

SCIENCE

VOL. 101

FRIDAY, JANUARY 12, 1945

No. 2611

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SCIENCE: A Weekly Journal, since 1900 the official organ of the American Association for the Advancement of Science. Published by the American Association for the Advancement of Science every Friday at Lancaster, Pennsylvania.

Editors: JOSEPHINE OWEN CATTELL and JAMES CATTELL.

Policy Committee: MALCOLM H. SOULE, ROGER ADAMS and WALTER R. MILES.

Advertising Manager: THEO. J. CHRISTENSEN.

Communications relative to articles offered for publication should be addressed to Editors of Science, The Science Press, Lancaster, Pa.

Communications relative to advertising should be addressed to MR. THEO. J. CHRISTENSEN, Advertising Manager, Smithsonian Institution Building, Washington 25, D. C.

Communications relative to membership in the Association and to all matters of business of the Association should be addressed to the Permanent Secretary, A.A.A.S., Smithsonian Institution Building, Washington 25, D. C.

Annual subscription, \$6.00

Single copies, 15 cents

ADDRESS OF THE PRESIDENT OF THE ROYAL SOCIETY¹

By Sir HENRY DALE, O.M., G.B.E.

THE annual number of *Obituary Notices of Fellows of the Royal Society*, published to-day, and the names which have just been read to us remind us of the losses the society has suffered.

Allow me first to make brief mention of the last service rendered to the society by one who had long been devoted to its interests, and whose name is among those of the fellows whom death has taken from us during the past year. Sir Henry Lyons, who was our foreign secretary for a year, and then achieved so much for the society in his full term of service as treasurer, had acquired in that period a deep interest in the handling of the society's business and in the changes in its structure and its administration over the centuries of its history. He devoted the last four years of his life, under conditions which must have deterred any less resolute enthusiast, to the writing of a historical account of the administration of the Royal

Society under its charters, and at the time of his death, last August, he was eagerly awaiting its publication, which war-time difficulties had long delayed. This long-expected contribution to our history was published a few weeks ago, and the society will welcome and cherish it, not only as a record of value and interest in itself, but in memory of one to whose devoted labors the society and its fellows owe so much.

A year ago I reported to the society that our biological secretary, Professor A. V. Hill, had left us on an important mission to India. The council of the society, at the invitation of the Indian Government, had nominated Professor Hill to visit India to see its problems for himself, so that he might offer his advice on scientific matters in general and, in particular, on the adoption for India of a new and progressive program of research and enterprise in science and its applications. From all sources—from the Viceroy and the Secretary of State with their official colleagues

¹ At the anniversary meeting, November 30, 1944.

and counsellors, and directly from our own colleagues, the Indian men of science—we have had evidence of the unqualified success of this mission of cooperation and good-will. We had nominated Professor Hill with a full confidence in his personal and scientific qualifications for such an undertaking. We knew, however, that the success of his mission would depend even more on the response made to his appeal by India's men of science. To succeed, he must find them sharing his own conviction, that only a large and generous promotion of scientific and technological development in India would open for the teeming millions of its peoples any prospect of the advances in nutrition, health, prosperity and culture required to fit them for their proper place in such a world civilization as we shall soon be striving to rebuild on firmer scientific foundations. The response of India's men of science has been no more in doubt than that of its Government. We sent Professor Hill to hold out the right hand of cooperation; India has sent us six of its scientific leaders to grasp it here in Britain, and we rejoice to have them with us to-day.

In accordance with a plan which I mentioned here a year ago, the first meeting of the society to be held outside this country, in all its long history, duly took place on January 3 of this year, on the occasion of the meeting of the Indian Science Congress in Delhi. The Viceroy, Lord Wavell, honored the meeting with his presence, and Professor Hill, as a vice-president, was able to give formal admission to two of our Indian fellows, Professor Bhabha and Sir Shanti Bhatnagar, and to receive their signatures on a special sheet of parchment. India's prompt and generous response to the invitation which Professor Hill extended has now brought Sir Shanti Bhatnagar here as a member of the return mission, so that he has been able already to sign the Charter Book itself. We shall hope that opportunities will yet occur for all Indian men of science who have been, or will in the future be, elected to our fellowship, to come here to the society's home and to inscribe their names in the book which our fellows have signed since 1662. This, our ancient and now historic Charter Book, is largely representative, in its earlier pages, of the springtime of modern science, not only in this country, but in all the western world; and we desire that it shall now also bear witness to a growing freedom of scientific contact and interchange with the great center of eastern culture, from which our visitors have come. Their journey to Britain, and later to Canada and the United States of America, should mark the beginning of a new era of collaboration in science between India and the rest of the world, growing ever easier and more intimate as the means of world transport, with the added impetus which war's demands have given, attain yet higher levels of speed and safety.

Our Indian colleagues are coming to the end of a visit which, we hope, has given them a new insight into the scientific activities and organization with which this country is still meeting the demands of war, and preparing for the tasks which will later have to be shouldered by a tired though triumphant country, in a largely devastated world. We hope that they will have learned, perhaps from our failures as well as from our achievements, lessons which will have applications of real value to their own country's scientific problems. All fellows of the Royal Society have been glad to know that our apartments have served our Indian guests as an official home and a point of departure for their various visits and engagements, and that Professor Hill has thus been able to keep a close and friendly eye upon this gratifying fulfilment of his hopes and his plans. Two days ago this visit of our Indian colleagues, nearing its end, reached also its climax, when their Majesties, the King and Queen, were graciously pleased to receive them, and thus to show their interest in the promise of a closer understanding and comradeship in science between India, the United Kingdom and the whole of the British Empire.

I made preliminary mention last year of the action taken by the council, in appointing a special committee to consider the prospective needs of fundamental researches in physics. As was then foreseen, the news of this response to an appeal from the sponsors of physics soon evoked similar pleas from those concerned for such researches in a number of other branches of science. The council agreed, accordingly, to appoint a series of other committees to advise upon the respective requirements, in the period following the war, of fundamental researches in chemistry, biology, geology, geophysics, geography and meteorology. Reports from all these committees have been received and considered, together with one of similar aim presented by the standing subcommittee, on oceanography, of the National Committee for Geodesy and Geophysics; and it is by no means certain that the tale of these special reports and appeals is entirely complete even now. It will be understood that the society, in undertaking this investigation, has endeavored to center its inquiry on researches aiming at the advancement of knowledge without immediate or even implicit reference to practical needs or objectives. It has done this, not because it regards those researches, which have in view the use of scientific methods and principles for the service of man's material needs, as of inferior status or interest, or as being, by their nature, less worthy of the society's consideration. We do not need to be reminded that researches seeking only the advancement of pure science have often revealed the shortest ways to practical developments, or that those undertaken with practical ends may

chance to open windows upon new vistas of knowledge. It may be hoped that the Royal Society will never lose the comprehensive aim defined in its charter, of "further promoting by the authority of experiments the sciences of natural things and of useful arts." It will be understood, however, that the council had to keep in mind the increasing extent to which support by public money is already given, through the three advisory councils, to those researches which are aimed, more or less directly, at obtaining and using scientific knowledge for the promotion of industrial and material progress, of human health and of agriculture; and they had to keep also in view the more immediate appeal which is made to private benevolence and enterprise, by researches with objectives thus already in view. As I said last year, the Royal Society must, in such circumstances, regard as its special concern the proper nourishment of the roots of the tree of knowledge. We hope that the report which the council have now adopted, based upon those of the special committees, will enable the society to evoke an effective response to its own conviction of the supreme importance, for the nation's future, of provision for the support of scientific researches at the frontiers of the unknown, on a scale more generous than any which has hitherto come within the range of official vision. The society is making representations to the appropriate departments and authorities, and stating its conclusions as to the nature and the dimensions of the various grants of funds and facilities which will be needed, to enable this country to keep its place in the general advance of science, in the altered world which will emerge from the war.

I ought to make further brief reference to another matter on which I spoke in some detail last year, namely, the accommodation provided by the nation for those scientific societies which, according to the pattern and tradition of our own, devote their activities to the promotion of natural knowledge for the general advantage, without reference to private interests or to professional status and discipline. Such provision had been accepted as a national obligation as early as 1778. The quarters at present provided, here in Burlington House, represent the allotment made in 1869 to the societies which then achieved such recognition. Since that date no enlargement or material alteration has been made, and there seemed to be no prospect of any, either for the societies admitted 75 years ago, or for others whose claims to such privilege have later appeared. Even the accommodation thus assigned in 1869 appears to have been only a remainder, after the major part of an earlier and more generous plan for science had been diverted to other purposes by intervening claims. In 1869, we

should remember, the study and promotion of the sciences had hardly been recognized as a life's occupation, except for a few determined devotees; science was at that date still largely a matter for the leisure of cultured amateurs. It is no matter for surprise, therefore, that accommodation then regarded as acceptable should now be found to make grossly inadequate provision for some of the more important of present scientific needs, and none at all for others.

After I had drawn public attention to this anomaly last year, we were asked by several of the specialist societies concerned, to take appropriate action with the Government. We approached the Lord President of the Council, Mr. Attlee, and on October 13, with the Chancellor of the Exchequer, Sir John Anderson, and the Minister of Works and Buildings, Lord Portal, he kindly received a deputation representing all the societies which have been housed here since 1869, and several others for which the Government has hitherto made no provision. Apart from the special and urgent needs of some of the societies, the case was fully presented for the inclusion, in any scheme for the rebuilding of London, of a center adequate to accommodate the principal scientific societies on a well-coordinated plan, and so placed and designed as worthily to symbolize the central importance of British science, for the cultural as well as the material aspects of the civilization of this nation, and, indeed, of the world. The ministers gave a careful and sympathetic hearing to the statement of our claims, and asked us to furnish quantitative data, as a basis for their further consideration of the problem.

With the outcome of the war even more certain, there can be no relaxation yet of the demand on what our scientific effort can contribute to the hastening of its end. It is none the less our duty to begin to look further ahead and to prepare for the part which science must play in the world which will follow. The needs of alliance in war have evoked, especially between the two great branches of the English-speaking nations, a closer interchange and collaboration in science, between men of different national traditions and loyalties, than has ever before been a matter of organized policy. It is not too early to begin to consider to what degree, and in what form, such a collaborative effort should be continued into the conditions of peace, and extended to scientists of international good-will throughout the world. Even in the twenty years of uneasy armistice which ended in 1939, a measure of cooperation among the world's scientists was achieved, which held promise as a potential agent of international understanding. Our traditions go back to days when our fellows belonged to a community embracing all Europe in its enthusiasm for the new experimental philosophy, and the Royal Society

will have a particular duty to be among the leaders in the resumption of international activities in science, and to use all its influence to establish these on an ever wider and firmer basis. We have a standing committee on international relations in science, with our foreign secretary appropriately as its chairman, to prepare for what action the society can usefully undertake or promote, as the opportunity presents itself. Meanwhile we may observe other signs that the spirit of international friendship and recognition in science is beginning to move again, even while the chaos of war is still with us. Among such signs, we may note that one of the committees which, since their foundation in Stockholm, have awarded the Nobel Prizes with unchallenged impartiality among the scientific discoverers of all nations, has resumed its awards this year. We in this society have welcomed the return to London of a group of distinguished French leaders in science from the United States of America, whither they had escaped from the hostile occupation of their country. We have been able to share their rejoicing at the liberation of France, and to welcome here others who had remained there, often in hiding and always in peril, as leaders in the steadfast resistance opposed by all but a negligible minority of the French men of science to the enemy's demands for their collaboration. The society had the pleasure of providing a special opportunity for our fellows to meet our French colleagues, with those from other allied countries who have long been in exile here during enemy occupation of their homelands. We are glad to think that new and lasting bonds of comradeship in science have been created for us with those who have been our country's wartime guests, and through them with all the men of science in the countries which they represent.

The society had recently the opportunity of showing its interest in the revival of international scientific cooperation in another special connection. From October 16 to 19 a small international conference met here, under the auspices of the Health Organization of the League of Nations, to discuss the creation of an international standard of reference for penicillin and the definition, in terms of this, of a unit of activity. Though the league has failed tragically of its central purpose, it has less conspicuous achievements to its credit, and science has an interest in ensuring the permanence of some of these. I have myself had the privilege of taking part in the activities of an international commission under the Health Organization of the league, which succeeded, in the years between the wars, in obtaining world-wide acceptance of standards and units of activity for a whole range of modern remedies—antitoxins, hormones, vitamins and certain drugs—the strength of which could only

be determined by direct biological measurements of the specific activity, in comparison with that of a fixed standard preparation in each case. Insulin was an early instance of a new remedy requiring such intervention; its general use for the treatment of diabetes could not have attained the present level of safety and effectiveness, unless a world-wide uniformity on these lines had replaced the chaos of widely different units in different countries, which was threatened in 1923. And now research has produced another new remedy, penicillin, the success of which, in the treatment of a range of dangerous infections, has also had such a dramatic quality that its reputation has spread rapidly beyond our scientific community and caught the interest even of a war-distracted world. Here, indeed, was a discovery which could rank as a major contribution of science and to the mitigation of the suffering which war inflicts, and, at the same time and no less, as a gift of healing to mankind at peace. The needs of war had given a stimulus to the researches which proved penicillin's remedial value, but its rapid production on an adequate scale had to face greater difficulties in our own country, where material and human resources had been more completely absorbed by earlier requisitions, than in the United States. So the present position was reached, in which, as we are proud to recognize, the existence of penicillin and then, after a decade, the methods by which it could be separated in sufficient purity to demonstrate its brilliant possibilities as a remedy, were discoveries made here in England, while, in the further researches and technical developments needed for its large-scale production, our American colleagues have played a major part.

Thus early in its history, therefore, penicillin and its applications had become a matter of international concern; and, though war had restricted the work in this field almost entirely to scientists of the English-speaking peoples, and had brought them into an unusual intimacy of cooperation, progress had been so rapid and action so urgent that there was a real danger of a divergence of meaning in the terms used to express its activity and define its dosage, even among the few countries already using it. Prompt action was required to avert this by accepting a common standard of reference; and, when the proposal of a conference for this purpose was made from this country to the League of Nations Health Section, we were grateful to our colleagues from the United States, as well as from Canada and Australia, for the generous promptitude with which they agreed to make the journey to England, so as to meet with us here in London. After all arrangements for the holding of the conference here had been completed, the liberation of Paris opened a new possibility; Dr.

Tréfouël, now director of the Pasteur Institute in Paris, was able at the last moment to accept an invitation to join us, and thus to give our deliberations, and our eventual agreement, a wider international basis. To illustrate how rapidly a divergence may arise under present conditions, I may just mention the fact that several different penicillins have now been recognized, produced by variations in the metabolism of the growth, possibly due to mutations of the mold itself, possibly to changes in the nutritive conditions offered to it by the medium or the cultural method employed. Three such varieties of penicillin have already been isolated in pure condition, and distinguished by certain chemical characters; but, while English workers had come to refer to these as Penicillin 1, 2 and 3, their colleagues in America spoke of Penicillin F, G and X; and it was not until they met round the table in our council room a few weeks ago, but then in less than 10 minutes, that they became quite certain of the identity of 1 with F, of 2 with G and of 3 with X. All these penicillins have the specific remedial action in high, though not quite identical degrees, and there are probably differences, still to be explored, in their proportional efficiencies against different infective organisms. When once their identities were thus put beyond doubt, however, the small conference had no hesitation in deciding, for the present, to use as the common basis of reference a sample of the penicillin which is predominant in most preparations now available, and most easily obtained as a pure salt in adequate quantities. The unit could then be defined as the activity of a precise, though very small weight—0.6 μg —of a particular sample of the perfectly dried, crystalline sodium salt of Penicillin 2 or G; and the unit thus chosen for definite fixation, and for international recognition henceforward, was, by a unanimous choice, so defined as to be as closely equivalent as possible to the unit first propounded by Sir Howard Florey's team of collaborators, and widely known as the "Oxford" unit.

The International Standard for Penicillin is thus added to an already numerous series, of which the custody, on behalf of the League of Nations Health Organization, has been shared by our own National Institute for Medical Research with the State Serum Institute of Denmark, at Copenhagen; and all these standards, we may hope, will be available for transfer to whatever international authority may be established in succession to the league, as a tangible and material result of genuinely international collaboration, which the league has been able to initiate and maintain among men of science, to the permanent advantage of the world.

Though penicillin has rightly made a special appeal

to the imagination and sympathetic interest of a wide public, it is, of course, only one out of a varied range of inventions and discoveries, hastened by the stimulus of war's demands and produced, in many cases, behind the veil of its secrecy, but ready, when peace returns, to take their proper place as new gifts to the welfare and the civilized progress of mankind. From what has already been made generally known, it is clear that we may look forward to revolutionary advances in the means of communication and in the speed and safety of travel across the world, and in methods of controlling insect pests and the diseases which insects convey; and these are but a few examples of the gains which we and the world may hope to set against the tragic loss and sacrifice of the years of war. There were probably few who even suspected in 1939 that science, in countries then so dangerously unready, would find itself, before the war ended, in its present position of central importance. None of us, I think, would claim more for science, even now, than to have played in this war a part of growing predominance in the provision for the fighting men of the material means of warfare, without which their heroism and sacrifice could not have prevailed. Even that duty, loyally accepted, is one from which the scientific community of the free nations must long for the release which victory will bring. But, while the operations of war have come to depend on science to a degree beyond all earlier experience, it can not be doubted that little more than a beginning has yet been made in exploiting the possibilities of destruction, which science could progressively offer, if the world should continue thus to misuse it, and if science were still on offer for such ends. Allow me to quote a passage from a letter which the Prime Minister, whom we are proud to number among our fellows, wrote a year ago to Professor Hill, in sending his greetings to Indian men of science.

"It is the great tragedy of our time," wrote Mr. Churchill, "that the fruits of science should by a monstrous perversion have been turned on so vast a scale to evil ends. But that is no fault of science. Science has given to this generation the means of unlimited disaster or of unlimited progress. When this war is won we shall have averted disaster. There will remain the greater task of directing knowledge lastingly towards the purposes of peace and human good." Noble words indeed, and a profession of faith which will find an immediate echo in the hope and the desire of every true man of science. "When this war is over we shall have averted disaster"—surely that is a confidence which every one of us will long to share. It must be clear, however, that Mr. Churchill's reference was to the present threat of disaster, from which the prospect of our escape is even more fully

assured to-day than when he wrote, a year ago. We may be certain that nobody sees more clearly than he that the threat of final disaster to all man's hopes and achievements will not be forever averted, if the possibility of the "monstrous perversion" of science is allowed to remain and to continue its evil growth. Even in the past year our enemies have thrown a new and vivid light on future possibilities, by the new weapons which science has enabled them to put on trial for our destruction. Though a people's unflinching courage and an answering effort of science and organization, together with the progress of the Allied armies over the launching areas, have given us confidence that flying bombs and the like will not affect the issue of this war, the warning which they give, as to what the future might hold, is not the less clear. The writing on the wall must be plain for all to read. If, when the memories of the present war begin to fade, the world should allow science again to be exploited by a nation grasping at predominance by conquest, science will no longer be invoked only as an aid to what valor can achieve by land, sea or air, but as an agent, in itself, of blind annihilation at an ever lengthening range. When we men of science regain that freedom, for the ultimate preservation of which we have loyally accepted, through these tragic years, the bonds of secrecy and submission to authority, we can not put aside with these our proper share in the new responsibility for the future of mankind,

which this war's experiences have laid upon the men of good-will in all nations. It is true, indeed, that neither the present abuse of science, nor any possibility of final disaster to civilization, which might come of a future perversion of its powers, can be charged as a fault to science itself; no more, indeed, than we could properly charge to religion, as such, the wars which once devastated much of Europe in its name. But we men of science can not escape from our growing share in the responsibility, in "the greater task," as Mr. Churchill has written, "of directing knowledge lastingly towards the purposes of peace and human good." No man of science has the right to prescribe for another his interpretation in detail of that duty; but there is one aim which may unite us, perhaps for the most effective action within our common grasp, and one which is worthy of all our common influence and effort. Let me quote again from Mr. Churchill's letter: "in this task," he writes, "the scientists of the world, united by the bond of a single purpose which overrides all bounds of race and language, can play a leading and inspiring part." To build anew, and on a firm and broadening foundation, a world community in science, is surely an aim worthy of our utmost effort and devotion; but there can be no swerving from the present duty, and the call on science by war may yet be sterner, before we have won the freedom thus to work for the future of the world.

THE SITE OF ANTIBODY FORMATION*

By Dr. W. E. EHRLICH and Dr. T. N. HARRIS

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EVOLUTION in science is brought about by the discovery of facts and the elaboration of patterns into which these facts will fit. The earliest facts about the formation of antibodies discovered by Metschnikoff and others fitted well into the pattern of the reticulo-endothelial theory of antibody production. However, in recent years additional facts have been brought to light which are difficult to reconcile with this theory,^{1, 2, 3, 4} and we have recently presented new facts which seem to be inconsistent with the old concept.^{5, 6} The latter lend themselves to the elaboration

of a theory which is consistent not only with the old facts but also with the new ones. This new pattern of antibody formation is the subject of the present presentation.

THE RETICULO-ENDOTHELIAL THEORY OF ANTIBODY FORMATION

The reticulo-endothelial theory of antibody formation was widely accepted, undoubtedly because it seemed plausible that the cells which phagocytose and destroy bacteria should also be concerned with the synthesis of antibodies.⁷ "It is chiefly this phagocytosis of formed antigens (erythrocytes, bacteria) which has directed the attention to the reticulo-endothelium as the possible source of the antibodies."⁸

There are two important arguments which have been

* From the Philadelphia General Hospital, The Children's Hospital of Philadelphia, and the Departments of Pathology and Pediatrics, The School of Medicine, University of Pennsylvania, Philadelphia. Aided by a grant from the Ella Sachs Plotz Foundation.

¹ L. Hektoen, *Jour. Infect. Dis.*, 17: 415, 1915.

² J. B. Murphy and E. Sturm, *Jour. Exp. Med.*, 41: 245, 1925.

³ W. E. Ehrlich and W. Voigt, *Beitr. Path. Anat.*, 93: 348, 1934.

⁴ A. R. Rich, M. R. Lewis and M. M. Wintrobe, *Bull. Johns Hopkins Hosp.*, 65: 311, 1939.

⁵ W. E. Ehrlich and T. N. Harris, *Jour. Exp. Med.*, 76: 335, 1942.

⁶ T. N. Harris, E. Grimm, E. Mertens and W. E. Ehrlich, *Jour. Exp. Med.*, in press.

⁷ Annotations, *Lancet*, 1: 654, 1943.

⁸ R. H. Jaffe, "The Reticulo-Endothelial System," *Handbook of Hematology*, Vol. II. New York: Hoeber. 1938.