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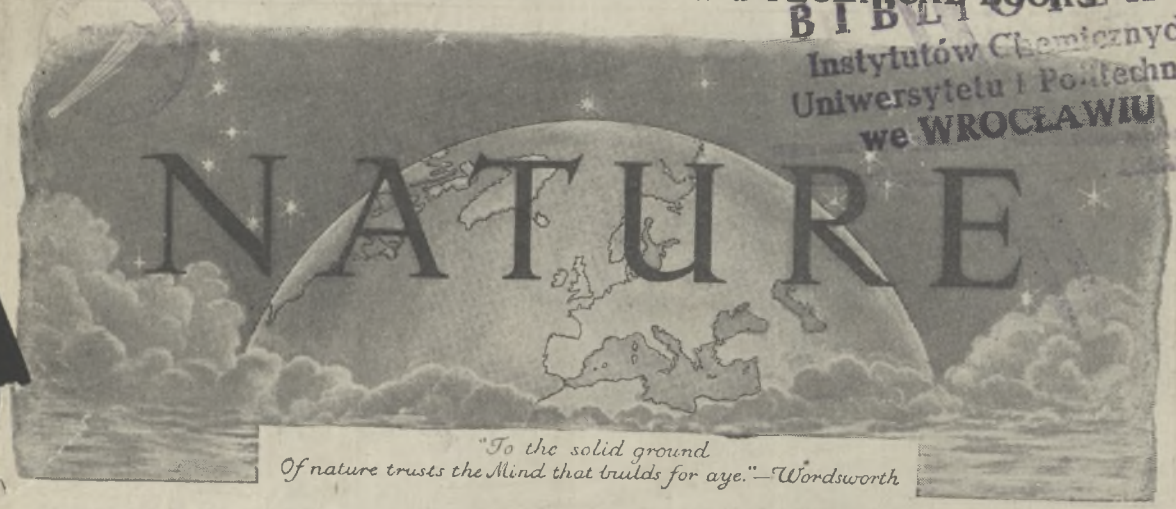

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CONTENTS

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PENICILLIN: A STUDY IN CO-OPERATION

MUCH has recently been heard of co-operation between scientific workers of Great Britain and of the United States in physical research, and the successful outcome of the work which culminated in the production of the atomic bomb has been widely quoted as an indication of the value of such co-operative effort and the desirability of its continuation in the future. With the publication of the statement on the chemistry of penicillin which appears in this issue of *Nature* (p. 766), there is revealed the existence of another co-operative effort in research, directed towards a very different end. This publication may serve to correct the general but mistaken impression that scientific work during the War has been mainly concerned with the destruction of man. It is of some interest to consider the background against which this extensive collaboration in work on penicillin was developed and the implications which it carries for the future.

As soon as the potential importance of penicillin as a therapeutic agent had been demonstrated by Florey and his collaborators, intensive chemical work on the substance was initiated in Florey's own laboratory and in the Department of Chemistry at Oxford. From the time of the formation in 1942, at the instance of the Ministry of Supply, of the General Penicillin Committee, which was charged with the duty of doing everything possible to increase production of penicillin, other academic and industrial laboratories in Great Britain were drawn into the work and a considerable measure of co-operation was achieved in this country.

As the work on the constitution of penicillin proceeded, and as the formidable difficulties of large-scale microbiological production of the substance were realized, the question of the development of a synthesis acquired considerable urgency, and through the Medical Research Council steps were taken to make the collaboration between British chemists engaged on the problem more intimate and effective. For this purpose the Council set up a Penicillin Synthesis Committee (under the chairmanship of Sir Robert Robinson, Waynflete professor of chemistry in the University of Oxford), which included distinguished chemists from both academic and industrial organizations working on this subject. By this time it had become apparent that, owing to the difficult situation in Great Britain, and to the greater resources of labour, material and technical knowledge of microbiological methods in the United States, it was from America that really large-scale microbiological production of penicillin was first to be anticipated. That this anticipation has been realized is now a matter of common knowledge ; what could not be foreseen at the time was that the most hopeful expectations would be far exceeded by an effort in the industrial application of microbiology which is probably without parallel in the past.

The development of the national effort in the microbiological production of penicillin in the United States naturally involved American chemists in work

similar to that which had already been begun in Great Britain on the constitution of penicillin with a view to its subsequent synthesis. The potentialities of penicillin not only in matters affecting the health of the civil population but also in directly assisting military operations by controlling infection of wounds, and thus reducing disability, were fully realized both in Britain and in the United States ; this realization brought the recognition that work directed towards synthesis, which at that time seemed to offer the best prospect of the rapid production of the substance in large quantities, was a matter of the greatest importance to both countries.

Since this conviction was shared on both sides of the Atlantic, it was possible for the Medical Research Council to arrange with the Office of Scientific Research and Development in Washington, which itself was co-ordinating American work on penicillin on behalf of the United States Government, for the complete and up-to-date exchange between the two countries of all research information bearing on the synthesis of penicillin. Thus, the Penicillin Synthesis Committee of the Medical Research Council referred to above became a co-ordinating centre in Britain not only for all British research on the constitution and synthesis of penicillin but also for the complete Anglo-American collaborative effort. The statement which is now published gives an outline of the unequivocal results obtained in Britain and in the United States both before and during the operation of this collaborative arrangement, up to the middle of 1944.

Full assessment of the value of the chemical work which has resulted from the international co-ordination of research on this subject must naturally await the complete publication of the results, which it is hoped may not be long delayed. In the meantime, however, the impressive amount of this work is immediately apparent from the preliminary statement, which also brings to light other facts of interest. The first is the extraordinary and unexpected difficulty of the problem. The molecule of penicillin is not large, and, as the statement indicates, the general features of its structure are revealed by identification of the products of acid hydrolysis ; on the other hand, some of the transformations undergone by penicillin are not easy to explain and it is clear that there has been difficulty in reaching finality about its constitution. A measure of the magnitude of the problem is afforded by perusal of the list of groups both in Britain and in the United States which have participated in the work, and this list is itself a second matter of interest to which attention may be directed. Not only have some of the most distinguished organic chemists in both countries directed their efforts to the problem, but also every potentially useful physico-chemical and physical technique has been brought to bear on it. Never before indeed can there have been such a concentrated attack on the chemistry of a single compound. It seems that penicillin is almost as remarkable in the tenacity with which it holds the secrets of its molecular structure as it is in the biological properties which give it its peculiar importance.

Whether or not we are ultimately to learn that the collaborative research on penicillin has led to success, the announcement that such a collaboration has been possible at all is an event of considerable significance. A few years ago it would have been quite inconceivable that a project with such possibilities of commercial development could have been the subject of pooled research, involving a completely free interchange of information, between a group of organizations such as those listed at the end of the statement ; this list includes, for both Britain and the United States, academic laboratories, government research institutions and the research departments of industrial firms which are normally commercial competitors. Those who have knowledge of the working of the arrangement are aware of, and have been impressed by, the complete loyalty with which all participants have observed the conditions of co-operation.

Even if it be admitted that such a collaboration in research on a subject of potential commercial value could only have been arranged under the special conditions prevailing in war-time, when the motive of commercial competition is submerged by that of defence of the country, the evident success of the temporary arrangement is certainly a good omen for the future. It becomes increasingly clear that for the advance of science in any country, particularly perhaps for the advance of chemistry and physics, a closer co-ordination is desirable than has hitherto existed between the research work which is done in universities, government institutions and industrial laboratories. Of the difficulties which have stood in the way of such co-ordination in the past, the greatest is probably the inevitable difference of outlook induced by the necessities of commercial practice. This has tended to set up a barrier between the academic research worker whose traditions demand free publication of all results and free interchange of information with his scientific colleagues, and the industrial research worker whose first duty is to the interests of his own firm. With the resumption in peace-time of normal commercial practice, this difficulty will necessarily reappear and it is useless to minimize its seriousness. Nevertheless, even the temporary breakdown of the barrier by a collaborative arrangement such as has operated during the last few years in the field of penicillin chemistry can scarcely fail to exercise a lasting effect for the good. On one hand, the academic participants will have had an opportunity, such as could not otherwise have been afforded to them, of learning something of the quality of research work which is carried out in industrial organizations, and they will certainly thereby have acquired a greater respect for this work ; on the other hand, it may be hoped that the industrial research workers may have become more impressed than they formerly were with the very real benefits which may be derived in scientific work from free consultation and discussion with colleagues. If such a conviction were established, it would probably also result in a change of policy in the direction of prompt and complete publication of scientific results from industrial research laboratories to the maximum extent consistent with adequate

protection for development ; no move could be more favourable to the recruitment of able scientific workers to industry than an increase in the opportunities afforded to them for publication and, through this, for the development of a scientific career.

If the collaborative research on penicillin has been effective in starting a move in the directions indicated, this may ultimately be counted a contribution to the advancement of science as important as the actual scientific work for which the collaborating parties have been responsible.

SCIENCE AND MYSTICISM

The Physical Basis of Personality

By Prof. V. H. Mottram. (Pelican Books, A.139.) Pp. 126. (Harmondsworth and New York : Penguin Books, Ltd., 1944.) 9*d*.

IN this book the reader will find a stimulating discussion of known facts about heredity, genes, endocrine organs and related biological conceptions. The terminology of these conceptions is freely used nowadays, often without a clear understanding of its meaning. It is therefore important that this meaning should be precisely understood. For this reason alone this book should be read.

Apart from this point, however, the book is worth reading for the sake of its last chapter entitled "Recapitulation and Coda". If some readers reject the author's criticism of the determinist materialist philosophy which is so popular nowadays (again often without adequate understanding of its full implications), others will welcome the method which the author adopts of avoiding the pessimism and unhappiness which materialism so often brings. The way indicated is a mysticism reconciled with scientific discovery. It will not be everyone's way of meeting the philosophical challenges of science. At least one other way is available, namely, the lonely way expounded by Sir Charles Sherrington in his "Man on his Nature", which book Prof. Mottram highly commends. Commendable Sir Charles Sherrington's book most certainly is, in spite of its difficult style ; but it counsels a solution which the mystic could not adopt. For Sherrington there can be no leaning for counsel and guidance upon a higher mind or personality. Man must shoulder his burden alone ; and by acceptance of that "loftier responsibility", he is raised, in Sherrington's opinion, to "a rank of obligation and pathos which neither Moses in his law-giving nor Job in all his suffering could present".

This attitude, admirable though it is, requires for its acceptance a mind too subservient to logic and the scientific method to be representative of the newest developments of human intelligence. Much recent writing indicates this. To mention only one example, Dr. Clark-Kennedy, in his lecture on "The Art of Medicine in Relation to the Progress of Thought" (Cambridge University Press, 1945), has ably set out some of the reasons why science is not enough for the proper practice of the art and science of medicine. Mottram, in the book under consideration, and the others, ancient and modern, whose work he quotes, remind us of an experience less tragic, if no less difficult, than that indicated by Sir Charles Sherrington—an experience which has been variously called communion with an inner spirit or reality, the quest of the world-soul, submission to the absolute (which does not, be it noted, necessarily involve acceptance or even understanding of Hegelian philosophy), the search for the spirit of the whole or accordance with the inner necessity. Yet others, like McTaggart and Younghusband, have frankly and simply called it love. It is an experience which all of us may have if we will ; we may have it, too, without any very esoteric disciplines. Most men of science, in any event, will probably be able, if they are honest with themselves, to apply to their own experience Sir Olaf Stapledon's description, quoted by Mottram from Stapledon's "Saints and Revolutionaries", of that "very comprehensive act of attention, an attending to everything at once, or to the wholeness of everything at once" which brought to Stapledon "a tension of fervour and peace" and might easily, he goes on to say, be regarded, if he were less sceptical, as some kind of contact with God.

One way of experiencing this kind of emotion—and of doing so without necessarily excluding God—is to watch, in the circle of green light beneath a microscope, the ways, say, of the trypanosome which can, and inevitably will, if conditions are favourable, kill a Christ and a Hitler alike. The proper understanding of the conditions necessary for this entirely inhuman and amoral act requires an intellectual discipline, maintained for many years of close and exacting study, which the orthodox mystic can scarcely comprehend. The mere act of looking down a microscope will not provide it, though the microscope can, like the rites prescribed by orthodox mysticism, shut out the disturbances of the immediate surroundings and focus the attention. It can focus the attention, moreover, upon those small details which, both by their cumulative effects and their individual significance, reveal to the experienced mind a good deal which the philosopher, who looks at the landscapes of science rather than at their several components, cannot possibly apprehend. It can focus the attention, in addition, upon those minute inexactitudes which at once justify the disciplines of the scientific method and at the same time reveal its limitations. It can endow the observer with a "snail-horn delicacy of perception" which is essential to any effort towards the understanding of those wider landscapes which the philosopher seeks to delineate.

The remainder of the mystic procedure will come naturally to the man of science. The elimination of the self, so far as this is possible to the Adam in us, is habitual to the scientific worker, who cannot, unless he achieve some considerable measure of it, begin to work at all. To him also comes naturally that deep and essentially religious awareness of abstract beauty, which goes so far beyond the appreciation of beauty of form—the realization, in other words, of the difficult beauty of adaptation, evolution, development and obedience to natural law. The slow and inspiring growth in the mind of all that this kind of beauty implies comes only, during the years, from the disciplines of study, disappointment and refusal to escape into easier ways ; and these are disciplines as difficult as any that the orthodox mystics have enjoined. When knowledge is thus gained in any field of scientific work, and is related, as only the experienced man of science can relate it, to the same kind of knowledge won from the similar study of other aspects of the universe, then the mind experiences, in rare moments of

synoptic insight, a reverent and exhilarating certainty of the essential unity of all phenomena appreciable by the mind, and of the omnipresence of an inner reality pervading all, which inspires and pervades the whole life and character of him who experiences it. It is this that equates the amœba with him who has thought his apprehension like a god's; it is this which has created, out of truth and beauty, the atomic bomb which awaits man's dedication of it, in action and not merely in a form of words, to the service of the good; it is the germ of this which Prof. Mottram offers to those who read his book.

For this reason, if for no other, this book can be commended to all those who are seeking at this moment—and desperately seeking—some reintegration of that belief in the existence and even in the good purpose of an inner reality which the recent War, and the evil of those who instigated it, may seem to have shattered beyond recovery. It shows beautifully the moral worth of the service of the truth. Read sincerely and with imagination, it spans the ages of man's experience. With the terrible charity which modern truth must exercise, it links the modern microscope with "the eye of my soul" which beheld, "above my mind, the Light Unchangeable".

G. LAPAGE.

A GREAT PHYSIOLOGIST

Léon Fredericq et les débuts de la physiologie en Belgique

Par Prof. Marcel Florkin. (Collection Nationale, Troisième Série, No. 36.) Pp. 104. (Bruxelles: J. Lebègue et Cie., 1943.) n.p.

PHYSIOLOGISTS the world over, and especially in Belgium, have reason to be proud of Léon Fredericq. Born in 1851, he became an outstanding figure in the classical period of physiology. Between 1870 and 1880, the institutes of physiology for the promotion of teaching and the encouragement of research, which came into being in various countries, necessitated the creation of whole-time chairs of physiology. In Belgium such innovations were encouraged by the State, and Léon Fredericq was appointed to the chair at Liège in 1879 in succession to Théodore Schwann, and charged with the creation of a new Institute of Physiology, which was completed in 1888. In the forty-two years during which he directed the Institute, it made history, and on reading this elegant little essay, one realizes why so high a place in world physiology is held by so small a country.

Fredericq's knowledge was encyclopædic, his experience wide and his talents manifold. Among the latter was high ability as a popular lecturer and as a water colourist. A great naturalist, we owe much to his researches in the comparative field, his most memorable discovery being that of hæmocyanin.

His contacts were closest with France and Germany, and though he had many friends in Britain too, his work was less well known here than it should have been. It is not generally known, for example, that he invented an apparatus, the oxygénographe, applicable for use on man, for reading off oxygen utilization, and recognized by Benedict as a prototype of the arrangement which he so extensively used. He was the initiator of the technique of crossed circulation, and his work on the respiratory exchange as revealed by tonometric determinations, on the left auricular pulsations as studied by œsophageal sounds, and of the time relations of events in the cardiac cycle, is widely known. Much of his work was biochemical and included investigations on blood coagulation: in the course of these he recognized the three main proteins of the plasma.

The book is full of interest, and is a valuable contribution to the history of physiology, with thoroughly painstaking bibliography and footnotes.

C. LOVATT EVANS.

ACCOUNTING FOR FARMERS

Good Farm Accounting

By A. C. Campbell. (Teach Yourself Farming Series.) Pp. 200. (Bickley: English Universities Press, Ltd., 1945.) 3*s*. 6*d*. net.

IF there is one branch of farming that can be learnt from books it must certainly be book-keeping. Formerly farmers were inclined to regard accounts as an unnecessary encumbrance in a life mostly spent in field and market; but recent changes in taxation have compelled practically all of them to provide statements of their affairs that will satisfy the Inland Revenue authorities.

If we must have accounts, however, let us have them in such a form as to give the maximum amount of information about the running of the business with the minimum of effort.

The author, who has had an extensive and varied farming experience, assumes no previous knowledge of bookkeeping on the part of his readers. Starting from first principles, he leads on through a series of farm accounts posted by double entry, the examples increasing in scope as the more intricate points are illustrated. Thus the treatment of the farmer's personal expenses, produce consumed in the farmhouse and payments in kind to farm workers, are discussed at some length. The interpretation of balance sheet and profit and loss account as a guide to management also receives attention.

For those who desire to keep their accounts in the simplest form consistent with accuracy and efficiency, the author proceeds to describe the single-entry system using an account book of his own design as an illustration.

A section on cost accounting follows. The author shows how cost accounts give a clearer view of the situation in the various farm departments than the purely financial treatment can provide. Further, when handled in mass by experts, they can form a basis for moulding agricultural policy. The nature of the records necessary to build up these accounts is explained with illustrations of the appropriate forms, but it is admitted that the procedure is too exacting for most farmers whose business is not big enough to justify the employment of a clerk.

Information relating to business methods and procedure forms an important part of the book. Certain tables of weights and measures, and valuers scales of compensation are given, some of which might with advantage have been included in an appendix.

The financial accounts are presented in sufficient detail to be readily followed by a beginner.

The Molluscan Family Planorbidæ

By Frank Collins Baker. Collation, revision and additions by Harley Jones van Cleave. Pp. xxxvi+530 (141 plates). (Urbana, Ill.: University of Illinois Press, 1945.)

THIS important monograph, based on exhaustive anatomical research, was nearing completion at the time of the author's death in May 1942; the collation, revision and additions necessary before publication having been carried out by H. J. van Cleave.

Frank Collins Baker's researches on the anatomy and ecology of North American freshwater Pulmonata have long been familiar to malacologists on both sides of the Atlantic, and valued for their accuracy and originality of concept; while the publication more than thirty years ago of his monograph on the Lymnæidæ of North and Middle America established his reputation as one of the few authorities on the subject. The present work, to which he devoted much time and labour during the last twenty-five years of his life, will long remain not only a lasting memorial to the man and his work, but also a standard text-book and work of reference. It fully confirms the importance of a study of the comparative anatomy of the soft parts of these molluscs as giving the only true key to a natural classification, for the shell cannot be relied upon entirely for this purpose, its characteristics often proving misleading on account of the presence of many cases of parallel development. That certain features of shell morphology, however, when used in conjunction with the anatomical details of the body, are of importance in establishing a satisfactory classification of the Planorbidæ is fully demonstrated both in the text and by the many admirable illustrations.

In the compilation of the work, the author had examined no fewer than 725 specimens representative of eighty-one species and races of the family; the number of species examined being divided among the four subfamilies as follows: Planorbinæ 19; Segmentininæ 11; Helisomatinæ 41; and Planorbulinæ 10. The wide geographical distribution of the Planorbidæ and their economic significance as the intermediate hosts of various disease-producing parasitic trematodes renders the intensive study of these freshwater molluscs one of prime importance, and one to which the work under review forms a valuable and authoritative contribution.

F. MARTIN DUNCAN.

The Economics of Advertising

By F. P. Bishop. Pp. 200. (London: Robert Hale, Ltd., 1944.) 7*s*. 6*d*. net.

A GOOD general dictionary tells you that advertising simply means making a thing widely known by circular, etc., but a scrupulously careful scientific handbook tells you that advertising means "the process of notifying *or persuading* people without personal solicitation" (italics ours). The difference between the two statements makes all the difference—notifying, yes, by all means; persuading, a much more hesitant yes. The kind of thing that bothers most people about advertising is the patent-medicine advertisement that blurs the distinction between palliatives and cures, the advertisement for pills that vulgarly disfigures a lovely landscape, the window-dressing that induces people to buy what they do not need and cannot afford. Evidently advertising touches psychology, ethics and æsthetics as well as economics. Of all this the author of this fine book is perfectly well aware. He promises to deal later on with "the various ethical and social problems raised by the practice of commercial advertising". In this volume he adheres to his purpose as indicated in the title. The book is packed with information and suggestions coming from one who is obviously master of his subject, who has lived it as well as studied it, and who helps the reader to form a judgment as to the immediate future of advertising.

Waveform Analysis

A Guide to the Interpretation of Periodic Waves, including Vibration Records. By R. G. Manley. Pp. xi+275+3 plates. (London: Chapman and Hall, Ltd., 1945.) 21*s*. net.

THE development of high-speed mechanical engines and similar devices has, during the last decade, brought forth a demand for both recording vibration amplitudes with accuracy and the analysis of such wave-forms as are thus obtained. The present author, while indicating methods of recording, is largely concerned with analysis, which is rendered complicated by the fact of frequencies which are not exact multiples. It is therefore necessary to extract beats and to endeavour to relate them to various other frequency components which are inherent in the wave-form. The precise analysis of the frequencies is essential in order that the source of the vibration component may be traced. It is important, therefore, that an exact record is taken simultaneously of any fundamental frequency of rotation in the machines being tested; but the author shows that variations in the actual speed of the record can be tolerated, provided this extra recording, as well as the time-scale, is also made. The author is to be congratulated on the completeness of his practical treatment, and the advice he has to give in interpretation; in particular, mechanical analysers are dealt with, especially that one devised by J. Harvey.

L. E. C. HUGHES.

Witchcraft in England

By Christina Hole. Pp. 168+16 plates. (London: B. T. Batsford, Ltd., 1945.) 21*s*. net.

THIS is an industrious and careful study of the voluminous records of various kinds of witchcraft and kindred practices, some of which survive to-day. The bibliography would have been more useful if dates of publication had been given throughout. The preliminary chapter on the "Art of Magic" follows Sir James Frazer's view that magic is "probably older than religion"; but doubt is cast on Miss Margaret Murray's belief in a "Witch Cult in Western Europe" transmitted from pagan times, though many rites and beliefs are of pre-Christian origin. The various forms of harmful magic are classified and illustrated in detail, with the ingenious and horrible methods of detecting witches within historic times, and the comparatively harmless practices of the 'white witch', which have survived the repeal of the statute against witchcraft in 1736 and the spasmodic panics, here and there, of later date.

As very few references are given, the result of so much labour is of no scientific value; and the more-than-Hogarthian illustrations by Merwyn Peake appear to be works of imagination. Only one has a place-name, but the church of Walton-in-le-dale does not look like that.

J. L. M.

CHEMISTRY OF PENICILLIN

THIS brief summary of results obtained by British and American chemists, issued under the joint auspices of the Committee on Medical Research (Office of Scientific Research and Development, Washington) and the Medical Research Council (London), is a preliminary notice of the principal findings secured up to the end of 1944 in a collaborative effort of a large number of investigators, unnamed at present. It implies some corrections of published data; authors of early publications are among those who have cleared up these points. For the sake of clearness, the account is not given in chronological order of development. The primary object of this communication is to disclose significant facts which have been confirmed by unequivocal synthesis and to record a few essential points which are still matter for conjecture. Full details will be disclosed at a later stage, together with an account of experiments not referred to in this report.

Several antibiotics of the penicillin class are known and all have the empirical formula $C_9H_{11}O_4SN_2R$. In penicillin-I (known in America as *F*-penicillin), R is Δ^2-pentenyl, $—CH_2.CH=CH.CH_2.CH_3$; in dihydropenicillin-I, R is *n*-amyl; in penicillin-II (known in America as *G*-penicillin), R is benzyl; in penicillin-III (also known as *X*-penicillin), R is *p*-hydroxybenzyl. In *K*-penicillin (a recent addition to the series) R is *n*-heptyl. The best elementary analyses are of pure crystalline sodium salts. Determinations of the molecular weights of the sodium salt and of the methyl ester of penicillin-II indicate that the empirical formulæ truly represent the molecular weights.

The penicillins are strong monobasic acids of *p*K about 2·8; electrometric titration does not disclose the presence of a basic group. Slow titration with perchloric acid in acetic acid solution indicates such a group, but the penicillin is biologically inactivated by this treatment; rapid titration gives a negative result.

The ultra-violet and infra-red absorptions, crystal structure (by X-ray methods including full electron distribution of the rubidium salt of penicillin-II), and polarimetric and polarographic behaviour of the penicillins and their derivatives have been studied.

Sodium penicillin-II contains one hydrogen atom replaceable by deuterium on equilibration with heavy water.

On treatment with hot dilute mineral acids the penicillins afford one molecule of carbon dioxide, an amino-acid termed penicillamine and other products. Penicillamine, obtainable by several other degradation processes, has been identified by analytic and synthetic methods as *d*-β,β-dimethylcysteine. Penicillamine with the same steric configuration is derived from penicillins-I and -II; it belongs to the *d*- or 'unnatural' series of α-amino-acids.

Synthetic penicillamine has been resolved and numerous derivatives of the optically active enantiomorphs and the racemic form have been prepared. These include penicillamine disulphide (tetramethylcystine) and penicillaminic acid (dimethylcysteic acid) as well as a long series of thiazolidines, and S- and N-substituted derivatives.

After removal of penicillamine from the acid hydrolysates, careful treatment of penicillin-I allowed of the isolation of an aldehyde, $C_8H_{13}O_2N$, in the form of its 2 : 4-dinitrophenylhydrazone and its condensation product with dimedone. Similarly, dihydropenicillin-I gave rise to derivatives of an aldehyde, $C_8H_{15}O_2N$. Penicillin-II afforded phenaceturic acid, phenylacetamide and an aldehyde, $C_{10}H_{11}O_2N$. Phenylacetic acid had previously been recognized as a hydrolytic product of penicillin-II.

These *penillo-aldehydes* have been identified by analysis and synthesis as follows: penillo-aldehyde-I, Δ^2-hexenoylaminoacetaldehyde; dihydropenillo-aldehyde-I, *n*-hexoylaminoacetaldehyde; penillo-aldehyde-II, phenylacetylaminoacetaldehyde.

It was inherently probable that the carbon dioxide liberated when penicillin is hydrolysed in hot acid solution was derived from an unstable carboxyl group and, taking into consideration the nature of penicillamine and the penillo-aldehydes, a probable precursor was penillo-aldehyde-carboxylic acid, $CHO.CH(CO_2H).NH.CO.R$, now termed a *penaldic acid*. This was conclusively demonstrated to be correct.

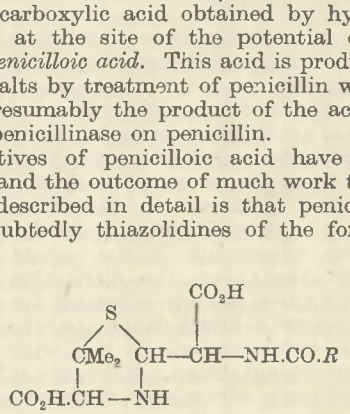
Penicillin-II and benzylamine afford a crystalline compound, $C_{30}H_{36}O_4N_4S.H_2O$, which has the composition of a hydrated addition compound of one molecule of penicillin-II and two molecules of benzylamine and is the mono-benzylamine salt of the mono-benzylamide of a dicarboxylic acid. Degradation of this substance by means of mercuric chloride afforded penicillamine and penaldic-II acid benzylamide which was catalytically reduced to hexahydrophenylacetylserine hexahydrobenzylamide, $C_6H_{11}.CH_2.CO.NH.CH(CH_2OH).CO.NH.C_7H_{13}$, identified with a synthetic specimen.

The penicillins are readily inactivated by methanol and the products are methyl esters. Methanol-inactivated penicillin-II was degraded to methyl-penaldate-II, $CHO.CH(CO_2Me).NH.CO.CH_2Ph$, the constitution of which was proved by its catalytic reduction to N-hexahydrophenylacetylalanine. The latter was identical with a specimen prepared by similar reduction of phenylacetylalanine. Penicillins-I and -II are converted by the action of diazomethane into mono-methyl esters and these are degraded by mercuric chloride in aqueous solution with formation of the methyl ester of penicillamine.

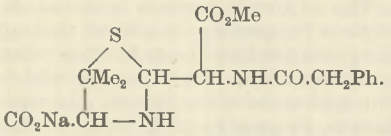
These observations serve to show (1) that the acidic group in penicillin is identical with the carboxyl group in penicillamine, (2) that by the addition of the elements of water to penicillin a second carboxyl group is produced, (3) that it is this new carboxyl which breaks down to carbon dioxide by the action of hot dilute mineral acids.

The dicarboxylic acid obtained by hydrolysis of penicillin at the site of the potential carboxyl is termed *penicilloic acid*. This acid is produced in the form of salts by treatment of penicillin with alkalis, and is presumably the product of the action of the enzyme penicillinase on penicillin.

Derivatives of penicilloic acid have been synthesized and the outcome of much work that cannot here be described in detail is that penicilloic acids are undoubtedly thiazolidines of the formula:



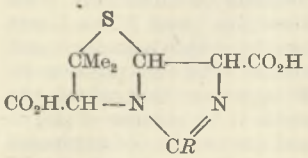
where *R* is one of the groups already particularized. Thus 'methanol inactivated' sodium penicillin-II is one of the stereoisomeric forms of the structure :



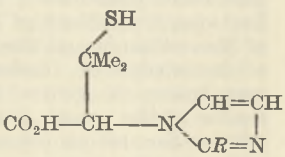
When any of the penicillins is held in dilute mineral acid solution at about 30°, a change occurs which may be followed polarimetrically. Crystalline isomerides of the penicillins termed *penillic acids* may then be readily isolated. These substances are shown by electrometric titrations to be dibasic acids containing a basic group : thiol groups are absent.

Treatment of the penillic acids with cold aqueous mercuric chloride involves loss of a molecule of carbon dioxide and formation of substances termed *penillamines*. These compounds are monobasic, mono-acidic and contain a thiol group.

Analysis and synthesis have shown that the annexed expressions represent the respective structures

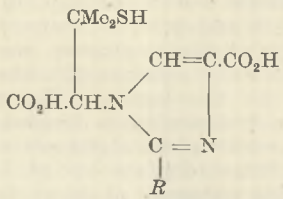


Penillic acids



Penillamines

Penillic-I and -II acids are convertible by baryta into the isomeric *iso*penillic acids.



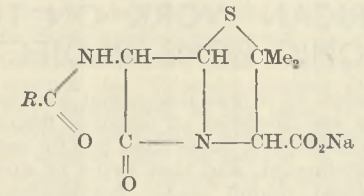
*Iso*penillic acids

Hydrolysis of the penillic acids by hot dilute acids affords penicillamine, the penillo-aldehydes and carbon dioxide ; but the penillamines are resistant to hydrolysis.

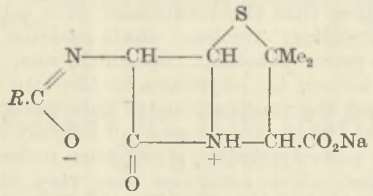
Methyl penicillin-II is changed by mercuric chloride in neutral media into the isomeric methyl penicillenate-II which, on hydrolysis by means of aqueous sodium hydroxide, affords the sodium salt of 4-hydroxymethylene-2-benzyloxazolone. The addition of the elements of thiocyanic acid to methyl penicillin and the transformations of the primary product have been investigated in detail with important results.

Finally, the action of Raney nickel catalyst on sodium penicillin-II in aqueous solution affords desthio-penicillin-II, $C_{16}H_{20}O_4N_2$, together with phenacetyl-*l*-alanyl-*d*-valine, $C_{16}H_{22}O_4N_2$.

Naturally the workers in this field have formed views as to the full constitution of the penicillins. At present it can be stated that the formulæ which are now receiving the most active attention contain respectively a β-lactam structure (I) and an incipient azlactone grouping (II) :



(I)



(II)

The following groups have participated in the joint programme for the chemical study of penicillin.

In Britain :

Boots Pure Drug Company, Ltd.*
British Drug Houses, Ltd.*
Cambridge University, Department of Chemistry.
Cambridge University, Department of Colloid Science.
Glaxo Laboratories, Ltd.*
Imperial Chemical Industries, Ltd. (Alkali Division).
Imperial Chemical Pharmaceuticals, Ltd.
Imperial College of Science, London, Department of Organic Chemistry.
The London Hospital Medical Unit.
Manchester University, Department of Chemistry.
May and Baker, Ltd.*
National Institute for Medical Research, Hampstead, London.
Oxford University, Department of Crystallography.
Oxford University, Dyson Perrins Laboratory.
Oxford University, Sir William Dunn School of Pathology.
Oxford University, Department of Physical Chemistry.
Wellcome Foundation, Ltd.*

In the United States :

Abbott Laboratories.
U.S. Department of Agriculture, Northern Regional Research Laboratory.
Cornell University Medical College, Department of Biochemistry and Russell Sage Institute.
Cutter Laboratories.
Federal Security Agency, Food and Drug Administration.
Harvard University, Department of Chemistry.
Heyden Chemical Corporation.
University of Illinois, Department of Chemistry.
Eli Lilly and Company.
Merck and Company, Inc.
University of Michigan, Department of Chemistry.
University of Michigan, Department of Physics.
National Bureau of Standards.
Naval Medical Research Institute.
Parke, Davis and Company.
Chas. Pfizer and Company, Inc.
The Rockefeller Institute for Medical Research.
Shell Development Company.
Squibb Institute for Medical Research.
The Upjohn Company.
Winthrop Chemical Company, Inc.

* Members of the Therapeutic Research Corporation of Great Britain, Ltd.

AMERICAN WORK ON THE ATOMIC BOMB PROJECT

JUST as soon as it was discovered that secondary neutrons are liberated in uranium fission to the extent of considerably more than one for each heavy nucleus transformed, and that types of nuclei exist which undergo fission under bombardment with neutrons of all energies, it became a reasonable scientific guess that the attainment of a self-propagating (divergent) nuclear chain-reaction would eventually prove possible. So much was, in fact, commonly known by physicists in the late summer of 1939—and the implications of this knowledge in relation to the likely development of military weapons of extreme power were not altogether unheeded by scientific men whose countries were very obviously slipping helplessly into war. In the United States, also, attempts to arouse official interest in the new possibilities were not entirely without effect. By slow degrees this latter interest quickened, and a few weeks before the Japanese attack on Pearl Harbour, American service chiefs were ready to sanction a greatly intensified effort on the problem. Early in 1942 a full-scale research and development programme was under way and plans for pilot production plants were in hand. Almost exactly three years later, what had appeared in sober estimate so distant was an actuality; the first bomb had not been dropped, but the scientific workers in charge of the project were satisfied that success was well-nigh inevitable, and large production plants were rapidly accumulating the fissile material which it was planned to use.

As is well known, the crucial trial was not staged until mid-July 1945—and it was not until August 6 that the new weapon was used offensively; but earlier in the year the scientists' efforts had progressed so far that some of them at least were able to relax a little and look beyond immediate problems of physical research to the impact which the employment of the weapon would be certain to have on the world at large. The heads of the Allied States concerned in the development of the bomb would obviously find it necessary to issue statements setting out briefly what had been done and indicating their policy towards the enemy if he remained unsubmissive; but it was felt that the peoples of the Allied Nations could not be left without further information, and that a popular exposition was needed which would allow them to appreciate the magnitude of the scientific achievement involved and—always within the limits imposed by considerations of security—permit them to look into the future with some guidance in their certain bewilderment.

The American scientists who acted on these conclusions are to be congratulated on the results of their efforts, first in obtaining the support of the military authorities in whose hands the question of security was vested, and secondly on the popular account itself which has been issued by the Government Printing Office in Washington* (and has also been reprinted and published by H.M. Stationery Office in Great Britain†), having been compiled by Prof. H. D. Smyth, chairman of the Department of Physics of Princeton University. This document, which was authorized for issue in America in August, very soon after the attack on Hiroshima, runs to 182 pages. The author's preface is dated July 1, 1945. The style is reasonably unhurried throughout; the whole thing cannot have been written overnight. It is to be repeated that the foresight which conceived the aim and scale of the report, and which led to its production, is greatly to be commended. In Great Britain we had less in the way of large-scale achievement to report upon, but it will be recalled that we also produced a 'popular' account for issue in August. The American account should be considered in one aspect, at least, in relation to the British one —to the necessarily incomplete but otherwise quite admirable White Paper* published by the Stationery Office. This is said in no spirit of criticism: it reflects merely the statement in Prof. Smyth's preface: "References to British and Canadian work are not intended to be complete since this is written from the point of view of the activities in this country".

The American report is divided into thirteen chapters each with a summary, and there are five appendixes. The first chapter (twenty pages) and the first two appendixes ("Methods of Observing Fast Particles from Nuclear Reactions" and "The Units of Mass, Charge and Energy") provide a background of knowledge of fundamental nuclear physics to supplement the general scientific outlook which the reader of the report is assumed to possess—"[It] is written for this professional group . . . of engineers and scientific men who can understand such things and who can explain the potentialities of atomic bombs to their fellow citizens". Chapters 2–5 give the administrative history of the project in its various stages, Chapter 6 describes in general terms the research carried out at Chicago in 1942, and Chapters 7 and 8 and 9 to 11, respectively, trace the development of the production methods used for plutonium 239 and uranium 235, the two fissile materials used for the bombs. The problem of bomb design and assembly is treated separately in Chapter 12, which gives a glimpse of the work of the special laboratory set up at Los Alamos precisely for this purpose. A short final chapter (13) summarizes the whole account—and ends with a call for an acute social consciousness to grapple with the weighty issues which the successful prosecution of the project has raised (Section 6, "Planning for the Future"; Sections 7 and 8, "The Questions before the People"). Lastly, Appendixes 3, 4 and 5 are included for the benefit of the semi-professional nuclear physicist. They give, as examples of the type of fundamental research work carried out in the course of the development programme, brief accounts of an investigation of the delayed neutrons of fission and of the construction and testing of the first self-sustaining chain-reacting pile (which was brought into operation on December 2, 1942, at an initial energy output of 0·5 watt)—also a representative list of eighteen titles taken from the index of reports written by the Chicago workers during 1942.

It will be evident from this brief digest of the contents of the Smyth Report that it cannot fail to make interesting reading. To the general reader the earlier chapters may appeal more than the later ones; the account of the administrative handling of this vast project will certainly be a revelation to the

* A General Account of the Development of Methods of Using Atomic Energy for Military Purposes under the Auspices of the United States Government, 1940–1945. By Prof. H. D. Smyth. Pp. vii+182. (Washington, D.C.: Government Printing Office, 1945.) 35 cents.

† Atomic Energy. (London: H.M. Stationery Office, 1945.) Pp. iv+144. 2*s*. 6*d*. net.

* Statements relating to the Atomic Bomb. (London: H.M. Stationery Office, 1945.) 4*d*. net.

industrialist—it is without question the history of the most complex and extensive industrial project ever brought into co-ordinated operation within a period of little more than two years; it is also, by implication, the story how, in a country of free institutions, under the stress of total war, many hundreds of millions of dollars were expended and many thousands of persons were employed without Congressional sanction or knowledge ("Because of the restrictions of military security there has been no chance for the Congress or the people to debate such questions").

To the scientist, however, the later chapters will probably have the greater appeal. Unless he has been associated with the project he will scarcely have heard of the 'transuranic' elements 93 (neptunium) and 94 (plutonium). To him, Chapters 7 and 8 will be particularly illuminating. He will be able to read for the first time a connected account of an altogether amazing achievement in transmutation. A chemical species which does not occur naturally on the earth, and for which the astrophysicist has never produced evidence of occurrence in the stars, has been manufactured on an industrial scale: kilograms—probably hundredweights—of uranium have been transformed, atom by atom, into something strange and new, and, as a by-product, energy has been released at a power which, if expressed in thousands of kilowatts, must certainly involve numbers which are large. He will be interested, too, to know something of the methods by which isotope separation has been achieved for the heaviest of the terrestrial elements—how many kilograms of the rare isotope uranium 235 (natural abundance 0·7 per cent!) have been separated, practically pure, by a bold development of the electromagnetic method, which before the War had been made to yield merely a few micrograms of the separated isotopes of lithium and boron for particular experiments (Chapter 11).

No one can possibly detract from the achievement of the scientists and engineers who brought this amazing project to success in the United States within days which were numbered; but a British reviewer may be pardoned for returning to the subject of the contribution which his colleagues belonging to this country made in the earlier (as to some extent, also, in the later) phases of the work. Let it be said, then, that the Smyth Report recognizes the reality of this contribution. It records the fact that a suggestion was made through the British scientific liaison office in Washington, late in December 1940, that plutonium 239 appeared worthy of serious consideration as material for a bomb (Chapter 3, Section 17), also that the definitive report of the Committee of the National Academy of Sciences dated November 6, 1941, was more conservative than the British report of July 15, 1941 (progressive action being taken on the former only in view of its reinforcement by the latter report; and because of "general urging by a number of physicists"—including Urey and Pegram, who had just returned from a visit to Britain: Chapter 3, Sections 21 and 23). It states quite clearly "The British, particularly J. Chadwick, were convinced that a U235 chain reaction could be achieved. . . . They feared that if the Germans got atomic bombs before the Allies did, the war might be over in a few weeks. The sense of urgency which Pegram and Urey brought back with them was of great importance" (Chapter 4, Section 47). More could scarcely be expected by way of acknowledgment from an ally and partner (if the reader wishes to learn more of the British effort he should consult the White Paper referred to above). In view of this, it is doubly unfortunate that a charge should be levelled against the "foremost nuclear physicist" of another ally, amounting, at the least, to an accusation of political unwisdom and irresponsibility. It would not appear that the section of the report in question (Chapter 3, Section 2) is factually correct, let alone temperate in utterance. This, however, is but one blemish in a generally admirable and objective presentation.

N. FEATHER.

PENICILLIN IN THE TREATMENT OF SYPHILIS

By DR. JAMES MARSHALL

IT is generally agreed that probability of cure in syphilis can only be assumed if, during five years after treatment, there have appeared no signs, clinical or pathological, of relapse or progression. Penicillin was first used in the treatment of syphilis as recently as 1943, and it is now known that the doses originally used were inadequate. We cannot, therefore, begin to estimate the value of penicillin as an agent for the permanent cure of syphilis.

It is possible, however, to describe the remarkable effects of penicillin on the lesions of syphilis at all stages and to give some indication of the short-term therapeutic results. Only the passage of time and careful observation of large numbers of cases treated by various methods will permit the place of penicillin in the treatment of syphilis finally to be evaluated.

Penicillin already bids fair to oust the arsenicals from their position as chief agents in the treatment of syphilis. It has one enormous advantage over arsenic, bismuth and mercury, in that it can be administered in any dosage without fear of dangerous toxic effects. (It must, however, be used cautiously in certain cases of late visceral syphilis for fear of therapeutic shock.) The immediate surface sterilizing action of penicillin in early contagious syphilis is profound and will doubtless have great repercussions in disease control in the future. One can predict that this advantage will, for a time at least, be offset by the fact that penicillin is already showing signs of producing a state of foolhardiness in those treated with it. Some patients with venereal diseases are already treating their conditions in the most light-hearted manner and repeatedly re-expose themselves to infection as soon as they think themselves cured. If penicillin were indeed a 100 per cent cure such people would harm only themselves; but, unfortunately, this is not the case.

Early Syphilis

The results of past experience allow certain generalizations to be made. It is not possible to cure human or animal syphilis by a single injection of penicillin no matter how high the dosage. Repeated injections are necessary. Intramuscular administration appears to give better results than the intravenous method, whether by multiple injections or by continuous infusion. Injections of penicillin in aqueous solution must be given every three to six hours. Penicillin does not penetrate into the cerebrospinal fluid; in spite of this, it is unnecessary to administer penicillin by the intrathecal route in neurosyphilis.

The original experiments on cases of early syphilis in the United States involved the giving of varying quantities of penicillin (60,000–1,200,000 units) divided into sixty doses injected intramuscularly every three hours for seven and a half days. Quite independent of the dosage, the immediate results were the same in all series. *Sp. Pallida* disappeared from surface lesions in an average time of twelve hours; lesions healed rapidly; and there was a rapid trend towards reversal of positive serological reactions.

Appraisal of results in patients treated with penicillin by these methods depends on the eventual appearance of evidence of relapse, clinical or serological, after some months. The indications are, however, that in the above dosage range, the lower the dosage the higher the relapse-rate. J. E. Moore[1] states that the indicated eventual early relapse-rate with a total dose of 60,000 units in seven and a half days is 100 per cent; with 300,000 units about 75 per cent; with 600,000 units about 40 per cent; and with 1,200,000 units about 15–20 per cent.

Variation of the time factor has also been studied. When doses between 600,000 and 2,400,000 units were given in thirty injections in four days, the results were not so good as when the same doses were given in sixty injections over seven and a half days. The results of further increasing the total time of administration are not yet known. It has been established that spacing injections at intervals of twelve hours is not satisfactory, but it is not known whether three- or six-hour intervals make any material difference.

These early results suggested that increased dosage of penicillin was likely to produce a further fall in the relapse-rate, and at present the standard dose of penicillin for early syphilis is 2,400,000 units given in sixty injections over seven and a half days. Experimental series are being treated with even larger doses. Very good results have been obtained in the United States in two small series of cases treated with penicillin (60,000 and 300,000 units) and 'Mapharsen' (320 mgm.) over eight days.

My own experience with penicillin in early syphilis in men, using a dose of 2,400,000 units, confirms the general impressions of other observers. *Sp. Pallida* disappeared from surface lesions, in my cases, in an average of nine hours, and serial observations showed an increase in motility of the organisms just before their disappearance or death. Surface lesions healed as rapidly as in cases treated with arsenic and bismuth. Positive serological reactions reversed to negative in about the same time as in cases treated with arsenic and bismuth by rapid methods. A transitory increase in positivity of serological tests or a rise into positivity was sometimes seen during treatment when serial blood tests were made. The results of sixty-seven cases followed for at least six months are shown below:

EARLY SYPHILIS TREATED WITH 2,400,000 UNITS PENICILLIN

Primary sero-negative	=	17 (of which 2 relapsed)
,, sero-positive	=	38 (of which 4 relapsed)
Secondary	=	12 (of which 4 relapsed)
Total	=	67 (of which 10 relapsed)

Average time for positive serological tests to become negative = 1·9 months

Analysis of relapse cases: cutaneous = 5; muco-cutaneous = 2; serological relapse = 1; sero-resistance = 2.

The incidence of relapse in this series was so high that, as will be described, the method of treatment was altered. Later observations and information have shown that failure after treatment of early syphilis with 2·4 million units of penicillin alone occurs in 7–8 per cent or more of cases followed up for six months or longer.

Relapse after Penicillin Treatment

Failure of penicillin treatment of early syphilis is usually manifested by (*a*) cutaneous, muco-cutaneous, or mucous relapse; or (*b*) serological relapse; or (*c*) sero-resistance; but a few rarer phenomena have been described.

(*a*) *Surface Relapse.* In most cases the surface lesions heal rapidly under treatment. Occasionally, however, cases are seen in which the chancre fails to heal completely and later breaks down again. Oftener the chancre heals completely but reappears on the original site after a latent period and may be accompanied by other surface manifestations of syphilis. Sometimes relapse phenomena are entirely 'secondary' in type, the primary lesion remaining healed. Evidence of serological relapse often, but not always, precedes or accompanies surface relapse.

Relapse lesions are often small and discrete and may entirely escape the notice of the patient. The ano-genital area should always be closely inspected at the routine follow-up examinations, as it is a common site for relapse phenomena of the condylomatous type. The interval between the end of treatment and the appearance of surface relapse has varied, in my experience, between 59 and 200 days, with an average of 83 days.

(*b*) *Serological Relapse.* In successfully treated cases of early syphilis, positive serum tests reverse to negative in two to five months. Serological relapse is diagnosed when serial quantitative serum tests show an increasing titre of positivity following a phase of negativity or of declining positivity.

(*c*) *Sero-resistance.* Sero-resistance is diagnosed at the end of an arbitrary period of six months in cases where serial tests have shown a maintained level of positivity. In some cases no decline in positivity follows treatment; in others there is a decline to a lower level, which is maintained.

Among the rarer relapse phenomena can be mentioned neuro-recurrence[2], ocular and osseous relapse, and the persistence of *Sp. Pallida* in surface lesions at the end of the treatment period.

The criteria used in the past in the differentiation between relapse and reinfection with syphilis will no doubt have to be revised, but in the consideration of difficult cases it is well to recall the advice of Dr. Harry Eagle[3]: "in the evaluation of a new therapeutic procedure any treated case in which dark-field positive lesions develop within one to two years must be adjudged a treatment failure unless the evidence for re-infection is overwhelming".

Combined Treatment with Arsenic and Penicillin

The results obtained in early syphilis with a treatment lasting only seven and a half days are quite remarkable, but even with doses of 2·4 million units an important percentage of early infectious relapses still occurs. This relapse-rate is higher, in my experience, than with the 'twenty-day treatment' with arsenoxide and bismuth.

With the view of evolving a treatment which would reduce the relapse-rate, I consulted Dr. F. R. Selbie, who has been engaged in parallel experiments with rabbit syphilis[4]. He was of the opinion that using only penicillin, a really high cure-rate might be attainable only at dosage-levels of 10 million units and more, and that the best line of experimental

approach in the circumstances was by combining arsenical and penicillin treatment.

As a speedy complete treatment was an essential for my patients, it was decided to combine a modified form of intensive arsenotherapy with penicillin at the previous dosage level. In order to give an adequate amount of arsenic and yet avoid so far as possible the toxic phenomena always associated with rapid arsenotherapy, the treatment evolved consisted in the administration of 0·09 gm. 'Neohalarsine' (arsphenoxide tartrate) or 0·06 gm. 'Mapharsen' on two days out of every three to a total of fourteen injections in twenty days. (Previous experience had shown this method of distribution of injections to be almost uncomplicated by toxic reactions.) The total amount of arsenoxide (840 mgm. 'Mapharsen' or 1,260 mgm. 'Neohalarsine') approximates to two thirds of the amount usually given in the 'twenty-day' arsenoxide treatment, and is the smallest quantity of arsenic, which, given by a rapid method, might be expected alone to cure a reasonable percentage of cases of early syphilis.

The results in seventy cases so treated and followed for at least six months are shown below.

EARLY SYPHILIS TREATED WITH 2,400,000 UNITS PENICILLIN AND ARSENOXIDE

Primary sero-negative	17		
Primary sero-positive	30	Relapse	0
Secondary	16		
Relapse sero-negative	2	Cases failing to show tendency to reversal of positive serological tests—0.	
Relapse sero-positive	5		
Total	70		

Average time for positive serological tests to become negative = 1·5 months

In a later series of patients, in order to reduce the time spent in hospital, the plan was changed and the arsenoxide part of the treatment was given in ten daily injections, each of 0·06 gm. 'Mapharsen' or 0·09 gm. 'Neohalarsine'. The incidence of minor toxic arsenical reactions was increased slightly by the closer approximation of the arsenical injections, but no major toxic effects have so far been encountered.

More than two hundred cases have now been treated by one or other of these methods of combined therapy, and the results, so far, appear better than with penicillin (2·4 million units) alone or with the 'twenty-day arsenoxide treatment'. Only three cases of relapse, all muco-cutaneous, have been seen or notified. It is of particular interest that two of the three patients who developed relapse phenomena had previously been treated for syphilis (one with 2·4 million units penicillin, the other with neoarsphenamine and bismuth) and the combined treatment was given as a result of failure of the original treatment.

Late Syphilis

The osseo-cutaneous lesions of late syphilis heal rapidly under penicillin treatment, and I have seen good clinical results in cases of gummata of the testicles. Interstitial keratitis in late congenital syphilis reacts equivocally.

My own relatively small experience with cases of late and latent syphilis with persistently positive serological reactions (in spite of arsenical and bismuth treatment) does not suggest that penicillin, in the dosage now employed, is very effective in producing reversal.

The results of treatment of visceral syphilis are difficult to assess. It may be noted, however, that the penicillin treatment of three cases of arterial syphilis (two of aortitis, one of aneurysm of the femoral artery) has been effected without evidence of therapeutic shock. Penicillin treatment was started without preparation with mercury or bismuth, the only precaution being that in the first forty-eight hours the individual doses were of only 10,000 units each.

In cases of late syphilis I have always used penicillin in a total dose of not less than 4 million units (for example, 100 injections of 40,000 units in aqueous solution). I consider it advisable to consolidate this treatment of attack with a long-term treatment with bismuth, or arsenic and bismuth, according to the type of case, over at least six months.

Neurosyphilis

Although penicillin does not penetrate into the cerebrospinal fluid in demonstrable quantities during the penicillin treatment of syphilis by the methods described, there is no doubt of its effect in neurosyphilis of all types.

Nelson and Duncan[5] report excellent clinical and pathological results in ten cases of early syphilitic meningitis treated with 600,000–4,000,000 units in seven and a half to eleven days. My own experience has been the same. One of my cases of secondary syphilis with meningitis is interesting in that the original abnormalities in the cerebrospinal fluid had disappeared two months after treatment with 2,400,000 units penicillin, and the fluid remained normal six months later when relapse became evident in a rising titre of positivity of serological tests and in the appearance of a general enlargement of lymph glands.

Stokes[6] reports that abnormal cerebrospinal fluids in late syphilis are improved by penicillin in 74 per cent of cases, and that improvement is marked in 33 per cent. The commonest change is a drop in the number of cells and in the quantity of protein. Symptomatic improvement of varying degrees can be achieved in general paresis, tabes dorsalis, meningovascular syphilis, recent ocular nerve palsies, optic papillitis and papillœdema. It remains to be seen whether such changes, clinical or pathological, will be maintained.

The optimum dosage in neuro-syphilis is as yet undetermined. Under investigation in America at present are: (1) repeated courses of relatively small doses, for example, 1,000,000 units at intervals; (2) single courses of 2,000,000–6,000,000 units within eight to twenty days; (3) malaria plus 2,000,000–4,000,000 units of penicillin simultaneously; (4) malaria followed by penicillin.

My own scheme of treatment in neurosyphilis now consists in the administration of 4,000,000 units penicillin followed by consolidatory treatment with an arsenical (trivalent or pentavalent according to the type of case) and bismuth for at least six months. Immediate results, clinical and pathological, have been good and improvement has been maintained in all cases. The speed with which gross abnormalities in the cerebrospinal fluid reverse to negative after penicillin treatment is often spectacular.

Congenital Syphilis: Prevention and Treatment

Lenz, Ingraham, Beerman and Stokes[7] have reported on the treatment of syphilis during pregnancy and infantile congenital syphilis with penicillin. Only a small number of cases was studied, but there are indications that penicillin has good effects on mother

and child in syphilis during pregnancy. Miscarriage, stillbirth and neonatal death can be averted, and infants are born apparently healthy.

Infants with congenital syphilis were given 28,600–34,200 units penicillin per kilo body weight, distributed in fractions at four-hour intervals over eight days. The results as shown by clinical and serological response and by X-ray observation of the bones were very good.

Platou and associates[8] have treated sixty-nine cases of infantile congenital syphilis with doses of 16,000–32,000 units penicillin per kilo distributed over seven and a half days with good symptomatic results. Of thirty-nine cases followed from four to twelve months, twenty-five remained apparently cured, nine were still sero-positive but progressing towards negativity, and five had relapsed serologically (of which two relapsed clinically). They recommend treatment with 40,000 units per kilo.

The few pregnant women I have treated for early syphilis have been given 2·4 million units penicillin and a standard ten-week course of neoarsphenamine and bismuth. Only one of the series has as yet come to term and she was delivered of a healthy child.

Treatment Reactions

Local pain, sometimes quite severe, may be caused by certain batches of penicillin. This may be due to impurities, and it has been noted that in such cases the penicillin powder is often a dark orange or brown colour. The therapeutic efficiency is not impaired.

Cutaneous eruptions of erythematous or urticarial type are sometimes seen during treatment but do not necessitate interruption of therapy. Shock, with pallor, sweating and rapid pulse, early in the treatment is sometimes seen. A few such cases have occurred in our series, but treatment was never interrupted. Such reactions may possibly be due to impurities in the penicillin.

An important and almost constant feature in cases of early syphilis is a fever, sometimes high, which begins about twelve hours after the first injection and lasts for twelve to twenty-four hours. This is probably a variety of Jarisch–Herxheimer reaction, as a transitory increase in cutaneous eruptions or œdema around the chancre often occurs at the same time. In the few cases of late syphilis we have treated, this febrile reaction has not been noted. American observers have, however, noted the occurrence of therapeutic shock (for example, transverse myelitis, convulsions) in patients with late syphilis of the nervous system, and advise a cautious start with reduced doses of penicillin in such cases.

Lloyd Jones[9] reports venous thrombosis as a complication in a series of cases treated with penicillin intravenously in large doses (up to 500,000 units).

Summary and Conclusions

Penicillin is an effective agent in the treatment of syphilis at all stages. The early results with the dosage schemes already used are encouraging, but final judgment must be deferred until a significant number of cases has been followed for a period of at least five years. There is some reason to believe that the relapse-rate in early syphilis is inversely proportional to the dosage of penicillin, so that a better cure-rate may be attained when larger doses are employed.

The use of aqueous solutions of penicillin necessitates the hospitalization of patients with syphilis. Until this difficulty is overcome, it must, for various reasons, reduce very considerably the number of patients who can have the treatment. Progress in the study of the effects of retarding media (for example, beeswax-peanut oil mixture) suggests that a method may soon be available for adequately treating syphilis with one or two injections of penicillin each day.

It appears that penicillin and the arsenicals have a synergistic action when used simultaneously. Pending the results of large-scale controlled experiments, and as a means of conserving penicillin, I would advocate for routine use in early syphilis some method of combined therapy. For patients requiring a rapid complete treatment (for example, merchant seamen) the arsenoxide-penicillin treatment described above is suggested; for those who can attend as out-patients, a week's hospitalization for 2·4 million units penicillin, during which time can be begun a standard ten-week course of injections of neoarsphenamine and bismuth.

Every case of late syphilis deserves individual assessment; but as a basic principle, I consider that penicillin should always be followed by a long-term treatment of consolidation with a suitable arsenical and bismuth.

In conclusion, I must point out that my present advocacy of combined therapy in the treatment of syphilis does not imply that penicillin alone is incapable of producing a cure. The optimum treatment for syphilis is still undiscovered. Penicillin in larger doses or by different methods of administration may provide the answer. In the meantime, the combination of penicillin with other anti-syphilitic remedies deserves further investigation.

[1] Moore, *Amer. J. Syph.*, **29** (March 1945).
[2] Leifer, *J. Amer. Med. Assoc.*, **126**, 67 (1944).
[3] Eagle, *J. Amer. Med. Assoc.*, 553 (Oct. 28, 1944).
[4] Selbie and Simon, *Brit. J. Exp. Path.*, **25**, 229 (1944).
[5] Nelson and Duncan, *Amer. J. Syph.*, **29**, 141 (1945).
[6] Stokes, Beerman and Ingraham, "Modern Clinical Syphilology" (3rd edit., 1944).
[7] Lenz, Ingraham, Beerman and Stokes, *J. Amer. Med. Assoc.*, **126**, 408 (1944).
[8] Platou, Hill, Ingraham, Goodwin, Wilkinson and Hansen, *J. Amer. Med. Assoc.*, **127**, 582 (1945).
[9] Lloyd Jones, paper read at Med. Soc. for Study of V.D., London (March 1945).

OBITUARIES

Prof. J. T. Wilson, F.R.S.

James Thomas Wilson, emeritus professor of anatomy in the University of Cambridge, died on September 2 at the age of eighty-four years.

An Edinburgh graduate and a pupil of Sir William Turner, Wilson went to Australia as a demonstrator of anatomy in the University of Sydney when he was twenty-six years old; three years later, independent chairs of anatomy and physiology were created and Wilson was elected as the first holder of the Challis professorship of anatomy. This position he held for the next thirty years, during which time he built up a fine department, a tradition for thoroughness in scientific investigation, and a great reputation as a university administrator of sound judgment and with an unusual breadth of vision. He was dean of the Faculty of Medicine, and, among many interests and responsibilities outside the University, he served with distinction in the Australian Intelligence Corps, being promoted honorary colonel in 1915.

During this period, Wilson collaborated with Sir Charles Martin and, more particularly, with Prof. J. P. Hill in research work, as a result of which many papers of fundamental importance were published on the structure and development of monotremes and marsupials. The late Sir Grafton Elliot Smith was one of his earliest pupils, and there is no doubt that Wilson's guidance and stimulating influence must have counted for much in laying the foundations for his later brilliant work.

In 1920, Wilson accepted the chair of anatomy at Cambridge. Although a comparative stranger, his outstanding abilities were quickly recognized, and he gained the respect and affection of all who worked with him in the University, and of the society of St. John's College, where he was elected to a fellowship in the same year. His work for the Cambridge Anatomy School is well known. During his fourteen years tenure of office, he enlarged and reorganized the course in anatomy for Part I of the Natural Sciences Tripos, created an excellent departmental library to which he gave a great part of his private collection of books and papers, and attracted each year a small number of students to take anatomy in Part II of the Tripos.

Wilson's scientific work was always characterized by meticulous care and thoroughness, and his papers were models in their exactness of expression and lucidity. The value of his contributions to natural science was recognized by his election into the fellowship of the Royal Society in 1909. In his later years, while at Cambridge, he spent a considerable part of his time in perfecting a technique by means of which a series of sections of large embryos could be exploited to the greatest advantage ; the enthusiasm which he showed in the development of the method, and in the demonstration of his specimens to those immediately around him, was wholly characteristic ; it is a great loss to embryology that but few of the many critical and original observations which he made as a result were published.

After his resignation from the chair at Cambridge in 1934, he continued to lead a full and active life ; that his judgment was held in the highest esteem to the end is evidenced by the fact that this year, at the age of eighty-four, he was asked to continue his Carnegie Reports for a further year. He was the first overseas member of the Anatomical Society of Great Britain and Ireland, and he acted as its president during the years 1922–24.

This record of scientific and administrative achievement alone would place Wilson high in the ranks of great medical teachers, but his greatness and influence were more profound and far-reaching than can be indicated by a mere statement of facts. His personal example and his friendship had a marked and lasting effect on generations of students ; medical men who were trained at Sydney during Wilson's time still say, when his name is mentioned, "Oh, you mean Jummy", and go on to speak of him with a spontaneous fervour delightful to hear. He had great charm of manner and a natural power of inspiring those around him ; he was actuated by the highest ideals, the sincerity of which was recognized and appreciated by the members of his staff and by his students. As with his scientific work, thoroughness and enthusiasm permeated every aspect of his teaching ; he gave without stint of his time, knowledge and experience, and no one could fail to be the better man for having met and worked with him.

H. L. H. H. Green.

Prof. W. H. Fraenkel

The death occurred on July 14, 1945, of Prof. Walter Fraenkel, who was living at Perth Amboy in the United States. He had been expelled from Germany early in 1939 by the Hitler Government and, after spending nearly a year at the University of Cambridge, as guest of the Metallurgical Laboratories, emigrated with his family to the United States.

Fraenkel's work covered problems of the age hardening of aluminium alloys, diffusion, segregation and crystallization and chemical reaction between metal and slag ; the latter in close co-operation with R. Lorentz. Fraenkel held a professorship in Frankfurt-am-Main and there most of his research work was done, with the help of a small band of enthusiastic and devoted pupils.

Two short periods in industrial research during the First World War and in the thirties gave him an opportunity of learning about industrial problems and the industrial way of technical development.

Prof. Fraenkel was a physical chemist (trained under Bredig and Lorentz) and his approach to problems of metallurgy was always from this angle, as was the method of his teacher in this field, Tammann. He even introduced the kinetics of reaction into metallurgy in his work on the age hardening of duralumin, a problem which fascinated him during almost the whole of his research work. His studies on this subject were among the earliest scientific work done on this important theme.

I happened to be the first student who chose a subject in Prof. Fraenkel's own line of research for a thesis. The work was carried on in closest collaboration with him. He knew and watched every step and, in long and almost daily discussions, an intimate view of the man and his work was obtained, and also no small inspiration from his general attitude towards science and scientific work. His rigorous criticism of any results, be it his own or other workers, without regard to name and reputation, his modesty and his complete devotion to the cause of truth and science, were among his outstanding characteristics.

In spite of the almost pessimistic severity of his general outlook and many personal disappointments, Prof. Fraenkel possessed a keen sense of humour and a caustic wit that spared nobody, least of all himself. All his pupils and his colleagues will honour his memory as that of a man of high principles, a most capable and careful man of science and teacher and a kind and reliable friend.

E. Scheuer.

Dr. William Cramer

William Cramer was born in the Rhineland on June 2, 1878. After taking his Ph.D. at the University of Berlin in 1901, he worked in its department of pharmacology. There he met E. F. Bashford, and their friendship resulted in his joining the staff of the Imperial Cancer Research Fund in 1903. Thus he came to collaborate with Bashford and Murray in that pioneer work which contributed so much to our knowledge of the growth of cancer under experimental conditions.

In 1905, Cramer went to Edinburgh as lecturer in chemical physiology in Sharpey-Schafer's Department, and took the degree of D.Sc. three years later. He published "Directions for a Practical Course in Chemical Physiology" in 1912, which ran to four editions. His position as a university teacher became somewhat difficult on the outbreak of the First

World War, and through the good offices of Dr. J. A. Murray, then director of the Imperial Cancer Research Fund, he rejoined its staff. Back in London, he completed his medical studies at University College Hospital and took the diplomas of M.R.C.S., L.R.C.P. in 1917. His intellectual versatility and wide scientific interests found expression in the numerous papers he published between 1915 and 1939, which embraced almost every aspect of the cancer problem. Never slow himself to enter the realm of scientific speculation, he protested only last year against a tendency in cancer research "to exalt theories over facts, to make facts fit into the Procrustean bed of a theory". He was specially interested in the hormonal factor in cancer, and a by-product of his investigations in this field was the book he published in 1928, entitled "Fever, Heat Regulation, Climate and the Thyroid-Adrenal Apparatus". He retired from the Imperial Cancer Research Fund at midsummer 1939.

After taking part in the Seventh International Genetical Congress in Edinburgh in August 1939, Cramer journeyed to America for the Third International Cancer Congress. Afterwards he joined the research group which Prof. E. V. Cowdry of St. Louis University organized at the Barnard Skin and Cancer Hospital for a special investigation into epidermal carcinogenesis. He became chief pathologist to the Hospital, and in 1941 delivered the Middleton Goldsmith Lecture to the New York Pathological Society.

Cramer died in Denver, Colorado, in August last, a victim of the disease to the study of which he had so assiduously devoted the greater part of his life.

R. J. Ludford.

We regret to announce the following deaths:

Sir Edward Farquhar Buzzard, K.C.V.O., emeritus regius professor of medicine, University of Oxford, on December 17, aged seventy-three.

Dr. E. W. Kemmerer, the well-known international economist, formerly professor of economics and finance in Princeton University, on December 16, aged seventy.

NEWS and VIEWS

Royal Institution: Appointment of Prof. E. K. Rideal, F.R.S.

As recently announced, Prof. E. K. Rideal relinquishes his post as professor of colloid science in the University of Cambridge to succeed Sir Henry Dale as Fullerian professor of chemistry in the Royal Institution and director of the Davy Faraday Research Laboratory. Prof. Rideal's great breadth of scientific interests and achievements, so befitting his new position, must have received considerable stimulus from an unusually varied career. A scholar of Trinity Hall, Cambridge, he graduated there in 1911. Upon the outbreak of the First World War he joined the Royal Engineers and was later invalided from France to the Munitions Inventions Department. During 1919–20 he was visiting professor of physical chemistry at the University of Illinois, and afterwards returned to Cambridge as Humphrey Owen Jones lecturer in the Department of Physical Chemistry.

In 1930 Rideal was elected a fellow of the Royal Society; and the University of Cambridge, assisted by a grant from the International Education Board, set up a Department of Colloidal Physics with Rideal as its first professor. Shortly after, the Plummer bequest enabled the original temporary professorship to be consolidated, and the Department became the Department of Colloid Science, its objects being the study of the physics and chemistry of colloids and their application to biology. Under his guidance a small but enthusiastic nucleus concerned themselves chiefly with the study of insoluble monolayers and catalysis by solid surfaces, laying the basis for a reputation which was soon to become international. The Department grew steadily in numbers; by 1939 it housed some twenty-five research workers, the variety of nationalities represented being paralleled by the diversity of activities, which had by now spread quite naturally into the field of high polymers. To all, however complex the problem, Prof. Rideal's stimulating discussions and detailed personal interest were a never-failing source of inspiration.

War brought inevitable changes in its train. Langmuir troughs were set aside and more urgent problems taken up at the request of Government and Service Departments. This entailed innumerable committees and considerable travelling; but despite enforced absences, Prof. Rideal still gave his usual courses of lectures and showed an almost uncanny acquaintance with the details of the by now incredible mixture of activities housed in his Department. His inspiration and optimism, which never visibly failed, are familiar to all who met him in those days. The return of peace saw the Department's numbers standing at thirty-five, an acute problem of accommodation but a testimony to his war-time leadership. His many friends in Cambridge and elsewhere, and that widely spread body of his past pupils, will join in expressing their great pleasure at his appointment, and will wish him every success in his new field of activity.

Chemical Engineering at the Imperial College: Prof. D. M. Newitt, F.R.S.

Prof. D. M. Newitt has been appointed to the Courtaulds chair of chemical engineering in the Department of Chemical Engineering and Applied Chemistry, Imperial College of Science and Technology, London. The recent munificent gift to the Imperial College by Courtaulds, Ltd., has made possible the establishment of this chair; a trust has been set up to administer the funds, which amount to about £118,000.

Prof. Newitt has been associated with the Department of Chemical Technology at the College since 1920, where he studied under Prof. Bone and Dr. Hinchley, who was then in charge of the chemical engineering section of the Department. For many years Prof. Newitt acted as one of Prof. Bone's chief assistants in researches on combustion, being particularly associated with the work on explosions at high pressures. This led him to his well-known studies of the behaviour of materials at extreme pressures up to 20,000 atmospheres, for which skill and originality in engineering design and special knowledge of the properties of highly stressed materials were required. In the development of industrial processes operating at high pressures he has been able to give most valuable advice, and he has

contributed to advances in the design of compressors and of vessels to withstand high pressures. During the War, Prof. Newitt was in charge of the research work of the Inter-Services Research Bureau and was responsible for many important developments. He is a member of the Heyworth Committee on the gas industry which has recently reported. He has also recently had the opportunity of visiting schools of chemical engineering in the United States of America. Prof. Newitt combines experience of research work in a wide field of engineering and physical chemistry with teaching experience which augurs well for the School of Chemical Engineering at the Imperial College.

Card File of Physical Constants of Substances

THE general plan of the American "Annual Tables of Physical Constants", started in 1941 under the National Research Council, called for publication of tables on loose sheets, by sections according to properties, and also of a card file of numerical data of physical magnitudes, by substances. The card file represents a departure from the customary method of recording and filing data dispersed in the literature. They are to be assembled in the card file for each substance in a permanent predetermined order of physical properties, instead of being tabulated for each property, for a list of substances. Thus all physical properties for a given substance are brought together, adding up to a complete numerical description of the substance; and the non-availability of certain data for the given substance becomes immediately noticeable by the absence of the section number of the corresponding property on the substance chart. The actual numerical values are inserted whenever they are expressible by a figure or a few figures; extensive tables of data are not as a rule reproduced. It is expected that microfilm distribution facilities and reading devices will be available in the near future, so that one may obtain microfilm copies of any scientific publication desired. This will render extensive reproduction of voluminous tables superfluous and further justify the present scheme.

The cards are being planned as follows: Elements in the alphabetical order of their symbols, inorganic compounds in the alphabetical order of their formulæ, organic compounds also in the usual order of their overall formulæ by increasing numbers of the carbon and hydrogen atoms. However, as the data are on loose cards, users, if they choose, can re-order their card files by any other principle which they may prefer. As new numerical material is published, additional cards will be issued for substances already covered. Likewise revised cards will be supplied whenever necessary to replace old cards which may become obsolete. It is planned to issue about two thousand substance cards a year in instalments of a hundred cards. One drawback of the use of the small-sized card, 5 in. × 3 in., is that it may involve a large number of cards per substance; for example, bromine requires eighteen cards. The subscription price is based on the rate of 5 cents a card, that is, 100 dollars a year for a set of 2,000 cards. Auxiliary cards will be supplied at 1·5 cents a card or 5 dollars for the set, whichever is the less. Publication at practically nominal prices has been made possible by grants and subsidies provided mainly by industrial corporations and a generous donation from the Carnegie Institution. Correspondence should be addressed to "Annual Tables of Physical Constants", Frick Chemical Laboratory, Princeton, New Jersey.

The Association for Planning and Regional Reconstruction

IN response to many requests, the Association for Planning and Regional Reconstruction has decided to develop its Information Service, and subscribers are now to be offered, in addition to copies of all the Association's broadsheets and reports and the services of the library and the information bureau, a bi-monthly bulletin containing a report of work being undertaken by the Association as well as a résumé of matters of interest in the planning world and pre-publication news of books produced by the Association to ensure subscribers being able to obtain these when published. The first information bulletin, October–November 1945, continues as No. 160 the progress sheets issued since February 1941. The bulletin includes a selected list of recent acquisitions to the Association's library, and a revised edition of Broadsheet O, dated September 1945, giving general information about the Association and containing a complete list of broadsheets issued to date, has also been published. The Association, which aims at serving as a centre for research in the planning field and undertaking factual investigations, as well as acting in an advisory capacity and furthering the establishment of technical and other standards, and the development of new conceptions of planning, works closely with the School of Planning and Research for Regional Development, which is under a separate board of management. The School has enrolled more than a thousand correspondence students in the Armed Forces and among prisoners of war, and those who on demobilization reach a certain standard are eligible for a three months completion course, the successful students in which will be exempt from the final examination of the Town Planning Institute.

Training of Engineers

IN his presidential address before the Institution of Mechanical Engineers, delivered on October 19, Prof. Andrew Robertson emphasized that the training of engineers is concerned very much with "a knowledge of science and the technique which must go with it", to which must be added qualities of character. The needs of a healthily advancing industry show that mechanical engineering can usefully absorb a considerable increase (twice the pre-war number is suggested), in the output of universities and technical colleges, of young men trained to the standards of engineering degrees or of higher national certificates. "There is a definite field for the technical college distinct from that of the faculty of engineering," the range of activity of the former being from crafts at one end to higher national certificate and specialized technological work at the other. "The aim of a university department should be to produce potential leaders of the profession."

National certificate courses, successfully begun twenty-four years ago, should be further developed; part-time day release should be encouraged; opportunities for superior technical college students to attend full-time courses should be provided; the universities and industry should co-operate intimately in the production of scientifically trained men, not omitting college apprentices; engineering faculties should consider the advisability of instituting 'general honours' and 'special honours' degrees; the educational scheme of Britain should be so designed that at every stage promising students may be transferred to the course best suited to them; "there is

a real need for an extension of post-graduate work both in research and in specialised studies in the fields of technology and administration, for established technical staff and executives"; some advanced students might with advantage work in the laboratories of the research associations. These and many other valuable suggestions are ably dealt with by Prof. Robertson in his discussion of engineering as a basis of a liberal education.

National Maps of Britain

A CIRCULAR from the Ministry of Town and Country Planning directs attention to a new series of maps of Great Britain constructed to illustrate various aspects of national life and resources. The scheme is a development of the idea of a National Atlas originally prepared by a committee of the British Association in 1939 and is now under the guidance of both the Ministry of Town and Country Planning and the Department of Health for Scotland. The maps are being published by the Ordnance Survey. All maps are to be on a scale of 1 : 625,000, or about ten miles to an inch, and all will bear the new national grid. Each map will be in two sheets, covering respectively (1) Scotland and the northern part of England and (2) the remainder of England and Wales. Those sheets already published are the base map, land utilization, administrative areas, topography, population density in 1931, types of farming and land classification. Several of these are new compilations. Shortly to be ready are sheets showing population of urban areas in 1938, roads, coal and iron resources, and iron and steel production. Others in hand include a physical map, with accepted terminology of physical features, grasslands of England and Wales, geology, electricity supply, gas, railways, population changes, various economic maps, and seaports. The price of the published sheets is generally five shillings.

Colorado Beetle in England during the War

THAT the freedom of the potato crop in England from the ravages of the Colorado beetle during the War was due not to good fortune but to the vigilance of the Ministry of Agriculture is evident from an article (*Agriculture*, 52, p. 210) describing the infestations that have occurred in various parts of the country in recent years. Since the outbreak at Tilbury in 1933 (which was only the second recorded in Great Britain) a close watch had been kept on potato crops, particularly in coastal areas. During 1936–39 a few beetles were reported in soils along the south-east coast and on ships in port, and, when military traffic across the Channel started, the precautionary measures were intensified. In 1941, however, beetles were discovered at six separate localities in the west of England, three of them being on inland farms in Devonshire. The special methods adopted for exterminating the pest were increased publicity and inspection, precautionary spraying of crops within a five-mile radius of an outbreak, and the restriction of potato growing to fields which had carried the same crop in the previous year. Approximately 30,000 acres of potatoes were inspected, beetles being discovered at five localities in the south-west counties in 1942. One further outbreak occurred in Wiltshire in the following year, and since then no infestations have been reported, though a few beetles were discovered on vessels and aeroplanes of cross-Channel services. The pest has evidently not yet established itself in Great Britain; but growers are asked to keep a constant watch and notify the Ministry at once of any circumstances which arouse suspicion that the beetle may be present. Unauthorized spraying is strongly discouraged as it may cause the beetles to spread.

Use of Fertilizers in Britain

THE need for maximum food production in Great Britain during the War called for the highest efficiency in the use of what fertilizers were available, and it is generally agreed that a drive for still further improvements must be made in the future if agriculture is to be put on a sound footing. In "Fertilizers During the War and After" (Pamphlet No. 13. Bath and West and Southern Counties Society. 2*s*.), Dr. E. M. Crowther gives a comprehensive and most lucid survey of the subject, which will both be a valuable guide to all concerned with crop production, and also of considerable historic interest. After comparing the pre-war consumption of fertilizers in Great Britain with that of neighbouring European countries and the United States, it describes the war-time rationing scheme for England and Wales, discusses the basis upon which it was founded and shows how the experience from large-scale field experiments has been utilized. It is impossible to give an adequate picture of the range of subjects dealt with, but among the newer aspects mention may be made of fertilizer placement. Results from field trials indicate that labour may be saved and the efficiency of fertilizers increased if small amounts of well-prepared fertilizer are placed in definite positions near the seed at the time of sowing. Another development that may well occur in the future is in the use of standardized compound fertilizers, which have proved so successful during the War. As regards the fertilizers themselves, Dr. Crowther considers that the technical efficiency of both making and using phosphate fertilizers needs to be improved, and he puts forward a plea for some revision of the Fertilisers and Feeding Stuffs Act Regulations, so that full advantage may be taken of current and future research.

The Tata Memorial Hospital

AMONG the buildings of Bombay the strikingly modern design of the Tata Memorial Hospital for the treatment of cancer and allied diseases must stand out with a distinctness which will direct attention to the beneficence of its purpose. Founded by the trustees of the late Sir Dorab Tata as a memorial to the philanthropy of Mr. J. N. Tata and his two sons, Sir Dorab and Sir Ratan, this fine hospital came into being in 1941 and has issued its first triennial report. Designed and built after consultation with experts from Manchester, London, New York, Cleveland, Paris, Stockholm and Brussels, the hospital is now staffed by Indian surgeons, anæsthetists, radiologists, pathologists and physicists, many of whom were sent abroad while the hospital was being planned and built, to gain special instruction and experience. The result is a hospital which can take its place beside any centre for the study and treatment of cancer, and it is not surprising that its superintendent, Colonel Sir J. N. Duggan, can report that it has, in spite of the handicaps of the war years, gained for itself a fine reputation. Any institution which can achieve, during a war like the one which has just ended, a standard of work like that which is here described, may congratulate itself. Future reports of its peace-time work will be awaited with interest.

Limitations of Science

In a paper "Methods of Research" (*J. Univ. Bombay*, **12**, March 1944, and **13**, March 1945), Prof. D. D. Kanga stresses the limitations of the scientific method in the modern world and the need for supplementing it, both in the world of affairs and in the sub-atomic world, by another training and discipline capable of transforming the present selfish, exploiting animal-man into a self-sacrificing, co-operating human being, willing to share with others. This technique Prof. Kanga terms the 'occult method', and emphasizing the importance of developing character, he believes that the chief drawback in our present system of education is the lopsided development of the individual. The university, he thinks, should address itself to this problem. In an earlier paper, "Knowledge Alone is not Enough to Solve our Problems" (*J. Univ. Bombay*, **12**, Part 3, November 1943), Prof. Kanga urged that it is the duty of a university to see that its curriculum provides for the development of its alumni equally from all sides; alongside science we require spiritual strength and spiritual qualities to enable us to resolve the many deadlocks confronting us in the world to-day.

Pitfalls in Prehistory

A short paper by Prof. C. van Riet Lowe of Johannesburg (*S. African J. Sci.*, **41**, 345; 1945) deserves to be noted by prehistorians elsewhere. It describes remarkable instances of artefacts transferred to surprisingly deep deposits by torrential river action; flaked pebbles from Carboniferous glacial gravels, betrayed by glacial striations; neolithic celts dispersed by a Norwegian settler in the last century; a soda-water bottle under 20 ft. of river-gravel; a wagon-wheel 23 ft. below a river bed, associated with a rolled palæolith; faked glass beads of German fabric, like those from Zimbabwe, reflecting a temporary fashion in amulets about 1908, and widely distributed in Transkei; a stone Chinese Buddha in undisturbed soil along the route of the Voortrekkers of 1837; and more Roman coins to add to those already known from various parts of South Africa and Rhodesia. The writer ends with an appeal to settlers, travellers, and field-workers not to discard any worked objects in situations where their presence may mislead.

Supernova in Canes

The June issue of *Sky and Telescope* contains a short reference to the discovery of a supernova in N.G.C. 5195, a satellite of the famous Whirlpool galaxy *M* 51. M. L. Humason was observing this satellite for the first time in three years, and on April 6 he noticed a faint star with which he was not previously familiar. The following evening he obtained its spectrum, which confirmed his suspicions that it was a supernova. At the time of discovery it had passed maximum by about 65 days. On April 12 the nova was at magnitude 16 photographic and 14 photovisual; its estimated maximum brightness was 11·0 photographic. It was fortunate that Humason had *M* 51 down on his observing programme on April 6, because the star was fading so rapidly that in a few weeks it would probably have been overlooked. A supernova appears in a spiral nebula on an average once in four hundred years, and this makes the coincidence all the more remarkable. In addition, the star would probably have escaped detection if it had not been so close to the central nucleus.

The Night Sky in January

New moon occurs on January 3d. 12h. 30m. U.T., and full moon on January 17d. 14h. 46m. The following conjunctions with the moon take place: Jan. 1d. 15h., Mercury 0·2° N.; Jan. 17d. 04h., Saturn 2° S.; Jan. 17d. 07h., Mars 2° N.; Jan. 24d. 11h., Jupiter 4° S. In addition to these conjunctions with the moon, Mars is in conjunction with Saturn on Jan. 22d. 17h., Mars being 4·4° N. Occultations of stars brighter than magnitude 6 are as follows: Jan. 12d. 17h. 39·1m., 147 *B* Aries (*D*); Jan. 14d. 01h. 57·8m., 85 H Tauri (*D*); Jan. 24d. 06h. 10·4m., 80 Virgo (*R*). The times are for Greenwich and (*D*) and (*R*) refer to disappearance and reappearance respectively. Mercury can be seen in the morning hours, rising at 6h. 25m. and 7h. 13m. at the beginning and middle of the month. Towards the end of the month the planet rises about the time of sunrise. Venus is too close to the sun during January for good observation, rising about 20 minutes before the sun on Jan. 1 and 15 minutes after the sun on Jan. 31. Mars, in the constellation of Cancer at the beginning of January, moving later into the constellation of Gemini, rises early in the evening and is well placed for observation throughout the night. The planet is in opposition with the sun on Jan. 14. Jupiter, in the constellation of Virgo, rises at 1h. 36m. on Jan. 1 and about midnight on Jan. 31. Saturn, in the constellation of Gemini, is visible throughout the night and does not set before the late morning hours. The earth makes its closest approach to the sun on Jan. 2. The Quadrantid meteor shower occurs during the first few nights of January.

Announcements

Prof. E. D. Hughes, professor of chemistry at the University College of North Wales, Bangor, will deliver the Tilden Lecture of the Chemical Society on January 17 at 5 p.m.

Mr. Paul G. 'Espinasse has been appointed lecturer and head of the Department of Zoology in the University College of Hull.

Standard Telephones and Cables, Ltd., have formed a central laboratory organization to undertake long-term research and development in the telecommunication, electronics and allied fields. The new laboratories, to be known as Standard Telecommunication Laboratories, Ltd., will be housed at Progress Way, Great Cambridge Road, Enfield, pending the erection of suitable permanent premises. They will have as their principal objective the intensification of research and development in all aspects of telephony, telegraphy, electronics, cables, radio, television, etc., and the various divisions of the Laboratories will be under the direction of specialists in the different spheres.

A Conference on "The Needs and Problems of the Family", arranged under the joint auspices of the British Social Hygiene Council and the Town and Country Planning Association, will be held at British Medical Association House, London, during January 24–25. Further information can be obtained from the Secretary, British Social Hygiene Council, Tavistock House North, Tavistock Square, London, W.C.1.

Erratum.—*Nature*, November 24, p. 626, col. 2, par. "British Bryological Society": *Dicranum strictum* is a recent addition to the flora of Surrey, not Britain as printed.

LETTERS TO THE EDITORS

The Editors do not hold themselves responsible for opinions expressed by their correspondents. No notice is taken of anonymous communications.

Determination of Factors Injurious to Plants in Acid Soils

Crop failures on acid soils are well known to farmers and to scientific workers interested in plant nutrition, and to both the remedy of liming is equally familiar. There exists, however, little knowledge concerning the relative importance of the various factors which produce the injurious effects observed on acid soils, and the subject is in need of intensive study. The evidence regarding the possible factors concerned are discussed by Russell[1], and it will suffice here to mention the main probable causes of injury: (1) direct injury of hydrogen ions; (2) lack of available calcium; (3) lack of available phosphorus; (4) excess of soluble aluminium; (5) excess of soluble manganese; (6) biotic factors (for example, mycorrhiza).

In examining crop failures, workers at Long Ashton have studied in particular the visual symptoms shown by plants in the field and in sand culture[2], and this technique has been applied during 1944 and 1945 to a detailed study of soil acidity effects on two plants, the runner bean (*Phaseolus multiflorus*) and the cauliflower.

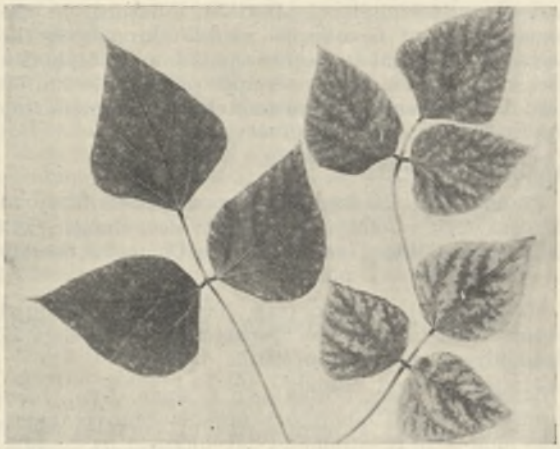


Fig. 1. Runner bean. High-manganese treatment. Comparison of manganese toxicity symptoms at high (left), medium (top right) and low (low right) calcium levels (June 18, 1945).

a *b* *c* *d*

Fig. 2. Cauliflower. *a*, Calcium deficiency symptoms with low-(normal)-manganese. *b*, *c* and *d*, High-manganese treatment. Comparison of manganese toxicity symptoms at high (*b*), medium (*c*) and low (*d*) calcium levels. (July 6, 1945.)

In these investigations we have endeavoured to determine in sand cultures whether certain common and striking field symptoms are related to lack of calcium or to excess of aluminium or manganese, the *p*H being kept at a constant level throughout.

The results have shown that the characteristic 'field acidity' leaf symptoms of these crops, namely, intervenal chlorosis and necrotic spotting of runner bean and incurled margins of cauliflower, are due to toxicity of manganese, though the toxicity effects are considerably modified by calcium status, being particularly severe when calcium is at a low level and substantially decreased by a high calcium status (Figs. 1 and 2). Using a plant-tissue test technique[3] as a measure of the solubility of manganese in the petioles, it has been shown that readily extractable manganese in the plant tissues is decreased by high calcium status.

The sand culture experiments were carried out according to a factorial design, using nutrient solutions with a constant *p*H of 5·2, with calcium, manganese and aluminium at the following levels. (Values are given as parts per million in the nutrient solutions.)

	Low (p.p.m.)	Medium (p.p.m.)	High (p.p.m.)
Calcium	0	67	400
Manganese	0·3 (normal)	12·8	25·3
Aluminium	0·3 (normal)	5·5	11·0

As a basis to these experiments the true symptoms of calcium deficiency were determined in other cultures, where calcium was withheld and effects of manganese and aluminium were ruled out. In these it was established that the visual symptoms of calcium deficiency are as follows: *Runner bean*—leaves slightly pale green as for moderate deficiency of nitrogen, with necrotic spots, especially near tips and around margins, and progressing inwards intervenally. *Cauliflower*—young leaves distorted, with tips brown and sharply hooked either backward or forward; older leaves, marginal and intervenal areas become wilted and finally brown.

In the special experiments typical symptoms of calcium deficiency were developed in all the low-calcium cultures of runner bean, though in cauliflower the symptoms to date have only been slight, and no special leaf effects due to aluminium have so far developed.

In the medium and high-manganese series, however, the symptoms have been striking, the observations for the high-manganese series after five and seven weeks being summarized in Table 1.

Table 1. Severity of manganese toxicity symptoms.

Calcium level	Severity of manganese toxicity symptoms	
	23/5/43 (after 5 weeks)	7/6/45 (after 7 weeks)
Calcium *low*		
Bean	Moderate	Severe
Cauliflower	Trace	Severe
Calcium *medium*		
Bean	Slight	Moderate
Cauliflower	Nil	Slight–Moderate
Calcium *high*		
Bean	Trace	Slight
Cauliflower	Nil	Trace

Results of tissue tests made on June 7 and 15, after seven and eight weeks growth, are given in Table 2. They reflect clearly the increased amounts of extractable material of both elements according to the increased concentrations in the nutrient solution

TABLE 2. RESULTS OF TISSUE TESTS FOR CALCIUM AND MANGANESE IN PETIOLES.

Runner Bean (7/6/45).

Calcium level	Low			Medium			High		
Manganese level	Low (normal)	Medium	High	Low	Medium	High	Low	Medium	High
Element tested	Tissue test assessment								
Calcium	L+	L+	M−	M+	M+	M	H	H+	H
Manganese	Tr	H++	H++++	Tr	H+	H+++	Tr−	H−	H

Cauliflower (15/6/45).

Element tested	Tissue test assessment								
Calcium	L+	L	L	M+	M+	M+	H+	H+	H+
Manganese	Tr	H++	H++++	Tr	H++	H++++	Tr	H−	H+

H = High; M = Medium; L = Low; Tr = Trace.

and also the effect of high calcium status in lowering the amount of extractable manganese.

These results bring out clearly the importance of manganese toxicity in acid soils, a point also demonstrated for tobacco in Kentucky by Bortner[4], who showed further that the toxicity was decreased by phosphate treatments. They further emphasize the importance of the visual method as a means of diagnosis of the causes of crop failures due to defective nutrition, and of the sand culture technique as a means of analysing complex soil problems of plant nutrition.

The results of the investigations will be reported more fully at a later date.

The work has been carried out under special grants made by the Agricultural Research Council, to which grateful acknowledgment is made.

T. WALLACE.
E. J. HEWITT.
D. J. D. NICHOLAS.

Long Ashton Research Station,
Bristol. July 16.

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Measurement of the Diameters of the Living Eye by Means of X-Rays

SEVERAL of the pioneer workers in röntgenology—Röntgen included—recorded the fact that X-rays are perceived by the dark-adapted eye. Similar observations were made on radium rays, which were even held to surpass ordinary light as a source of illumination to the partially blind: radium rays were in fact used by one observer[1] for teaching at a blind school. Conflicting reports rapidly led to loss of all interest in the matter, until Taft[2] in 1932 clearly established the visibility of X-rays, and Pirie[3] simultaneously and independently directed attention to the possibility of 'reading with closed eyes' by means of X-ray light.

Possible applications to clinical ophthalmology were suggested by both these observers and by Gifford and Barth[4], and Newell and Borley[5]; while Rushton[6] in 1938 showed the axial length of the eye could be measured by throwing a beam of X-rays laterally on the posterior segment of the eye and moving this beam backward until its image became a point corresponding to the posterior apex of the globe. By noting the position of this point in relation to the image of the cornea reflected in a mirror, the axial length was obtained. Goldmann and Hagen[7] confirmed and extended this observation by recording the axial length of eighteen eyes.

The visibility of X-rays to the dark-adapted eye offers the opportunity of visualizing the shape and measuring all the diameters of the living eye. Such visualization and measurements can with advantage replace the 'schematic eye' (that is, a statistically computed average eye) in such practical problems as the localizing of intra-ocular foreign bodies and in the theoretical discussions on the nature and the varieties of the factors in the refraction of the eye.

Technique and findings. The subject undergoes fifteen minutes preliminary dark adaptation. He is then seated facing the X-ray apparatus in a darkened room with his head immobilized in a clamp. A slit beam of Röntgen rays, 0·5 mm. × 50 mm., is projected so that it traverses the eyeball with the plane of the beam at right angles to the diameter to be measured. This excites the sensation of vision where the beam transects the retina. By moving the beam from side to side without changing its direction with respect to the diameter and questioning the patient as to his visual sensations, it is possible to determine a position where the beam is tangential to the retina, that is, the position where the reported sensation is that of a point of light.

This position is marked by an exposure on a film introduced in front of the eye. The beam is then moved until it is again tangential at the opposite pole and its position again marked. On the developed film the distance between the two images gives the length of the diameter; thus any selected diameter can be measured provided its ends abut on the retina. As to the axial length, this is measured by determining the lateral projection of the posterior pole of the eye on a film by the method already described. A true lateral radiograph of the cornea is then taken on a dental film held at the inner canthus. A special cone is used carrying a cross-wire in its central ray, which impresses its image on both films. After development, the films are related to each other by superimposing the images of the cross-wire and the axial length measured between the corneal image and the slit image. With slight variations this technique can be employed in the localization of foreign bodies.

Dosage estimations show that, during the examination, no part of the skin receives more than 15 r.

and no part of the eye more than 7 r.—values well within safe limits.

The average anatomically determined measurements of the transverse, vertical and antero-posterior diameters of the eye are: 24·1, 23·5 and 24·2 mm. respectively[8]. There are, however, considerable individual variations. This is, broadly speaking, confirmed by the following X-ray measurements in five eyes:

Case No.	Measurements of diameters in millimetres Transverse	Vertical	Antero-posterior
1	23	22	23
2	23	21·5	26
3	24	23	25
4	22	21	22
5	24	23·5	24

In one case we had the opportunity of checking the X-ray measurements when the globe was excised for a malignant tumour. The X-ray measurements were 13 mm., 14 mm., and 22·75 mm. in the transverse, vertical and antero-posterior diameters respectively. In the excised eye the length of the antero-posterior diameter was identical with that obtained by X-ray measurement; low readings for the transverse and vertical diameters were found to correspond to the diameters formed by the inner and lower walls of the bisected eye with the apex of the tumour, which was situated in the upper and outer quadrant of the globe.

We are indebted to Dr. J. W. McLaren for advice and interest, and to Dr. G. Spiegler for the measurement of X-ray dosage.

Arnold Sorsby.
A. D. O'Connor.

Royal Eye Hospital,
London, S.E.1. Sept. 30.

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An Induced Carcinoma in the Fowl

However applied, or wherever injected, blastogenic agents, including tar and carcinogenic hydrocarbons, viruses and radium, usually induce in fowls mesoblastic tumours, that is, sarcomata or leukæmias. So far as we are aware, the only exception to this statement are the carcinomata which Japanese workers claimed to have obtained by injecting Scarlet Red and related azo compounds into fowls[1,2,3,4].

It is of some interest therefore that we have obtained a carcinoma of the kidney in a cock with another nitrogen-containing carcinogen, 2-acetyl aminofluorene. War-time conditions have prevented a repetition of the experiment on a larger scale.

Five one-month old Rhode Island Red cocks received 2-acetyl aminofluorene in the food for forty-five weeks; the daily dose commenced at 3 mgm. and was gradually increased to 30 mgm. at the end of the experiment (total 5·5 gm.). Three animals died during the first year but no tumours were found. The two survivors appeared healthy for about eighty weeks, when they began to lose weight. They were killed when they were moribund in the eighty-seventh week of the experiment, forty-one to forty-two weeks after the drug was withdrawn. In one of them the cause of death was a rather atypical leukæmia. The liver was grossly enlarged, weighing 367 gm. (quarter of the total weight of the bird) and almost the entire liver tissue was replaced by immature blood cells. The myelopoietic process affected the spleen (5·5 gm.) in much less degree, and the peripheral blood contained relatively few immature leucocytes. It was impossible to decide whether the leukæmic process was due to a virus or to the action of 2-acetyl aminofluorene, as the incidence of spontaneous leukæmia in fowls is rather high.

In the other bird, however, the findings from the etiological point of view were less ambiguous. Both kidneys were enlarged, especially the right (18 gm.), and converted into irregular masses. The surfaces were covered with whitish-yellow nodules together with several cysts, and on cutting the rather tough organs the nodules were found to replace the greater part of the kidney tissue. Histologically, these nodules were seen to be composed of polyhedral epithelial cells which were invading normal kidney tissue. The tumour bore no resemblance to the so-called embryomal nephroma and had all the characteristics of an anaplastic carcinoma. Since such a carcinoma is not known to arise spontaneously in the fowl, it seems justifiable to attribute its development to the action of 2-acetyl aminofluorene.

Our thanks are due to Drs. W. E. Gye and E. Vazquez Lopez for their opinion on the tumour morphology.

F. Bielschowsky.
H. N. Green.

Department of Pathology,
and Cancer Research Laboratories,
University of Sheffield.
Aug. 24.

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A Fatal Case of D.D.T. Poisoning in a Child

The following is an account of what is possibly the first recorded human death from D.D.T. poisoning.

On August 22, 1945, an African child aged one year seven months and weighing 10 kgm. found a bottle of 5 per cent D.D.T. in kerosene, and drank (about) 1 oz. of the mixture. Within ten minutes he began to cough and vomit, whereupon he was given palm oil by the neighbours. His general condition became progressively worse, and after one and a half hours the child became comatose, and had convulsions which, so far as can be ascertained, consisted of generalized fine tremors. He was later seen by an Army medical officer, who gives the following account: "Child was comatose, collapsed with no perceptible pulse, froth at the mouth. Atropine, grs. 1/400 was given and the stomach washed out, the stomach washings proving to be a yellow pultaceous mass of paw-paw (native fruit). No smell of kerosene was detected. Artificial respiration was given but the child died at 15.00 hours", that is, four hours after ingestion of D.D.T.

Post-mortem performed two hours after death showed pulmonary œdema as the only demonstrable macroscopic lesion. The main histological findings

were a cloudy swelling of the liver and of the kidneys and a marked œdema of the lungs.

Full details of this case will be published elsewhere*.

K. R. Hill.
G. Robinson.

Medical Research Institute,
Accra, Gold Coast.
Oct. 1.

* See *B.M.J.*, Dec. 15, p. 845.—Editors.

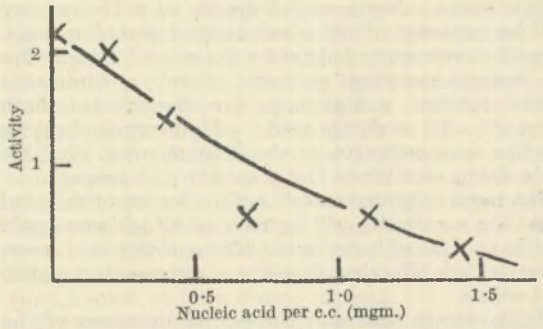
Adsorption of Enzymes on Solid Nucleic Acid

In the course of experiments on an improved method for isolating and purifying the amylases of malt, I have found that solid yeast nucleic acid is a very powerful adsorbent of these enzymes. The figure shows an experiment in which varying quantities of the solid nucleic acid (B.D.H.) were added to a diluted malt extract containing 0·12 mgm. nitrogen per mil, most of which is protein. The solution was gently shaken for a few minutes and then filtered. It can be seen that 1 mgm. of nucleic acid per ml. of solution removes the greater part of the enzymic activity. The enzyme can be recovered from the residue by the simple expedient of dissolving it in a few mils of dilute phosphate buffer of *p*H 6. For example, the following figures were obtained by the addition of 10 mgm. of nucleic acid to a malt solution containing 0·24 mgm. nitrogen per mil.

Activity in original solution	2·2
Activity in filtrate	0·6
Activity recovered from nucleic acid ..	1·5
Activity in wash water	0·2

The presence of nucleic acid in the solution appears to have no effect on the enzymic activity.

The malt extract used in these experiments contains both α- and β-amylases, but predominantly the latter. The activity was determined by adding 1 c.c. of the solution to 10 c.c. of 1 per cent soluble starch in a *M*/10 phosphate buffer of *p*H 6, for 10 (or 20) minutes at 37°, when the amount of maltose formed is determined by the method of Willstätter *et al.*[1]. This method determines primarily the β-amylase; but observations of the colour of the products with iodine indicates that the nucleic acid does not differentiate between the α- and β-amylases.



Compound formation between proteins and nucleic acid has been demonstrated in the past[2] by mixing solutions of protein and of nucleic acid and precipitating the complex with acid, and nucleic acid has been used in this way to precipitate enzyme as a step in purification[3]. I have not found any record of the observation of the reversible adsorption of enzymes on the solid acid. In view of the probable importance of nucleic acid in the processes of gene reduplication and protein synthesis[4], this phenomenon appears to be of considerable interest and is being further investigated.

I am much indebted to Mr. Adam Tait, of Messrs. Wm. Younger and Co., Ltd., for the gift of the malt.

J. A. V. Butler.

King's Buildings, West Mains Road,
Edinburgh, 9. Aug. 23.

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Inhibition of the Development of *Fusarium oxysporum cubense* by a Growth Substance produced by Meredith's Actinomycetes

In a discussion which we had early this year with Dr. Portheim of Kew Gardens, the latter raised the question of the use of antibiotics in the control of plant diseases caused by bacteria and fungi, and suggested that preliminary work which he had carried out supported his contention that gliotoxin-producing fungi might be found useful in combating such diseases. Dr. Portheim's views would appear to have been in part substantiated by the recent observation of Brian and McGowan[1].

At the suggestion of Dr. Portheim, we undertook to determine the gliotoxin production of a culture of *Trichoderma viridans*, supplied by him, when grown on the waste water used in the cleaning of beer casks, a medium claimed by him to be suitable for the cultivation of this fungus. As test organism for gliotoxin production a standard strain of *Bac. subtilis* was used which, on trial, had been proved to be inhibited in its growth by gliotoxin, supplied by Dr. Portheim, in concentrations of 6 parts per million.

Though the culture of *Trichoderma viridans* used grows abundantly on the beer wash water at temperature between 25° and 30° C., at no time did the growth liquid have an inhibitory action on the development of *Bac. subtilis*; and it was concluded that, under the conditions employed, the *Trichoderma* culture had failed to produce gliotoxin.

When these experiments were in progress, we became acquainted with Meredith's[2] observation that certain Jamaican soils are inhibitory to the spread of Panama disease, caused by *Fusarium oxysporum cubense*, and that certain Actinomycetes inhabit such soils. On isolation and subsequent cultivation of these Actinomycetes in extracts from their own soils, some of these organisms were found by Meredith to inhibit or retard the development of *Fusarium oxysporum cubense*.

Though Meredith does not ascribe the function of his antagonistic Actinomycetes to growth-inhibiting substances produced by them, we felt it worth while to explore to what extent this might be the case, and in this way possibly to bring further evidence in support of Dr. Portheim's contention that certain plant diseases can be controlled by antibiotics. For this purpose we secured cultures of Meredith's Actinomycetes from the National Type Culture Collection and grew them on Portheim's beer wash medium and on the waste liquors resulting from food yeast manufacture.

In both these media the Actinomycetes grew well; in the latter particularly when the liquor was diluted with equal parts of water.

After incubation at 30° C. for one month, the inoculated waste liquor from food yeast manufacture was covered by a pink pellicle of Actinomycetes. When 4 ml. of this medium, freed from living cells by centrifuging, was added to 10 ml. of wort agar, the mixture allowed no growth of *Fusarium oxysporum cubense*, even when the plate was heavily inoculated with a fresh culture of the fungus. Wort agar plates which had had 3 ml. and 2 ml. of the centrifuged Actinomycetes growth-liquor incorporated allowed restricted growth of the fungus. Control plates made up of wort agar with 4 ml. of the original medium, on which the Actinomycetes was to grow, showed abundant growth of the *Fusarium* within two days.

After five weeks growth in food yeast waste liquor, the concentration of the inhibitory substance produced by Meredith's organism had increased to such an extent that 1 ml. of the liquor sufficed to prevent growth of *Fusarium oxysporum cubense*.

Having established the toxic action of Meredith's organisms, preliminary attempts were made to isolate the active substance. These attempts, so far, have shown that the substance is thermolabile and that it fails to pass through a porcelain filter.

Further investigations on its action, its isolation, and its nature are in progress.

A. C. Thaysen.
Colonial Microbiological Research Institute,
Trinidad.

K. R. Butlin.
Chemical Research Laboratory,
Department of Scientific and
Industrial Research,
Teddington.

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Insecticidal Properties of *Euphorbia* Extracts

In the June number of the *Tropical Diseases Bulletin* (p. 502) there is a review of a paper by Mülhens[1] on the insecticidal properties of *Euphorbia dendroides* in Crete. I thought it might be desirable to place on record some tests on the insecticidal properties of *Euphorbia tirucalli* Linn. which were carried out during 1943 and 1944 in Tanganyika.

This, with other species of African *Euphorbia*, have been used for centuries as a fish poison; it is a common shrub throughout the whole of East Africa. The natives mash the green shoots with water and throw this into the pond or river; the fish float paralysed on the surface after a few minutes. It was thought that extracts might provide a cheap insecticide especially against mosquito larvæ.

Aqueous extracts of the fresh material had no effect on mosquito larvæ, but seemed to possess some insecticidal effect on adult Diptera. Extracts were then prepared by steeping 50 gm. of young shoots that had been dried in an oven at 100° C. in 100 c.c. kerosene for 48 hours. These extracts gave 100 per cent kill of adult *Glossina* and other Diptera, compared with 20–30 per cent kill given by the untreated kerosene. This recipe was sent to the Industrial Research Board, Nairobi, for further testing; however, it was reported that extracts made there had no appreciable insecticidal properties. The original extracts were then retested at Shinyanga with the same results as recorded above; but when further extracts were prepared from sun-dried shoots of *E. tirucalli*, no appreciable insecticidal properties were found. Owing to pressure of other work this investigation was stopped.

I mentioned these experiments to Mr. Culwick, district commissioner, Mahenge, who stated that the African tribes in his district used *Euphorbia calycina* N.E.Br., the common candelabra euphorbia of Africa, as an insecticide and claimed that it was very successful. Further investigation also revealed that Africans used fresh branches of *E. tirucalli* to protect young plants from the ravages of grasshoppers, slugs, snails and other insects. I witnessed a test carried out by Mrs. Fairbairn using young shoots of *E. tirucalli* laid around various young vegetable plants. Some plants were left untreated to serve as controls, and these were all devoured, whereas the *Euphorbia* afforded 100 per cent protection for the others.

I suggest that this subject would be worth further investigation.

F. L. Vanderplank.
Tsetse Research Department,
Tanganyika.

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Aerial Bactericides

In an earlier letter[1] we discussed the bactericidal action of lactic acid, mandelic acid and triethanolamine against airborne organisms freshly sprayed from the respiratory tract. Since then we have investigated the aerial disinfectant action of the homologous series of aliphatic α-hydroxy carboxylic acids RR_1C.OH.COOH, including glycollic acid, lactic acid, α-hydroxy valeric acid, α-hydroxy *n*-hexoic acid, α-hydroxy *n*-octoic acid, α-hydroxy *n*-decoic acid, α-hydroxy isobutyric acid, α-hydroxy-α-methyl butyric acid, cyclopentanol-1-carboxylic acid, and cyclohexanol-1-carboxylic acid. We have also investigated the aerial disinfectant action of the mono esters of maleic acid *R*OOC.CH=CH.COOH, including the methyl, ethyl, allyl, butyl and hexyl esters, and two mono esters of succinic acid, the ethyl and hexyl.

All the compounds which are listed above were effective in destroying the organisms of sprayed saliva (*S. salivarius* and others) and could be of use as aerial disinfectants. Some useful degree of activity may well be expected of other substituted glycollic acids. The effectiveness, as judged by the rate of destruction of bacteria-carrying particles, from a simulated sneeze, reached a maximum for the straight-chain series (R_1=H) at lactic acid. α-Hydroxy *iso*-butyric was the most effective of the disubstituted glycollic acids, being similar to lactic acid in this respect.

The most effective maleic acid ester was the ethyl ester, the maximum killing rate of which was again similar to that of lactic acid. The succinic acid esters appeared less effective than the corresponding maleic acid esters.

Unlike lactic acid and the earlier members of the straight-chain series, the disubstituted acids and the maleic acid esters can be volatilized, without appreciable decomposition, by simple heating. Also the rate of vaporization from relatively large surfaces at room temperatures is sufficient to maintain a useful bactericidal concentration.

Tests of these substances were carried out in an 800 cu. ft. room at temperatures between 60° and 75° F. and over a relative humidity range of 60–75 per cent. The bacteria were sampled on to serum

agar plates in a slit sampler[2]. Further details of the bactericidal action of vapours of these substances under varying conditions will be published later.

J. E. Lovelock.
National Institute for Medical Research,
Hampstead, N.W.3.
Nov. 2.

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Unit Cell and Space-Group of Co_2Al_9

In an investigation of cobalt-aluminium alloys by X-ray methods, Bradley and Seager[1] identified a phase Co_2Al_9 or Co_3Al_{13}, thus confirming the findings of earlier workers. The composition of the phase appeared to be invariable, but it could not be fixed exactly in the absence of knowledge of the structure. A phase $FeNiAl_9$ (or $FeNi_2Al_{18}$), found in the ternary system of iron, nickel and aluminium, is isomorphous with the cobalt-aluminium phase, and in a paper on aluminium-rich alloys of the ternary system, Bradley and Taylor[2] suggest that this phase is monoclinic. The work described below was carried out in order to test this suggestion.

An alloy containing 32·7 per cent cobalt and 67·3 per cent aluminium was made up in a high-frequency induction furnace under a low pressure of hydrogen. The alloy was annealed *in vacuo* at 900° C. for 48 hours and allowed to cool in the furnace, after which it was found to be brittle and could be easily crushed. Powder photographs were taken, but it was not found possible to interpret these satisfactorily on the basis of a structure with higher symmetry than monoclinic. Interpretation on the basis of a monoclinic unit cell, that is with four unknown quantities, is not practicable. It was therefore decided to try to isolate single crystals of the phase, so that the unit cell could be obtained directly from oscillation and Weissenberg X-ray photographs.

An examination of the crushed fragments under a microscope showed a small percentage of regularly shaped pieces. Some of these were mounted with shellac on glass fibres and photographed in an X-ray camera of 2·8 cm. diameter specially designed to reduce exposure time in these preliminary experiments[3]. The photographs so taken usually contained an irregular distribution of spots, showing that the fragment consisted of a number of crystals, but sometimes traces of layer lines could be detected. From the orientation of these layer lines the crystal could be set with one axis parallel to the axis of oscillation. When this was achieved it was often found that other crystals were also present, giving spots lying between the layer lines. Finally one fragment was found which gave layer lines with no spots between them; this was then known to be a single crystal.

From the single crystal obtained in this manner, the unit cell was found to be monoclinic with $a = 6{\cdot}18 \pm 0{\cdot}02$ kX., $b = 6{\cdot}24 \pm 0{\cdot}02$ kX., $c = 8{\cdot}59 \pm 0{\cdot}02$ kX., $\beta = 95° \pm 0{\cdot}5°$. With these parameters it was possible to index the lines on the powder photograph, thus showing that the fragment selected was of the same phase as the bulk of the material. From the unit cell dimensions combined with density measurements it is found that there are four cobalt and eighteen aluminium atoms per unit cell; the density calculated on this basis is 3·62 gm./c.c., which agrees with the observed density of 3·673 gm./c.c. Thus the composition is represented by the formula Co_2Al_9. The space-group is $P\,2_1/c$ which has four general equivalent positions per unit cell. Hence two of the aluminium atoms must lie on special positions on one of the four sets of centres of symmetry, but it is probable that all the other atoms are in general positions.

Further work on the complete determination of the structure is in progress.

Audrey M. B. Parker.
Cavendish Laboratory,
Cambridge.
Sept. 12.

[1] Bradley, A. J., and Seager, G. C., *J. Inst. Met.*, **64**, 81 (1939).
[2] Bradley, A. J., and Taylor, A., *J. Inst. Met.*, **66**, 53 (1940).
[3] Parker, A. M. B., *J. Sci. Instruments*, **22**, 131 (1945).

A New Test for 2 × 2 Tables

May I reply briefly to some of Prof. R. A. Fisher's remarks[1] on my suggested test[2]?

First, Prof. E. B. Wilson[3] was concerned with tables in which all marginal totals were equal ($m = n = r = s$ in my notation). He calculated the distribution of the difference $(a - b)$ on the assumption that p was given by the column totals to be $\frac{1}{2}$; and his test was based on this distribution. Apart from the facts (*a*) that my proposal involves neither $m = n$ nor $r = s$, and (*b*) that my test is not based on the difference $(a - b)$, there is an essential difference of principle between my proposal and that of Prof. Wilson, in that he assumes p to be given by the column totals, while I make no such assumption. My validity condition explicitly covers all possible values of p.

Prof. Fisher's criticism[4] of Prof. Wilson was based primarily on this assumption about the unknown p, and it seems a valid criticism of this assumption; but my proposal is unaffected by it.

Secondly, I wish to emphasize that I do not believe that the conditions stated in my earlier letter for the validity of the test I proposed are *always* satisfied in practice. If they were, there would have been little point in stating them. Conditions can arise where it is altogether false to assume p constant. In such circumstances, we can only try to randomize beforehand; and then, if this is done, Prof. Fisher's test remains valid—a fact not always realized (for example, Wald[5]).

Thirdly, concerning Prof. Fisher's remark that the result where all animals die is irrelevant to the null hypothesis, it may be that this difference of opinion results from a difference of attitude. Suppose we consider two 'null hypotheses': (1) blue-eyed people are just as likely to catch colds as non-blue-eyed people; (2) taking a daily dose of *XYZ* does not affect the chance of having a cold. Each of these hypotheses might be tested by an experiment yielding a 2 × 2 table. But there is a difference of attitude. In case (1), we do not have in mind any proposal to do away with blue-eyed people in order to reduce colds; in case (2) we do have in mind giving people *XYZ*, if it should turn out to be good. In case (1) we *study* the world; in case (2) we propose to *change* it. Our conceptual universe in case (1) is a single four-fold one, in which a given individual can be classified by two distinct attributes—'blue-eyed' and 'cold'. In case (2) we have in mind two distinct two-fold worlds; one possible world, in which everybody has *XYZ*

and each individual is classified according to the single attribute 'cold', and another world, in which people go without *XYZ* and again are classified by 'cold'. In case (2) we wish to decide which of these two possible worlds should be made the real one.

Now suppose all our experimental subjects catch colds. In case (1) we might say we learn nothing. But in case (2) we do learn—in fact it would seem not worth while to give people *XYZ*, since they seem to catch colds anyway. Of course, the evidence may not be conclusive; but such as it is, it is surely relevant.

Other points will, I hope, become clear in a forthcoming paper.

G. A. Barnard.

Mathematics Department,
Imperial College,
London, S.W.7.

[1] Fisher, R. A., *Nature*, **156**, 388 (1945).
[2] Barnard, G. A., *Nature*, **156**, 177 (1945).
[3] Wilson, E. B. *Science*, **93**, 557 (1941).
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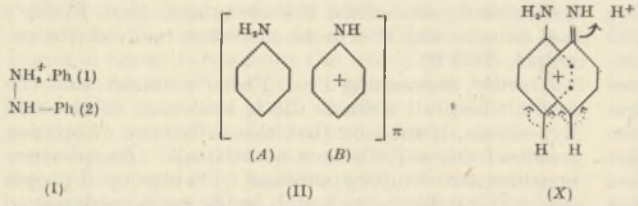
[5] Wald, A., *Ann. Math. Statistics*, **16**, 167 (1945).

Mechanism of the Benzidine and Related Rearrangements

Two electronic theories have been proposed for the benzidine rearrangement[1,2], but both are open to criticism. The present theory is an elaboration of the Robinson[2] mechanism in terms of the quantum theory[3] of aromatic structure.

It is suggested that, in the initial hydrazobenzene salt (I), a non-localized π-electron migrates from ring 2 to ring 1 with consequent fission of the N–N bond to produce the complex molecule (II), composed of the aniline derivative *A* and the ion-radical *B*. Since the electron levels of the latter are incompletely filled, and since the π-orbitals of the rings will overlap, exchange forces should hold *A* and *B* together. The product will be called a π-complex. The 'π–π' bond in it will be of novel type, joining aromatic systems and not a pair of atoms, but it will be otherwise analogous to the bond in the helium molecule ion He_2^+. Rotation about the bond will be possible, but three positions of stability with intermediate energy-hills will be defined by the alternating polarities round the rings; in them the nitrogens will be opposite each other or 120° apart. The rings in the π-complex will be parallel and co-axial.



(I) (II) (X)

If the *p*-substituents in the π-complex can be eliminated as positive ions, process *X* will be possible (dotted arrows indicate displacements of single electrons), leading to a benzidine. If reaction is delayed, rotation to a 120° position will allow the formation of a diphenyline by a type *X* process. Thirdly, process *Y*, involving a 60° or 180° orientation of the π-complex, will lead to a semidine; this involves a configuration corresponding to an energy-hill and should be less facile than *X*. If we assume that process *X* is in fact easier than *Y* only if it involves a *p*-position of component *A*, all the data[4] on the benzidine rearrangement can be interpreted in detail.

The products formed will depend not on the 'migratory aptitudes' of the groups but on the point of attack of the proton catalyst; thus in *Y* the more basic ring will function as component *A* and carry the free amino-group in the product. A diphenyline can form only if the more basic ring has a free *para* position. These conclusions are confirmed in detail by the existing evidence. Moreover, in naphthalene derivatives, where rotation of the π-complex should be inhibited since the rings are not symmetrical, diphenylines and *p*-semidines are in fact never formed.

Similar π-complex intermediates can be written for other analogous rearrangements (for example, N-bromacetanilide, *para* Claisen, Hofmann, etc.).

The theory will be investigated and full details published elsewhere in due course.

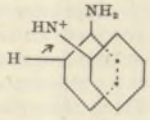
M. J. S. Dewar.

Dyson Perrins Laboratory,
University, Oxford.

[1] Ingold and Kidd, *J. Chem. Soc.*, 984 (1933). Hughes and Ingold, *ibid.*, 608 (1941).
[2] Robinson, *J. Chem. Soc.*, 220 (1941).
[3] For non-mathematical summaries, see Coulson, *Proc. Roy. Soc. Edin.*, **61**, 115 (1942). Hückel, *Z. Electrochem.*, **43**, 752, 827 (1937).
[4] Jacobson, *Ann.*, **428**, 76 (1922).

Properties of Optically Isomeric Mepacrines

In a recent communication, Hammick and Chambers[1] report that whereas the racemic form of the well-known antimalarial drug mepacrine is given to human patients, only the lævo isomer of this drug is excreted in their urine. It seems appropriate to record here that the problem of biological relations of optically isomeric mepacrines has been dealt with in a number of Russian publications during the last few years. After the resolution of racemic mepacrine into its isomers by Chelintsev and Osetrova[2] in 1940, Gause and Alpatov[3] noticed that both isomers of this drug are equally effective against malaria, whereas the dextro isomer is about twice less toxic than the lævo form for mammals and birds. Further, Gause[4] recorded that the dextro isomer differs from the lævo form in the mechanism of its permeability into the living cell. Finally, extensive clinical studies made under the supervision of Prof. Tareev in the clinical department of this Institute confirmed the observations of Gause and Alpatov and showed that the pure dextro form of mepacrine is less toxic for human patients than the usual racemic form, but the strength of antimalarial action in both forms is the same. It is hence clear that the dextro isomer of mepacrine is very interesting from the therapeutic point of view.



(Y)

G. F. Gause.

Institute of Tropical Medicine,
Moscow.

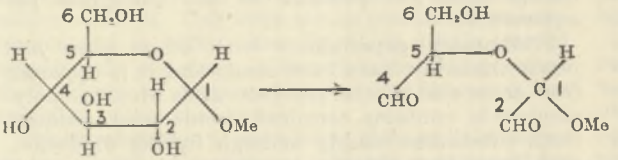
[1] Hammick and Chambers, *Nature*, **155**, 141 (1945).
[2] Chelintsev and Osetrova, *J. Gen. Chem. U.S.S.R.*, **10**, 1978 (1940).
[3] Gause and Alpatov, *C.R. Acad. Sci. U.S.S.R.*, **32**, 526 (1941).
[4] Gause, *Bull. Exp. Biol. Med. U.S.S.R.*, **16**, 48 (1943).

APPLICATION OF NEW METHODS OF END-GROUP DETERMINATION TO STRUCTURAL PROBLEMS IN THE POLYSACCHARIDES

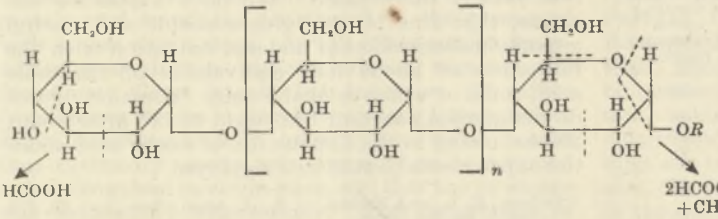
By F. BROWN, SONIA DUNSTAN, T. G. HALSALL, Prof. E. L. HIRST, F.R.S., and J. K. N. JONES

The University, Manchester

THE oxidative degradation of α-glycols by periodic acid has found many applications in carbohydrate chemistry, one of the most important of these being C. S. Hudson's[1] investigation of the reaction between this reagent and the methyl hexopyranosides, which are attacked with disruption of the ring and elimination of the third carbon atom of the hexose as formic acid. In the case of reducing disaccharides consisting of 1 : 4-linked hexopyranose residues, the reducing



hexose residue should yield a further 2 mol. of formic acid, giving three in all. The corresponding methyl biosides, on the other hand, contain the requisite system of contiguous hydroxyl groups only in the terminal residue, and should yield only 1 mol. of formic acid. It follows that polysaccharides built up on the pattern of starch or cellulose with chains of 1 : 4-linked hexopyranose residues should yield formic acid only from the reducing residues (if any) and from the terminal residues. If, therefore, the reaction could be carried out quantitatively, an estimation of the formic acid produced would give a measure of the number of end-groups present.



On the other hand, polysaccharides containing 1 : 6-linkages will give rise to 1 mol. of formic acid for every such monose residue which contains no other substituent. If, therefore, end-group determinations by the periodic acid method and by the methylation method agree, evidence is provided that no 1 : 6-linked sugar residues containing three unsubstituted hydroxyl groups occur in the polysaccharide.

The marked tendency for oxidation of polysaccharides by periodic acid to proceed beyond the stage depicted above[2] has hitherto restricted the usefulness of the method, but the reagent has been used in other ways in the study of polysaccharides. For example, Barry and Dillon[3] showed that by use of periodic acid the stepwise degradation of the 1 : 3-linked polysaccharide laminarin can be effected, and in the case of starch dextrins an attempt has been made to measure the formaldehyde produced from the reducing end of the chain[4].

Our interest in these reactions originated in attempts to gain further insight into the structure of plant gums, suitably bound side-chains of which we hoped to remove with the aid of periodic acid. We at once encountered difficulties due to over-oxidation, and a detailed study of the experimental conditions was undertaken. We have now found that suitable conditions for the quantitative liberation of formic acid from methyl hexopyranosides, methyl biosides of appropriate structure, cellulose, starch, glycogen and certain plant gums, are provided by the use of a solution of sodium periodate to which potassium chloride has been added. Potassium periodate is precipitated, but sufficient remains in solution to effect oxidation under conditions such that the formic acid is liberated quantitatively from the terminal sugar residues in about 180 hr. at 15° C. The concentration of reactants is important and the amount of starting material is so chosen that approximately 7 mgm. of formic acid are liberated per 100 c.c. of solution. The excess of potassium periodate is destroyed by addition of ethylene glycol, and the formic acid is then titrated by 0·01 *N* baryta. Alternatively, the formic acid can be extracted by ether and estimated by the mercuric chloride method or gasometrically from the amount of carbon monoxide produced by the action of sulphuric acid on the sodium salt. The utility and economy of the method are shown by the fact that an end-group determination can be completed in the starch series using as little as 0·5 gm. of material.

Experiments were carried out with the methyl pyranosides of xylose, arabinose, glucose, galactose, mannose, cellobiose and maltose, and also with sucrose, all of which give quantitatively 1 mol. of formic acid. A study was then made of the action of periodic acid on starch and amylopectin. In these materials the proportion of reducing end-groups is small in comparison with the proportion of non-reducing end-groups, and the observed values for the amounts of formic acid liberated can be used to calculate directly the proportion of non-reducing end-groups. It is to be noted, however, that for long straight-chain molecules such as amylose and cellulose, in which both reducing and non-reducing end-groups may be present, formic acid may be liberated from both the first and the last glucose residues, and the calculation must be adjusted accordingly. Nevertheless, for the mixtures of amylose and amylopectin which are present in starches the amount of formic acid given by the long-chain molecules of the amylose portion may be neglected, as a first approximation, in comparison with that given by the many non-reducing end-groups present in the branched chain molecules of amylopectin. The results (see table) have been expressed as the average number of glucose residues in the molecule for every end-group present (estimated experimental error ± 2 units).

In some instances independent end-group determinations were made by the standard methylation procedure. In these experiments the chromatographic method[5] was used for the quantitative separation of the tetramethyl glucose, and it was found to be easily

possible to complete an end-group determination using less than 10 gm. of starch.

We then measured by potentiometric titration[6] (using a modification of the standard method kindly placed at our disposal by Mr. R. S. Higginbotham) the iodine-binding power of the various samples. The available evidence, which does not, however, cover the full range of starches, indicates that all amyloses possess similar iodine-binding powers[7], and on this assumption we proceeded to evaluate the amylose contents of the samples (column 2 of table). Since the amylose constituent contributes only negligibly to the formic acid liberated by the action of KIO_4 on starch, the figures in columns 2 and 3 of the table enable a calculation to be made of the chain-length of the repeating unit of the amylopectin portion of the starches. The results (column 5) show that for a wide range of starches the amylopectin component contains approximately twenty glucose residues per end group. Exceptions are the amylopectins of sweet potato (27) and arrowroot (25), but we prefer to postpone discussion of possible causes for these divergences until more is known concerning the iodine-binding power of the corresponding amyloses. Indeed, until further evidence is forthcoming, the possibility cannot be entirely ruled out that materials intermediate in structure between unbranched amylose and much branched amylopectin may yet be encountered. The rice starch examined differed from the previous sample in that for the whole starch there were 24–27 glucose residues per end group in contrast with the earlier figure of 30 [8]. The possibility arises that the proportions of amylose and amylopectin may vary considerably for different samples, and this may be true for other starches also; for example, maize, in which widely different amylose contents have been recorded, and waxy maize, for which a higher figure (26) was previously observed[9] for the number of glucose residues per end group. Our present sample of waxy maize starch consisted entirely of amylopectin.

Substance	Amylose content %	Number of glucose residues per end-group		Calculated chain-length of repeating unit of amylopectin fraction
		By KIO_4 method	By methylation method	
Potato starch	18	28	25	23
Crude potato amylopectin	7	21		20
Sago starch	26	24		18
Banana starch	21	27	24	21
Sweet potato starch	18	32	30	27
Arrowroot starch	20	31		25
Tapioca starch	17	25		20
Pearl manioc starch	16	24		20
Rice starch	14	24	27	20
Maize starch	23	25		19
Waxy maize starch	0	20	20	20
Wheat starch	19	26		21

We have applied the method also to various samples of glycogen kindly supplied to us by Dr. D. J. Bell. For all these, the sources being respectively horse muscle, rabbit liver, human muscle, rabbit muscle (fasted), *Mytilus edulis* and *Ascaris lumbricoides*, our results indicated within the limits of experimental error a repeating unit of twelve glucose residues. The same figure was obtained by Bell[10] for horse muscle and rabbit liver glycogen, using the methylation method, and for *Mytilus edulis* glycogen by K. H. Meyer[11] (the others have not yet been examined by the methylation technique). The new results considerably extend the list of glycogens which have been found to contain a repeating unit of twelve glucose residues.

For cellulose, after making allowance for the formic acid produced at the reducing end of the chain, a value of at least 1,000 residues per chain has been obtained. The range of application of the method is further shown by the results obtained with: (*a*) inulin[12] (repeating unit approximately 25 fructose residues, calculated on the amount of formic acid liberated from the reducing end of the chain); (*b*) gum arabic (our results show that the repeating unit of mol. wt. 1220 found by Smith[13], using the methylation technique, contains two end-groups which liberate formic acid, support being thus given to the molecular structure for gum arabic advanced by Smith); (*c*) ε-galactan of larch wood (there are three end-groups per repeating unit of mol. wt. 1104, in agreement with our previous results[14] and with the formula suggested by White[15]; (*d*) pershore plum gum (the equivalent by acidimetry is 1,200 and the present results show the presence of one end-group per equivalent).

Preliminary experiments with other gums and pectic materials have been made and it is apparent from these that special problems arise when the polysaccharide contains terminal uronic acid residues. Such substances readily undergo further oxidation, with breakdown of the molecule and liberation of additional amounts of formic acid[16]. The probable reason for this behaviour is that after the initial oxidation is complete there are two $>\overset{|}{C}=O$ groups attached to the $-\overset{|}{C}-O-$ ring linkage of the original uronic acid residues. Similar conditions exist when α-methylmannofuranoside is treated with potassium periodate, the sixth C-atom being removed as formaldehyde, leaving two aldehyde groups attached to the $-\overset{|}{C}-O-$ ring linkage. Here also further oxidation readily takes place. We have found, for example, that zinc borneol glucuronoside and methyl α-methylgalacturonoside undergo oxidation with the formation of about four equivalents of titratable acid, some of which is oxalic acid. Titration figures do not remain constant but begin to fall after about 200 hr. owing to the destruction of oxalic acid under the experimental conditions employed.

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[2] Davidson, G. F., *J. Textile Inst.*, **32**, T, 109 (1941).

[3] Barry, V. C., *Nature*, **152**, 538 (1943). Dillon, T., *Nature*, **155**, 546 (1945).

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[5] Jones, J. K. N., *J. Chem. Soc.*, 333 (1944).

[6] Bates, L. F., French, D., and Rundle, R. E., *J. Amer. Chem. Soc.*, **65**, 142 (1943).

[7] Higginbotham, R. S., and Morrison, G. A., *Chem. and Ind.*, 77 (1945). See also Kerr, "Chemistry and Industry of Starch" (1945), 333.

[8] Hirst, E. L., and Young, G. T., *J. Chem. Soc.*, 1471 (1939).

[9] Haworth, W. N., Hirst, E. L., and Woolgar, M. D., *J. Chem. Soc.*, 177 (1935).

[10] Bell, D. J., *Biochem. J.*, **31**, 1683 (1937).

[11] Meyer, K. H., *Naturwiss.*, **29**, 287 (1941).

[12] Haworth, W. N., Hirst, E. L., and Percival, E. G. V., obtained the value 30 by the methylation method (*J. Chem. Soc.*, 2384 (1932)).

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[14] Hirst, E. L., Jones, J. K. N., and Campbell, W. G., *Nature*, **147**, 25 (1941).

[15] White, E. V., *J. Amer. Chem. Soc.*, **64**, 2838 (1942).

[16] Compare Heubner, C. F., Lohmar, R., Dimler, R. J., Moore, S., and Link, K. P., *J. Biol. Chem.*, **159**, 503 (1945).

MAMMARY CANCER IN MICE

IN the introduction to this collection of essays*, Dr. M. B. Shimkin sketches the historical development of our knowledge of mammary cancer in mice. Dr. E. F. Bashford and his colleagues of the Imperial Cancer Research Fund were instrumental in establishing the validity of using animal tumours in experimental cancer research. Then Leo Loeb and others showed the important part played by hormones in mammary cancer. By developing and using inbred strains of mice, American workers were able to investigate the inheritance of mammary cancer and reveal the existence of extrachromosomal influence. The cytology, morphology and histogenesis of the mammary gland and mammary tumours are discussed in four illustrated contributions. In general, only minor advances have been made in the morphology of mammary tumours since the classical work carried out early in the present century. Dr. W. E. Heston reviews our knowledge of the genetics of mammary cancer in mice and describes the origins and characters of the inbred strains of mice used in cancer research. This work can be considered to have commenced in 1909, when Dr. C. C. Little started breeding the *cba* strain, although some evidence that the tendency to mammary cancer was inherited was available before that time.

The development of knowledge of the milk influence on the genesis of mammary tumours is reviewed by Dr. H. B. Andervont. Early experiments showed that in reciprocal matings between strains with high and low mammary tumour-rates, the mice born to high-cancer strain mothers develop cancer, while those born to low-cancer strain mothers remain relatively free of tumours. The extra-chromosomal factor influencing the incidence was shown by Dr. J. J. Bittner, in a series of foster-nursing experiments, to be present in the milk of high-cancer strain mice. The relative incidence of tumours and the latent period for the appearance of tumours in certain strains of mice vary with the dose of the milk factor, and the response can be used for the biological assay of the factor. The milk factor appears to be a nucleoprotein and is widely distributed in the tissues of high-cancer strain mice. As the effect can be transmitted through mice without inducing tumours, the factor acts like a latent virus infection. It differs from known viruses in its relatively long latent period. Early experiments with heterozygous mice showed that mammary cancer was generally more common in breeding than in virgin mice, and that the incidence was reduced by ovariectomy. The importance of œstrogenic hormones in the incidence of mammary cancer could only be clearly shown by treating male mice of high-cancer strains which had both chromosomal and extra-chromosomal factors for cancer.

The relatively uniform behaviour of mice from inbred strains also makes it possible to study the effects of diet on the incidence and growth of mammary tumours. Dr. H. P. Morris describes many different experiments in which restriction of food intake or utilization has reduced the incidence of cancer or retarded the growth of existing tumours. In their chemical constituents and biochemical processes, mammary tumours resemble other tumours more closely than normal breast tissue. Dr. J. P. Greenstein points out that the end results of neoplastic growth are tissues which are chemically similar. The range of activity of several enzymes is much smaller among different tumours than among normal tissues. Mammary tumours in mice have been used extensively for experiments on chemotherapy of cancer, and Dr. Helen H. Dyer, in summarizing and tabulating the work in this field, concludes that no effective remedy has yet been found. Breast tumours in mice form the most valuable material available for such experiments. The probability that the cure for one type of cancer may not work on all types of tumour, however, makes it advisable that more than one type of tumour should be used in therapeutic experiments.

In the concluding essay, Dr. M. B. Shimkin considers the possible implications of the work on mice to human cancer. Whether mammary cancer in women is inherited is not yet known with certainty, so that we cannot say if a milk factor operates in humans or not. Even so, Dr. J. J. Bittner has suggested that it might be desirable to interrupt completely the nursing of daughters in whose family history carcinoma of the breast has occurred.

Mammary tumours in mice have been extensively studied, and the facts which have been obtained are well presented in this symposium. To what extent other tumours, or mammary tumours in other species, resemble these mouse tumours, particularly from the point of view of heredity, remain as interesting problems for the future. E. BOYLAND.

* Mammary Tumours in Mice. A Symposium by Members of the Staff of the National Cancer Institute, National Institute of Health, United States Public Health Service. Publication No. 22. Pp. v+223. (Washington, D.C.: American Association for the Advancement of Science, 1945.)

STUDIES ON COMPREGNATED WOOD

EXPERIMENTS carried out at the Forest Research Institute, Dehra Dun, indicate that compregnated wood which compares favourably with foreign samples (tests on a foreign specimen of compregnated birch are given) can be produced from Indian timbers. In Indian Forest Leaflet No. 77—1945 (Utilization) entitled "Preliminary Studies on Improved Wood, Part III. Compregnated Wood" (published by Forest Research Institute, Dehra Dun, 1945), it is stated that wood of highly improved properties can be obtained by a suitable combination of impregnation, lamination and compression. In the case of compressed wood and lignostone, whole wood scantlings are used and, by application of great compression, the properties of the material are made uniform in the main direction. In the case of compregnated wood, the timber is sub-divided into veneers, and impregnated with resins, or thin films of glue are placed between the veneers; finally the pack is compressed at a high pressure at a suitable temperature. Alcoholic solutions of resin or film glues, such as Tego film, etc., are used. It is said that by suitable choice of the species of wood, thickness of the veneers, pressure and temperature employed, and the direction of laying the veneers, the properties of the resulting material can be varied to meet particular requirements. The uses of this material, it is held, are very varied—aeroplane propeller blades are given as an example. The main defects of natural wood in this connexion are low hardness; low cleavage strength; low shear strength and great hygroscopicity. Compregnated wood, on the other hand, has high tensile strength; high shear strength to cope with the high centrifugal stresses at the boss,

which at the same time are reduced to a minimum due to the low density of the material in contrast to metal; high damping capacity; favourable strength density ratio; lightness (weight of such blades are a third of metal ones); increases in efficiency (about 6 per cent) by the use of such blades; ease of repair; and finally, it is claimed, freedom from tiring, which is so frequently the cause of fatal air accidents in aeroplanes fitted with metal propellers. Other uses are gear wheels, bearings (ships' tail shafts, rolling mills, textile mills, etc.), fish plates, press forms, gun stocks, electrical machinery and so forth.

For the preparation of compregnated wood in the investigations, rotary cut, sawn or sliced veneers of different Indian timbers were used, some twenty-three species being experimented with. The adhesives employed were tar acid formaldehyde resins prepared in the laboratory, prolamin-formaldehyde dispersions, casein-formaldehyde dispersions or a suitable combination of these materials. The Leaflet, which is illustrated with photographs and tabular diagrammatic statements, discusses the methods and procedure employed in the investigation.

FORTHCOMING EVENTS

Saturday, December 29

ROYAL INSTITUTION (at 21 Albemarle Street, London, W.1), at 2.30 p.m.—Sir Robert Watson-Watt, F.R.S.: "Wireless" (Christmas Lectures adapted to a Juvenile Auditory, 2).

Tuesday, January 1

ROYAL INSTITUTION (at 21 Albemarle Street, London, W.1), at 2.30 p.m.—Sir Robert Watson-Watt, F.R.S.: "Wireless" (Christmas Lectures adapted to a Juvenile Auditory, 3).

TELEVISION SOCIETY (at the Institution of Electrical Engineers, Savoy Place, Victoria Embankment, London, W.C.2), at 6 p.m.—Mr. F. A. Inskip: "A Test Signal Generator for Television Receivers"; Mr. A. M. Spooner: "Cathode Ray Tube Quality Measuring Apparatus".

Wednesday, January 2

ROYAL SOCIETY OF ARTS (at John Adam Street, Adelphi, London, W.C.2), at 2.30 p.m.—Dr. C. B. Williams: "The Migration of Butterflies" (Dr. Mann Juvenile Lectures, 1).

Thursday, January 3

ROYAL INSTITUTION (at 21 Albemarle Street, London, W.1), at 2.30 p.m.—Sir Robert Watson-Watt, F.R.S.: "Wireless" (Christmas Lectures adapted to a Juvenile Auditory, 4).

ROYAL COLLEGE OF SURGEONS OF ENGLAND (at Lincoln's Inn Fields, London, W.C.2), at 5 p.m.—Mr. N. L. Capener: "Physiological Rest—the Orthopædic Principle".

ASSOCIATION FOR SCIENTIFIC PHOTOGRAPHY (in the Theatre of the British Council, 3 Hanover Street, London, W.1), at 6.15 p.m.—Dr. A. J. Holland: "Glass and Photography".

Friday, January 4

BRITISH ECOLOGICAL SOCIETY (in the Washington Singer Laboratories, Prince of Wales Road, Exeter), at 10 a.m.—Annual General Meeting.

INSTITUTE OF PHYSICS, ELECTRONICS GROUP (at the Royal Society, Burlington House, Piccadilly, London, W.1), at 5.30 p.m.—Prof. N. Feather, F.R.S.: "Artificial Radioactivity".

Saturday, January 5

ROYAL INSTITUTION (at 21 Albemarle Street, London, W.1), at 2.30 p.m.—Sir Robert Watson-Watt, F.R.S.: "Wireless" (Christmas Lectures adapted to a Juvenile Auditory, 5).

Monday, December 31—Saturday, January 5

TWENTY-NINTH ANNUAL CONFERENCE OF EDUCATIONAL ASSOCIATIONS (at King's College, Strand, London, W.C.2).

Wednesday, January 2

At 5 p.m. (in the Great Hall).—Lady Simon: "The School, the Teacher and the Home" (Presidential Address).

Thursday, January 3

At 2.30 p.m. (in the Great Hall).—Discussion on "The Teacher's Profession" (to be opened by Mrs. M. D. Stocks and Mr. Nigel O. Parry).

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

ASSISTANT BURSAR—The Bursar, Queen's University, Belfast (January 10).

PRINCIPAL—The Clerk and Treasurer, Dundee Institute of Art and Technology, Bell Street, Dundee (January 12).

PATENT AGENT (qualified), preferably holding an Engineering Degree or equivalent qualification, by a large Engineering Company, electrical and mechanical—The Ministry of Labour and National Service, Appointments Department, Technical and Scientific Register, Room 572, York House, Kingsway, London, W.C.2, quoting F.5222.XA (January 12).

DEPUTY BOROUGH ENGINEER AND SURVEYOR—The Town Clerk, Town Hall, St. Marylebone, London, W.1, endorsed 'Deputy Borough Engineer and Surveyor' (January 12).

LECTURER IN HAUSA—The Director, School of Oriental and African Studies, University of London, London, W.C.1 (January 15).

ARCHÆOLOGIST (man or woman)—The Keeper of the Museums, Yorkshire Museum, York (January 31).

PROFESSOR OF CHEMISTRY—The Principal, Heriot-Watt College, Edinburgh (April 22).

PROFESSORSHIP OF INDUSTRIAL CHEMISTRY at Istanbul University—The British Council (Appointments Department), 3 Hanover Street, London, W.1.

BACTERIOLOGIST to work on the intestinal flora, a BIOCHEMIST with good bacteriological knowledge for microbiological assay of the vitamins, and an ORGANIC or BIO-CHEMIST for other work involving vitamin assay—The Secretary, National Institute for Research in Dairying, Shinfield, Reading.

CHEMISTS (male), Inter. B.Sc. standard, as Assistant Works Chemists with large firm of cement manufacturers—The Ministry of Labour and National Service, London Appointments Office, 1–6 Tavistock Square, London, W.C.1, quoting Ref. No. C.N.68.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

Radar: a Report on Science at War. Released by the Joint Board on Scientific Information Policy for Office of Scientific Research and Development, War Department, Navy Department. Pp. 50. (London: H.M. Stationery Office; Washington, D.C.: Government Printing Office, 1945.) 1*s.* net. [259

The Scientific Civil Service: Reorganization and Recruitment during the Reconstruction Period. (Cmd. 6679.) Pp. 16. (London: H.M. Stationery Office, 1945.) 3*d.* net. [269

The Administrative Class of the Civil Service. (Cmd. 6680.) Pp. 16. (London: H.M. Stationery Office, 1945.) 3*d.* net. [269

Report by the Geological Sub-Committee of the Nature Reserves Investigation Committee. Memorandum No. 5: National Geological Reserves in England and Wales. Pp. iv+42. (London: Society for the Promotion of Nature Reserves, c/o British Museum (Natural History), 1945.) 1*s.* 6*d.* [279

A New Deal for Government Scientists? Pp. 12. (London: Institution of Professional Civil Servants, 1945.) [289

British Trust for Ornithology. Eleventh Report for the Year 1944. Pp. 16. (London: British Trust for Ornithology, c/o Zoological Society of London, 1945.) [410

West India Royal Commission Report. (Cmd. 6607.) Pp. xviii+480+16 plates. (London: H.M. Stationery Office, 1945.) 7*s.* 6*d.* net. [1110

Other Countries

Bulletin of the American Museum of Natural History. Vol. 84: The North and South American Ascidians. By Dr. Willard G. Van Name. Pp. vii+476+31 plates. (New York: American Museum of Natural History, 1945.) [98

Contributions from the United States National Herbarium. Vol. 29, Part 2: Mexican Phanerogams described by M. E. Jones, by C. V. Morton; Asteraceae described from Mexico and the Southwestern United States by M. E. Jones, 1908–1935, by S. F. Blake. Pp. xi+87–138. (Washington, D.C.: Government Printing Office, 1945.) 20 cents. [98

Proceedings of the United States National Museum. Vol. 96, No. 3193: The Ichneumon-Flies of the Genus *Cryptanura* Brullé, mainly Tropical American. By R. A. Cushman. Pp. 139–176. Vol. 96, No. 3194: Neotropical Lanternflies of the Genus *Phrictus* in the United States National Museum, with Descriptions of Four New Species. By John S. Caldwell. Pp. 177–184. (Washington, D.C.: Government Printing Office, 1945.) [98

Biological Abstracts. Report for 1944. By John E. Flynn. Pp. 12. (Philadelphia: University of Pennsylvania, 1945.) [98

Gold Coast Colony. Forestry in the Northern Territories of the Gold Coast. By R. C. Marshall. Pp. 12. (Accra: Government Printing Office, 1945.) 1*s.* [98

American Philosophical Society. Year Book 1944, January 1, 1944–December 31, 1944. Pp. 394. (Philadelphia: American Philosophical Society, 1945.) [98

Catalogues

High Vacuum for Industry. Pp. 30. (Boston, Mass.: National Research Corporation, 1945.)

Books of All Ages on Varied Subjects. (Catalogue No. 676.) Pp. 70. (London: Francis Edwards, Ltd., 1945.)

Libros de medicina, farmacia y veterinaria. Pp. 64. (Madrid: Libreria Casas y Buendia, 1945.)

COMMONWEALTH OF AUSTRALIA

COUNCIL FOR SCIENTIFIC AND INDUSTRIAL RESEARCH

DIVISION OF INDUSTRIAL CHEMISTRY

APPOINTMENT OF SENIOR RESEARCH OFFICER FOR X-RAY CRYSTALLOGRAPHY

Applications are invited for one position of Senior Research Officer, Division of Industrial Chemistry, Melbourne. *Duties:* To undertake X-ray crystallographic investigations of a fundamental nature within the Division's Chemical Physics Section. *Qualifications:* University degree in science or equivalent qualifications together with several years experience in X-ray crystallography. *Salary:* Dependent on qualifications and experience, commencing salary will be within the range of Senior Research Officer (Male, £A625 to £A750 p.a. nominal; Female, £A563 to £A688 p.a. nominal; five equal increments, first automatic, remainder discretionary). *Note.*—The present cost-of-living adjustment to the above nominal salaries is an additional £40 p.a. in the case of a male appointee and £27 p.a. in respect of a female.

Subject to a satisfactory medical examination, the successful applicant will be appointed initially on probation; after the expiry of a period of twelve months, if confirmed in his or her appointment as an officer of the Council, will be eligible to contribute to, and receive benefits from, either the Commonwealth Superannuation Fund or the Commonwealth Provident Fund.

Applications stating date of birth, nationality, present employment, particulars of qualifications and experience, and accompanied by copies of not more than four testimonials, should reach the Secretary, Australian Scientific Research Liaison Office, Australia House, Strand, London, W.C.2, not later than February 8.

G. A. COOK,
Secretary.

Council for Scientific and Industrial Research,
314 Albert Street,
East Melbourne, C.2, Victoria.

HOME OFFICE FORENSIC SCIENCE LABORATORIES

Applications are invited for men and women for the following posts at the Home Office Forensic Science Laboratories:

(*a*) BIOLOGISTS at (i) the North Eastern Laboratory at Wakefield; (ii) the West Midland Laboratory at Birmingham; (iii) the South Western Laboratory at Bristol; (iv) the North Western Laboratory at Preston. (Ref. No. F.5063A).

(*b*) CHEMISTS at (i) the North Eastern Laboratory at Wakefield (Ref. No. F.5387A); and (ii) the South Western Laboratory at Bristol (Ref. No. 5388A).

Only well qualified candidates of British birth and parentage should apply. The Biologist should be an Honours Graduate in Botany, with subsidiary qualifications in Zoology and/or Bacteriology. The Chemist should have an Honours degree in Chemistry; experience of micro-analysis and the use of physico-analytical instruments is also required.

Commencing salary for men would be on the range of £275 to £650 per annum plus Civil Service War Bonus (at present £60 per annum), and for women £275 to £520 plus War Bonus (at present £48 per annum), both according to age and qualifications. The ranges of salary are subject to review in the light of the White Paper on the Scientific Civil Service. The scales of salary recommended in the White Paper are: Scientific Officers £255 to £470 per annum, Senior Scientific Officer £520 to £710 per annum, plus bonus, with slightly lower scales for women. There are opportunities for promotion to ranks carrying salaries at present up to £1,250 per annum.

A temporary appointment only can be offered at the present time, but candidates born on or after August 2, 1915, will be eligible to compete in the post-war reconstruction competitions with a view to being established. It is not possible to offer prospects of establishment to candidates born before that date unless the circumstances are very exceptional.

Applications received by the Home Office in reply to earlier advertisement for similar posts will be considered and applicants need not apply again.

Write quoting appropriate reference numbers to Ministry of Labour and National Service, Appointments Department, Technical and Scientific Register, Room 572, York House, Kingsway, London, W.C.2, for application form which must be returned completed, with three copies of recent testimonials, by January 19, 1946.

Physicist required on Research Staff of glass manufacturers in North East. Honours degree and about five years industrial or research experience (not necessarily in glass) preferred. Salary according to qualifications. Box 488, T. G. Scott & Son, Ltd., 9 Arundel Street, London, W.C.2.

DEPARTMENT OF SCIENTIFIC AND INDUSTRIAL RESEARCH

Applications are invited for (a) two vacancies on the staff of the Water Pollution Research Laboratory, Watford, mainly for research on methods of treatment of water, sewage and trade waste waters (Ref. F.5087.A) and (b) one vacancy on the staff of the Chemical Research Laboratory, Teddington, for research on the methods of separation of tar components, including distillation (Ref. F. 5216.A). Candidates should have a 1st or 2nd Class Honours Degree in Chemistry, or equivalent qualifications, with postgraduate experience, preferably in research. One of the posts at the Water Pollution Research Laboratory calls for training or experience in biochemistry or bacteriology; at the Chemical Research Laboratory a Physical Chemist with good knowledge of thermodynamics is required. In the first instance, pending the application of the new scheme for Scientific Staff in the Government Service recently published, (Cmd. 6679), the appointments will be in the grade of either Temporary Junior Scientific Officer or Temporary Scientific Officer. The initial salary will be between £300 and £500 plus Civil Service war bonus.

Write, quoting appropriate reference number, to the Ministry of Labour and National Service, Appointments Department, Technical and Scientific Register, Room 572, York House, Kingsway, London, W.C.2, for application form which must be returned completed by January 18.

Manchester Municipal COLLEGE OF TECHNOLOGY

(Faculty of Technology in the University of Manchester).

Appointment of

(*a*) LECTURER IN PHYSICAL CHEMISTRY.

(*b*) LECTURER IN MATHEMATICS.

The Governing Body invites applications for:

(*a*) a LECTURESHIP IN PHYSICAL CHEMISTRY in the College of Technology, with the title and status of Lecturer in the University of Manchester;

(*b*) a LECTURESHIP IN MATHEMATICS in the College of Technology, with the title and status of Lecturer in the University of Manchester.

Salary: £425 per annum, rising by annual increments of £15 to £550 per annum, plus war bonus (which at the present time is £52 per annum). Commencing salary according to qualifications. Revised salary scales are at present under consideration.

Conditions of appointment and forms of application may be obtained from the Registrar, College of Technology, Manchester, 1. The last day for the receipt of applications is January 14, 1946.

Canvassing, either directly or indirectly, will disqualify a candidate for appointment.

J. E. MYERS,
Principal of the College.

NATAL UNIVERSITY COLLEGE

(DURBAN)

Applications are invited for the post of PROFESSOR OF SOCIAL ANTHROPOLOGY. Salary will be on the scale: Men £750—£25—£1,000. Women £650—£25—£900, plus current cost of living allowance. The initial salary will be determined in accordance with the qualifications and experience of the successful candidate. Allowance for travelling expenses. Membership of the University Teachers' Provident Fund is compulsory. Appointment will be in the first place for probationary period of one year. Successful applicant will be expected to take up his duties in 1946 but applications will be considered from members of the Armed Forces who are not able to comply with this condition. Further particulars may be obtained from the Secretary, Universities Bureau of the British Empire, c/o University College, Gower Street, London, W.C.1.

BRADFORD EDUCATION COMMITTEE

TECHNICAL COLLEGE, BRADFORD

IMPERIAL CHEMICAL INDUSTRIES RESEARCH SCHOLARSHIP

A Research Scholarship for research on new textile fibres is now available. The Scholarship is of the annual value of £100 and has been provided by Imperial Chemical Industries, Ltd.

The Scholarship may be held for one or more years.

Applications should be forwarded as soon as possible to the Principal, Technical College, Bradford.

Bacteriologist (graduate woman) required for diagnostic and anærobic culture work in veterinary pathological laboratory. Superannuation scheme. Apply: The Director, The Wellcome Physiological Research Laboratories, Langley Court, Beckenham, Kent.

THE POLYTECHNIC

REGENT STREET

DEPARTMENT OF MATHEMATICS AND PHYSICS

A course of lectures on advanced MATHEMATICAL STATISTICS, designed to meet the needs of scientists and engineers, will commence on Tuesday, January 15, 1946.

Full particulars may be obtained on application to the undersigned.

J. C. JONES,
Director of Education

The Polytechnic,
309 Regent Street,
London, W.1.

UNIVERSITY OF MELBOURNE

Applications are invited for appointment as SIR THOMAS LYLE RESEARCH FELLOW IN PHYSICS, commencing duty early in 1946. Salary £600 (Australian) per annum. Tenure two years with a possibility of extension to third year. Further particulars may be obtained from the Secretary, Universities Bureau of the British Empire, c/o University College, Gower Street, London, W.C.1. Closing date for receipt of applications (in Australia) February 15, 1946.

UNIVERSITY COLLEGE OF WALES ABERYSTWYTH

Assistant Lecturer in Zoology required to commence duties as soon as possible. Salary £400. Applications should be sent to the Registrar, from whom further particulars may be obtained, by January 19.

Chemist (Male) required in the Mineral Resources Department of the Imperial Institute. Candidates must have a University degree (not lower than 2nd Class Hons.) or its equivalent. The duties are concerned with the investigation of Empire raw materials of mineral origin with a view to assessing their commercial value or market possibilities. Age limit 30 years. Salary £275 p.a. with annual increments of £18 plus war bonus (at present £60 p.a.). Appointment temporary with a view to permanent pensionable employment. Further information from Establishment Officer, Imperial Institute, S.W.7.

Three Senior Dietitians (Technical Officers), all women, required by Ministry of Food, Food Advice Division. Candidates should possess a science degree or domestic science teacher's diploma and diploma in dietetics. Only candidates with a science degree and diploma in dietetics will be considered. All candidates must be prepared to lecture and may be out-stationed in provinces.

Salary: Seniors, £320 to £480, plus war bonus £48, according to qualifications and experience.

Write quoting F.4631.A to Ministry of Labour and National Service, Appointments Department, Technical and Scientific Register, Room 572, York House, Kingsway, London, W.C.2, for application form, which must be returned completed by January 15, 1946.

Library Assistant: graduate in chemistry, man or woman; industrial company in Home Counties; permanent and progressive post. Ministry of Labour approval will be sought to the appointment of the successful applicant. Please write fully Box 484, T. G. Scott & Son, Ltd., 9 Arundel Street, London, W.C.2.

British Nylon Spinners, Limited, require Physicist, age 30–35, Ph.D. or Hons. B.Sc. Physics essential. To undertake research on textiles and yarn production. State salary required. Written applications only to the Secretary, 72 Lockhurst Lane, Coventry.

Electrical Manufacturing Company's Patent Department in London area requires assistants for general patent work. Applicants should possess a good honours degree in General Science, Physics or Engineering. A knowledge of patent work would be an advantage but is not essential. Applications should be addressed to Box 485, T. G. Scott & Son, Ltd., 9 Arundel Street, London, W.C.2.

A Dietitian required by Food Research Laboratory in Oxford engaged in carrying out Nutritional Surveys and research into large-scale cooking problems. Box 486, T. G. Scott & Son, Ltd., 9 Arundel Street, London, W.C.2.

A Chemist required by Food Research Laboratory in Oxford. A knowledge of the Warburg apparatus an advantage but not essential. Box 487, T. G. Scott & Son, Ltd., 9 Arundel Street, London, W.C.2.

Assistant required for routine Biological testing, and to help in research. Newly qualified graduate or Inter.B.Sc. Apply Personnel Officer, May & Baker, Ltd., Dagenham, Essex.

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