

HENRY HALLETT DALE
1875-1968
A portrait on his 85th birthday by Allan Chappelow, M.A., F.R.S.A.

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On July 23, 1968, an era came to an end with the death of Sir Henry Dale, who was regarded by physiologists and pharmacologists in every part of the world with the affectionate veneration we reserve for our greatest masters. He exerted a farreaching influence not only over physiologists and pharmacologists, but over scientists in general. Whenever he voiced an opinion or took a stand on an issue which affected science, it was the voice of the true scientist we heard. Not that he was asked or wanted to act as the spokesman of scientists; he spoke because he felt the necessity to do so. But by his intuitive judgement, his intellectual courage, and the clarity of style with which he could formulate his ideas and express his doubts, which were held and felt by his scientific colleagues, he became their conscience. That is part of the secret how, up to his death at the age of 93, he exerted such a profound influence on the scientific world, although he had ceased to be actively engaged in research over 30 years earlier.

Dale's discoveries, which have gone into medical history, are still very much alive in the sense that they influence the stream of present-day research to an astonishing degree; they contained the seed, often hidden from his contemporaries, of the progress now being made. Dale lived with his scientific colleagues until the end, and not through his past achievements alone. Impressive was the grip he had on any problem related to his previous work that turned up. Until a few years ago, his discussion remarks at meetings of the Pharmacological and the Physiological Society were most penetrating and sometimes initiated new series of experiments to be carried out by those who had given the papers. Until the very end, his colleagues loved to visit him at the nursing home in Cambridge to which he was confined during the last years, to listen to his stimulating criticism and, the most enjoyable reward of all, to find him enthusiastic about their new observations and ideas.

His outstanding achievements in medical research and his far-reaching influence in science have found national and international recognition. He was elected Fellow of the Royal Society in 1914. In 1936 he shared the Nobel Prize with his old friend O. Loewi. In 1943 he received the Knight Grand Cross Order of the British Empire and in 1944 he was awarded the highest honour that the King could confer upon a scholar—the Order of Merit. Another Pour le Mérite was bestowed upon him in 1955 by the German Bundesrepublik, and as he once pointed out, he shared the unique position of being holder of two orders of merit with only one other person in this country, the late T. S. Elliot. Belgium honoured him in 1944 with the Grand Croix de l'ordre de la Couronne. During the war years, from 1940 to 1945, he was President of the Royal Society, and as such became Chairman of the Scientific Advisory Committee to the War Cabinet. He was President of the British Association in 1947, of the Royal Society of Medicine from 1948 to 1950, and of the British Council from 1950 to 1955. In 1959 a medal, the Dale Medal, was struck in his honour by the Society of Endocrinology, awarded annually, and a lecture—the Sir Henry Dale Lecture—delivered by the recipient. In 1961 the Royal Society established the Henry Dale Research Professorship, endowed by

the Wellcome Trustees, who wished to commemorate his unique services as Chairman of their Trust for twenty-two years, as well as his outstanding contributions to science and medicine in a wider context. Several years earlier, in 1956, the Wellcome Trust had shown their deep appreciation of Sir Henry Dale in a more personal way by naming a boat "Lady Dale," a boat the Trust had given to the Medical Research Council Unit at Fajara, and that now cruises on the Gambia River.

Long is the list of honorary membership of foreign societies and academies, and more than twenty universities have awarded him honorary degrees. It was said during the war—Dale receives new honours with each new ration book!

Dale began his scientific career immediately after having obtained a First Class in the Natural Sciences Tripos in 1898. He stayed in Cambridge for another two years before he took his clinical course at St. Bartholomew's Hospital, London, and worked in the Physiological Laboratory under Langley. Here he came under the stimulating influence of Gaskell and Anderson, and in 1900, at the age of 24, published his first scientific paper in the *Journal of Physiology*. His main discoveries, however, were to come later and extended over a period of thirty years, from 1906 to 1936. The first eight years of these creative three decades Dale worked in the Wellcome Research Laboratories and afterwards in the laboratories of the Medical Research Council, or, as it was called until 1920, the Medical Research Committee, first as a member of the scientific staff, and from 1928 onwards as the Director of the National Institute for Medical Research, which became famous under his leadership.

In 1952, when Dale was asked to make a selection for republication of his papers, which at that time exceeded 250, he chose thirty, of which twenty-six were publications of his main experimental work during these thirty years, and four were lectures given between 1920 and 1937 in which he reviewed this work. To the collection he gave the revealing title "Adventures in Physiology," and through arrangements with the Wellcome Trustees and the Board of Directors of the Wellcome Foundation, the volume was reprinted in 1965 to mark the occasion of Sir Henry's ninetieth birthday.

His "Adventures in Physiology" give us not only a clear picture of his scientific achievements, but through the introduction he wrote and through the comments he made to each paper, he succeeded in reviving the past. We are given the rare pleasure of taking part in the excitement surrounding his experiments, we can admire how discoveries logically follow each other, how they reach into the future, were taken up and developed to act in the course of time as the solid foundation on which much of present research is still building.

Dale began his research at the Wellcome Laboratories with ergot, and the fungus ergot turns up again and again in his research. By discovering that extracts of ergot reversed the pressor effect of adrenaline and sympathetic nerve stimulation, Dale introduced the first adrenaline blocking agent into pharmacology. In his "Adventures in Physiology" he stresses the role played by lucky accidents in his research, and his ability to recognize the chances provided by such lucky accidents played a decisive role also in the discovery of this new action of ergot. He had been asked to determine the adrenaline content of a sample of dried adrenal glands delivered to him by the Burroughs Wellcome factory. By chance he tested it, at the

end of an experiment, on a spinal cat on which he had studied the actions of ergot. To his surprise the sample when injected did not raise but lowered the arterial blood pressure, and, as he said, "with the confidence of inexperience I condemned the sample without hesitation." But when by "an almost incredibly fortunate coincidence the same sequence of events was repeated in detail a week later" his interest was alerted with the result that he discovered the adrenaline reversing action of ergot.

From an accidental observation made in the course of these experiments on ergot stems another of Dale's important discoveries, that of the oxytocic action of pituitary extract. He had used such an extract in one experiment as a control, and it happened that in this experiment he was also recording the tone and rhythm of the cat's uterus, and thus "by chance" as he said, observed the potent stimulating action on the uterus muscle, a discovery which probably led to the most frequent application in practical medicine of pituitary extract.

Another example of a fundamental discovery which, as Dale tells us, "arose from one of my most fortunate accidents," was his demonstration that the anaphylactic contraction of smooth muscle resulted from the formation of cell-fixed antibodies. Whilst studying the effects of horse serum and comparing them with those of histamine on the isolated guinea-pig uterus, he encountered one preparation which responded with a maximal contraction to the application of the serum in a usually inactive dilution. He made enquiries about the guinea-pig because he knew that, at that time, the Wellcome Laboratories were using guinea-pigs for the assay of antitoxins which involved many small injections of horse serum. His suspicions were confirmed: he had been supplied with a guinea-pig used for these assays. The results of his subsequent experiments which were initiated by this "most fortunate accident" have changed our conception of anaphylaxis and have given us an understanding of the relation between hypersensitivity and immunity. As Dale expressed it, anaphylaxis results from a predominantly cellular fixation of an antibody which, when it circulates in excess, is recognized as the cause of immunity.

The main topics of Dale's other research were concerned with the physiology and pharmacology of sympathomimetic amines, histamine and acetylcholine. In each instance the work began with the identification of the substance in extracts of ergot; of tyramine and histamine, in 1910 together with G. Barger, and of acetylcholine three years later as the result of an accidental observation—"the lucky encounter with a peculiar ergot extract." The extract, which had been sent to him for routine examination, had aroused Dale's interest because of its unusual activity; it caused profound inhibition of the heart beat and had other actions resembling those of muscarine. He secured the whole batch of the extract for further investigation by his chemist colleague, A. J. Ewins, who succeeded in obtaining a few milligrams of the abnormal active constituent as a platinum salt. Its properties, however, were not those of the stable muscarine but rather those of a very labile ester, and there seemed little hope of identifying the substance until Dale, as he said, "recalled into conscious memory an observation made some eight years earlier" by Hunt and Taveau on the enormous potency of the unstable ester acetylcholine. When Ewins accordingly made Dale some acetylcholine for comparison, its identity with the substance from the ergot extract was put beyond doubt. Fifteen years later, in 1929, and again as the result of an "incidental" and "quite unexpected" observation whilst studying the distribution of histamine in animal tissue, Dale, together with H. W. Dudley, isolated acetylcholine in extracts of horse spleen and provided the first direct proof for its occurrence in tissues of the animal body.

The discovery of tyramine in ergot was in part responsible for the research he and Barger carried out, in 1910, on the relation between chemical structure and pharmacological action of a number of amines related to adrenaline. For these amines he coined the term "sympathomimetic amines" now in general use. In later years this paper, which is a mine of information, gave Dale some cause for regret because it "shows evidence of missed opportunities" as he expressed it. Having found that the N-propyl members of the amino-aceto-catechol and of the amino-ethanolcatechol series had a weaker action than their lower homologues, they did not examine the N-isopropyl member of the amino-ethanol-catechol and thus missed the discovery of the therapeutically valuable isoprenaline, with its strong inhibitory actions. Further, having pointed out that adrenaline, which only incompletely reproduced sympathetic actions, could not be the transmitter of sympathetic nerve impulses, they discussed but discarded the possibility of noradrenaline being the main transmitter because at that time noradrenaline was nothing but a synthetic curiosity and was not known to occur in the body. admire the caution, but it is frustrating to read the few sentences in the discussion dealing with this problem and to realize how very near he was to the correct solution. "I failed to jump to the truth, and I can hardly claim credit for having crawled so near and then stopped short of it" he says, to which we may reply, with Molière, "c'est le privilège d'un grand homme de faire impunément des défauts."

From the discovery of histamine and acetylcholine in ergot arose the study of their pharmacological actions. Our present knowledge of the actions of these two potent substances is mainly derived from these studies which were published between 1910 and 1920. They form some of the finest pharmacological analyses ever made, particularly those of the circulatory effects. They have become models for the analysis of drug actions, and we admire the simplicity of the methods Dale used to reveal the mechanisms of their actions.

The pharmacological studies of histamine which were begun with P. P. Laidlaw brought to light nearly all its main actions, those on plain muscle, on capillaries, gland cells, the suprarenal medulla and on the central nervous system; the one important action missed, because they did not look for it, was the action on the oxyntic cells of the gastric mucosa which results in strong acid gastric secretion.

Having shown that the fall in arterial blood pressure produced in cats and dogs by small doses of histamine resulted from vasodilatation, Dale, together with A. N. Richards and later with J. H. Burn, analysed this effect and was able to show where in the vascular tree histamine produced its dilator effect. Simply by observing the changes in skin colour of unpigmented pads of the feet in cats, and by measuring in a limb the volume changes during the fall in blood pressure, or in perfusion experiments during the changes in outflow, he was able to distinguish between the dilatation of capillaries and that of arteries and arterioles. From the results obtained with these methods he could conclude that in cats histamine dilated the capillaries in contrast to acetylcholine, which dilated the arteries, but that in dogs, histamine dilated capillaries and arterioles. But histamine had a vasoconstrictor action as well, which was revealed particularly in perfusion experiments. In later writings Dale has summarized the position in different species and pictured "the action of histamine on vascular tone, in those species in which it has been possible to analyse its incidence, as changing in every case, but at different levels in the vascular branching from a more central arterio-constrictor to a more peripheral dilator effect; and

this change occurs at levels moving towards the periphery, as the species are considered in the following order—monkey (and presumably man), dog, cat and, finally, rabbit." Time has not changed the validity of this statement.

With the knowledge of a predominantly capillary site of the vasodilator action of histamine, Dale and Laidlaw, in 1918, studied the mechanism of histamine shock. This study was "undertaken as a contribution to a co-operative war study of conditions of varied origin, then being included in a general description as 'secondary wound shock'—conditions apparently resulting in most cases from haemorrhage, exposure, infection and toxaemia in unknown proportions." They hoped that a study of the artificially reproducible histamine shock might indicate by analogy some common factor in the resultant syndrome and suggest some appropriate treatment.

Using the simple method of measuring the corpuscular content of blood with the haematocrit, Dale and Laidlaw showed that large doses of histamine given intravenously, particularly by slow infusion, not only dilated the capillaries but also caused a general increase in their permeability, thereby allowing plasma to escape from the vessels into the tissues as seen by the striking increase in corpuscular content of blood withdrawn when the shock had fully developed. The ensuing reduction in circulating blood volume and the tendency of the remaining blood with its increased viscosity to stagnate in the dilated capillaries and venules instead of returning to the heart were the characteristic features of histamine shock. These findings emphasized "a deficiency in the volume of blood in effective currency, as a common factor in conditions of so-called secondary wound shock and pointed to the addition, by transfusion to the circulating blood of a fluid which the morbidly-permeable capillaries might retain—blood or plasma—as the most immediately effective remedy."

To Dale we also owe our knowledge of the occurrence of histamine as a natural constituent in many animal tissues, as was convincingly shown in 1929, when he, together with C. H. Best, H. W. Dudley and W. V. Thorpe, isolated histamine from alcoholic extracts of fresh liver and lung, and together with Dudley from alcoholic extracts of spleen, and in amounts sufficient to account for the histamine-like activity of such extracts. Once again, circumstances of an accidental kind had provided the immediate stimulus for this study. A liver extract had been acquiring some reputation in Canada for high blood pressure, and Dale, as he tells us, was asked to examine this extract to verify and standardize its activity, and if possible to find out the substance responsible for it.

In 1918, however, histamine was not known to be a natural constituent of animal tissue, and Dale and Laidlaw not only avoided any premature assumption of a direct participation of histamine in traumatic shock or in the local vascular reactions of the tissues to injury or irritation, but as he later wrote, "I have been quite shocked on reading anew one passage of our discussion to discover how we seem to have gone almost out of our way even to preclude this possibility from consideration." Naturally, Dale was aware of this possibility, but to be cautious in making generalized conclusions based on analogy alone was characteristic of him. In this attitude, this ability to be able to wait, we recognize the true scientist who humbly pays his respects to nature's secrets. His attitude may serve as a warning to those of us—for whom it does not come too late—to be cautious when speculating about the physiological significance of newly discovered facts and not to try to prove more

than they warrant. Dale never erred in this direction and thus failed to experience what Thomas Huxley described as "the great tragedy of science—the slaying of a beautiful hypothesis by an ugly fact."

Even after his discovery of histamine in animal tissues, when discussing its function for the symptoms of cell injury or irritation, of anaphylaxis or of shock-like conditions, he emphasized not the similarities but the discrepancies between these symptoms and those produced by histamine, and did not attribute to histamine a role greater than it could possibly play. As Adrian once said about Dale, he has been more concerned to apply the brake than to be first in the gold rush, but the gold he has found will keep its value. Dale's critical discussion of the role of histamine in physiological and pathological reactions given in his Croonian Lectures of 1929 has not diminished in significance; his arguments are as pertinent today as they were forty years ago.

In 1914, when Dale published his experiments on the action of some esters and ethers of choline, including acetylcholine, he could scarcely have foretold that in the course of time these investigations would lead to a revolutionary change in our concept of neuromuscular and synaptic transmission. In this paper Dale did not describe just this or that action of these derivatives of choline, but by recognizing that they shared some of their actions with muscarine, others with nicotine, he established the dual action of acetylcholine. It acted like muscarine on smooth muscles, heart and gland cells, and these muscarinic actions were abolished by atropine. But Dale showed that acetylcholine acted also like nicotine, in that it activated or excited the cells of the adrenal medulla and of the sympathetic ganglia and, as shown later, that it depolarized the motor endplates of striated muscle; and these nicotinic actions were abolished by large paralysing doses of nicotine. The real importance of the dual action of acetylcholine, that is, its physiological implication, became evident only about twenty years later, when Dale and his colleagues demonstrated the role of acetylcholine in the transmission of nerve effects. But already in 1914 Dale pointed out that if there were any evidence for the presence of acetylcholine in animal tissues—the evidence was later supplied by him and Dudley in 1929 acetylcholine would be a most suitable transmitter substance of nerve effects at certain divisions of the autonomic nervous system. He also suggested that the evanescence of the acetylcholine effects might be due to the activity of an esterase; thus he predicted the presence of cholinesterase in the animal body sixteen years before it was discovered independently in two places: by Matthes in Dale's laboratory, and by Engelhardt and Loewi in Austria.

The publications concerning the role of acetylcholine as transmitter of nerve effects that appeared between 1934 and 1937 from the National Institute for Medical Research are based on Dale's original discovery of the dual action of acetylcholine; they all, whether he is one of the authors or not, bear his stamp. Those who took part in these exciting investigations were G. L. Brown, J. H. Gaddum, Marthe Vogt and myself.

Acetylcholine was shown to be the transmitter not only of postganglionic parasympathetic but also of some postganglionic sympathetic fibres, for instance, of those innervating the sweat glands in cats. Thus the transmitter function of acetylcholine was not limited to one of the two anatomical divisions, parasympathetic or sympathetic, of the autonomic nervous system. However, the discovery of the nicotinic transmitter function of acetylcholine entailed a much wider implication—it

came as a real shock. The finding that acetylcholine was the neuromuscular transmitter at the motor endplate of striated muscle and the synaptic transmitter in a sympathetic ganglion went against all the, often ingenious, ideas which had been propounded up to that time by those working in this field because it had been taken for granted that these transmission processes were physical—purely electrical events. How many today realize or recall the complete change in concept that took place as a result of the discovery of the nicotinic transmitter function of acetylcholine.

When these discoveries were made, Dale at once realized the necessity, in order "to promote clear ideas", of a terminology which would distinguish nerve fibres not with regard to their anatomical origin, but with regard to their chemical transmission, due in one case to acetylcholine, in the other to a substance like adrenaline, now known to be noradrenaline. Therefore as early as 1933 he coined the terms "cholinergic" and "adrenergic" for use in this sense and to be applied to nerve fibres, neurones or transmission processes. Our present knowledge of the distribution of cholinergic and adrenergic neurones in the peripheral nervous system is based on the results obtained in the thirties by Dale and his associates.

Very soon Dale had to defend his new terminology when the expressions "cholinergic" and "adrenergic" were used not only to designate neurones but substances as well. In 1935 Dale protested and wrote: "The application of the term cholinergic to a substance supposed to act like acetylcholine threatens a loss of precision in the use of these words and therewith of their value." However, the misuse continued and in 1953 Dale implored the writers in this field to resist the impulse to widen the application of these terms by allusion or "transference of epithet." "This can be attractive in a poem, no doubt, but for a scientific term it is destruction of its only value, precision." And in 1954 Dale again complained that he suffered, as he expressed it "from the actions of colleagues in kidnapping my verbal offspring for what I regard as improper uses." Later, Dale realized the need for an additional terminology, one which would denote the sensitivity of a structure to the transmitter substances, and he suggested the terms "cholinoceptive" and "adrenoceptive."

Dale had not only to defend his terminology, but also the theory of the transmitter functions of acetylcholine, and we again admire the pungency of his style when refuting the suggestion of some authors that acetylcholine was the transmitter not only for synaptic transmission, but also for the propagated nerve impulse along the nerve. "Such a conception," he wrote, "offers of course the kind of intellectual satisfaction which many minds obtain from a simplifying and co-ordinating generalization." "But," he continued, "the ingenuity of its supporters is sorely taxed to discover even plausible ways of escape from the facts which contradict it."

One other major contribution to science and particularly to therapeutics for which humanity owes a great debt to Dale must not be forgotten. It concerns his work on the standardization of drugs, of posterior pituitary extract, neoarsphenamine, insulin and digitalis. He showed that it is essential to use a common standard reference preparation when estimating the potency of a preparation containing one of these substances, and he was able, as the chairman at a conference of the Health Organization of the League of Nations at Geneva in 1925, to persuade the other members to adopt international standards for these substances. The benefit of this arrangement became so obvious that at later conferences international standards were adopted almost as a matter of course for a number of other substances. "How great a

contribution this has been to therapeutics throughout the world," writes J. H. Burn on the occasion of Dale's eightieth birthday, "it is quite impossible to indicate or measure. It is very largely due to Dale's skilful persuasion that instead of confusion there is order and co-operation in a field where national prejudices are sometimes just as capable of preventing agreement as in politics generally."

Of the many great scientists Dale met during his life there were two he particularly admired: Rutherford and Ehrlich. About Lord Rutherford, Dale has left us "Some personal memories" in a lecture given in New Zealand and republished in the delightful little book An Autumn Gleaning, a selection made by him in 1954 of his lectures and addresses. For a time Dale even contemplated writing a biography of Rutherford, writing it so, as he said, that a schoolboy of 14 would enjoy it. Ehrlich he had met when, as a young man, he had gone to Frankfurt to work in his Institute. He wanted to make a more direct contact with Ehrlich's way of thinking, but the work he was asked to do did not appeal to him. So he stayed for only four months, but as he often pointed out, he was glad to have seen something of this special genius who fascinated him during his whole life. After the last war Dale was responsible for the publication in this country of Ehrlich's collected papers. They make up three large volumes compiled and edited by Dr. F. Himmelweit, but under the editorial direction of Sir Henry, who wrote an introduction to each volume. These introductions, particularly the first one, reveal Dale as a fine historian, and rank as outstanding contributions to the history of medical science. Here a great scientist pays homage to the greatness of another genius of a different kind. Because different they were! And yet what Dale wrote about Ehrlich's way of working is a true reflection of Dale's own approach to research. This is perhaps not surprising, for psychology works in both directions, exposing the biographer as well. When Dale writes of Ehrlich's readiness, on occasion, to talk freely about what he regarded as his own special methods and experiences in research, and how Ehrlich at times thought of himself as essentially an opportunist, owing his successes mainly to a quick recognition of chances presented by lucky accidents of observation, do we not recognize in this description nearly the same vocabulary Dale liked to use, and with such relish, when speaking of his own successes? "By one of my greatest strokes of good fortune," said he, referring to his first attempt in practical pharmacology which led to the discovery of the adrenaline reversal by ergotoxin—"it was to give me an immediate opportunity of making a mistake of my own—a really shocking 'howler'!" Dale was endowed with the same quasi-intuitive subconscious reasoning that he attributed to Ehrlich. Of Dale we can say what he said about Ehrlich when quoting Helmholtz, who exclaimed in admiration of Faraday: "He smells out the truth." Those who have worked with Dale were struck by just this ability of his, and many have testified to it with submissive admiration.

Full justice to Sir Henry Dale's personality and deep humanity would not be done without recalling his attitude to the grave problems which confront the scientist of today. He knew that relentless vigilance is required to prevent any undue curtailment of the freedom of science. We are grateful to him for having defended that freedom whenever and wherever in the world it was threatened. Let us again listen to some of his warnings, for instance those he expressed during the war in his Presidential address to the Royal Society in 1941. "I see danger," he said, "if the name of science, or the very cause of its freedom, should become involved as a battle cry in a campaign on behalf of any political system, whether its opponents

would describe it as revolutionary or reactionary." And, he went on, "This Society, with its firm and unbroken tradition of complete aloofness from political controversy, may still find it an important part of its function to keep watch and, if necessary, to stand without compromise, for the right and the duty of science to seek the truth for its own sake, in complete freedom from any kind of extraneous influence." It was in the defence of the freedom of science that at the height of the Lysenko controversy Dale resigned from the Academy of Sciences of the U.S.S.R. This he made clear in his letter of resignation in which he expressed concern that as a result of the policy adopted—by not allowing criticism of Lysenko's conclusions and by dismissing from positions of authority those who persisted in applying scientific standards to the argument—"The whole great fabric of exact knowledge still growing at the hands of those who have followed Mendel, Bateson and Morgan, is to be repudiated and denounced."

We are proud of the stand Sir Henry took with regard to the atom bomb. In a review written in 1951 about a book on the second atom bomb that fell on Nagasaki he wrote, "We begin to talk glibly, almost with wry humour, of the possibility of a hydrogen bomb which, with its yet incalculable range and power of devastation, could serve no visible or conceivable purpose of peace but only that of an immeasurable destruction or the threat of it." He warned us that in considering a possible atomic war in merely quantitative terms we easily lose our sense of human values, "And," he concluded, "nothing, it seems, but a general resurgence of human ideas can halt the world now on the ever more precipitous slope."

And when on his ninetieth birthday he was asked in an interview by the B.B.C. about a letter he had written to *The Times* in August 1945, and about the hope expressed in this letter that science should become international once again after the war with Japan was over, he reiterated his creed. Let us again hear this, his final appeal, which gave voice to the uneasiness that is felt as strongly now as it was at that time by every true scientist and bears witnesses to the deep responsibility Dale felt towards science and humanity. "We have tolerated much, and will tolerate anything to ensure victory for freedom, but when the victory has been won we shall want the freedom. I still believe that freedom of scientific knowledge among nations should be the aim of national policy. I still believe that the true spirit of science working in freedom, seeking only truth and fearing only falsehood and concealment, would still offer a lofty and austere contribution to man's moral equipment, which the world cannot afford to lose or to diminish."

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