SCURVY IN RETROSPECT

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TWO hundred years ago, in 1753 at Edinburgh, was published Lind's "Treatise on Scurvy"—or to give it its full title: "A Treatise of the Scurvy, in Three Parts, Containing an Inquiry into the Nature, Causes and Cure of that Disease, together with a Critical and Chronological View of what has been Published on the Subject". This is almost the first book to deal exclusively with what we should now call a vitamin-deficiency disease. But it is not quite the first, because in 1650 Glisson of Cambridge had published his famous work on "Rickets"; and five years earlier still Whistler from Oxford had brought out, in Leyden, as his M.D. thesis, the less well known but important "De morbo puerili Anglorum quem patrio idiomate indigenæ vocant, The Rickets".

To mark the bicentenary of Lind's noted book, and imbued no doubt with a due sense of civic pride, Drs. C. P. Stewart and A. P. Meiklejohn, of the University of Edinburgh, recently organized a series of celebrations in that city. These included: a scientific conference on vitamin C, held under the auspices of the Nutrition Society of Great Britain and attended by leading experts from other parts of the world; an honorary degree ceremony, together with other academic and social occasions; and the re-issue of Lind's "Treatise", complete with new explanatory notes.

Dr. C. P. Stewart and Dr. D. Guthrie, who have been responsible for the editing of this reprint of Lind's first edition, have done their work admirably. In this volume*, in addition to the careful re-issue of the "Treatise" in modern typography, there are included also contributions by C. P. Stewart (a description of "The Third Edition of the *Treatise*"), Surgeon Vice-Admiral Sir Sheldon F. Dudley ("The Lind Tradition in the Royal Naval Medical Service"), D. Guthrie and A. P. Meiklejohn ("James Lind and Some of His Contemporaries"), C. P. Stewart ("Scurvy in the Nineteenth Century and After"), E. L. Hirst ("The Chemistry of Vitamin C"), and A. P. Meiklejohn, C. P. Stewart and R. Passmore ("The Rôle of Ascorbic Acid in the Human Body"). Every worker on vitamins, and every medical historian, can now be proud to possess, on his own bookshelf, a copy of the famous Lind "Treatise".

It is sometimes said that Lind was the first to discover how scurvy could be cured or prevented, namely, by the use of orange or lemon juice. This is a slight, if pardonable, exaggeration. Others before Lind had, in fact, recorded how scurvy might be controlled by the consumption of such 'antiscorbutics' as a decoction of spruce pine needles (Jacques Cartier, 1535), or by oranges and lemons (Sir Richard Hawkins, 1593). Most notably, in 1601, Sir James Lancaster had introduced into the ships of the East India Company the regular use of oranges and lemons as a sure preventive of this dreaded scourge of mariners. Then, during the seventeenth and eighteenth centuries, many others repeatedly confirmed the fact that fresh fruits and vegetables were effective in curing or preventing scurvy (for example, Woodall, 1639, Kramer, 1739).

But, as with so many scientific discoveries, what had been discovered was later to be forgotten and had to be re-discovered. Knowledge generally grows little by little, by developing what is already known rather than by some spectacular, unpredicted leap into the unknown. Just as no one individual can claim to have been the first to discover the existence of vitamins or to recognize the nature of the vitamin-deficiency diseases, so the knowledge of how to prevent scurvy empirically by means of fresh fruits or vegetables, or other fresh foods, emerged little by little.

Perhaps the juster claim to make on Lind's behalf is that he was the first, or one of the first, to carry out an accurately controlled clinical test, to prove conclusively how scurvy could be cured. To say that is not to belittle Lind's fame, but perhaps to enhance it.

Lind's own account of his test has been more than once quoted before, but bears repetition:

> "On the 20th May, 1747, I took twelve patients in the scurvy, on board the *Salisbury* at sea. Their cases were as similar as I could have them. . . . Two of these were ordered each a quart of cyder a-day. Two others took twenty-five gutts of *elixir vitriol* three times a-day. . . . Two others took two spoonsfuls of vinegar three times a-day upon an empty stomach. . . . Two of the worst . . . were put under a course of sea-water. . . . Two others had each two oranges and one lemon given them every day. . . . The two remaining patients, took the bigness of a nutmeg three times a-day, of an electuary recommended by an hospital surgeon. . . .
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> "The consequence was, that the most sudden and visible good effects were perceived from the use of the oranges and lemons; one of those who had taken them, being at the end of six days fit for duty. . . . The other was the best recovered of any in his condition; and being now deemed pretty well, was appointed nurse to the rest of the sick. . . ."

Elsewhere, he writes:

> "Some persons cannot be brought to believe that a disease so fatal and dreadful can be prevented or cured by such easy means. They would have more faith in some elaborate composition dignified by the title of an antiscorbutic golden elixir or the like. . . . Facts are sufficient to convince the unprejudiced. It is no easy matter to root out old prejudices or overturn opinions which have acquired an establishment by time, custom and great authorities."

In Lind's own day it was rightly said that scurvy had done more to reduce the fighting strength of the Royal Navy than enemy action and shipwreck combined. Lind himself, venerated as the 'father of nautical medicine', was the medical director of the Naval Hospital at Haslar, near Portsmouth, during 1758–83. This was, and still is, the largest hospital ever built. In his time, one-quarter of all the patients in it were suffering from scurvy.

The havoc which had been wrought by the disease among navigators is apparent from records going back to the fifteenth and sixteenth centuries. For example, when in 1498 Vasco da Gama had sailed around the Cape of Good Hope, a hundred of his men had perished from scurvy, out of a crew of a hundred and sixty. In 1593, Admiral Sir Richard Hawkins mentioned that ten thousand seamen had

* Lind's Treatise on Scurvy. A Bicentenary Volume containing a reprint of the first edition of "A Treatise of the Scurvy by James Lind, M.D.", with Additional Notes. Edited by Dr. C. P. Stewart and Dr. Douglas Guthrie. Pp. xi+440+4 plates. (Edinburgh: At the University Press, 1953.) 45s. net.

died from scurvy within his own personal experience. On one occasion a Spanish galleon had been found adrift at sea, its entire crew dead from scurvy.

But for centuries scurvy was of common occurrence not only among seafarers and explorers and armies in the field but also among civilian populations in most regions of Northern Europe. The reason for this was that throughout the dark months of winter vegetables and fruits were unobtainable. The principal factors which led ultimately to the decline of scurvy were the introduction of the potato into Europe, and the development of modern methods of transport—and, in more recent times, to the growth of exact, scientific knowledge about the existence of, and the properties of, the anti-scurvy vitamin.

After Lind's time the puzzle of scurvy was to be unravelled in gradual stages, both on the practical and on the theoretical side. In 1772, Captain Cook's voyage around the world owed its success to the measures taken by the Admiralty to protect the sailors from scurvy. Captain Cook himself was awarded the Copley Medal of the Royal Society in 1776 for his account of how the disorder had been prevented on board his ship. In 1804, at the instigation of Sir Gilbert Blane, regulations were introduced into the British Navy enforcing the consumption of daily rations of lemon juice. In consequence, the incidence of scurvy at the Haslar Naval Hospital fell from 1,457 cases in 1780 to vanishing point by 1806.

Later, the unwarranted substitution of preserved lime juice (unhappily inactive) for the fresh lemon juice (a potent antiscorbutic) was to lead to misunderstandings and misfortunes. The disaster which befell Captain Scott's expedition to the South Pole in 1912 can be attributed largely to a failure to supply active antiscorbutic articles of food.

Then again, during the First World War, outbreaks of scurvy still occurred in Britain: fifty cases were reported at a poor-law infirmary in Glasgow, eighty-two cases in a prison camp in another part of Scotland, and sixteen cases at an infirmary in Newcastle. The cause was considered to be a national shortage of potatoes; but a failure to apply existing knowledge might as justly be blamed.

As late as the beginning of the present century, infantile scurvy was still rife among bottle-fed babies, as a result of the wide use of sterilized or boiled milk, or of farinaceous milk substitutes, in place of fresh milk. The modern infant welfare movement, with its insistence on the provision of antiscorbutic supplements, has changed all that. Nevertheless, in a recent survey at the Johns Hopkins Hospital in Baltimore, Maryland, U.S.A., microscopic evidence of scurvy was found to be present, *post mortem*, in 31 per cent of those babies examined, between the fifth and eleventh month of age, who had been fed on cows' milk alone.

Scientific, as distinct from empirical, knowledge about scurvy starts from 1907. In that year—following the earlier recognition that beriberi could be produced experimentally in birds, and was a disease of deficiency—Holst and Frölich, in Oslo, stumbled across experimental scurvy in guinea pigs, and they were quick to recognize it as another deficiency disease.

Writing in 1906, Hopkins had already referred to scurvy as a disease of which "for long years we have had knowledge of a dietetic factor", and he rightly added that the error in the diet was "still obscure" but "certainly of the kind which comprises the minimal qualitative factors". (And one recalls here, too, that as long previously as 1840 another far-sighted writer, G. Budd, had predicted that scurvy was due to the "lack of an essential element which it is hardly too sanguine to state will be discovered by organic chemistry or the experiments of physiologists in a not too distant future".) By 1912, Funk was able to postulate the existence of a distinctive anti-scurvy "vitamine", and to enumerate four separate disorders, namely, scurvy, beriberi, rickets and pellagra, as being "vitamine" deficiency diseases. In 1920, J. C. Drummond introduced the current alphabetical nomenclature, the letter "C" being reserved for the then unidentified anti-scurvy factor.

The earliest attempts to isolate vitamin C, by Zilva and by others, were rendered difficult by its instability and its power to undergo reversible oxidation. However, in 1928, the Hungarian biochemist, Szent-Györgyi, then working in Cambridge, isolated from the adrenal cortex, as well as from oranges and cabbage, a silver-reducing substance, first to be known as hexuronic acid. The suggestion was made by Harris in Cambridge, and by Tillmans and Hirsch in Germany, that this substance might, in fact, be identical with vitamin C. In 1932, when Waugh and King in the United States had at length succeeded in isolating an undoubted specimen of pure, crystalline vitamin C, they reported that it possessed all the properties of hexuronic acid; and almost simultaneously Svirbely and Szent-Györgyi in Hungary confirmed the antiscorbutic potency of hexuronic acid. The identity was not universally accepted at first; but tests soon proved that there was, in fact, an unfailing and quantitative correlation between the presence of hexuronic acid and antiscorbutic potency. Doubts were finally set at rest when the chemical structure was worked out, and the synthetic product was found to have identical activity with the substance isolated from natural sources. The vitamin was then renamed ascorbic acid.

Later advances have included, for example, the development of chemical methods for the estimation of vitamin C; and techniques have been devised for the assessment of vitamin C status in human subjects. Another point of interest is the recognition of the fact that the requirements for the vitamin are increased in infection. Among animal species, primates and guinea pigs are unique in needing vitamin C in their diet; all other animals, so far as is known, synthesize it in their bodies, the precursor apparently being glucose.

During the Second World War, the accumulated scientific knowledge on vitamin C which had so recently been won could be put to good service. Government action was taken to ensure an adequate supply of concentrated orange juice, or of black-currant juice, or synthetic ascorbic acid, for mothers and young children; encouragement was given to the cultivation by householders of fresh fruit and vegetables on 'allotments'; housewives were advised what measures should be taken to minimize losses on cooking; and procedures were worked out for manufacturing dehydrated vegetables, to be used, for example, in the desert campaign, which still retained their vitamin C. No outbreaks of scurvy were seen during the Second World War, in contrast with the conditions referred to above in the First World War, when outbreaks had occurred among the civilians in all the belligerent countries (including Great Britain and the United States), as well as among the armed forces at the various fronts, the total number of cases running into many thousands.

Little is yet known about the detailed physiology of vitamin C action, except that it is needed for the elaboration of the intercellular cementing substance, collagen, or, in a more general way, for the functional activity of the formative cells in general. Chemically, the vitamin is concerned in the conversion in the animal organism of folic acid (pteroylglutamic acid) into folinic acid, and in the metabolism of tyrosine. Vitamin C itself has intense reducing activity, but it has not yet been shown that its characteristic anti-scorbutic action can be attributed intrinsically to its redox properties.

Among various new points brought out at the Lind Bicentenary Conference, held in Edinburgh between May 22 and 23, was the suggestive fact, mentioned by C. G. King, that ascorbic acid may also have a role to take in the metabolism of cholesterol. At this meeting, contributions relating to vitamin C and allied topics were made by the following : Surgeon Vice-Admiral Sir Sheldon Dudley ("The Lind Oration"), Sir Edward Mellanby (opening remarks), Dame Harriette Chick ("Early Investigation of Scurvy and the Antiscorbutic Vitamin"), Dr. C. G. King ("The Discovery and Chemistry of Ascorbic Acid"), Dr. M. van Eekelen ("The Occurrence of Vitamin C in Foods"), Prof. H. A. Krebs ("The Sheffield Experiment"), Prof. S. B. Wolbach ("The Histology of Scurvy"), Prof. V. P. Sydenstricker ("The Impact of Vitamin Research on the Practice of Medicine"), Dr. J. H. Crandon ("Ascorbic Acid Deficiency in Human and Experimental Subjects"), Dr. R. M. Kark ("Ascorbic Acid in Relation to Scurvy, A.C.T.H. and Surgery"), Prof. E. J. Bigwood and Dr. J. P. Dustin ("Amino-aciduria in Infancy and Ascorbic Acid Deficiency"), Dr. C. P. Stewart ("Dehydroascorbic Acid in Human Blood Plasma"), Mr. A. J. Lorenz ("Pre-Lind Writers on Scurvy"), Dr. H. Gounelle and Dr. H. Teulon ("Contribution à l'étude de le Vitamine C dans certains états physiologiques et pathologiques chez l'homme"), Dr. W. J. Darby ("The Relationship of Ascorbic Acid to Tyrosine and to Hæmopoietic Vitamins"), Dr. L. W. Mapson and Dr. F. A. Isherwood ("Synthesis of Ascorbic Acid in Plants and Animals"), and Dr. Leslie J. Harris (chairman's summing-up). The proceedings are to be printed in full in a special, forthcoming issue of the *Proceedings of the Nutrition Society*. Obviously, anyone interested in the field of vitamins, whether from the separate aspects of biochemistry, physiology, dietetics or public health, will have need to consult this issue of the *Proceedings*. Together with the reprint of Lind's "Treatise", this record will form a fitting and permanent memorial to the pioneer whose memory was honoured at the bicentenary meeting.

HIGH-FREQUENCY ELECTRICAL MEASUREMENTS

CONFERENCE IN WASHINGTON, D.C.

THE third of the biennial conferences organized jointly by the American Institute of Electrical Engineers, the Institute of Radio Engineers and the National Bureau of Standards was held during January 14–16 in the Auditorium of the Interior Department in Washington, D.C. It was divided into four technical sessions dealing respectively with the measurement of frequency, length and time, power and attenuation, transmission and reception, and impedance. A list of the authors[1] and the briefest abstracts of the twenty-seven papers that were read would occupy the space of this article, and it will perhaps be preferable to select for more detailed treatment those subjects of particular interest to the writer.

Before the first session Dr. A. V. Astin gave a short address of welcome to the seven hundred delegates, and stressed the importance of the conference in helping specialists to keep abreast of this rapidly developing field of work. The chairman of the session, Dr. Harold Lyons, then introduced Dr. L. Essen, who described the frequency standards developed at the National Physical Laboratory, Teddington, their application to microwave measurements and, in particular, to the determination of the velocity of electromagnetic waves and the refractive indices of gases. The experiments involve the accurate measurement of both frequency and wave-length. Extensions of well-known techniques have given an accuracy of frequency measurement, throughout the radio-frequency spectrum, of one part in 10^8, and microwave optics have been developed to give an accuracy of wave-length measurement of one part in 10^6. Dr. Essen made use of a cavity resonator which is the microwave analogue of the Fabry–Pérot interferometer, while K. D. Froome used the analogue of the Michelson interferometer. The final accuracy that can be given for the value of the velocity of light, c, depends on the analysis and elimination of systematic errors due, in one case, to the imperfections of the surface of the resonator and, in the other, to the diffraction of the beam of radio waves at the transmitting horn and reflector. The values obtained are $299{,}792{\cdot}5 \pm 1{\cdot}0$ km./sec. and $299{,}792{\cdot}6 \pm 0{\cdot}7$ km./sec.

Dr. K. Bol then gave some previously unpublished details and the final result of the velocity determination initiated by Prof. W. W. Hansen at Stanford University. One of the main experimental difficulties had been the measurement of the length of the resonator, and this is probably mainly responsible for the spread of 2·2 km./sec. in the results. The final result of the measurements was given as $299{,}789 \pm 0{\cdot}5$ km./sec.

In view of the interest in the subject, a special discussion meeting was arranged by Dr. Lyons. The presence of so many of those concerned with the recent determination of the velocity of light would, he thought, afford a good opportunity for discussing the discrepancies between the various results, the question which is still sometimes raised of the variation of the velocity with time or frequency, and the best approach to a number of new measurements which are being planned. The result diverging most from the average of recent values is that obtained by D. H. Rank and his co-workers, from an examination of the infra-red and microwave spectra of hydrogen cyanide. Prof. Rank, although not at the meeting, had said earlier that there is some dissatisfaction with the wave-length measurements and that a new determination now in progress should give a considerably higher accuracy. In view of this and of some criticisms that were made about the way in which the final result is derived from the measurements, there was a general feeling that too much importance should not at present be attached to the discrepancy, although the method is one of great interest and potential importance.

The difference between the two cavity-resonator results was discussed at some length, but was not