THE ANALYST

EDITORIAL

THE BERNARD DYER MEMORIAL LECTURE

WITH this issue of *The Analyst* we publish photographs of the Bernard Dyer Memorial Medal.

The Council of the Society decided soon after Bernard Dyer died that it would be fitting to commemorate the great services he rendered to analytical chemistry by instituting a lecture in his memory, to be known as the Bernard Dyer Memorial Lecture and to be given every second year.

The first of these lectures was given in 1950 by Sir E. John Russell, F.R.S., and the second in 1952 by the Hon. Mr. Justice Lloyd-Jacob, and both have appeared in *The Analyst*.

It was intended from the first that the giving of these lectures should be marked by the presentation of a medal to the lecturer, and, accordingly, Mr. T. H. Paget was commissioned to design and produce one. The choice of artist was a very happy one, his work being well known to the world as the designer of the obverse of coins of the last reign, and to chemists as responsible for the Castner Medal of the Society of Chemical Industry. Mr. Paget's design was accepted by the Council last year, and the medal was struck from it by the Royal Mint. Copies were presented to the first two Bernard Dyer Lecturers on the occasion of the Society's Biennial Dinner in March, as reported elsewhere in this issue. The photographs we publish are by the Honorary Secretary of the Society.

This handsome medal forms a fitting memento both of the occasion of the lecture and of the eminent chemist in whose memory it has been struck. The obverse carries an excellent likeness of "B. D." in his habit as he lived, and the reverse bears a symbolical reminder of his activities—a ploughed field to mark his lifelong interest in the land, a Kjeldahl flask in memory of his laboratory researches on fertilisers and a full sheaf of corn as an emblematical representation of the benefits conferred on mankind by his life's work.

PROCEEDINGS OF THE SOCIETY OF PUBLIC ANALYSTS AND OTHER ANALYTICAL CHEMISTS

ANNUAL GENERAL MEETING

THE seventy-ninth Annual General Meeting of the Society was held at 2.45 p.m. on Friday, March 6th, 1953, in the meeting room of the Chemical Society, Burlington House, London, W.1. The Chair was taken by the President, Dr. J. R. Nicholls, C.B.E., F.R.I.C. The financial statement for 1952 was presented by the Honorary Treasurer and approved, and the Auditors for 1953 were appointed. The Report of the Council for the year ending March, 1953 (see pp. 264–271), was presented by the Honorary Secretary and adopted.

The Scrutineers, Messrs. J. B. Attrill and G. B. Thackray, reported that the following had been elected officers for the coming year—

President—D. W. Kent-Jones, B.Sc., Ph.D., F.R.I.C.

Past Presidents serving on the Council—Lewis Eynon, G. W. Monier-Williams, J. R. Nicholls and George Taylor.

Vice-Presidents—A. J. Amos, T. McLachlan and Eric Voelcker.

Honorary Treasurer—J. H. Hamence.

Honorary Secretary—K. A. Williams.

Other Members of Council—The Scrutineers further reported that 434 valid ballot papers had been received and that votes had been cast in the election of Ordinary Members of Council as follows—A. L. Bacharach, 343; R. C. Chirnside, 334; D. C. Garratt, 334; H. M. N. H. Irving, 257; Miss Mary Corner, 239; H. W. Hodgson, 210; E. G. Whittle, 175; A. L. Williams, 175; Osman Jones, 167; R. H. Morgan, 125.

The President declared the following to have been elected Ordinary Members of Council for the ensuing two years—A. L. Bacharach, R. C. Chirnside, D. C. Garratt, H. M. N. H. Irving, Miss Mary Corner and H. W. Hodgson.

C. A. Adams, N. L. Allport, B. S. Cooper, N. Heron, H. E. Monk and H. C. S. de Whalley, having been elected members of the Council in 1952, will, by the Society's Articles of Association, remain Ordinary Members of the Council for 1953.

T. W. Lovett (Chairman of the North of England Section), R. S. Watson (Chairman of the Scottish Section), A. M. Ward (Chairman of the Microchemistry Group), J. Haslam (Chairman of the Physical Methods Group) and H. O. J. Collier (Chairman of the Biological Methods Group) will be *ex-officio* members of the Council for 1953.

After the business outlined above had been completed, the meeting was opened to visitors, and the retiring President, Dr. J. R. Nicholls, C.B.E., F.R.I.C., delivered his Presidential Address (see pp. 271–280).

NEW MEMBERS

William John Bayley, B.Sc. (Lond.), A.I.M., F.R.I.C.; Ronald Blunt, B.Sc. (Lond.), F.R.I.C.; Robert Buckley, B.Sc. (Lond.), A.R.I.C.; William Thomas Carter, B.Sc. (Lond.); Miss Janet Cartmel, B.Sc. (Birm.); Miss Laura Mary Cleverly; Geoffrey Lionel Coulter, B.Sc. (Wales); Miss Olive Lucy Drage, B.Sc. (Lond.), A.R.I.C.; Alfred James Feuell, B.Sc. (Lond.), A.R.I.C.; Derek Guthrie Forbes, B.Sc. (Lond.), A.R.I.C.; Ronald John Hanson; Henry Arthur Harbottle, B.Sc. (Dunelm.); Thomas Hewitt, B.E.M., B.Sc. (Lond.), A.R.C.S., A.R.I.C.; Kenneth John Jarrett, B.Sc. (Lond.), A.R.I.C.; Richard Keith Lewis, B.Sc. (Lond.), A.R.I.C.; Norman Nix, B.Sc. (Notts.), A.R.I.C.; Donald Albert Pantony, B.Sc. (Lond.), Ph.D. (Leeds), A.R.C.S., A.R.I.C.; Reginald Jewitt Peace, B.Sc. (Lond.), A.R.I.C.; Anthony William Charles Phillips, B.Sc. (Lond.); John Alexander Pickard; Wynn Price-Davies, B.Sc. (Wales), A.R.I.C.; Victor William Reid, B.Sc. (Q.U.B.); Gordon Edward Simons Richards, A.R.I.C.; Derek Wilson Smith; Ronald Alan Watkins, B.Sc. (Lond.), A.R.I.C.; Robin Albert Woolf, B.Sc. (Lond.).

DEATH

WE regret to record the death of

John Robert Stubbs.

PHYSICAL METHODS GROUP

THE thirty-ninth Ordinary Meeting of the Group was held at 6.30 p.m. on Tuesday, March 3rd, 1953, in the Meeting Room of the Chemical Society, Burlington House, London, W.1. Dr. J. Haslam was in the Chair and about fifty-five members and visitors were present.

The following papers on "Absorptiometry" were presented and discussed: "The Use of High Absorbancy Reference Standards in Absorptiometry," by H. M. Irving, M.A., D.Phil., F.R.I.C.; "The Determination of Titanium by Precision Absorptiometry," by W. T. L. Neal, M.A., A.R.I.C., and H. G. Short, M.Sc., A.R.I.C.

COMMITTEES, 1953–1954

THE Council of the Society has appointed the following Committees—

FINANCE COMMITTEE

D. W. Kent-Jones (Chairman), N. L. Allport, Lewis Eynon, J. H. Hamence, H. W. Hodgson, E. B. Hughes, G. W. Monier-Williams, G. Taylor, A. M. Ward, K. A. Williams (Honorary Secretary).

PUBLICATION COMMITTEE

J. R. Nicholls (Chairman), N. L. Allport, A. J. Amos, A. L. Bacharach, R. C. Chirnside, B. S. Cooper, Lewis Eynon, D. C. Garratt, J. H. Hamence, J. Haslam, H. M. N. H. Irving, G. Roche Lynch, F. L. Okell, G. H. Osborn, J. E. Page, A. A. Smales, G. Taylor, L. S. Theobald, Eric Voelcker, C. Whalley, K. A. Williams, E. C. Wood.

POLICY COMMITTEE

G. Taylor (Chairman), R. C. Chirnside, J. A. Eggleston, J. H. Hamence, J. Haslam, N. Heron, H. M. N. H. Irving, D. W. Kent-Jones, J. R. Nicholls, A. M. Ward, K. A. Williams.

ANALYTICAL METHODS COMMITTEE

E. B. Hughes (Chairman), N. L. Allport, R. C. Chirnside, Norman Evers, J. H. Hamence, J. Haslam, D. W. Kent-Jones, R. F. Milton, J. R. Nicholls, F. L. Okell, G. H. Osborn, J. E. Page, R. W. Sutton, G. Taylor, H. C. S. de Whalley, K. A. Williams, D. W. Wilson, E. C. Wood, D. C. Garratt (Honorary Secretary).

PUBLIC ANALYSTS AND OFFICIAL AGRICULTURAL ANALYSTS COMMITTEE

G. Taylor (Chairman), C. A. Adams, F. W. F. Arnaud, H. H. Bagnall, W. Gordon Carey, H. Childs, J. F. Clark, S. Dixon, J. H. Hamence, E. S. Hawkins, N. Heron, E. T. Illing, D. W. Kent-Jones, J. King, A. Lees, J. B. McKean, T. McLachlan, C. H. Manley, S. Ernest Melling, G. W. Monier-Williams, H. E. Monk, J. R. Nicholls, C. J. Regan, J. G. Sherratt, R. W. Sutton, R. G. Thin, K. A. Williams, E. C. Wood, Eric Voelcker (Honorary Secretary).

STANDARD METHODS OF ANALYSIS COMMITTEE

G. Taylor (Chairman), N. L. Allport, D. C. Garratt, J. H. Hamence, D. W. Kent-Jones, J. R. Nicholls, K. A. Williams.

LIAISON COMMITTEE

G. Taylor (Chairman), J. H. Hamence, K. A. Williams.

SOCIETY'S REPRESENTATIVES ON THE JOINT COMMITTEE OF THE SOCIETY AND THE ROYAL INSTITUTE OF CHEMISTRY

W. Gordon Carey, S. Dixon, J. H. Hamence, T. McLachlan, J. G. Sherratt, G. Taylor, Eric Voelcker.

Annual Report of the Council: March, 1953

THE roll of the Society numbers 1592, an increase of 14 over the membership of a year ago.

HONOUR—During the year Professor D. N. McArthur has been awarded the C.B.E., and the Council offers him its congratulations.

LONG MEMBERSHIP—The congratulations and good wishes of the Council are extended to F. W. F. Arnaud, A. H. Bennett, H. Harman and E. M. Hawkins, who have completed 50 years of membership of the Society, and to S. Elliott, H. Lowe and A. J. Parker, who have completed 40 years of membership.

DEATHS—The Council regrets to have to record the deaths of the following members—

R. E. L. Davies	J. F. H. Gilbard	H. G. Reeves
Sir Jack Drummond	L. O. Newton	R. H. Slater
F. C. Dyche-Teague	A. Rayner	F. E. Thompson

Davies became a Bachelor of Science of Liverpool University with first class honours in 1924 and was elected Associate of the Institute of Chemistry in 1926. He joined the consulting practice of A. Norman Tate & Co., in Liverpool, in 1924, and succeeded to it on the death of his father, Joseph Davies, in 1948. He joined the Society in 1949.

Drummond was born in 1891 and was educated at King's College School and East London College, taking his degree in 1913. He was for a short time at the Government Laboratory and then went to the Cancer Hospital Research Institute, where he became Director of Biochemical Research. In 1919 he was Reader in Chemical Physiology at University College, London, and was made the first Professor of Biochemistry in the University in 1922. Here his work on the vitamins became famous. In 1939 he offered his services to the Ministry of Food and in due course became their Scientific Adviser, holding this post until 1946. His work now was to advise on the problems of feeding the people of an island almost isolated by enemy action. To this end it seemed that he ignored to a large extent any question of vitamins, and concentrated on the principle that in the circumstances it was calories that counted. He initiated measures that helped greatly in the effort to prevent any real malnutrition. He was knighted in 1944 and in the same year was elected a Fellow of the Royal Society. In 1946 he became Director of Research to Boots Pure Drug Co., Ltd. He served on the Council of the Society in 1924–5, and on the Council of the Institute of Chemistry. He was an Examiner of the Institute for six years, and Chairman of its London Section. He was a member of the Interdepartmental Committee on Food Standards from 1942, and more recently a member of the Food Standards Committee of the Ministry of Food. He died tragically, with his family, in France in the summer of 1952 at the hand of an unknown assassin.

Dyche-Teague obtained the degree of Bachelor of Science in the University of Birmingham. He became an Associate of the Institute of Chemistry in 1910 and a Fellow in 1914. He was elected a member of the Society in 1912. At that time he was a consulting analytical chemist and bacteriologist, and he had earlier been with F. E. Parkes and J. W. Gatehouse, Public Analysts. He was a pioneer in the production of British chlorinated rubber and founded Detel Products, Ltd., of which he was managing director.

Gilbard died in his 83rd year, 62 years after his election to membership of the Society. He was educated at Vermont College, Clapton, and at Finsbury Technical College under Meldola and Streatfeild. He became assistant to Bernard Dyer in 1888 and remained with him all his life. He became a Fellow of the Chemical Society in 1895 and of the Institute of Chemistry in 1899. About then he was appointed a Gas Examiner to the London County Council and later to West Ham as well.

Newton was educated at Tiffins Boys' School, Kingston-on-Thames and King's College, London, and Sir John Cass Technical Institute. He served an apprenticeship with the Locomotive Co. of America and in 1902 became assistant works manager to the Locomotive Co. of Great Britain Ltd. He joined Lassen and Hjort, water purification engineers, in 1907 and became manager of Sofnol Ltd. in 1912, of which company he was managing director from 1921 until his death. He was also retained as consultant to United Water Softeners Ltd. He was a member of the Institution of Chemical Engineers and acted as Honorary Secretary of the Institution for a period of seven years. He was a member of Gray's Inn.

protection should be envisaged and applied before a possible danger shows signs of becoming an acute reality. The measures proposed to minimise one risk must be equally applicable to many others and all should be considered together.

I should like to put before you my views on how the policy should be implemented, and as there are a few risks that may arise from sources other than consumer goods, I propose briefly to survey the whole field of public health hazards before indicating how the general problem might be tackled, as far as possible within the framework of existing legislation. I shall not consider industrial hazards, as these are more appropriate for particular treatment and, in themselves, are essentially medical questions.

Survey of public health hazards

Public health hazards may arise from—

(1) Air;
(2) Water;
(3) Food;
(4) Clothing;
(5) Cosmetics;
(6) Household materials.

(1) Air hazards—

Human beings are continually exhaling carbon dioxide, and the amount in the air is augmented by the burning of all types of fuel. In view of the vast extent of the atmosphere and the capacity of vegetation to utilise carbon dioxide for photosynthesis, the normal hazard from this gas is negligible. There are, however, other polluting substances that arise from the combustion of fuel, including unburned and partially burned coal dust, ash dust and grit, coke particles, tarry soot and gaseous sulphur dioxide. Much of this is fine particulate matter conducive to the production of fog, and during this last winter there were periods when fog prevailed for some days, and excessive and unexplained fatalities occurred to human beings and animals. Some medical authorities were of the opinion that local and unusual concentrations of carbon dioxide and other contaminants could not be excluded as a possible cause, even if only contributory. Whether or not this is correct, it is possible that traffic congestion in busy streets may produce a hazard over and above those mentioned, as the exhaust gases from car engines include, in addition, carbon monoxide and the products of pyrolysis of oils with their increasingly varied additives. The exhaust fumes from factories contribute in a similar way; and while national and local authorities take appropriate measures if there is a nuisance, the aspect should not be overlooked that there may be a public health hazard. Particulate matter in the atmosphere, not sufficient to cause a nuisance, may settle as dust and subsequently be blown about to be inhaled. These particles, no doubt, remain in the lungs after breathing.

(2) Water hazards—

Water authorities are very conscious of their responsibility to supply a pure article. They make sure that no contamination occurs in their plant or filter beds. But the water comes from a large catchment area and there is always the possibility of contamination either of the natural sources or from polluted areas. We know that certain waters contain high proportions of fluorine; and although the effect of this has been described as only a cosmetic blemish, there are pathological effects if the amount of fluorine is too high. The complete absence from very pure water of certain trace elements, such as iodine and fluorine, may raise the question of deficiencies, for which counter measures may be necessary. This is so closely connected with public health hazards that it must be considered with it.

The general problem of water pollution is a wide one and goes far beyond my present survey. But there are many ways in which the public health may be involved and this aspect must not be lost sight of. Special problems may be created by the more widespread occurrence of radioactive elements.

(3) Food hazards—

As already mentioned, food is a potential source of many hazards and these may be divided into a number of general classes.

(*a*) *Metallic contamination*—The possible dangers from poisonous metals are well known and good commercial practice tends to reduce the amounts present to negligible proportions. One has to consider not only the quantity present in a particular food but also that which may be present in the complete diet, as absorption of some metals is cumulative. For this reason it is desirable that steps should be taken to reduce the quantity of a poisonous metal present in any one food to the lowest commercially practicable amount. With very poisonous metals, such as arsenic and lead, ordinary commercial practice may not be the best possible to eliminate risks of contamination, and the ideal should be that of the most up-to-date and well-equipped producer. There is a consensus of opinion that the plant used in preparing food for sale should not yield harmful metals to food. Lead pipes should not be used for conveying liquids such as beer and cider. This has been recognised by the trade and it is largely the difficulty of obtaining replacements during recent years that has prevented their abandonment. It can be hoped that this hazard will be removed within a reasonably short time. Cooking utensils for household use should not contaminate food. Reputable manufacturers are aware of the possible danger, but it is doubtful if our present legislation is adequate for the necessary control.

(*b*) *Bacterial contamination*—For manufactured foods this is essentially a matter of hygiene, and good commercial practice results in a negligible risk. Some foods eaten raw, such as salad crops, may be grown on land treated with fertilisers or compost made from sewage sludge and this may entail a risk.

(*c*) *Extraneous matter*—Foods are subject to contamination by rodent residues, insects and mould at all stages of their history. This contamination is minimised by proper hygiene and good commercial practice; but as such matter is largely avoidable, some control may be necessary.

(*d*) *Wrapping materials*—Pre-packed food comes in contact with a variety of packing materials, and these should not contribute harmful substances to food. Suitable metal foils and plastic materials are known and recommended; but it must be remembered that not all plasticisers and breakdown products of plastics are harmless.

(*e*) *Insecticidal residues*—This is a very difficult problem, whether considered from the point of view of the chemist or from that of public health. It may be essential to use insecticides to obtain the maximum supply of natural foods, and it may be inevitable that traces remain in the food that reaches the public. Very potent insecticides have recently been developed and it may be economically essential to use them rather than less dangerous ones. This may be an instance where we are obliged to take a risk; but we ought to know how much remains in the food, what is the fate of the excess used and the nature of any decomposition products. A balance will have to be drawn between economic necessity and possible dangers. If it is essential to accept a risk, the extent of that risk should be known with some degree of exactitude.

(*f*) *Chemicals in food*—Here I shall deal with chemicals that are deliberately added for what may be called technical reasons, and I am using the term "chemical" in its widest sense. First, I should emphasise that improvements in food technology should be encouraged in every way, as they help to make the best use of the world's inadequate food supplies. Many alarmist statements have been made about the addition of chemicals to food, and most of these are generalisations from particular and exceptional examples. Hence they must be severely discounted, but they cannot be ignored. All reasonable people agree that the addition of either natural or synthetic chemicals to food may involve a risk to the consumer if there is inadequate knowledge of the pharmacological action of the chemical. Synthetic chemicals as a class cannot be regarded as potentially more toxic than natural ones, for some of the most dangerous poisons are isolated from natural material. It would be completely unreasonable to forbid the use of all chemicals in food manufacture; each must be considered on the information available. But I would suggest as a general guide that if a chemical has little or no food value, it should not be added to food if there is any doubt of its harmlessness and only then if there is justification for its use. Now it is very difficult, if not impossible, to prove that a substance is completely harmless. What can, however, be done, is for pharmacologists to lay down what tests should be carried out to obtain information upon which an opinion can be based. As knowledge increases, the criteria and tests may need to be revised. This increase in knowledge may have to be sought deliberately by planned research as recommended by the Zuckerman Committee. An important point will be upon

whom shall lie the responsibility for carrying out the tests laid down; this I shall come to later, when I make suggestions as to control.

Assuming that tests are prescribed and the responsibility for carrying them out has been localised, I foresee no practical difficulty with such substances as anti-oxidants, emulsifying agents, anti-staling agents and preservatives, as they are relatively pure substances of simple constitution and their numbers are not likely to be great. The position is not so simple if there are many substances of a class, any one of which may be used, and particularly when the members are of widely varying and complicated chemical structure. What I have in mind is food colours, and I must spend a little time in discussing them. These are used legitimately for improving the appearance or attractiveness of foods and, as they are used in quite small proportions, it may be suggested that the risk from them is negligible. This is not so, as we are all aware that certain colours are dangerous and some are already prohibited for use in food. The prohibition of these colours was made over 25 years ago and it cannot be accepted that these are the only ones that are harmful. Synthetic colours are usually made by coupling intermediates that in some instances are known to be toxic. Some of these intermediates are closely allied in constitution to substances that have been proved to be carcinogenetic and we do not know if they are re-formed in the body by breakdown of the colour. What happens to the characteristic linkage of the azo dyes during their passage through the body? How much of the colour is broken down and what are the resulting products? Is the body capable of removing sulphonic acid groupings? These are all questions that ought to be answered at some time. Meanwhile, no colour should be used in food if there are serious doubts as to its harmlessness. Manufacturers would still have a wide choice of colours that are not suspect in our present state of knowledge; and many additional shades can be produced by appropriate blending. The special action that may be necessary for controlling colours used in foods will be dealt with later.

A new development of recent times concerning the presence of chemicals in food is the specialised use of certain drugs in the breeding of poultry and animals for human food. Stilboestrol is used for the tenderization of poultry flesh and this involves the slow absorption of the drug by the birds over a long period. The unabsorbed drug is removed when the head and neck are cut off before the bird is sold to the consumer; and although the practice may result in the production of more marketable birds, what of the affect, if any, on the consumer of the meat? Antibiotics are used for increasing the rate of growth of pigs. The action appears to be rather the prevention of a depression of growth by specific action on the gut flora, and there may be a risk of the appearance of resistant strains, so that more and more of the antibiotic is required, with subsidiary effects not now apparent. Apart from the probably small risk to the public of normal use in this way, there is clearly a possible danger in placing powerful drugs in the hands of poultry breeders and stockfeeders.

(4) Clothing hazards—

The risks from clothing are few, but the effects of dyes, particularly in furs, must be considered. Furs are also sold permanently moth-proofed, and this involves the retention of chemicals that may be in contact with warm skin for several hours. Special detergents are sold for washing undergarments, and a property that makes a good advertising point is that no rinsing is required. The washed article, therefore, contains small but significant amounts of substances that remain in contact with the skin for many hours, with the possibility of absorption. Optical bleaching agents for white garments depend for their value upon substances remaining in or on the article treated, and which remain after washing. Although some of these substances are claimed to show their effect after repeated washings, and therefore must be very insoluble, there is no guarantee that absorption does not take place when in contact with the skin and perspiration. Crease-resisting agents are incorporated in some fabrics. These are likely to be made up into external garments; but the material may be in contact with the skin.

(5) Cosmetic hazards—

This country has no special legal control over the ingredients of cosmetics, and it does not seem sufficient protection to the public that anything can be sold for application to the external surface of the human body without consideration being given to the possible harmful effects. While we can assume that no manufacturer would include in his preparations a substance known to be harmful, can we be certain that all the substances used are, in fact,

harmless? If there is a hazard, it is likely to affect nearly half of the population of most countries. What of the purity of the dyes and colours used? These are applied regularly, in some instances in considerable amounts, and consideration must be given to their effects.

(6) HOUSEHOLD HAZARDS—

A variety of substances are now being sold as household detergents. They are very suitable for the purpose, but one of their characteristics is a tenacious adherence as a surface film on the article cleaned. They are so efficient that little rinsing appears necessary. The amount remaining after wiping may be minute, but there must be an accumulation on the drying cloth used and this may mean that no household plate, dish or glass is completely free from these powerful surface-acting agents, and significant amounts might remain on the crockery of catering establishments. Many of these detergents contain in addition a foaming agent, which contributes to the efficiency of the cleansing action. These foaming agents pass into sewers and rivers, and if there is a sufficient accumulation, patches of foam may collect and remain for days. While this is normally only a nuisance, there may be instances where water is drawn from a river for subsequent household use and filter beds may be incapable of removing the foaming agents. To remove the effect of the foaming agents in effluents other chemicals have been proposed, and the addition of these may bring other problems.

Detergents and foaming agents are also used in shampoos and here an incidental and unsuspected hazard has recently arisen. When hair is shampooed the liquid may run into the eyes, and irritation and slight damage has been caused by certain preparations.

There are some minor household hazards, such as the risk of children sucking toys coloured with soluble paint, which need not be dealt with except to say that it might be desirable if powers existed for their general control.

CONTROL OF PUBLIC HEALTH HAZARDS

Having considered the whole field of public health hazards somewhat comprehensively, but certainly not exhaustively, I should like to give my views of the sort of control I think necessary, bearing in mind the policy outlined by the Advisory Council. On principle the people of this country do not look kindly on controls, and this is a worthy attribute that should be encouraged. On the other hand, there is little antipathy to controls that are proved necessary. Everyone is agreed that where people cannot protect themselves some controls are necessary, and rarely is a voice raised against any reasonable measure to ensure public health.

The various hazards to which I have referred can be broadly divided into three classes, *viz.*—

(1) Hazards due to lack of hygiene;
(2) Hazards due to contamination;
(3) Hazards due to "chemicals," using that term in the widest sense.

(1) HAZARDS DUE TO THE LACK OF HYGIENE—

These are preventable or largely minimised by proper hygiene and are almost negligible with good commercial practice. In the household, control is the concern of the housewife, and education and common sense are sufficient safeguards. As regards food for sale to the public, we have already legislation to cover the cleanliness of food, and Government departments and local authorities have power to make any regulations in respect of places where food is prepared. Reputable manufacturers are little concerned with such control, as their domestic standards are generally higher than any officially prescribed minima.

(2) HAZARDS DUE TO CONTAMINATION—

These arise from traces of material unavoidably present even with good commercial practice, such as metallic contamination, or from substances remaining as traces after legitimate use for other purposes, such as insecticidal residues, or from substances permitted to be added in particular instances, such as preservatives. For these, statutory tolerances are appropriate, and as regards food, powers exist under Public Health or Food Acts to prescribe such limits. Similar powers would be appropriate for cosmetics and any other consumer goods liable to the hazard. The Atmospheric Pollution Research Committee

concerns itself with obtaining data on air contamination, but possibly rather more on the side of the prevention of nuisances than that of hazards; these two aspects clearly overlap.

At the present time the Food Standards Committee of the Ministry of Food has a Sub-Committee dealing with Metallic Contamination of Food and several reports have been published with suggested tolerances (copper, M. of F. Bulletin No. 611, 1951; arsenic, M. of F. Bulletin No. 616, 1951; lead, M. of F. Bulletin No. 628, 1951; tin, M. of F. Bulletin No. 685, 1953).

The Minister of Agriculture and Fisheries appointed a Working Party on Precautionary Measures against Toxic Chemicals used in Agriculture and its first report was published in 1951 (H.M. Stationery Office, Code No. 24–190). This Working Party was subsequently asked by the Ministers concerned (Joint Announcement by the Ministry of Agriculture and Fisheries, the Ministry of Health, the Ministry of Food and the Department of Health for Scotland, June, 1951) to enquire whether any risks arise, from the point of view of the consumer of the final product, in the use of toxic chemicals in agriculture and in the storage of food, and to make recommendations for protective measures should these appear to be desirable. No report has yet been issued.

It is in connection with hazards due to contamination that our Society can play a most important and essential part. Any tolerances allowed must be capable of being enforced, and it is the chemist who must develop the methods for determining all the contaminants and he is likely to be more and more called upon in connection with insecticidal residues and the like.

(3) HAZARDS DUE TO CHEMICALS—

These arise where the harmlessness of the chemical has not been proved, and here statutory tolerances are, in general, inappropriate; either the chemical should be permitted or its use should be forbidden. At present, powers exist for forbidding by regulation the use of a substance in food if it is known to be harmful. But the position as regards other consumer goods is not so clear.

In general, all sales are subject to the Sale of Goods Act, which requires any article sold to be reasonably fit for its normal purpose. The emphasis here is on fitness for use rather than the possibility of a hazard; even where there is a risk, the idiosyncracy of certain individuals may be raised as a defence. Other Acts, *e.g.*, the Factories Act and the Petroleum Acts, have some bearing on public health, but they are really more concerned with particular dangers and with nuisances. The Public Health Acts and the Food and Drugs Act have already been referred to, and Government departments and local authorities have powers to make regulations and bye-laws under various Acts.

Whatever control measures are envisaged, it seems generally agreed that provision must be made for periodical review. This can be achieved only by a permanent body such as was recommended by the Zuckerman Committee and approved by the Advisory Council.

The idea of a permanent or standing body is not new. The Pharmacy and Poisons Act, 1933, established a Poisons Board, and we now have twenty years' experience of its working. The Board meets periodically and considers what control is necessary over the sale of poisons to the public. The Board's recommendations are reported to the Home Secretary, who considers them and, if he thinks fit, makes Regulations that are laid before Parliament and to which objection can be raised. If necessary, control action can be taken very rapidly, and can equally quickly be amended. I do not think that any objection has been raised to any action that has been taken as a result of the recommendations of the Poisons Board; and this confirms my earlier statement that no objection is taken to reasonable controls designed solely to protect the public.

The standing committee should cover the whole field of public health hazards and there should not be difficulty in defining its relation to the authorities that now are responsible for some form of control. A new function would be the consideration of those hazards arising from chemicals whose harmlessness has not been reasonably proved. This is an important problem and, as it is likely to become of increasing magnitude, the earlier it is considered the better. It is also a very controversial problem, especially as regards food. I propose, therefore, now to consider chemicals in foods, being sure that hazards from chemicals in other materials can be fitted in on similar and easier lines.

Our present laws make it an offence to add any substance to any food so as to render

the food injurious to health. There is little direct evidence on the matter, but it is thought to have worked reasonably well in the past, and many people would like the position to continue. Some of us, however, consider that the time is rapidly coming, if not already here, when we must go a little further. Manufacturers of food are continually looking for some substance that will perform a particular function in improving their products, and chemical manufacturers are often able to supply something that will do the job. New chemicals may be found to have particular properties that could be useful in improving food, and the makers will doubtless advocate their use for that purpose. All these are legitimate objects and make for technological progress. But the substance chosen for use may be quite different in composition from any normal ingredient of food, and its fate and effect in the human body may be quite unpredictable. Consider the recent history of mineral oil in food. Such an oil has been taken internally as a medicine by many people in large amounts for long periods, and when of pharmaceutical quality it might have been presumed to be perfectly harmless as an ingredient of food, for which it is an efficient emulsifier. Recently it was found that in an emulsified form mineral oils seriously affect the absorption and utilisation by the body of some of the vitamins and provitamins, with the resulting possibility of deficiency effects. A further risk with such oils is that impure grades have been found to contain carcinogens, and once an oil has been added to food it is difficult, if not impossible, to ascertain the grade used. For these reasons restrictions were placed by Order on the use of mineral oil in food. At the time the Order was made there was no extensive use in food, and in consequence few manufacturers were affected and little dislocation of trade occurred. It might happen, however, that a particular substance was used on a large scale before it was found to be harmful, and any sudden embargo on its use might cause considerable trade embarrassment. An example to illustrate this point is that of nitrogen trichloride (Agene) used for treating flour. This substance had gained very widespread use before it was discovered that the treated flour contained about 2 parts per million of a potentially toxic substance, methionine sulphoximine. This substance produced substantial physiological effects in dogs, rabbits and ferrets; but the amount that might be consumed by a man in a year is extremely small and may well be within the ineffective dosage range. The only difference between the protagonists for and against the use of nitrogen trichloride is whether the margin of safety is wide enough. It might, however, have been found that the treated flour was definitely harmful to man, in which event the question of banning its use might have been acute. But what was found was that neither its harmlessness nor its harmfulness to man was proved; nevertheless it is pertinent to mention that, when an officially appointed committee reported in 1950 on improvers in flour, the Ministry of Food, the Ministry of Health and the milling industry accepted the recommendation that it was desirable eventually to discontinue the use of nitrogen trichloride and to use chlorine dioxide instead.

In considering any action to be taken on chemicals in food, a case can be made out for making a distinction between those that are already in use and new ones that might be suggested for use. To deal with the latter first, I would maintain that it is reasonable to insist that all new substances should pass appropriate pharmacological tests before being used for purposes that might otherwise involve a possible public health hazard. The responsibility for carrying out those tests should, in my view, rest upon those who make the article for such use or upon those who wish to use it for that purpose or upon both.

In fixing this responsibility, I have in mind two facts. The first is that for many years it has been an offence to add any substance to any food so as to render the food injurious to health. This principle should, I think, apply to all consumer goods. The second is that if a person is charged with unlawfully using a harmful substance, he has the defence that he did not know, and could not with reasonable diligence have ascertained, that it was harmful as used. This is a protection to him if not to the person harmed. I think the time has come to regard reasonable diligence as including the necessity of testing pharmacologically any novel substance to be used in or on the human body.

As regards the tests to be applied, it should be the responsibility of the standing committee to issue them and to assess officially the results obtained. In doing so, the relative pharmacological effects of the substance should clearly be related to the amount that is likely to be taken. Professor Frazer has suggested (*Endeavour*, 1953, **12**, 43) that dosage levels can be classified as ineffective, effective, toxic and lethal, and with man the general ratio of these is approximately 1:10:100:1000. He suggests that an acceptable dosage level of a chemical

to be used in food should be one-tenth of the ineffective dosage level, calculated as milligrams per kilogram of body weight. He, therefore, arrives at the following table—

Dosage group	Result	Approximate dose relationship
Lethal	Death	10,000
Toxic	Demonstrable tissue damage	1,000
Effective	Significant modification of structure or function ..	100
Ineffective	No significant modification of structure or function	10
Acceptable	—	1

He is satisfied that pharmacologists can specify appropriate short-term and long-term tests on different species of animals, which would enable non-cumulative dosage levels to be assessed.

It is known that several of the big organisations making food additives in this country recognise their responsibilities and carry out tests on these lines. It is desirable that such tests should be standardised and officially prescribed; clearly the right time for them to be carried out is before the substances are used and not while they are being used. It is not a new principle to apply special control to new substances. The Dangerous Drugs Acts place an embargo upon the manufacture and trade in certain drugs not known before a particular date; when satisfactory evidence is produced, the restrictions on a particular drug can be relaxed by Order.

When considering pharmacological properties, it is necessary to refer to carcinogens, because everyone is in agreement that no potentially carcinogenetic substance should be added to food. But here a difficulty arises; we do not always know when a particular substance has this characteristic. At a recent meeting on the apparently increasing incidence of cancer in modern times, it was stated that after affection of a person by a carcinogenetic substance a latent period of up to ten years may elapse before any effects are noticed. Once the body has become affected the process cannot be halted, and it may be years before any detection is possible, so making uncertain the possible cause. Any substance, therefore, that is reasonably suspected of possible carcinogenetic properties should be excluded from food.

There remains to consider what action, if any, should be taken with respect to chemicals at present in use. These, I think, should be reviewed by the standing committee, and an official pronouncement made regarding those for which there are reasonable grounds for doubting their harmlessness. All others should be tentatively permitted, but should be reviewed if evidence becomes available of possible risk. In some instances it might be desirable to take steps to ensure that positive evidence is available upon which a review could be made. At the present time certain Research Associations are examining some classes of products; but the whole field needs covering and this can best be done under the general direction of the standing committee so that no hazard is overlooked. In certain instances it might be appropriate to prescribe the purity of the substance used.

I will illustrate the suggested action by examples of two types of chemicals. The first is artificial sweeteners. For many years there has been a need for such substances, and two found favour in this country, *viz.*, saccharin and dulcin. Neither of these was thoroughly tested toxicologically until recent years, but the results of extended tests have now been published. For saccharin there was no evidence that it was in any way harmful, at any rate in the maximum amounts ever likely to be consumed. Dulcin, however, showed harmful effects in different species of animals at certain concentrations and under specified conditions. If the standing committee were in existence, it should review the evidence and decide whether it justified banning the use of dulcin. Such a pronouncement, whether for or against, would be of great value to the public and to industry. There are other artificial sweeteners that have been proposed for use, *e.g.*, P 4000, and as far as this country is concerned they may be regarded as new chemicals. P 4000 was advertised abroad as completely harmless to humans. The tests used to justify this statement were not disclosed, and many people were chary of accepting the assurance on the grounds that a substance containing nitro-groups, and which at high concentrations was a local anaesthetic, must be subjected to unequivocal tests before its use could be permitted in food. Later, more extended tests were carried out in the United States, and harmful effects were produced in animals. This shows the importance of prescribing the tests to be employed. Under my suggestions, P 4000 would not be permitted for use in food until the standing committee had reviewed the results of adequate tests.

The second illustration that I should like to give is that of food colours. I have already mentioned some of the hazards that might occur from their use and the lack of complete

knowledge of their fate in the human body. A sub-committee of the Food Standards Committee is dealing with preservatives, etc., and this includes food colours. This sub-committee has not yet reported and the nature of any recommendations that may eventually be made cannot be presumed. It is, however, carrying out in a limited field the functions that I think the standing committee should perform for the whole of the field. Without anticipating any conclusions of this sub-committee, I will illustrate how food colours fit in with my general picture.

Some hundreds of synthetic food colours are or have been used for colouring food. They are produced by chemical reactions from intermediates, some of which are known to produce toxic effects. For this reason colour manufacturers take particular care to supply for use in food those that are as pure as possible and free from harmful impurities. A certain amount of pharmacological work has been carried out on some of these colours over many years and in many countries; but the results of such work can be applied only to a colour conforming to the specification of the sample tested. Some of the colours used in food are produced in less pure grades for purposes other than food, and in order to avoid any unnecessary risk it is important that a colour permitted for use in food should conform to an appropriate chemical specification. This can only be achieved by defining that specification, and this leads to the conclusion, as I think inescapably, that a list of permitted colours is essential, each with its definite chemical specification. At present our law specifies a short list of prohibited colours and any colour not on that list may be used in food, unless its use can be challenged under the Food and Drugs Act. If it should be thought proper to protect the public more fully from a risk that might arise from harmful colours, then inevitably the policy must be changed to a permitted list specifying those colours that, after examination of the evidence, are considered suitable for use. It should be the function of the standing committee to compile this list from the colours now in use having regard to the pharmacological evidence available. No new colour should be added to the list without having been adequately tested and approved, and any colour on the list found to have harmful effects should be withdrawn at once or, according to the risk, after a specified time. Provision could easily be made for notification of intention and an opportunity given for commercial interests to express their views.

Colours in cosmetics should also be under review and there should be legal powers of control. This, I think, would be accepted by industry, as it would provide a protection for manufacturers from a risk that, although small, is ever present as a civil liability to them.

The field that I have attempted to survey is a large one, and difficult because it is concerned with a great number of risks, most of which, in themselves, are relatively small. Taken together they cannot be ignored, and the public is entitled to expect that consideration will be given to its protection. I hope that my survey will help to give a picture of the whole field and that what I have suggested is a rational, realistic and reasonable implementation of the policy of the Advisory Council on Scientific Policy.

Anniversary Dinner

In the evening following the Annual General Meeting, a Dinner to celebrate the seventy-ninth anniversary of the Society was held, by kind permission of the Master, in the Hall of the Worshipful Society of Apothecaries of London, Blackfriars Lane, London, E.C.4. The members and guests, numbering 100, were received by the President, Dr. J. R. Nicholls, C.B.E., F.R.I.C., and Mrs. Nicholls. The President afterwards took the Chair at the Dinner.

The guests of the Society and of the President included: Dr. Charles Hill, M.A., M.D., D.P.H., LL.D., M.P., and Mrs. Hill; H. W. Cremer, C.B.E., M.Sc., M.I.Chem.E., M.Inst.F., F.R.I.C.; Norman C. Wright, B.A., D.Sc., Ph.D., F.R.I.C., and Mrs. Wright; L. H. Lampitt, D.Sc., F.R.I.C., M.I.Chem.E., and Mrs. Lampitt; Stanley Robson, M.Sc., D.I.C., M.I.Chem.E., M.I.M.M., F.R.I.C., and Mrs. Robson; G. Roche Lynch, O.B.E., M.B., B.S., D.P.H., F.C.G.I., L.M.S.S.A., F.R.I.C.; Sir E. John Russell, O.B.E., D.Sc., F.R.S., and Lady Russell; The Hon. Mr. Justice Lloyd-Jacob, and Lady Lloyd-Jacob; Mrs. S. B. R. David, B.Sc., A.R.C.S., A.R.I.C.; R. A. Beck; J. Lee; and the Clerk of the Worshipful Society of Apothecaries, E. Busby.

After the loyal toast had been honoured, the President, Dr. Nicholls, presented Bernard Dyer Memorial Medals to the first two Medallists, who had given the first two Bernard Dyer Memorial Lectures to the Society and were present as guests. He recalled that Bernard Dyer had been one of the original members of the Society, remaining a member for 73 years until his death in 1948. He was an agricultural chemist, which made it most appropriate that the first Memorial lecturer should have been Sir E. John Russell, who was also an agricultural chemist. The President then presented the Medal to Sir John.

Sir John Russell, in thanking the President, said that he had happy memories of Bernard Dyer, Chaston Chapman and Augustus Voelcker, and had enjoyed a long connection with the Society.

Before presenting the second Medal to the Hon. Mr. Justice Lloyd-Jacob, the President said that the Bernard Dyer Memorial Medal had been designed by Mr. T. H. Paget, who had been responsible for the obverse designs of the coins and medals of the reign of King George VI. He much regretted that Mr. Paget had been unable to attend the dinner owing to illness. The President then presented the Medal to Mr. Justice Lloyd-Jacob, and said that it had been only chance that had turned him from chemistry to the legal profession.

The Hon. Mr. Justice Lloyd-Jacob, in thanking the President, said that he found himself in the position of a junior following an eminent leader, Sir John Russell. His own connection with the Society was more recent, being with members who had given evidence in the court in which he sat.

Mr. H. W. Cremer, President of the Royal Institute of Chemistry, proposed the toast of the Society. He said he was impressed by the large number of members of the Society who were also Fellows or Associates of the Royal Institute of Chemistry. He complimented the Society, now in its eightieth year, on its growth; there were now many more members concerned with analysis of articles other than foods, and in the subject groups of the Society and in the topics chosen for lectures the Society's field had been widely extended of recent years. The Society had played a very full part in the Analytical Congress at Oxford in September, 1952. He paid tribute to the President elect, Dr. Kent-Jones, and said that on his becoming President the Royal Institute of Chemistry had lost a greatly honoured Honorary Treasurer. In that capacity Dr. Kent-Jones had shown great wisdom, sympathy and understanding. The Institute's Benevolent Fund had benefited enormously by the sympathy with which Dr. Kent-Jones sought to relieve those in distress. He wished the Society every success, and coupled his toast with the name of the President.

The President, Dr. Nicholls, in reply, thanked Mr. Cremer for his appreciative remarks about the Society. He, too, knew that the majority of the members of the Society were members of the Royal Institute of Chemistry. The Institute was a qualifying body and, as such, might be described mathematically as the lowest common denominator of chemistry; if, so, analytical chemistry was the greatest common measure in all other branches of chemistry.

Dr. A. J. Amos, in proposing the toast of the guests, said that it was fitting that he should refer first to Dr. Charles Hill. Chemists would recognise in him the phenomenon of allotropy—existence in several forms of one and the same body; first he appeared as Secretary

to the British Medical Association, then as the "Radio Doctor," and then he reappeared as the Parliamentary Secretary to the Ministry of Food. There had been a great deal of liaison between our Society and the Ministry of Food. Dr. Hill's training, although in medicine, had been scientific, so that he understood the analyst's language. The Ministry had in many ways earned the gratitude of the Food Industry. He was sorry that the Ministry's very valuable Advisory Service had ceased. Dr. Norman Wright, Scientific Adviser to the Ministry of Food, had been a most successful Chairman of the Food Standards Committee, on which there was great scope for co-operation between the Ministry, the Food Trade and the analyst. Dr. Amos welcomed Mr. Cremer both as chemist and engineer; his Presidency of the Royal Institute of Chemistry was linked with his Past Presidency of the Institution of Chemical Engineers—a record which he believed was unique. Dr. Lampitt represented the President of the Society of Chemical Industry; the choice of him as proxy was very welcome, as he had been responsible for the formation of that Society's Food Group. Mr. Stanley Robson, the President of the Institution of Chemical Engineers, was also doubly welcome, for he was a Past President of the Society of Chemical Industry. Dr. Roche Lynch, representing the Master of the Worshipful Society of Apothecaries, was both host and guest, for he was the immediate Past Master of the Society of Apothecaries and a Past President of the Society of Public Analysts. He was pleased to welcome the Bernard Dyer Memorial Medallists as guests; Sir John Russell's outstanding contributions to analysis were well known, and Mr. Justice Lloyd-Jacob might well have been as eminent an analyst as he was a judge. Finally, but by no means least, he welcomed the ladies, without whose presence the Dinner would not have been complete. The toast of the guests was coupled with the name of Dr. Charles Hill.

Dr. Charles Hill, replying on behalf of the guests, said that he thanked the Society in general, and the President in particular, for the valuable co-operation they had extended to the Ministry of Food in the past 13 or 14 years. He understood Dr. Amos's regret at the disappearance of the Advisory Service, but although as analysts they might be sorry that the Ministry's functions grew less in number, as ordinary citizens they might well hope for the speedy departure of the whole Ministry. He felt sure that the work of the Society would succeed just as well in the absence of the Ministry. The guests had appreciated and enjoyed the Society's hospitality.

The President, Dr. Nicholls, then invested Dr. Kent-Jones with the presidential badge and wished him success during his term of office. Dr. Kent-Jones expressed his thanks to the Society for the honour it had conferred upon him.

Evaluation of Anti-Viral Compounds

By LÖIS DICKINSON

(*Presented at the meeting of the Biological Methods Group on Friday, October 26th,* 1951)

The desiderata and difficulties involved in any scheme of testing for anti-viral compounds are discussed and illustrated by the use of one such scheme making use of (*a*) a bacteriophage of *Pseudomonas pyocyanea*, (*b*) influenza-A virus, (*c*) vaccinia virus, (*d*) sheep abortion virus and (*e*) Rous sarcoma virus; (*b*) to (*e*) are *in ovo* tests. Extended to *in vivo* work, the tests cover influenza, ectromelia and mouse pneumonitis (Nigg) viruses in mice and Rous sarcoma virus in chicks. Correlation between the *in ovo* and mouse tests has been found for Nigg virus.

In this paper viruses are defined as "organisms or particles ranging in size from about 10 mμ to about 300 mμ with a common property of requiring the presence of living host cells (animal or bacterial) for growth." Current views on the nature of viruses range from conceptions of them as degraded bacteria to the idea that they are gene-like structures, which direct the infected cells' metabolism to produce more virus particles.

The evaluation of possible anti-viral compounds is complicated by the fact that, except for the larger viruses, there is no known active drug that can be used as a standard to justify a scheme of testing. Furthermore, all tests have to be *in vivo* tests, with the complication that toxicity to the host (bacteria, egg, tissue culture or animal cell) has to be considered from the beginning.

The fact that viruses are intracellular parasites does not mean that the task is impossible. Drugs could conceivably act by—

(*i*) direct inactivation of *extracellular* virus,
(*ii*) prevention of adsorption of virus on the cell, or its penetration into the cell,
(*iii*) prevention of release of virus from infected host cells, or
(*iv*) inhibition of the multiplication of *intracellular* virus.

The intracellular approach is perhaps the most important and certainly the most fascinating one. One virus particle enters a cell and, after a certain, definite interval of time, many particles, up to 300 for some bacteriophages (*i.e.*, bacterial viruses), come out.

We know almost nothing about virus metabolism, if any, or indeed whether the smallest viruses (about 10 mμ in size) are similar to the largest ones (about 250 mμ). Even in the group of the largest ones, the viruses differ considerably in their response to the various drugs, in the experimental animal and in man (Table I). The variation would be much

TABLE I

CHEMOTHERAPY OF THE LARGER VIRUSES

(Host not indicated)

Virus	Acridines	Penicillin	Sulphonamides	PABA	Chloromycetin	Aureomycin	Terramycin
L.G.V.	0, +	+	+	Stimulates	+	++	++
Trachoma	...	±	+	...	+	+	...
Psittacosis	±	+	0 (most strains)	0	+	+	...
Feline pneumonitis ..	+	±	0	...	±	...	...
Mouse pneumonitis ..	0	+	+	0	++	+++	+++
Sheep abortion ..	...	0	0	0	++	+++	+++

0 = No action; ±, +, ++, +++ = various degrees of activity.
Data taken from Findlay[1] and Dickinson and Inkley.[2]

greater if the tests had been carried out with different strains of each virus against a range of hosts.

Hence the problem of evaluating anti-viral compounds resolves itself into the choice of virus and host, since it is obviously impossible to test every virus in various host animals.

Man would be the ideal host and, in fact, for the common cold he is used as the experimental animal, although an inconvenient and expensive one. One might expect mammals to give a better host-picture than the chick embryo or a bacterial cell, but at the moment there are no grounds for such a view. Therefore, most workers choose the convenient laboratory hosts, bacteria, fertile eggs and mice. There appear to be as many different testing procedures as there are papers in the literature on virus chemotherapy. We have devised our own scheme (Fig. 1), and it is this scheme that is discussed here. It is far from perfect, still tentative, and we are prepared to alter it at any time. No one scheme can hope to cover every virus infection; it must be a compromise between the ideal and the practical.

Any virus used must obviously be conveniently handled in the laboratory, *i.e.*, it must not be very highly infectious to workers or to stock animals. The host animals must be available in quantity and must be free, as far as possible, from latent infections; pure-line strains are advantageous. The test viruses should be easily titrated and reasonably stable, so that stocks at constant titre are at hand. Some viruses, *e.g.*, sheep abortion virus, maintain their titre almost indefinitely at −20° C, but others, *e.g.*, mouse pneumonitis (Nigg) virus, lose activity even at −70° C. Freeze-drying is quite satisfactory for virus preservation, but there is usually a considerable loss of titre during the process.

Owing to the risk of cross infection of animals, it is not good policy to work with many viruses at once. On the other hand, it is not wise to limit the testing to only one host-virus system, for it is not known whether or not different small viruses have different points of attack; the individual response of the larger viruses does vary. We therefore test all compounds against a bacteriophage and regard the phage merely as one convenient test

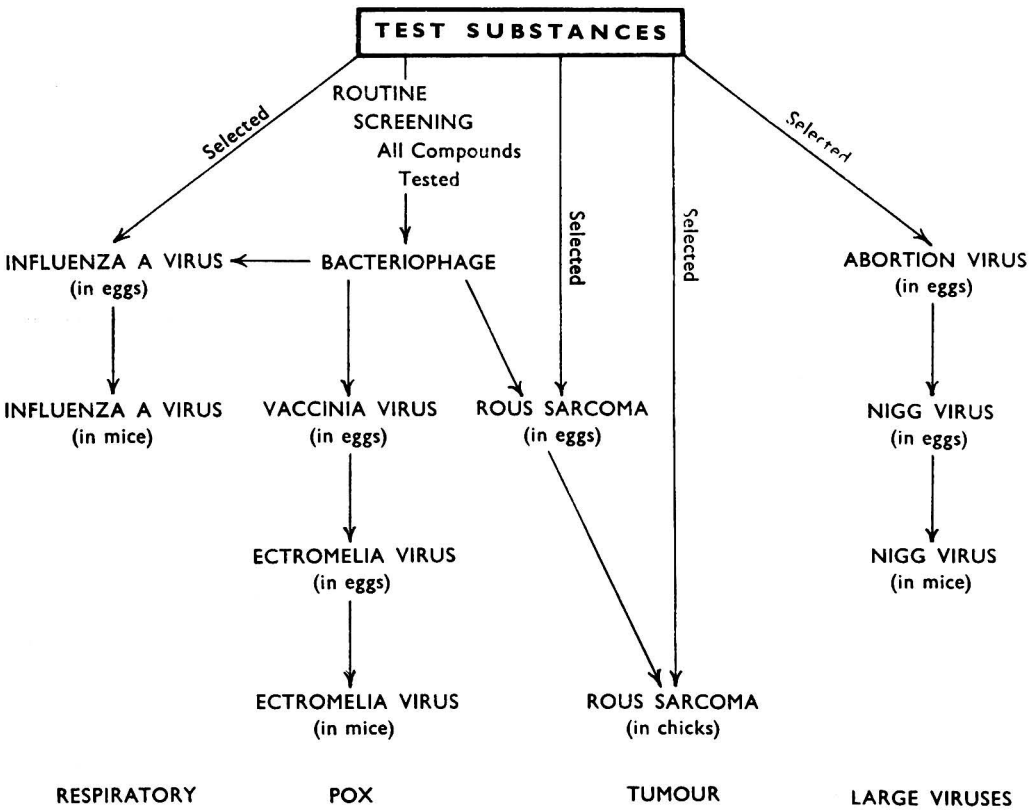

Fig. 1. Evaluation of possible anti-viral agents

virus; one junior assistant can carry out hundreds of such tests. For safety, however, many selected compounds are tested against other viruses, an attempt being made to cover the main groups of viruses as far as they can be classified at present, *e.g.*, the respiratory, pox and tumour groups of infections.

For the bacteriophage we use a phage of *Pseudomonas pyocyanea*. This has several advantages. The host cell is particularly resistant to drug action and grows readily in a simple medium of ammonium lactate and salts.

The test itself is very simple.[3] The drug is diluted in lactate medium and inoculated with a heavy inoculum of host cells plus about 20 phage particles per ml. After incubation for 24 hours, a control culture contains about 10^8 phage particles per ml. A loopful of such a culture, when spotted on a previously prepared plate of nutrient agar seeded with the host cell, lyses the area on which it has been spotted. If the phage has not multiplied, and provided that the host cells in the tube have grown (as observed visually), there is an area of "no lysis." With this system it is fairly easy to find out how the drugs are acting. One difficulty in this test has been that compounds are often active in the synthetic medium, but not when the test is carried out in broth. This is easy to understand when the drugs act by a direct viricidal effect, since proteins do "protect" many viruses. Sometimes, however, this inactivation by broth occurs when the drug concerned is neither acting by "contact" nor stimulating host growth.

Compounds active against phage are tested against other viruses. In addition, many compounds (and all new types of molecules) are tested against influenza-A virus in fertile eggs, regardless of the phage test results. Influenza A typifies a large and important group of viruses (the respiratory group) and, in addition, is in world-wide use as a test virus.

Compounds, *e.g.*, chloromycetin-like compounds, that are expected to show activity against the larger viruses are tested against the virus of sheep abortion.[2] The phage test would not be expected to detect such activity and, in fact, does not, as the phage is a small virus. The sheep abortion virus is most satisfactory for chemotherapy experiments in eggs. It is very stable and gives clear and consistent lesions on the chorioallantoic membrane of the developing chick embryo. The other virus used in this group is the virus of mouse pneumonitis (Nigg).

We cover the pox group of viruses by egg tests against vaccinia virus, and then by ectromelia virus. Both these are stable and easy to estimate on the chorioallantoic membrane.

The tumour-producing group of viruses is typified by Rous sarcoma 1 virus.

In ovo TESTING—

For tests in eggs against influenza-A virus, both drug and virus (100 egg-infective doses) are given via the allantoic sac, the drug being given 1 hour before the virus.[3] This test is so simple that influenza A has become our main virus for general screening. After incubation for 48 hours, the increase in virus is judged by the haemagglutination of fowl red blood cells by the allantoic fluid. The merits of this test are—

(*i*) It is simple and rapid.
(*ii*) It should indicate activity by contact, prevention of adsorption, release of virus or multiplication of virus. We believe that a compound should be active in this test if it has any activity at all.
(*iii*) The allantoic sac, the extra-embryonic bladder of the embryo, withstands larger amounts of drugs than can be administered by any other route.

The test may be modified so that the virus is given first and the drug several hours afterwards but, even so, it is difficult to exclude a contact action of the drug on the virus. For example, certain plant extracts are active 4 hours after infection[3]; however, the tannins in the extract inactivate the virus in the allantoic fluid, which is virtually protein-free. Incidentally, the active plant extracts are highly active against phage, and this effect is also one of direct contact. When the tannins are precipitated by serum or phenazone, the extracts are inactive against both phage and influenza.

An alternative route, to avoid this type of contact action, is to give the drug via the yolk sac. Unfortunately, drugs are much more toxic by this route and contamination is a more serious problem, although addition of penicillin and streptomycin (200 units of each per millilitre) usually prevents any trouble if the material cannot readily be sterilised.

There are two doubtful features in this yolk-sac test, namely, doubt as to the permeability of the embryonic membranes compared with that of mammalian cells, and doubt whether an effective drug concentration can be attained in the allantoic sac (*i.e.*, the site of virus proliferation), when drugs are given via the yolk sac. So far, although we have had compounds active in the allantoic sac, none have been active when given via the yolk sac.

Ginsberg, Goebel and Horsfall[4] found that a polysaccharide given via the yolk sac only reached the allantoic sac in 50 per cent. of the eggs; it prevented influenza growth in these eggs. The compounds we have tested may have been too toxic or not active enough to give the required concentration in the allantoic sac; this applies particularly to impure antibiotics or other natural products. Perhaps they are inactivated or broken down in the yolk sac.

To avoid the difficulties just described, influenza-A virus can be adapted to grow on the chorioallantoic membrane and the drug can be given via the yolk sac. This type of test works well for the larger viruses. For example, abortion and Nigg viruses are inhibited by chloromycetin, aureomycin and terramycin.[2] Other workers in this field use the yolk-sac route for infection and treatment, judging activity of compounds by their ability to prolong the survival of the embryos, but we find the membrane technique more satisfactory.

Difficulties arise when Rous sarcoma virus is used in this type of test because of the occasional irregularities of the response. Sometimes, enormous bean-sized sarcoma develop, even without any obvious damage to the membrane to account for it, and it is difficult to know whether one large tumour is equivalent to many little ones. We therefore fix, dry and weigh the membrane for quantitative assessment.[5]

The egg tests offer the following advantages—

(*i*) Small amounts of drug are required; usually a single dose. The compound cannot be excreted from the egg and is not normally inactivated.
(*ii*) Eggs have no known latent viruses of their own, provided that they come from a reliable source.
(*iii*) The tests are rapidly made.
(*iv*) The system is very simple.

Any compounds found active in the egg tests are investigated further in animals.

In vivo TESTING—

If a compound is active in eggs against influenza-A virus, it is tested in mice against the same virus adapted to mouse lungs. The virus is given intranasally and the drugs subcutaneously; results are assessed on deaths, survival times and on the extent of pulmonary lesions.

When a drug is active against vaccinia and ectromelia viruses in eggs, it is examined against ectromelia in mice. Ectromelia or "mouse pox" virus, given intraperitoneally to mice, causes death within 7 days. It is a highly infective natural pathogen of mice, and great care must be taken to prevent the spread of infection.

Compounds suppressing the growth of sheep abortion and Nigg viruses are tested against Nigg virus in mice by a similar technique to that used in the influenza test. For the Nigg virus, results in eggs and mice agree well with each other (Table II) and the clinical picture

TABLE II

CHEMOTHERAPY OF THE LARGER VIRUSES

Drug	Inhibitory dose, mg per egg, for Abortion virus	Inhibitory dose, mg per egg, for Nigg virus	Activity in mice against Nigg virus (drug given subcutaneously from day of infection)
Chloromycetin	1·0	2·0	++ (0·02 mg per g per day)
Aureomycin	0·25	0·25	+++ (")
Terramycin	0·06	0·06	+++ (")
Penicillin	Inactive 2,000 u.	2,000 u.	+ (4,000 u. per mouse per day)
Sulphathiazole	" 14·7	14·7	+ (0·2 mg per g per day)
p-Aminobenzoic acid ..	" 27·4	Inactive 13·7	0 (2 mg per g per day, orally)

+ = Prolongation of life only; ++ = no deaths, but lungs involved;
+++ = no deaths, lungs not involved.

in the treatment of the larger viruses is in agreement with these results. It is for this reason that we feel that the egg test should pick out a potential anti-viral compound in the other groups of viruses.

When the Rous sarcoma virus is used, two aspects of chemotherapy, the anti-viral and the anti-tumour, must be distinguished. The egg test should pick out a potential anti-viral agent, whereas the chick test should reveal both types of activity. Many compounds

are therefore tested in young chicks regardless of the results of the egg test. We have found several anti-mitotic agents to be active in the chick test, but inactive in the egg test.[5]

It will be seen that we have not included a very small virus in this scheme. Nigg and abortion viruses are in the 200 to 300-mμ size group, vaccinia is about 150 mμ, and influenza A about 100 mμ. Rous sarcoma is 75 mμ and *Pseudomonas pyocyanea* phage about 60 mμ. Foot-and-mouth disease and poliomyelitis viruses are only about 10 mμ in size. If necessary, however, we could include a mouse encephalomyelitis virus (10 mμ) in the scheme, but we should be satisfied if we found anything of use in the treatment of viruses in the groups we are studying at present. The larger ones are already fairly well covered and give some hope that the task is not impossible. The latent infections that may arise from such treatments are another problem.

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The Colorimetric Determination of Fructose and Sorbose

BY F. J. T. HARRIS*

When a fructose or sorbose solution is heated with the Folin - Denis reagent and tri-sodium phosphate a blue colour is produced. This colour can be used in determining the amount of sugar in the solution, with an accuracy of about 2 per cent. Sugars other than fructose or sorbose give much fainter colours.

DURING the course of other work the need arose for a method of determining fructose in the presence of small amounts of other sugars and the method of Englis and Miles[1] was investigated and extended to other sugars.

When fructose is mixed with the Folin - Denis phosphotungstic - phosphomolybdate reagent and tri-sodium phosphate, a blue colour develops on heating in boiling water. This colour is also produced by other sugars, but, except for sorbose, with them the colour is much less intense.

Experimental

The colour produced was measured on a Spekker absorptiometer. Ten millilitres of a 12·5 per cent. fructose solution and 5 ml of the phosphotungstic - phosphomolybdate reagent were mixed in a 100-ml calibrated flask, which was set aside for 4 minutes. Ten millilitres of a 0·5 *M* tri-sodium phosphate solution were added and the flask was placed in boiling water for 10 minutes. The mixture was then cooled and diluted to 100 ml. It was found that the transmittance of the mixture decreased at the longer wavelengths, so a red No. 608 filter was used for further work (see Table I).

Table I

EFFECT OF FILTERS ON OPTICAL DENSITY MEASURED IN A 1-cm CELL

Filter No.	601	602	603	604	605	606	607	608
Approximate wavelength at peak, mμ	431	467	489	515	548	570	598	682
Optical density with 0·125 g of fructose	0·112	0·141	0·158	0·172	0·199	0·210	0·228	0·246
Optical density of blank solution	0·011	—	—	0·013	—	0·015	—	0·020

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The effect of varying the interval between the addition of the reagent and the addition of the phosphate was investigated. The final optical density of the solution increased as the interval increased up to 5 minutes and then decreased with further increase in the interval (see Table II). A 5-minute interval was used in all subsequent work instead of the 4-minute interval specified by Englis and Miles.[1] The tri-sodium phosphate solution used was 0·5 *M* (19 per cent. w/v) instead of 20 per cent. as used by the American workers.

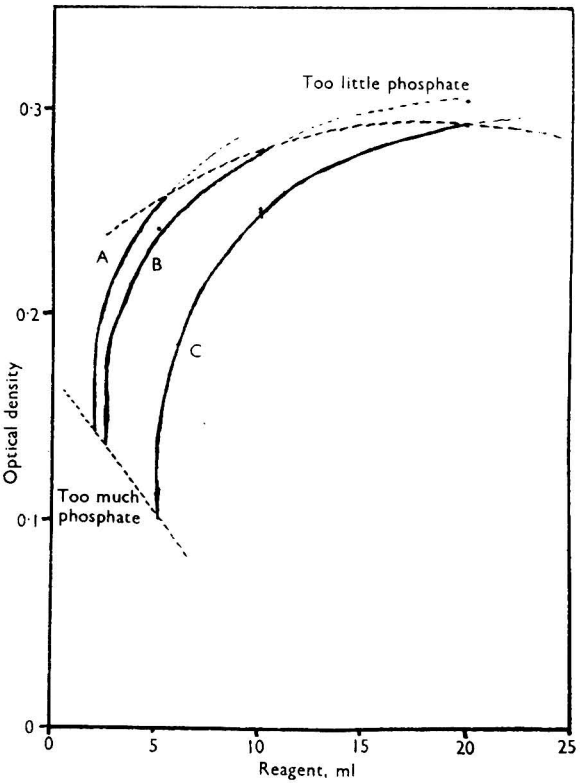

Fig. 1. Effect of Folin-Denis reagent and phosphate on optical density. Curve A, 5 ml of phosphate; curve B, 10 ml of phosphate; curve C, 20 ml of phosphate

The stability of the colour was investigated and it was found that the decrease in optical density proceeded steadily, but was only 2½ to 3 per cent. over a period of 21½ hours. The decrease in, say, 1 hour is consequently negligible.

The variation in the optical density produced by varying the amounts of reagent and phosphate was investigated. An increase in the amount of reagent used increased the colour, whilst increase in the amount of phosphate decreased the colour (see Fig. 1). If the volume

TABLE II

EFFECT OF VARIATION OF INTERVAL BETWEEN ADDITIONS OF REAGENT AND PHOSPHATE

1-cm cell, No. 608 filter

Interval, minutes	2	4	5	8	10
Optical density of 0·125 g of fructose ..	0·210	0·246	0·251	0·226	0·212
Optical density of blank solution	—	0·020	0·021	—	0·021

of the phosphate was less than that of the reagent, or if the volume of phosphate was more than about four times that of the reagent, results were erratic and the green colour produced varied greatly. The amounts finally adopted were 5 ml of reagent and 10 ml of phosphate.

Variation in time of heating was also investigated. The optical density increased as the time of heating increased, but the greatest optical density was almost reached in about 10 minutes.

TABLE III

EFFECT OF TIME OF HEATING IN BOILING WATER

Time, minutes	0	2	5	7	10	12	15	30
Optical density of 0·125 g of fructose less blank value, measured in a 1-cm cell	0·011	0·174	0·205	0·220	0·241	0·237	0·241	0·254

Variations in the volume of the sugar solution caused variations in the final optical density, so the volume of sugar solution was standardised at 10 ml.

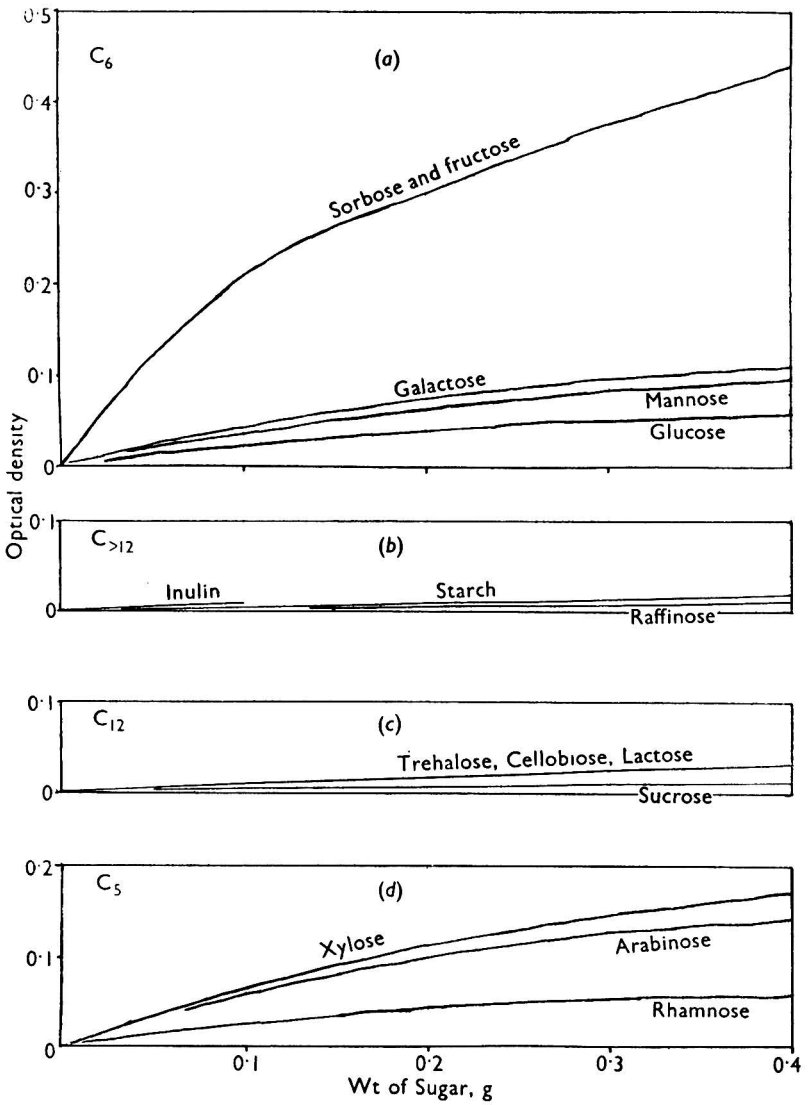

Fig. 2. Optical densities produced by various sugars, with 1-cm cell and No. 608 filter. (*a*), C_6 sugars; (*b*), $C_{>12}$ sugars; (*c*) C_{12} sugars; (*d*), C_5 sugars

Method

Reagents—

Folin - Denis phosphotungstic - phosphomolybdate reagent[2]—To 100 g of sodium tungstate and 20 g of phosphomolybdic acid, add 100 g of phosphoric acid and 700 ml of water. Boil for 2 hours, cool, filter if necessary and dilute to 1 litre.

Tri-sodium phosphate solution, 0·5 M—Dissolve 190 g of pure tri-sodium phosphate in water and dilute to 1 litre.

Procedure—

Mix 10 ml of sugar solution and 5 ml of the Folin - Denis reagent. After 5 minutes, add 10 ml of the 0·5 *M* tri-sodium phosphate solution and place the flask in boiling water. After 10 minutes remove the flask from the boiling water and at once dilute the solution with cold distilled water to about 95 ml. Allow to cool, dilute to the mark and measure the optical density of the solution (compared with water) in a 1 or 4-cm cell using a red No. 608 filter.

Prepare a comparison solution by substituting 10 ml of water for the 10 ml of sugar solution.

Results

The method was tried with starch, raffinose, inulin, maltose, trehalose, cellobiose, lactose, sucrose, sorbose, fructose, galactose, mannose, glucose, xylose, arabinose and rhamnose. The sugars used were nearly all either of analytical reagent grade or bacteriologically pure. It was found (see Tables IV and V and Fig. 2) that the only two ketohexoses investigated (sorbose and fructose) gave identical optical density - concentration graphs. The other sugars all gave much less colour.

Different batches of reagent were found to give slightly different results.

Table IV

Optical density of sorbose and fructose in a 4-cm cell

Amount of sugar, g	..	..	0·02	0·04	0·06	0·08	0·10
Optical density	..	..	0·236	0·424	0·600	0·770	0·924

Table V

Optical density of 0·1 g of various sugars in a 4-cm cell

Sugar	Optical density	Sugar	Optical density
Starch	0·020	Sucrose	0·005
Raffinose	0·010	Galactose	0·210
Inulin	0·061	Mannose	0·132
Maltose	0·141	Glucose	0·082
Trehalose	0·042	Xylose	0·269
Cellobiose	0·042	Arabinose	0·248
Lactose	0·042	Rhamnose	0·079

In a number of determinations with known amounts of fructose the error was found to be about 1 to 2 per cent.

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A Critical Examination of the Ferrocyanide Determination of Zinc

By MARY R. RICHARDSON and ALEXANDER BRYSON

The titration of zinc with potassium ferrocyanide has been critically examined and the end-point of the titration when internal indicators are used has been correlated with the potential drop occurring at the end of the potentiometric titration.

The determination of zinc by titration with potassium ferrocyanide in acid solution with diphenylamine or diphenylbenzidine as an internal indicator was first proposed by Cone and Cady[1], and the method was subsequently investigated by Kolthoff[2] and Kolthoff and Pearson.[3] These last workers carried out an extensive survey on the influence of various factors on the accuracy of the method and advised the general use of back-titration, stating that the direct titration was too slow. However, when applied to the analysis of a number of ores in this laboratory, the procedure they recommended proved to have unexpected difficulties and, in the hands of students, gave widely divergent results. Consequently a thorough investigation of the problem was undertaken. In this paper we have examined critically the method as applied to pure zinc solutions and have described the influence of inorganic salts and operating conditions on the accuracy of the method. The results of this research are the outcome of more than 300 potentiometric titrations and as many titrations with indicator alone.

The reaction of zinc ions in acid solution with potassium ferrocyanide closely follows the equation—

$$3ZnSO_4 + 2K_4Fe(CN)_6 \rightarrow K_2Zn_3[Fe(CN)_6]_2 + 3K_2SO_4$$

The reaction is not completely stoicheiometric and the results are influenced by the operating conditions. Variations of ± 3 per cent. in zinc values are common. Many workers have attempted to define the conditions necessary to ensure zinc values equal to the theoretical, but none has succeeded. It is generally agreed that under the best operating conditions the error is about -1 per cent. and our investigations confirm this. Hitherto the reaction has been followed with an internal indicator such as diphenylamine,[1,2,3] or potentiometrically,[4,5,6] but no attempt seems to have been made to correlate the potentiometric and indicator end-points. When diphenylamine or diphenylbenzidine is used as an internal indicator, it is necessary to add a small amount of potassium ferricyanide to the solution. The redox potential of the system is governed by the ratio of the ferricyanide to the ferrocyanide ions and is sufficiently high at about 0·6 volt against a saturated calomel electrode to convert the indicator into the purple form. As the reaction proceeds, this colour is replaced by a blue, which persists until shortly before the true end-point and afterwards fades (the "false end-point"). On setting aside or titrating slowly, the original purple colour re-appears and sharply changes to a yellow-green at the final end-point. The reasons for these changes will be discussed.

The reaction has been investigated in respect of the variables: concentration of sulphuric acid; effect of the salts ammonium sulphate, ammonium chloride and potassium sulphate; ferricyanide concentration; direct and back-titrations; effect of the speed of titration and the rate and point at which excess of ferrocyanide is added for the back-titration; zinc concentration; effect of temperature; and interferences.

Experimental

Reagents—

All materials used were of analytical reagent grade.

The 0·05 *M* zinc solution was prepared by dissolving 14·34 g of zinc sulphate ($ZnSO_4.7H_2O$) in distilled water and diluting to 1 litre. It contained 3·26 g of zinc in 1000 ml. The zinc content of the solution was checked by the pyrophosphate method.

The 0·05 *M* and 0·025 *M* potassium ferrocyanide solutions were prepared by dissolving 21·12 and 10·56 g, respectively, of potassium ferrocyanide ($K_4Fe(CN)_6.3H_2O$) in distilled water and diluting to 1 litre. The solutions were standardised potentiometrically against a standard

ceric sulphate solution. The ferrocyanide solution should be kept in a dark bottle, since on exposure to light it deteriorates rapidly by forming ferricyanide (easily observed by the gradual changing of the colour of the solution from pale green to orange-yellow) and the deposition of a brownish flocculent precipitate, presumably ferric hydroxide. These solutions should not be used because an excess of ferricyanide is detrimental to the sensitivity of the indicator end-point.

The diphenylbenzidine and diphenylamine solutions were made up to 1 per cent. in concentrated sulphuric acid. The potassium ferricyanide solution was a 1 per cent. solution of potassium ferricyanide in water. The indicators were made up freshly every few days.

BASIC PROCEDURES—

Many determinations were made potentiometrically with indicator present for comparison, others with indicator alone. Because of the need for taking readings during the potentiometric titrations these titrations were carried out at a slower rate than those with indicator alone. Potentiometric titrations were carried out with a Cambridge pH meter, a saturated calomel half-cell with ground-glass sleeve and a platinum electrode. Automatic stirring was used throughout.

Micro-burettes were used for all titrations requiring less than 10 ml of titrant.

Except where otherwise stated all chemicals were added before the commencement of titration. Concentrations of reagents are given as at the end-point, since all our work indicates that this, rather than the commencement of the titration, is the critical point.

CHARACTERISTICS OF THE POTENTIOMETRIC TITRATION—

Fig. 1 shows a typical potentiometric graph. The potentiometric end-point occurs from 0·50 to 0·52 volt against a saturated calomel electrode at an acid normality of 1 to 2;

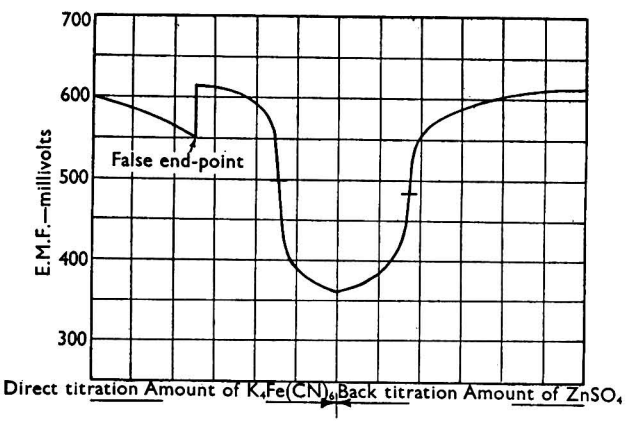

Fig. 1. Characteristics of the potentiometric titration graph

this agrees well with the transition potential of diphenylamine and diphenylbenzidine, found by Kolthoff and Sarver[7] to be 0·51 ± 0·1 volt.

The interesting phenomenon is the dip in the curve before the potential drop, which coincides with the indicator "false end-point." At the normal rate of potentiometric titration of 150 mg of zinc, this occurs about 2 ml before the end-point. With slow titration it may occur as much as 4 or 5 ml before. With smaller amounts of zinc it tends to occur later and with larger amounts earlier. Its position and size are affected by the sulphuric acid concentration (see below), and any substance that decreases the potential drop at the end-point also decreases the false end-point dip, without eliminating it.

De Koninck and Prost[8] suggested that the zinc ferrocyanide first formed slowly changes into potassium zinc ferrocyanide. Kolthoff and Pearson[3] suggest that at the false end-point the ferrocyanide concentration decreases owing to the transformation of the precipitate into the stable and less soluble salt. We are not in agreement with these views. The potential during the titration to within 2 to 3 ml of the false end-point is fairly constant and is determined by the ratio of the ferricyanide to ferrocyanide ions, which is controlled

by the solubility of the double salt potassium zinc ferrocyanide produced. As the potential remains fairly constant, it seems that the same molecular species is present at the time. The steady drop near the false end-point and the sudden rise of potential thereafter, accompanied by the change of colour from blue to purple are indications of desorption and it is suggested that the precipitate adsorbs zinc ions and the positively charged indicator ions during the greater part of the titration. At the iso-electric point, which occurs before the true end-point, flocculation occurs and the zinc ions are desorbed together with the indicator. The formation of fresh potassium zinc ferrocyanide then raises the value of the potential. It is noteworthy that no appearance of this dip in the potential curve occurs in the back-titration. The adsorption theory also explains the earlier appearance of the false end-point at slow rates of titration. The final precipitate, however, is still deficient in ferrocyanide and no stated explanation of this appears to be convincing. It appears that further work is necessary to determine the structure of the double ferrocyanide formed in these titrations.

ACID CONCENTRATION—

Kolthoff and Pearson[3] recommend a sulphuric acid normality of approximately 1 at the end-point, and they state that although the most favourable acidity is from 0·5 to 1·5 *N*, the degree of acidity is of minor importance.

Results of potentiometric titrations carried out by us at various sulphuric acid normalities are indicated in Fig. 2.

Evaluation of the potentiometric curves and figures presented in Tables I and II indicates that the sulphuric acid concentration should be about 2 *N* at the end-point of the titration. At sulphuric acid concentrations of between 1·7 and 2·1 *N* the indicator end-point coincides with the potentiometric end-point. The indicator changes are improved, the colour develops quicker and the end-point is made sharper. At low concentrations of zinc the speed of the reaction is considerably increased and the colour change at the "false end-point" takes place more rapidly. At still higher acid concentrations the indicator end-point, although brilliant, takes place after the potentiometric end-point; the potential drop is also decreased (Fig. 2).

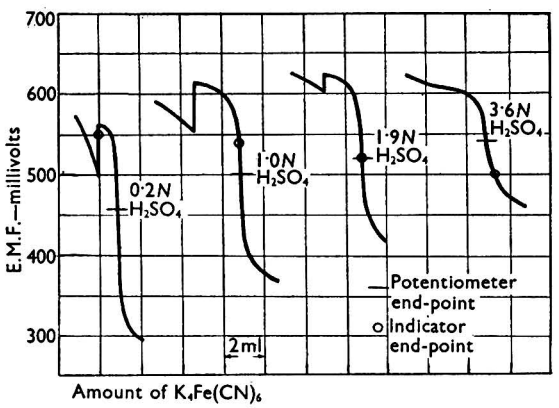

Fig. 2. Potentiometric titration graphs for various concentrations of sulphuric acid

Hydrochloric acid and perchloric acid were also tried at 1 *N* concentration with or without ammonium sulphate in potentiometric and indicator titrations. They gave lower results and poorer indicator end-points than sulphuric acid, and are not recommended.

INFLUENCE OF INORGANIC SALTS—

In Tables III and IV are shown the errors produced in presence of various amounts of ammonium sulphate, ammonium chloride and potassium sulphate.

Table III shows that at least 1·5 g of ammonium sulphate per 100 ml are required to give consistent results and in all further experiments 1·5 g of ammonium sulphate per 100 ml of solution were added as standard practice.

TABLE I

EFFECT OF SULPHURIC ACID CONCENTRATION ON POTENTIOMETRIC TITRATIONS

Experiment	Temperature	Total zinc present, mg	Zinc concentration at end-point, mg per ml	Deviation from theory: Acid concentration 2 *N* at end-point, Potentiometrically, %	Deviation from theory: Acid concentration 2 *N* at end-point, Indicator, %	Deviation from theory: Acid concentration *N* at end-point, Potentiometrically, %	Deviation from theory: Acid concentration *N* at end-point, Indicator, %
1	Room temperature	250	1·2	−0·8	−0·8	−1·1	−1·2
2	"	150	1·5	−0·8	−0·8		
3	"	150	0·8	−0·8	−0·9	−1·0	−1·1
4	"	75	0·4	−0·8	−0·8	−1·2	−1·5
5	"	30	0·3	−0·8	−0·8		
6	"	30	0·15	−0·3*	−0·2	−0·5*	−2·0§
7	"	15	0·4	−0·8*	−0·8	−0·3	−0·3
				−0·5*	0·0	−0·4‡	−1·5
				−0·3*	−0·3		
8	"	15	0·2	−0·6†	0·0	−0·8‡	−1·6
				−0·2†	0·0	−0·4‡	−1·0
9	"	15	0·08	−2·1‡	−2·4	−2·0‡	−5·7§
				−1·7‡	−1·6	−1·1‡	−4·9§
				−1·6‡	−1·6		
				−1·3‡	−1·6		
10	50° to 60° C	15	0·4	−2·7*	−2·2	−3·0†	−3·0
				−2·2*	−2·1	−2·8†	−3·0
				−0·3*	−0·8		
11	"	15	0·2	−1·5†	−2·2§	−1·1†	−4·4§
				−0·5†	−1·5§	−1·0†	−3·8§
12	"	15	0·08	−2·0‡	−3·0§		

* Titration slower than usual (10 to 15 minutes).
† Titration slow (20 to 30 minutes).
‡ Titration slow (up to 60 minutes).
§ Poor indicator end-point.

TABLE II

EFFECT OF SULPHURIC ACID CONCENTRATION ON TITRATIONS WITH INDICATOR ALONE

Experiment	Total zinc present, mg	Zinc concentration at end-point, mg per ml	Deviation from theory: Acid concentration 2 *N* at end-point, at room temperature, %	Deviation from theory: Acid concentration 2 *N* at end-point, at 50° to 60° C, %	Deviation from theory: Acid concentration *N* at end-point, at room temperature, %	Deviation from theory: Acid concentration *N* at end-point, at 50° to 60° C, %
13	150	0·8	−0·8	—	−1·0	—
14	75	0·4	−0·8	—	−1·3	—
15	30	0·15	−0·9	—	—	—
16	15	0·4	−0·5	−0·8	−0·2	−2·0
			−0·5	−0·8	+1·1	−0·5
			−0·1	−0·8	+1·7	0·0
			+0·3	−0·5		
				−0·5		
17	15	0·2	−1·4	−2·2	−0·8	−3·0*
			−0·5	−1·7	−0·2	−2·2*
			+0·1	−0·5	+1·4	
				+0·8		
				+0·8		
18	6	0·3	−0·8	−0·7		
			−0·8	−2·2		
			−1·5			

* Poor indicator end-point.

The authors could not confirm Kolthoff and Pearson's claim[3] that high concentrations (7 g per 100 ml) of ammonium sulphate produced errors of about +4 per cent. except in the slowest titrations. When the ferrocyanide was added with the burette tap fully open until within 0·2 ml of the known end-point (total titration time, 45 seconds), the results were about 3 per cent. too high. But a pause of only 10 to 15 seconds before the dropwise addition gave results equal to those with smaller amounts of ammonium sulphate at an acid

TABLE III

EFFECT OF AMMONIUM SULPHATE ON THE TITRATION ERROR

Amount of ammonium sulphate per 100 ml, g	Time of titration, minutes	Error at acid normality of	
		1 *N*, %	2 *N*, %
0	4 to 5 (normal)	−2·7	−2·3
0·5	"	−1·9	—
1·5	"	−1·0	−0·8
7	"	−1·0	−0·8
7	1 (slight pause before end-point)	+0·2	−0·7
7	¾ (straight through to end-point)	—	+3·2

TABLE IV

EFFECT OF AMMONIUM CHLORIDE AND POTASSIUM SULPHATE ON THE TITRATION ERROR

Salt per 100 ml added, g	Error with NH_4Cl, %	Error with K_2SO_4, %
1·5	−1·6	−1·9
2·0	−1·5	−1·6
3·0	—	−1·0
5·0	−2·0	−1·0
12·5	−4·2	—

NOTE—Values are means of two or more titrations.

normality of 2 and about 1 per cent. higher at a 1 *N* acidity. However, a high concentration of ammonium sulphate does tend to retard the initial colour development and gives a less well defined end-point. These effects are less marked at 2 *N* than at 1 *N* acidity.

Potassium sulphate can replace ammonium sulphate if present in amounts greater than 3 g per 100 ml; therefore, it appears that ammonium ions are not indispensable to the colour change as Kolthoff states.[2]

Although Cone and Cady[1] advocate the use of 10 g of ammonium chloride in a volume of about 150 ml, its substitution for ammonium sulphate is not satisfactory (see Table IV). Large amounts of ammonium chloride lower both potentiometric and indicator results, make the indicator end-point indistinct and decrease the potential drop at the end-point.

FERRICYANIDE—

Two to three drops of a 1 per cent. solution of potassium ferricyanide in water were used per 100 ml of solution. An increase in the number of drops has at first no apparent influence on the end-point, but in presence of larger amounts the colour change of the indicator becomes increasingly indistinct and eventually the false end-point can no longer be observed. We confirmed Kolthoff and Pearson's[3] finding that with large amounts of ferricyanide (1 ml of 10 per cent. solution) the indicator turns dull green instead of purple and that the amount of ferricyanide suggested by Bradley[9] is too high.

DIPHENYLBENZIDINE SULPHATE AND DIPHENYLAMINE SULPHATE INDICATORS—

Although diphenylbenzidine sulphate was the indicator used generally throughout this work, most results were confirmed with diphenylamine sulphate indicator, a correction of 0·03 ml per drop of diphenylamine sulphate being added, as recommended by Cone and Cady[1]

and confirmed by Kolthoff and Pearson[3] and ourselves. No correction is necessary with the diphenylbenzidine sulphate and its omission has no effect on the potentiometric curve. Diphenylamine sulphate appears to have no advantages to offset the necessity for a correction. Two to four drops of diphenylbenzidine sulphate were added per 100 ml.

COMPARISON OF DIRECT AND BACK-TITRATION—

Direct titrations with potassium ferrocyanide for amounts of zinc greater than 40 mg in a solution 2 *N* with respect to sulphuric acid at the end-point and containing 1 to 2 g of ammonium sulphate per 100 ml, give results that are about 0·8 per cent. low and reproducible to within 1 or 2 parts per thousand. For greater amounts of zinc the speed of titration has little effect.

Titrations carried out by adding an excess of ferrocyanide after such a direct titration (*i.e.*, one in which the ferrocyanide is added at normal speed as far as the false end-point and then dropwise to the direct end-point) give potentiometric results that are the same as those from direct titration. The indicator end-point is not as sharp as in the direct titration and results tend to be lower (see Table V). With smaller amounts of zinc this effect is more marked.

TABLE V

COMPARISON OF RESULTS (POTENTIOMETRIC AND INDICATOR) FROM DIRECT TITRATION AND SUBSEQUENT BACK-TITRATION

All titrations were at a final acidity of 2 *N*, at ammonium sulphate concentration of 1 to 2 g per 100 ml and at room temperature. A 5 to 10 per cent. excess of ferrocyanide was added for the back-titration

Total zinc present, mg	Concentration of zinc at end-point, mg per ml	Deviation from theory: By direct titration, Potentiometrically, %	By direct titration, Indicator, %	By back-titration, Potentiometrically, %	By back-titration, Indicator, %
150	0·8	−0·8	−0·8	−0·8	−1·1
75	0·4	−0·8	−0·9	−0·8	−1·1
30	0·3	−0·8	−0·8	−0·7	−1·5
30	0·15	−0·3	−0·2	−0·2	−2·0*
15	0·08	−1·5	−1·6	−1·6	−7·0*

* Poor indicator end-points.

NOTE—Results are means of two or more titrations, which varied by 0·2 per cent. or less.

It is apparent that back-titration with indicator under these conditions produces greater errors.

Kolthoff and Pearson[3] claim to have brought the error of the titration almost to zero by their recommended back-titration procedure after the ferrocyanide has been added fairly rapidly until an excess of 5 to 15 per cent. is present, *i.e.*, without waiting for the appearance of the false end-point during the addition of the ferrocyanide. No stress is laid on the speed of the ferrocyanide addition, although in a footnote to (their) Table IV they explain that in the titration of 25 ml of 0·05 *M* zinc sulphate solution "the ferrocyanide (about 35 ml) was added fairly rapidly (70 to 90 seconds). Near the end-point the speed of the ferrocyanide was decreased."

Our work confirms that of Urbasch[10] and previous work of Kolthoff himself,[2] namely, that results are affected by the rate at which the excess of ferrocyanide is added.

It seems that Kolthoff and Pearson[3] succeeded in approximating to the conditions shown in experiment 2 of Table VI, aided no doubt by the fact that they were working with zinc solutions of known strength and so knew the ferrocyanide titre in advance. With unknown solutions slight overshooting is inevitable at this rate of titration and conditions are more likely to approximate to those in experiment 3 of Table VI.

We further confirmed Kolthoff and Pearson's finding that the amount of excess ferrocyanide has no effect on results.

In view of our findings, those of Urbasch[10] and Kolthoff's previous work[2] it seems certain that the back-titration procedure recommended by Kolthoff and Pearson is unsatisfactory

except with the most carefully-controlled titration time after a preliminary direct titration to find the direct end-point.

EFFECT OF ZINC CONCENTRATION—

Both the total amount of zinc present and the zinc concentration affect the titration as shown in Tables I and II.

Results 1 to 6 in Table I are the average of at least three titrations, which varied by 0·2 per cent. or less.

Results 13 and 14 in Table II were both averages of four determinations, which varied by 0·2 per cent. or less. Experiments 16, 17 and 18 were carried out fairly slowly, but more

TABLE VI

EFFECT OF SPEED OF ADDITION OF EXCESS FERROCYANIDE ON POTENTIOMETRIC AND INDICATOR RESULTS OBTAINED BY BACK-TITRATION

All titrations carried out at an acidity of 2 *N*, at ammonium sulphate concentration of 1 to 2 g per 100 ml and at room temperature

Experiment	Speed of addition	Total zinc present, mg	Deviation from theory: Potentiometrically, %	Deviation from theory: Indicator, %
1	Ferrocyanide added steadily to false end-point, then dropwise to a 10 per cent. excess	150	−0·6	−0·7
			−0·8	−0·8
		75	−0·8	−1·0
			−0·9	−0·9
		15	−0·1	−0·4
			−0·3	−0·3
2	Ferrocyanide added steadily to 0·5 ml before direct end-point, then dropwise to a 10 per cent. excess	150	0·0	−0·1
		75	−0·2	−0·4
		15	—	+1·6
3	Ferrocyanide added steadily to 0·5 ml after direct end-point, then dropwise to a 10 per cent. excess	75	+0·7	+0·6
4	Ferrocyanide added steadily to a 10 per cent. excess	150	+1·3	+1·2
			—	+1·3
		75	+1·7	+1·6
			+1·5	+1·3
			+1·7	+1·5
		15	+3·3	+2·9

NOTE—Steadily means a titration rate of 30 ml per minute.

rapidly than corresponding experiments 7 and 8, in which speed was governed by the mode of titration. Experiments 1 to 5 (Table I) and 13 to 15 (Table II) show that titration with a 2 *N* concentration of sulphuric acid at the end-point at room temperature gives satisfactory results with 30 mg of zinc or more, provided the zinc concentration at the end-point is not less than 0·3 mg per ml.

With 15 mg of zinc the titration is not so reliable, even when the zinc concentration is 4 mg per ml. The initial indicator colour is slower to develop, as noted by Brennecke[11] and when the zinc concentration is only 0·08 mg per ml with the sulphuric acid normality at 1, the indicator colour will not develop until the false end-point is reached. Increased acid concentration gives some improvement. The indicator change in the potentiometric titration occurs more rapidly than the potential change. Hence the difference between indicator results in experiments 7 and 8 in Table I and results in 16 and 17 of Table II. However, the indicator end-point with these small quantities of zinc is quite good when the acid is 2 *N* and the zinc concentration not less than 0·3 mg per ml at the end-point.

EFFECT OF TEMPERATURE—

Kolthoff[2] and other workers recommended titration at 50° to 60° C because the titration can be carried out at greater speed than at room temperature. We found that the colour

change is much less well defined at elevated temperatures, and when more than 30 mg of zinc are present there is no need to increase the speed of the titration. With less than 30 mg of zinc the results for both potentiometric and indicator titrations are worse at 50° to 60° C. (Compare experiments 7, 8 and 9 with 10, 11 and 12 of Table I.)

SPEED OF TITRATION—

In repeated experiments it was found that the direct titration of 50 mg or more of zinc (acid 2 *N* at end-point, total volume ranging from 40 ml to 200 ml) gave results that were 0·8 ± 0·1 per cent. low, regardless of whether the rate of titration was normal (30 ml in 3 to 4 minutes) or slow (30 ml in 15 minutes). If the ferrocyanide was added to within 0·3 ml of the end-point at the maximum speed possible (30 ml in 30 seconds) and then titrated dropwise (total time 55 seconds) results were only 0·3 to 0·5 per cent. higher. Results were unaffected by either waiting for the false end-point to come to completion or titrating through it. Rate of stirring had no effect provided there was some agitation. It seems that the direct titration of 50 mg or more of zinc with any normal titration procedure is unaffected by the speed of titration. Overshooting is less likely than with most methods because of the timely warning of the false end-point.

With less than 50-mg amounts of zinc the reaction becomes progressively slower with decreasing concentrations of zinc. Table I gives some indication of the times required for potentiometric titrations. Nevertheless, provided the zinc concentration is at least 0·3 mg per ml, a careful titration with indicator alone gives results 0·4 ± 0·4 per cent. low for 15 mg of zinc and 1·1 ± 0·4 per cent. low for 6 mg of zinc, regardless of whether the titration takes 5 or 15 minutes. However, a slow addition of the ferrocyanide is essential after the false end-point, which should be allowed to come to completion before continuing the titration.

INTERFERING SUBSTANCES—

Reducing substances such as hydrogen sulphide and sodium thiosulphate must be absent, as they interfere with the redox potential of the system. Nitrates at low concentrations have no effect, but even small amounts of nitrites render both the potentiometric and indicator end-point unsatisfactory.

METHOD

RECOMMENDED PROCEDURE—

On summarising the influence of the various factors, the following procedure is recommended for the determination of zinc by titration with potassium ferrocyanide and with diphenylbenzidine sulphate as an internal indicator.

Direct titration at room temperature should be used. The volume of the solution should be such that the concentration of zinc at the end-point will be at least 0·4 mg per ml. Before commencing the titration sufficient sulphuric acid to make the acidity 1·7 to 2·1 *N* at the end-point, ammonium sulphate sufficient to make its concentration at the end-point 1 to 2 g per 100 ml, 2 to 4 drops of a 1 per cent. potassium ferricyanide solution and 2 to 4 drops of 1 per cent. diphenylbenzidine sulphate per 100 ml are added to the zinc solution, which is then titrated with potassium ferrocyanide solution until the indicator colour changes permanently from purple to yellowish-green. For amounts of zinc greater than 30 mg the rate of titration has no effect, and it is not necessary to wait for the false end-point to come to completion. With smaller amounts of zinc a slower rate of titration, waiting for the false end-point and subsequent dropwise titration is advised.

This procedure gives results that are 0·8 ± 0·2 per cent. low for 30 to 300-mg amounts of zinc. With smaller amounts of zinc results are as much as 1·5 per cent. low. Standardisation of the potassium ferrocyanide solution against a known solution of zinc eliminates this error.

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The Separation of Zinc and Cadmium by the Use of Activated Copper

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A method of separating 5 to 200-mg amounts of cadmium and zinc is presented. Metallic copper in complex cyanide solution containing tartrate as an additional complexing agent displaces cadmium but not zinc from solution. Zinc is precipitated from the filtrate as zinc sulphide by adding sodium sulphide, filtered, re-dissolved in acid and determined either volumetrically or gravimetrically. Cadmium is recovered from the copper by extraction with an alkaline potassium cyanide solution containing small amounts of hydrogen peroxide. It is precipitated as cadmium sulphide by sodium sulphide and can be determined with 8-hydroxyquinoline after filtering and dissolving in acid.

THE determination of zinc is one of the more difficult analytical operations. This arises from the lack of variable valency states in the zinc atom and because gravimetric and volumetric methods for zinc are subject to interference from other elements, notably cadmium. The potassium ferrocyanide titration method involving internal indicators is specially liable to error. In the preceding paper,[1] the optimum conditions were established for this titration. They require a fairly close control of pH, the presence of ammonium sulphate within certain limits and the absence of copper, cadmium, iron, aluminium, nitrite and thiosulphate. In the usual method for determining zinc the elements of the copper group are removed with hydrogen sulphide. In the presence of cadmium double precipitation is essential to recover co-precipitated zinc sulphide. The iron-group metals are precipitated as hydroxides in the presence of a considerable excess of ammonium chloride and ammonium hydroxide, in order to prevent co-precipitation of zinc hydroxide. This procedure violates the specified requirements for ammonium ions and should be avoided if possible. Undoubtedly the most satisfactory method is to precipitate zinc sulphide from a solution buffered to a pH of 2 to 3, after removing copper, cadmium, lead and so on, but it has the serious disadvantage of requiring prolonged and vigorous gassing of the solution with hydrogen sulphide. Many attempts have been made to avoid these difficulties. Waring and Stone[2] recommended boiling an acid solution of cadmium and zinc with aluminium, whereby cadmium would be precipitated and zinc would remain in solution, but Fales and Ware[3] have stated that cadmium cannot be separated from zinc by this method. The property of the complex acid H_2CdI_4 of forming insoluble compounds with organic bases has been used by several investigators. Allyl iodide and hexamethylenetetramine,[4] brucine,[5] β-naphthoquinoline[6] and the *tris*-dipyridylferrous ion,[7] in the presence of potassium iodide, have all been suggested as suitable methods for the separation of zinc from cadmium. Chalupný and Breisch[8] recommend adding thiourea to a boiling solution of zinc and cadmium containing potassium hydroxide and potassium cyanide, the cadmium being precipitated as cadmium sulphide. A second precipitation is recommended, which indicates co-precipitation of some zinc sulphide. More recently, Evans[9] recommended the separation of zinc from cadmium in alkaline cyanide solution in the presence of ammonium hydroxide. Evans claimed that under these conditions only cadmium sulphide is precipitated by sodium sulphide. The zinc is subsequently precipitated as zinc sulphide in the filtrate by adding an excess of sodium hydroxide and

boiling. We have investigated this method under varied conditions, with the addition of colloids, such as agar-agar and gelatin, to prevent co-precipitation or post-precipitation of the zinc sulphide. Separation was never complete and the recovery of zinc ranged from 90 to 95 per cent. The possibility of using magnesium or aluminium as reducing agents in alkaline cyanide solution was then investigated. Magnesium proved too active, depositing most of the zinc as well as the cadmium. Aluminium used in the form of thin foil was more successful, particularly when potassium sodium tartrate was present as an additional complexing agent. But even under the best conditions the recovery of the zinc never exceeded 98 to 99 per cent. and the method was therefore abandoned. But it had been noticed that if the complex cyanide solution contained copper as well as cadmium and zinc, first the cadmium was deposited on the aluminium foil, then the copper, and the zinc remained in solution. As cadmium was precipitated before the copper it seemed that copper might be a suitable reducing agent for cadmium. This was found to be so and a method is now described for the complete separation of zinc and cadmium in the range of 5 to 200 mg of either metal. It is probable that the method will lend itself to the separation of even smaller amounts of zinc and cadmium, but no experimental work has been carried out in that direction. The method has been extended to the separation of zinc from tin, lead, bismuth, arsenic, manganese, iron and aluminium, which will be the subject of a later paper.

The standard electrode potentials for the reactions—

$$Cu + 4CN' \rightleftharpoons Cu(CN)_4''' + e \quad .. \quad .. \quad .. \quad .. \quad (1)$$

$$Cd + 4CN' \rightleftharpoons Cd(CN)_4'' + 2e \quad .. \quad .. \quad .. \quad .. \quad (2)$$

$$Zn + 4CN' \rightleftharpoons Zn(CN)_4'' + 2e \quad .. \quad .. \quad .. \quad .. \quad (3)$$

have not been measured, but they can be estimated from the published values[10] of the dissociation constants (K) of the cyanide complexes and the standard electrode potentials of the metals in non-complex-forming solutions. The dissociation constants of the substances $K_3Cu(CN)_4$, $K_2Cd(CN)_4$ and $K_2Zn(CN)_4$ are 2×10^{-27} (Sidgwick[11]), $1{\cdot}4 \times 10^{-10}$ and $1{\cdot}3 \times 10^{-17}$, respectively. From the equation—

$$E'_0 = E_0 - \frac{RT}{nF} \log K,$$

the values of the electrode potentials E_0' of the reactions (1) to (3) above can be calculated, E_0 being the standard electrode potential for the metal in non-complex-forming media. ($Cu/Cu^{\cdot}$, $-0{\cdot}51$ V; $Cd/Cd^{\cdot\cdot}$, $0{\cdot}40$ V; $Zn/Zn^{\cdot\cdot}$, $0{\cdot}76$ V.) The calculated values for E_0' are $+1{\cdot}27$, $+1{\cdot}09$ and $+0{\cdot}91$ V for zinc, copper and cadmium, respectively. These can be compared with the polarographic half-wave potentials in cyanide solution, which, for cadmium, is $-1{\cdot}18$ V, against the saturated calomel electrode, whilst copper and zinc are not reduced at the dropping-mercury electrode. It follows, therefore, from theoretical consideration, that copper will displace cadmium, but not zinc, from cyanide solutions.

The method involves the addition of specially prepared copper to a boiling solution of cadmium and zinc containing potassium cyanide and potassium sodium tartrate, when cadmium is precipitated in metallic form on the copper, leaving the zinc in solution. The zinc is precipitated in the filtrate as zinc sulphide by addition of sodium hydroxide and sodium sulphide. The zinc sulphide is dissolved in sulphuric acid and titrated under specified conditions. The cadmium is re-dissolved from the copper in an alkaline potassium cyanide solution containing hydrogen peroxide, precipitated from the solution as cadmium sulphide with sodium sulphide and determined by 8-hydroxyquinoline after filtering and dissolving in acid.

Experimental

Reactivity of copper—

A great deal of experimental work was carried out to prepare copper metal of high purity and satisfactory reactivity. Copper foil and copper filings were found suitable for small quantities of cadmium only. For instance, to deposit 20 mg of cadmium, 4 g of copper filings were required. A commercial brand of copper powder was found to contain zinc. An attempt was made to prepare finely divided copper by reducing copper sulphate solution with magnesium, iron or aluminium, but none of these preparations was satisfactory in all respects. Satisfactory copper powder was prepared eventually by reducing copper oxide

powder with hydrogen. It is a coarse, crystalline powder of light-reddish copper colour. It is so reactive that it dissolves in 3 per cent. potassium cyanide solution with vigorous evolution of hydrogen and 4 to 5 g of this material precipitate up to 0·3 g of cadmium in 15 minutes. It is best to use the copper powder after it has been freshly prepared. Alternatively, it may be stored in a sealed tube.

CONCENTRATION OF CYANIDE AND TARTRATE—

Experiments were carried out to determine the most satisfactory concentrations of potassium cyanide and potassium sodium tartrate. Although cyanide is the chief complexing agent, tartrate is essential to give a clean separation of cadmium. Experimental results are shown in Table I. They indicate that if the cyanide concentration falls below a certain level cadmium is incompletely precipitated, whereas at high concentrations of cyanide there might be a small loss of zinc. However, the range is fairly wide and an amount of potassium cyanide in 100 ml of solution equal to 7 to 17 times the weight of metal in solution is adequate. A weight of potassium cyanide equal to 10 times the estimated weight of metals in solution is recommended. The concentration of potassium sodium tartrate is not critical; 10 g per 100 ml solution is suitable.

TABLE I

INFLUENCE OF POTASSIUM CYANIDE ON THE SEPARATION OF ZINC FROM CADMIUM

Each solution was made up from 25 ml of 0·1 *M* zinc solution (160 mg of zinc) and 25 ml of 0·1 *M* cadmium solution (280 mg of cadmium) together with 10 g of potassium sodium tartrate

25 ml of zinc solution ≡ 32·96 ml of 0·05 *M* potassium ferrocyanide solution

Amount of 10% KCN solution, ml	Copper powder added, g	Reaction	Reaction time, minutes	Colour of ZnS ppt.	Amount of 0·05 *M* $K_4Fe(CN)_6$, ml
20	12·0	no gassing	great	yellow	— (discarded)
30	3·5	slight gassing	30	white	33·10
45	4·5	moderate gassing	↓ decreasing	"	33·00
60	4·0	strong gassing	↓ decreasing	"	33·00
75	4·0	"	↓ decreasing	"	32·96
90	4·5	"	15	"	32·78

METHOD

REAGENTS—

All reagents should be of recognised analytical purity.

Copper oxide powder.

Sulphuric acid, concentrated and 5 N.

Potassium cyanide solution, 10 *per cent.*

Sodium hydroxide solution, 5 N.

Sodium sulphide solution, 10 *per cent.*

Sodium chloride solution, 2 *per cent.*

Potassium ferrocyanide solution, 0·05 M.

Hydrogen peroxide solution, 3 *per cent.*

Potassium ferricyanide indicator solution, 1 *per cent.*

Diphenylbenzidine indicator—A 1 per cent. solution of diphenylbenzidine in concentrated sulphuric acid.

PROCEDURE—

Preparation of copper powder—Fill a ¾-inch diameter silica tube loosely with fine A.R. copper oxide powder and slip a closely fitting brass sleeve about 2 inches long over the tube. Attach a small bubble counter to the exit end of the tube. Pass hydrogen, which has been washed by bubbling through an alkaline permanganate solution and then through concentrated sulphuric acid, through the tube to remove air. Then start heating the silica tube at the hydrogen inlet with a medium bunsen flame, using the brass sleeve as a shield. Move the sleeve and burner along the tube as the reduction proceeds. The tube should be inclined slightly to allow the water formed to drain. When the reduction is complete, cool the tube

in a stream of hydrogen and grind the slightly-caked material in a mortar. If not used immediately, store in a sealed tube.

Separation of zinc and cadmium—The solution should contain cadmium and zinc as the sulphates and not more than 0·5 g of the combined metals. Neutralise the solution with solid sodium carbonate until a permanent precipitate forms, then add 10 times the weight of potassium cyanide, calculated on the estimated total weight of metals present, *e.g.*, for 0·5 g add 50 ml of 10 per cent. potassium cyanide solution. Add 10 g of potassium sodium tartrate and dilute to 100 ml with distilled water. Bring almost to boil and add copper powder in small amounts at a time, boiling for several minutes after each addition. The red copper powder turns grey as it becomes coated with cadmium. The reaction is at an end when added copper powder remains red after boiling for several minutes. The reaction takes 15 to 30 minutes, depending on the amount of cadmium to be removed. Filter immediately through a Whatman No. 530 or No. 30 filter-paper and wash rapidly several times with water.

Determination of zinc—To the filtrate, which has a volume of 150 to 200 ml, add 20 ml of 5 *N* sodium hydroxide solution, heat to boiling and add 25 ml of 10 per cent. sodium sulphide solution with stirring. Boil for several minutes to coagulate the zinc sulphide and allow to digest on the hot-plate for 1 to 3 hours. Filter through a Whatman No. 42 filter-paper and wash with 60 to 80 ml of 2 per cent. sodium chloride solution. Place the precipitate and filter-paper in the precipitation beaker, add 50 ml of 5 *N* sulphuric acid and heat carefully on the hot-plate until the zinc sulphide is dissolved and the hydrogen sulphide has completely boiled off. Add small amounts of water if necessary to prevent charring. Cool, dilute to 80 ml with distilled water, add 2 g of ammonium sulphate, 4 drops of a 1 per cent. solution of potassium ferricyanide in water, and then 4 drops of a 1 per cent. solution of diphenylbenzidine in concentrated sulphuric acid. Titrate the purple solution with 0·05 *M* potassium ferrocyanide solution to a pale green end-point. Usually there is a premature fading of the colour close to the end-point ("false end-point"), but the purple colour re-appears in a few seconds. Titrate the solution dropwise until the colour changes sharply to a pale green. Standardise the potassium ferrocyanide solution against a 0·1 *M* standard zinc solution under the same conditions.

Determination of cadmium—To the beaker containing the copper and the precipitated cadmium add 10 ml of 10 per cent. potassium cyanide solution, followed by 1 ml of 3 per cent. hydrogen peroxide solution and 1 ml of 5 *N* sodium hydroxide solution. The grey coating of cadmium disappears and is replaced by the red colour of copper. Stir for several minutes and pour the liquid through the filter-paper previously used for the filtration of the copper suspension. Repeat the extraction with 5 ml of 10 per cent. potassium cyanide solution, 1 ml of 3 per cent. hydrogen peroxide solution and 1 ml of 5 *N* sodium hydroxide solution and filter. Repeat until the filtrate shows no sign of a yellow precipitate when heated after sodium sulphide solution is added. This is necessary since one extraction will not dissolve the cadmium completely. Add 10 ml of 5 *N* sodium hydroxide solution and dilute to 200 ml with distilled water. Boil for several minutes to destroy hydrogen peroxide, then add 20 ml of 10 per cent. sodium sulphide solution with stirring. Digest the precipitated cadmium sulphide for 30 minutes, filter through a Whatman No. 42 filter-paper, and wash thoroughly with 2 per cent. sodium chloride solution. Pierce the filter-paper and wash the precipitate into the precipitation beaker. Traces of cadmium sulphide on the filter-paper are dissolved by washing with 30 ml of hot 2 *N* hydrochloric acid and again with water, the solution being collected in the precipitation beaker. Heat gently until the cadmium sulphide dissolves. A small insoluble residue of copper sulphide remains, which is filtered off, if necessary. The cadmium is precipitated as the hydroxyquinolate, filtered through a sintered glass crucible, dried at 100° to 105° C and weighed as $Cd(C_9H_6ON)_2.1\frac{1}{2}H_2O$.

Results

Recovery of zinc—

For amounts of less than 30 mg, the zinc was determined gravimetrically as zinc ammonium phosphate, because the end-point in titrations of small amounts of zinc was not satisfactory. Belcher, Nutten and Stephen[12] have recently described alternative indicators derived from dinaphthylamine, which, they claim, are useful for even minute amounts of zinc, but we have had no experience of them.

Recoveries of 6 to 160-mg amounts of zinc in the presence of up to 220 mg of cadmium are shown in Tables II and III. In the experiments (Table II) in which different amounts of

cadmium were added, the zinc sulphide precipitates were all perfectly white and the amounts of copper powder and potassium cyanide solution used were in accordance with the directions given in the procedure, p. 301. The 0·1 *M* standard zinc solution was prepared by dissolving 6·508 g of Merck's "Zinc *pro analysi*" in water and 60 ml of concentrated sulphuric acid and making up to 1000 ml with water. The 0·01 *M* solution was prepared by diluting 50 ml of the 0·1 *M* zinc solution to 500 ml.

1 ml of 0·1 *M* zinc solution contained 0·006508 g of zinc.

TABLE II

SEPARATION OF 162·7 mg OF ZINC FROM CADMIUM

Cadmium added, mg	220	160	110	50	20	10
Zinc found, mg	162·5	162·5	162·7	162·6	162·6	162·6

TABLE III

SEPARATION OF ZINC FROM 220 mg OF CADMIUM

Concentration of zinc solution added	Volume of zinc solution added, ml	Zinc added, mg	Zinc found, mg
0·1 *M*	20	130·2	129·9
0·1 *M*	15	97·6	97·7
0·1 *M*	10	65·1	64·8
0·01 *M*	25	16·3	16·5*
0·01 *M*	10	6·5	6·3*

* Zinc determined gravimetrically as zinc ammonium phosphate.

RECOVERY OF CADMIUM—

From 5 to 140-mg amounts of cadmium were separated from up to 160 mg of zinc. Results are shown in Table IV.

The 0·05 *M* standard cadmium solution was prepared by dissolving 12·826 g of cadmium sulphate ($3CdSO_4.8H_2O$) in water and diluting to 1000 ml. The 0·005 *M* cadmium solution was made by diluting 50 ml of the 0·05 *M* cadmium solution with water to 500 ml.

1 ml of 0·05 *M* cadmium solution contained 0·005621 g of cadmium.

TABLE IV

SEPARATION OF CADMIUM FROM 163 mg OF ZINC

Concentration of cadmium solution added	Volume of cadmium solution added, ml	Cadmium added, mg	Cadmium found, mg
0·05 *M*	25	140·5	140·7
0·05 *M*	10	56·2	55·8
0·005 *M*	50	28·1	28·4
0·005 *M*	25	14·1	14·4
0·005 *M*	10	5·6	5·5

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The Determination of Zinc in Lubricating Oils by Amperometric Titration

Part I. Amperometric Titration of Zinc with Versene

By D. PICKLES and C. C. WASHBROOK

Zinc is titrated amperometrically with di-sodium ethylenediaminetetra-acetate (versene) at the dropping-mercury electrode in a strongly alkaline solution containing *cyclo*hexylamine, or in a buffered solution containing ammonium acetate. A potential of −1·4 volts against the saturated calomel electrode is used with a mercury drop-time of 3 to 4 seconds. A simple polarising unit is used. Advantages are that bulky precipitates, which might foul the electrodes, are not formed, and titration can proceed quickly because of rapid attainment of equilibrium after addition of titrant.

The method is applied to the determination of zinc in new and used lubricating oils, and methods of dealing with interfering elements are discussed. Determinations are made in new oils and additives containing barium and phosphorus, and in used lubricating oils containing barium, calcium, iron, copper, lead and phosphorus. Copper and iron are removed by ethereal extraction of cupferron complexes; barium and lead are removed as sulphates, and calcium is suppressed by addition of sodium fluoride. The acetate buffer method is suitable for solutions containing appreciable amounts of phosphates.

An accuracy of ±0·3 per cent. is attained in the titrations at the level of 1 mg of zinc. A precision of better than 2 per cent. can be attained in the analysis of new lubricating oils and additives.

The determination of zinc in fractional milligram quantities and at low concentrations is required in the analysis of many materials. For routine analysis it is desirable to have a reasonably accurate and rapid method that makes use of robust and relatively inexpensive apparatus. Small quantities of zinc are often determined by means of diphenylthiocarbazone (dithizone) and a photometric technique or a partition titration method. Such methods are troublesome because of the great precautions necessary in the preparation and storage of the reagents. Sylvester and Hughes[1] used dithizone for the separation of zinc from other metals, with subsequent determination by a micro-modification of the Lang procedure in which iodine is liberated by ferricyanide. This method is only successful for amounts of zinc within a narrow range, 0·1 to 0·3 mg, and moreover requires highly skilled operation for dependable results. Many workers prefer the polarographic method, but this involves the use of expensive apparatus or the tedious use of a manual instrument. However, by the use of a simple and inexpensive polarising unit of the type described by Stock,[2] zinc can be determined by amperometric titration.

Amperometric titrations have been made with ferrocyanide,[3,4,5] with 8-hydroxyquinoline[6,7] and with quinaldinic acid.[8] All these methods have the disadvantages of forming sparingly soluble complexes, some very bulky in nature, and of requiring some little time for the system to come to equilibrium after each addition of reagent. Moreover, Stock's quinaldinic acid method[8] requires the operation to be carried out at 60° C, which is a drawback for routine application. None has the virtue of making use of a specific reagent for zinc, but this factor is obviated if the essential measurements depend on the progressive reduction of the diffusion current due to zinc.

An amperometric titration method has now been devised in which zinc is titrated with di-sodium ethylenediaminetetra-acetate solution (for brevity referred to as "versene"). This reagent was shown by Schwarzenbach[9] and others to form un-ionised water-soluble complexes with barium, calcium, magnesium, cadmium, lead, manganese, mercury, strontium and zinc, and it has been applied successfully to the determination of hardness in waters. For this purpose an indicator, Eriochrome black T, is used; this changes colour when the calcium and magnesium ions have been inactivated by the formation of complex ions.

In the proposed method, zinc in aqueous solution is buffered in a highly alkaline medium with *cyclo*hexylamine and placed in a cell containing a dropping-mercury electrode. After deoxygenation with nitrogen, the solution is titrated amperometrically with versene. The dropping-mercury electrode is maintained at a fixed potential of −1·4 volts with respect

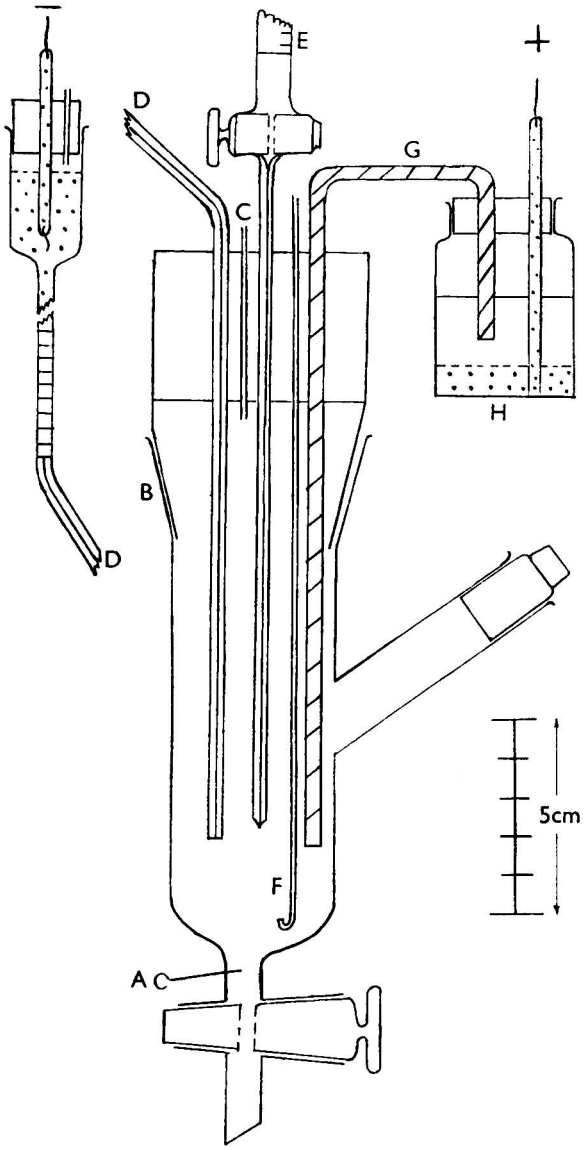

Fig. 1. Titration cell. A, platinum electrode; B, ground-glass joint; C, gas exit; D, capillary tube; E, burette; F, gas entry; G, agar bridge; H, calomel cell

to the saturated calomel electrode as anode. Versene is added in regular increments from a semi-micro burette and the diffusion current due to zinc is measured by a sensitive galvanometer. The zinc is combined in an un-ionised water-soluble complex and in this form does not contribute to the diffusion current, which therefore decreases in proportion to the decrease of the $Zn^{\cdot\cdot}$ concentration. There is a considerable difference between the reduction potentials

of zinc and of both the zinc complex and the reagent, so that when all the zinc has been titrated the diffusion current remains constant at a low value. When values of diffusion current (galvanometer readings) are plotted against volumes of versene added, two intersecting straight lines can be drawn through the points. The point of intersection of the lines corresponds to the equivalence point of the titration.

Advantages of this method are that: (*i*) no precipitate is formed, so that there is no risk of contaminating the electrodes; moreover, the cell can be easily and quickly washed out ready for the next titration; (*ii*) the combination of the zinc is rapid, entailing an interval of approximately 15 seconds between addition of reagent and attainment of equilibrium at normal laboratory temperature; in methods involving precipitation, an interval of 5 to 10 minutes is usual; (*iii*) the apparatus is simple to construct and consists of a titration cell, a simple polarising unit and a sensitive galvanometer.

Experimental

Apparatus for amperometric titration—

Polarising unit—The unit described by Stock[2] can be used. This has been modified by including 6-way double-bank switches so that the polarity of the electrodes can be reversed, if necessary (see Fig. 2). This refinement was required for experimental work with other electrode systems.

Titration cell—This is shown in Fig. 1. The platinum electrode is not used.

Semi-micro burette—A 0 to 2-ml burette graduated at each 0·02 ml.

Scalamp galvanometer (variable sensitivity)—The instrument used was made by W. G. Pye Ltd., Cambridge. Its characteristics were: resistance, 390 ohms; time of swing, 2 seconds; maximum sensitivity, 98 mm per microampere.

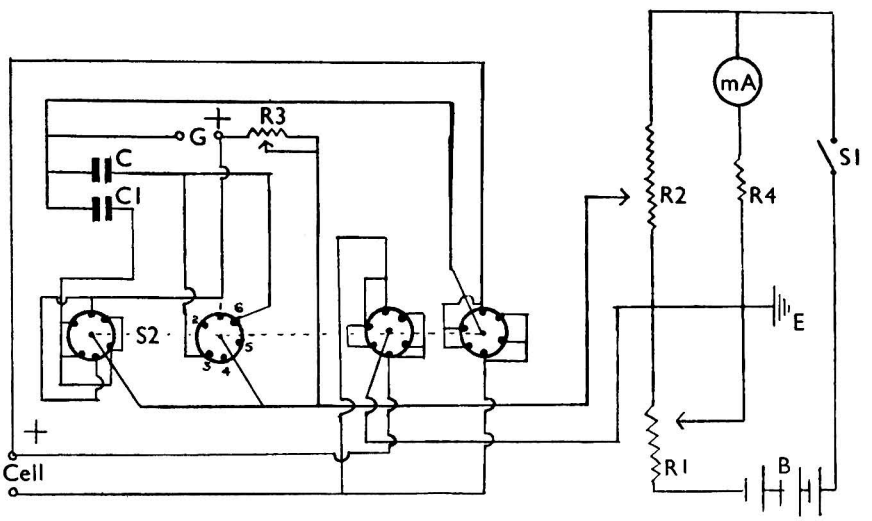

Fig. 2. Circuit for polarising unit

Establishment of suitable conditions—

Colour indicator titration of alkaline earth metals with versene is carried out at a high pH value in ammoniacal buffer solution.[10] Koryta and Kössler[11] have published values for the stability constants of ethylenediaminetetra-acetic acid and its zinc salt; it was necessary to find the polarographic behaviour of versene under possible test conditions. Fig. 3 shows polarograms of versene in ammonium chloride solutions at a series of pH values, the instrument being used as a manual polarograph. The values of pH were measured with a Cambridge pH meter and a glass electrode. It has been established that versene is not reduced at pH values greater than about 4 until the potential of the dropping-mercury electrode is −1·7 volts with respect to the saturated calomel electrode. At low pH values,

diffusion currents appear and are observed to be connected with hydrogen evolution, which makes the galvanometer difficult to read.

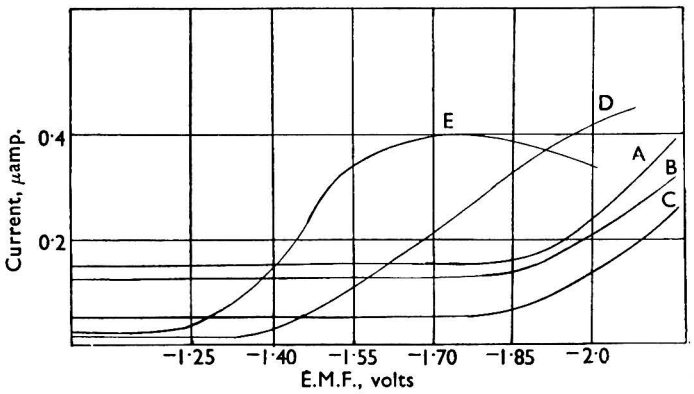

Fig. 3. Polarograms of versene in ammonium chloride base solution. Curve A, pH 10·0; curve B, pH 8·5; curve C, pH 4·1; curve D, pH 2; curve E, pH 0·5

Ammonium chloride - ammonium hydroxide mixture, sodium hydroxide solution, and neutral solutions were unsatisfactory as base solutions, but a 10 per cent. aqueous solution of *cyclo*hexylamine formed a suitable buffer, which was strongly alkaline and less volatile than the ammoniacal mixture. The polarographic behaviour of zinc and versene in a *cyclo*hexylamine solution has been studied and the results are shown in Fig. 4. It is found that *cyclo*hexylamine solution in water gives no appreciable diffusion current until the dropping-mercury electrode is at −1·9 volts with respect to the saturated calomel electrode. The

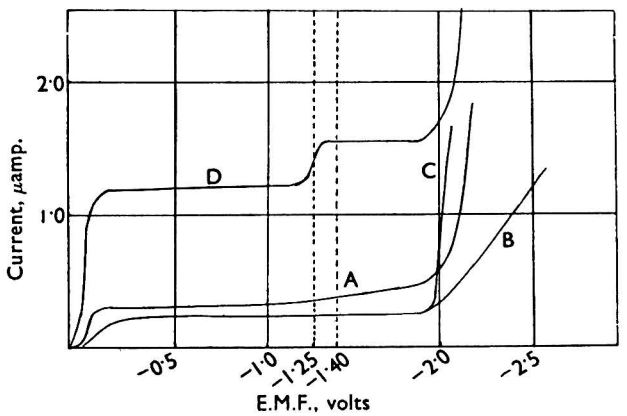

Fig. 4. Polarograms in *cyclo*hexylamine base solution. Curve A, base; curve B, sodium versenate; curve C, zinc and sodium versenate; curve D, 1 mg of zinc

same value is found for versene and the zinc - versene complex (obtained from a mixture of zinc and *cyclo*hexylamine solutions with excess of versene present). In this base solution the half-wave potential of zinc is −1·25 volts against the saturated calomel electrode. A potential for the dropping-mercury electrode of −1·4 volts against the saturated calomel electrode was selected for the amperometric titration of zinc with versene in a *cyclo*hexylamine base solution and satisfactory titration curves were obtained under these conditions. Typical plots are shown in Fig. 5.

Method

Reagents—

cyclo*Hexylamine*—Redistil technical grade *cyclo*hexylamine and collect the fraction boiling over the range 132° to 133° C.

Nitrogen—Preferably oxygen-free.

Versene solution—Dissolve 5·0 g of ethylenediaminetetra-acetic acid, di-sodium salt (dihydrate),* in 1 litre of distilled water; 1 ml of this solution is equivalent to approximately 1 mg of zinc.

Standard zinc solution—Accurately weigh 0·1 g of pure electrolytic zinc metal and dissolve it in a small volume of 50 per cent. hydrochloric acid solution and make up to 1 litre with distilled water; 1 ml of this solution contains 0·100 mg of zinc.

PROCEDURE—

Adjust the mercury head of the dropping-mercury electrode to give a drop-time of about 3 seconds in distilled water.

Standardise the polarising unit. This involves adjustment of R1 until a full-scale deflection is shown by the micro-ammeter, mA. Set the potentiometer, R2, so that the dropping-mercury electrode is at a potential of −1·4 volts against the saturated calomel electrode. Connect the galvanometer and set this at a suitable sensitivity, *e.g.*, 2·5 mm per microampere.

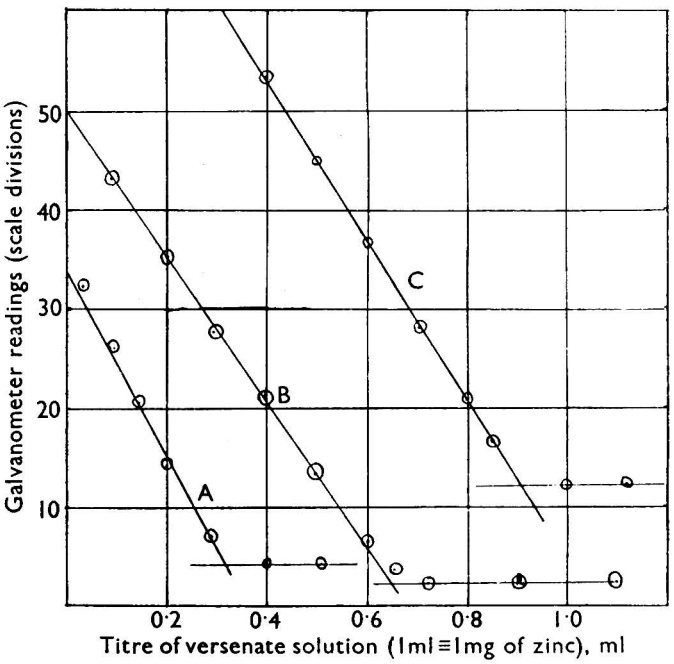

Fig. 5. Amperometric titration of zinc *cyclo*hexylamine base solution. Curve A, 0·31 mg of zinc; curve B, 0·64 mg of zinc; curve C, 0·94 mg of zinc

Transfer by pipette 10·0 ml of standard zinc solution to the titration cell. Alternatively, place in the cell a suitable volume of test solution containing about 1 mg of zinc. Add 1 ml of *cyclo*hexylamine and 19 ml of distilled water. Pass nitrogen for 10 minutes.

Stop the flow of nitrogen and wait a few seconds for the last few bubbles to come out of solution. Read the galvanometer at the maximum point of its swing (see Note 1).

Add a fixed increment, *e.g.*, 0 1 ml, of versene solution from a semi-micro burette. Bubble nitrogen for 15 seconds, allow the bubbles to subside and read the maximum point of the galvanometer swing.

Repeat the procedure described in the foregoing paragraph until further additions of versene solution give no change in the galvanometer reading. Take several more readings after this point is reached.

Plot galvanometer readings as ordinates against the volumes of versene solution added

* Obtainable from Genatosan Ltd.

as abscissae. Draw two straight lines through the points. The end-point is given by the intersection of the two lines.

Note 1—The excursions of the galvanometer are large at first, but diminish as the titration proceeds, and so indicate the approach to the end-point. Normally no damping is required, as the swings, although rapid, are repeated with each drop and give the same value as before.

Note 2—Points very near to the end-point may not lie exactly on either of the two lines drawn. This is evidently due to slight instability of the zinc - versene complex in the region where dissociation of the complex is not repressed by the common ion effect. Such points are well known in amperometric titrations depending on solubility effects,[12] and it has been shown that they have no special significance and can be ignored.

Note 3—If the volume of titrant added is small compared with the volume of the solution in the cell no correction for dilution is necessary. If the volume added is appreciable, galvanometer readings should be corrected by multiplying by the factor $(V + v)/V$, in which V denotes original volume and v the volume of reagent added at any point.

The stoicheiometry of the reaction was investigated by titrating zinc solution with 0·0136 *M* versene solution, each having been prepared by accurate weighing. Pure electrolytic zinc was used for the zinc standard, whereas the versene was dried to constant weight at 105° C. The results are shown in Table I.

TABLE I

TITRATION OF STANDARD ZINC SOLUTION

Volume of 0·00158 *M* zinc solution, ml	Titre of 0·0136 *M* versene solution, ml	
5·0	0·585,	0·585, 0·585
10·0	1·170,	1·175, 1·175
	1·170,	1·170, 1·175
Mean titre on basis of 10 ml of zinc solution ..		1·171 ml
Standard deviation ..		0·003
Hence, 1 mg of zinc ≡ 5·177 mg of versene.		

The experimental data show a deviation of 0·7 per cent. from the calculated value of 5·143 mg for the versene equivalence of zinc, which is close to the limits of accuracy as determined. The calculated value is based on the equation—

$$Na_2H_2O_4V_e + Zn^{\cdot\cdot} \rightarrow ZnH_2O_4V_e + 2H^{\cdot}$$

where the ethylenediaminetetra-acetyl radical—

$$[(CO.CH_2)N.CH_2.CH_2.N(CH_2.CO)]''''$$

is represented by V_e.

The reaction is therefore stoicheiometric.

This amperometric titration procedure gives a degree of precision higher than that attained by conventional polarography, in which a value of ±2 per cent. is considered satisfactory. Moreover it has the merits of making use of simple apparatus, of not requiring careful drying of apparatus, such as cells, and of finishing in a graphical procedure that gives a clearly indicated end-point. It is not necessary to recalibrate the instrument when minor changes in technique occur, and reasonable variations in the drop-time of the mercury cathode have no effect.

The procedure as applied to the determination of zinc in lubricating oil and additives is described below.

Part II. The Determination of Zinc in Lubricating Oils

The determination of metals in engine lubricating oils of the Heavy Duty and Premium types involves a number of analytical difficulties because of mutual interference and the presence of phosphorus. Zinc can be determined by spectroscopy of an ash by procedure I.P.122/48(T) of the Institute of Petroleum.[13] The simpler methods described in I.P.117/47(T) are suitable only when there is no interfering element present, and they are unsuitable for used oils. The alternative procedure, A.S.T.M. D–811,[14] is suitable both for used and for new oils, but is very tedious in use.

Methods involving amperometric titration have been described by Parks and Lykken[15,16] for the determination of copper, iron and silver in lubricating oils. The amperometric

procedure described in Part 1 of this paper has been applied to the determination of zinc in used and unused lubricating oils of the Heavy Duty type. The removal and suppression of interfering elements has been studied and suitable conditions are recommended for the determination.

TREATMENT OF USED OIL—

Our usual method for treatment of oil ashes and deposits has been adopted. The ash or deposit is treated with concentrated sulphuric acid and, after oxidation of organic matter, barium and lead are precipitated as sulphates together with acid-insoluble grit. The acid conditions used are chosen to give the minimum solubility of lead sulphate. After removal of the sulphates and grit, the filtrate is diluted to a standard volume and aliquot portions are taken for the determination of copper, iron, zinc, calcium and other metals.

Determinations are made on a single sample, which avoids sampling difficulties with used oils; the conditions, however, require the use of sensitive methods suitable for dealing with amounts of material in the range 0·2 to 1 mg in a suitable aliquot. The zinc content of oils analysed is usually of the order 200 to 600 p.p.m. Formerly zinc was determined by the method of Sylvester and Hughes,[1] but this was found to be far too tedious for routine application. The present method has been applied in the presence of major amounts of calcium, magnesium, copper and iron after removal of lead or barium as sulphate.

In devising suitable conditions for the test, unsuccessful attempts were made to suppress iron by various means, including the addition of fluoride ions, complexing with citric acid, mannitol and ethylene glycol, and reduction with thioglycollic acid. Finally, it was found expedient to remove copper and iron from solution by co-extraction of the cupferron (ammonium nitrosophenylhydroxylamine) complexes in ether. This treatment also removes traces of tin and vanadium. Interference by calcium and magnesium is prevented by addition of sodium fluoride, when the insoluble fluorides are precipitated in a semi-colloidal form and do not settle out for a considerable time. This usually takes from 6 to 8 hours, which gives ample time for completing batches of titrations. Normally, other metals that form complexes with versene, such as aluminium, cadmium and bismuth, are only present in traces and so do not constitute a serious problem.

TREATMENT OF NEW OIL AND ADDITIVES—

In the analysis of new oils and additives an alternative procedure has been used in which a sulphated ash is subjected to perchloric acid digestion as described in Part B of I.P.110/47(T) for the determination of barium. This procedure was originally described by Osborn.[17] After removal of barium sulphate by filtration, the filtrate is used for the determination of zinc by amperometric titration. This operation is very rapid, as the preliminary extraction of copper and iron is normally unnecessary, and precision equal to that of the oxine procedure of I.P.117/47(T) is attained.

MODIFICATION FOR SAMPLES OF HIGH PHOSPHORUS CONTENT—

When certain additives having high zinc and phosphorus concentrations are analysed, the ash often contains considerable amounts of phosphate. This is fixed during the combustion by reaction of organic phosphorus compounds with the zinc oxide formed. When the phosphate concentration of the aqueous solution does not exceed 500 p.p.m., the *cyclo*-hexylamine base solution is satisfactory. However, when the phosphate content is appreciably higher, zinc ammonium phosphate is precipitated under the strongly alkaline conditions of the test. To avoid this precipitation, conditions have been devised for titration in a solution buffered at pH 4·5 with ammonium acetate. Typical zinc polarograms and titration curves were obtained in this base solution and were considered to be satisfactory.

METHOD FOR THE DETERMINATION OF ZINC

REAGENTS—

Reagents should be of recognised analytical purity.
Ammonium hydroxide, sp.gr. 0·880.
Ammonium hydroxide, 2 N.
Cupferron—A 5 per cent. w/v aqueous solution.
Ammonium acetate—A 57 per cent. aqueous solution.

Ethyl ether—Anaesthetic grade, B.P.
Phenolphthalein—A 1 per cent. solution in ethyl alcohol.
Sodium fluoride—A 4 per cent. w/v aqueous solution.
Other reagents as described in Part 1 (see p. 307).

PRELIMINARY EXTRACTION OF COPPER AND IRON—

Transfer 25 ml of acid solution, containing 0·5 to 1·5 mg of zinc together with copper, iron and calcium, to a 100-ml separating funnel. Add 1 ml of cupferron solution (which is adequate for 1 mg of iron, 1 mg of copper and the usual traces of other metals) and 10 ml of ethyl ether. Stopper the funnel and shake it vigorously to extract the metal complexes. Release the pressure developed and set the funnel aside for a few minutes to allow the ether layer to separate cleanly. Run the lower aqueous layer into a second separating funnel. Wash the ether layer in the first funnel with about 5 ml of water and run the separated washings into the second funnel. Add to this second funnel a few drops of phenolphthalein solution and then ammonium hydroxide, sp.gr. 0·880, dropwise until the solution is just pink. Extract again with 10 ml of ether; this second ammoniacal extraction prevents undue partition of ethereal cupferron solution into the aqueous phase. Finally, run the aqueous layer into a 50-ml calibrated flask, wash the ether layer as described above and add the washings to the main solution. Add 10 ml of sodium fluoride solution and 1 ml of *cyclo*hexylamine and dilute to volume with distilled water. Use this solution for the amperometric titration of zinc.

MODIFICATION FOR SOLUTIONS OF HIGH PHOSPHATE CONTENT—

When solutions of high phosphate content are expected, reserve the combined acid extracts from the cupferron extraction and proceed as follows: to the combined washings add a few drops of thymol blue indicator solution and ammonium hydroxide, sp.gr. 0·880, dropwise until the indicator shows the first signs of colour change, and then add 2 *N* ammonium hydroxide dropwise until the solution just turns yellow. At this stage the solution should have a pH of about 3·0. Add 5 ml of 57 per cent. ammonium acetate solution and dilute the solution to 50 ml. This solution should have a final pH of about 4·5 and is used for amperometric titration.

TITRATION OF ZINC—

Transfer 30 ml (or other suitable amount) of the solution to the titration cell. When the zinc content is expected to be less than 0·5 mg, add 5 ml of standard zinc solution (*i.e.*, 0·5 mg of zinc); otherwise proceed directly. De-oxygenate the solution by passing nitrogen for 10 minutes and then titrate with versene as described in Part 1 of this paper. Standardise the versene solution by titration of a suitable volume of standard zinc solution, *e.g.*, 10 ml, treated with 1 ml of *cyclo*hexylamine and 10 ml of sodium fluoride solution and then diluted to 30 ml.

Subtract the versene titre for 5 ml of zinc solution from the test titre if zinc has been added.

RESULTS

A prepared solution containing interfering metals was subjected to the separation and titration procedure described above. This solution was typical of those occurring in the analysis of used oil after removal of lead and barium as sulphates. It contained 1·28 mg of zinc, 1·00 mg each of copper, iron and calcium, 0·10 mg each of aluminium, magnesium and tin, and 0·03 mg of lead in 25 ml of 2 *N* sulphuric acid. Six replicate titrations with 0·0136 *M* versene solution gave results of 0·86, 0·87, 0·87, 0·89, 0·87 and 0·87 ml; the theoretical titre is 0·88 ml.

Table II shows the results of analyses of a series of oils prepared by adding various amounts of an additive containing barium, zinc and phosphorus. Phosphorus and zinc were present in equal proportions. The oils were treated by the method described. A sulphated residue was prepared and then treated with sulphuric acid. The barium was removed as sulphate and weighed, and the filtrate provided aliquots for the determination of zinc by amperometric titration and gravimetrically as the 8-hydroxyquinoline complex as described in I.P.117/47(T). The spectrographic analysis was performed on a separate ash as described in I.P.122/48(T), the zinc determination being made with the maximum accuracy.

The amperometric titration method shows good correlation with the two comparative techniques. All the results are within the precision limits quoted for reproducibility in I.P.117/47(T).

The separated barium sulphate precipitates were also subjected to spectrographic analysis for zinc; in every instance the zinc content was less than 0·1 per cent. of the precipitate. This showed that adsorption of zinc under the conditions of the test is negligible.

Table II

Determination of zinc additions in lubricating oil

Sample No.	Zinc content by: Amperometric titration, p.p.m.	Zinc content by: Oxine method, p.p.m.	Zinc content by: Spectrographic method, p.p.m.	Barium content by I.P. 110/47 (B) method, %
1	247	257	250	0·35
2	186	193	190	0·26
3	124	129	124	0·18
4	82	64	77	0·09

Table III

Determination of zinc in new lubricating oil and additives

Sample	Zinc content by: Amperometric titration, %	Zinc content by: Oxine method, %	Barium content by I.P. 110/47 (B), %
Heavy Duty Oil No. 1	0·025	0·026*	0·41
Heavy Duty Oil No. 2	0·026	0·025*	0·38
Heavy Duty Oil No. 3	0·028	0·028*	0·38
Heavy Duty Oil No. 4	0·046	0·048*	0·37
Heavy Duty Oil No. 5	0·063	0·064	0·35
Heavy Duty Oil No. 6	0·075	0·076	0·41
Additive No. 1	0·90†	0·89	9·95
Additive No. 2	1·78†	1·78	9·58
Additive No. 3	1·75†	1·77	9·44
Additive No. 4	5·79†	5·84	nil
Additive No. 5	4·94†	4·96	0·33
Additive No. 6	4·67†	4·70	nil

* Determination by independent laboratory.
† Acetate buffer procedure.

Table IV

Analysis of used lubricating oils for metals

Sample No.	Zinc, p.p.m. (a)	Zinc, p.p.m. (s)	Barium, p.p.m. (s)	Calcium, p.p.m. (s)	Copper, p.p.m. (c)	Iron, p.p.m. (c)	Lead, p.p.m. (s)
1	165	150	10	300	150	30	230
2	200	180	5	360	150	35	370
3	210	210	10	390	10	10	440
4	220	180	5	430	200	50	181
5	255	230	5	350	90	20	200
6	280	270	30	420	150	70	610
7	320	260	10	360	30	10	1000
8	370	380	20	390	20	10	230
9	400	450	20	450	5	10	580
10	450	490	20	480	10	5	260

(*a*) By amperometric titration.
(*s*) By spectrographic analysis.
(*c*) By colorimetric analysis.

The method has been successfully applied to a large number of samples of used and new lubricating oils and additives. Table III shows a typical range of results for new Heavy Duty lubricants both by amperometric titration and by separate oxine determinations. Agreement is good, and the authors have now adopted the amperometric titration procedure as a rapid alternative to the standard oxine method. Analyses for a typical range of filtered used lubricating oils are shown in Table IV. These lubricants were taken from petrol engines operating under arduous conditions and were filtered through "Sterimat" G.S. filters. The zinc figures were derived from amperometric titration and by spectrographic analysis of separate ashes. Other metals reported are shown as being derived from spectrographic or colorimetric analysis.

On occasion spectrographic and chemical analyses differ widely in values for zinc and other metals. This is due to a number of factors, including difficulty of sample reproduction, losses of metals during ashing, mechanical difficulty in removal of ashes from crucibles for spectrographic analysis and mutual interference by other metals present. The values quoted in Table IV are typical of the range covered and are not intended to record gross variations.

The authors are indebted to the Spectrographic section of their department for the values quoted in Tables II and IV.

Acknowledgment is made to the Chief Scientist of the Ministry of Supply for permission to publish this communication. Crown Copyright is reserved in respect of the figures to Part I of this paper, which are reproduced with the permission of the Controller of H.M. Stationery Office.

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Ministry of Supply
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August 12th, 1952

Erratum: April (1953) issue, p. 219. The paper by Rây should bear the date "August 14th, 1952."

An Improved Randles-Type Cathode-Ray Polarograph

By G. F. REYNOLDS and H. M. DAVIS

(*Presented at the meeting of the Polarographic Discussion Panel of the Physical Methods Group on Friday, November 16th,* 1951)

An introductory description of an improved Randles-type cathode-ray polarograph that has been developed in the Chemical Inspectorate is given.

The principle of the linear-sweep cathode-ray polarograph is briefly described, and some details are given of the modifications and improvements that have been made in the present instrument. These modifications and improvements have been designed to enhance the performance of the instrument and to simplify its operation, so that it can be used by relatively unskilled workers. The panel controls are described and the method of operation is given.

The interpretation of cathode-ray polarographic curves is briefly discussed and a reduced form of the Randles equation, applicable to this instrument, is presented. The advantages of the present cathode-ray polarograph in sensitivity and rapidity of operation are described, and its limitations in certain types of research work are mentioned.

The principle of the linear-sweep cathode-ray polarograph has been discussed by Randles[1,2] and Delahay,[3,4] and instruments embodying this principle have been described by Randles, Airey,[5] Weidmann,[6] and Snowden and Page.[7]

The design of the instrument described here is based upon that of the experimental apparatus constructed by Randles and Airey in the laboratories of the Chemical Inspectorate. As the new instrument was designed to be used in routine analysis by operators with little or no experience of electronic apparatus, steps were taken to reduce the number of panel controls to the minimum. This has been accomplished without serious loss of the flexibility that characterised the older equipment, and it has proved possible to extend the range of measurements that can be undertaken.

In this type of polarograph, the entire change of potential difference between the cell electrodes is effected during the life of only one mercury drop, instead of being spread over the lives of many such drops, as in the conventional instrument. The potential sweep is applied through a load resistor in series with the cell by means of a compensation circuit. The function of this compensation circuit is to maintain a constant rate of change of potential across the cell, irrespective of the iR drop in the load resistor.

The potential difference existing across the cell is amplified by means of a D.C. amplifier and applied to the X deflector plates of a long-afterglow cathode-ray tube. The potential difference appearing across the load resistor is a function of the current flowing in the cell, and it is similarly applied to the Y plates. The spot of light on the cathode-ray tube screen is made to trace out the polarographic curve under the influence of these two potentials.

It is necessary to ensure that no major change in the surface area of the drop occurs during the potential sweep, as such a change would cause variations in the cell current other than those it is desired to measure. Also, in order to secure a reproducible trace, the sweep must always commence at the same point in the life of each drop. These requirements are met by means of a triggered delay circuit that is actuated as each drop falls and which delays the electrolysis until late in the life of the succeeding drop.

Instrumental modifications

The modifications made fall into two classes: those designed to simplify operation and those designed to enhance performance.

In the first class the following points have received attention.

THE RATE OF POTENTIAL SWEEP—

The rate of change of cell potential has been fixed at 0·3 volt per second. This value has been found satisfactory under a wide range of conditions, and it was considered that retention of a variable sweep-rate would render the instrument unnecessarily complicated for routine purposes.

THE DELAY TIME BEFORE APPLICATION OF THE SWEEP—

A fixed delay time of five seconds has been allowed in an average drop time of seven seconds. This setting gives the largest practicable ratio of delay to drop time, and enables a trace corresponding to a change in cell potential of 0·5 to 0·6 volt to be displayed on the screen.

THE CELL CURRENT (Y) AMPLIFIER—

The voltage gain of this amplifier has now been pre-set, and the only means provided for variation of the instrument's sensitivity is a selector switch controlling the resistance in series with the cell.

THE CELL POTENTIAL (X) AMPLIFIER—

In view of the decision to fix the rate of cell potential change (see above), it was possible to fix the gain of the X amplifier so that the horizontal displacement of the spot could readily be used as a measure of cell potential change. The factor relating potential change to spot displacement is 50 millivolts per cm.

TRIGGER DELAY CIRCUIT—

The delay circuit used by Randles and Airey has been replaced by a multivibrator, which provides a fixed delay time of five seconds and a sweep period of two seconds. The multivibrator is of the free-running type, but has been arranged to trigger to the delay condition on the fall of each drop.

Two advantages are gained by this circuit change: (*i*) the potential sweep is automatically terminated should triggering not occur, and (*ii*) that synchronisation can automatically be established merely by setting the drop time of the mercury cathode to be slightly less than the total period (7 seconds) of the multivibrator.

SYNCHRONISATION CIRCUIT—

An improved method of triggering the delay circuit has been used, which enables synchronisation to be maintained over a wide range of sensitivity settings.

Changes designed to enhance performance are as follows.

Y-SHIFT CALIBRATION—The Y-beam shift has been so arranged that the shift potential can be accurately related to that of a Weston standard cell. This enables peak heights to be measured directly in terms of millivolts and hence, from a knowledge of the cell load resistance, the peak current to be calculated. The use of this control is explained in greater detail later.

COMPENSATION FOR CELL CAPACITANCE—As is well known, the polarographic cell has a high internal capacitance and, when the potential sweep is applied, an approximately constant current—

$$i = C \frac{dv}{dt}$$

flows, which generates a voltage across the cell load resistor. This voltage is troublesome when high values of cell load resistor are in use, as it may be sufficiently great to deflect the spot from the screen.

In the present apparatus, this jump in potential has been eliminated by supplying the constant current required by the cell capacitance from an external source, with the result that it no longer flows through the cell load resistor.[8]

DERIVATIVE WORKING—Provision has been made for the use of the instrument in derivative polarography.

Full details and complete circuit diagrams of the cathode-ray polarograph will be published elsewhere in the near future.[9]

Controls and operation

The latest Randles-type cathode-ray polarograph constructed in these laboratories is shown in Fig. 1. The panel controls fitted to this instrument (reading from left to right) are as follows.

Top panel—

The start potential control—This determines the potential difference across the cell electrodes before the potential sweep is applied.

The X-shift control.

The condenser current compensator—This controls the supply of current to the cell capacitance, as already mentioned.

Centre panel (upper row)—

The sensitivity control—This selects the value of the cell load resistor used.

The Y-shift control.

Centre panel (lower row)—

The derivative selector switch—This prepares the instrument for either "straight" or "derivative" polarography.

The beam-brightness control.

The beam-focus control.

The calibration control—This is used in the calibration of the Y-beam shift control.

Bottom panel—

The main switch.

No special type of cell or dropping-mercury electrode is required, but the drop time must be about 7 seconds. As can be seen in Fig. 1, a Cambridge stand and thermostat bath is used with this instrument. The only modification that has been made is in replacing the twin cable from the anode and cathode terminals by a screened lead.

To take a polarogram, the solution is placed in a polarographic cell and de-oxygenated in the usual manner. The start potential control is set to a value about 0·1 volt more positive (British convention) than the half-wave potential of the ion species to be determined. The X- and Y-shift controls are then used to set the spot on the "start point," which is a point marked on the graticule near the bottom left-hand corner. The voltage applied to the cell electrodes at the commencement of the sweep is then that indicated on the dial of the start potential control. The sensitivity control is set to give a convenient step height.

The instrument is then allowed to sweep several times in order to become synchronised with the mercury drops. This usually takes place in about two sweeps, but can be hastened, if desired, by detaching the mercury drop by tapping sharply as the spot nears the end of the sweep. Synchronisation is indicated when the trace is sharply cut off and the spot flies back to the start point. When synchronisation has been attained, the height of the step can be read from the graticule. This method of measurement is quite satisfactory for routine analytical work, but, if a more accurate value of the current is required, the height of the step can be measured by use of the calibrated Y-shift. This is done by setting the foot of the step on the centre line of the graticule and noting the setting of the Y-shift dial. The Y-shift is then re-set to bring the top of the step on to the same line.

Calibration of the Y-shift can be carried out when necessary by setting the control to zero, rotating the appropriate switch to "Calibrate" and adjusting a pre-set resistor until the trace on the screen ceases to have a toothed wave-form and becomes linear.

Steps produced by other reductions in the same solution can be examined simply by re-setting the start potential control and bringing the spot back to the start point. For each step the sensitivity control must, of course, be altered as necessary.

Interpretation of results

In view of the fact that the change of potential applied across the electrodes of the polarographic cell is carried out in the life of only one mercury drop, the steps obtained are not of conventional shape and are not governed by the Ilkovič equation. Instead, the current first rises to a peak and then falls off exponentially to the steady state normally attained. This step shape arises because the rapid application of a changing potential causes a "stripping out" of the reducible ions near the drop surface. This process is not

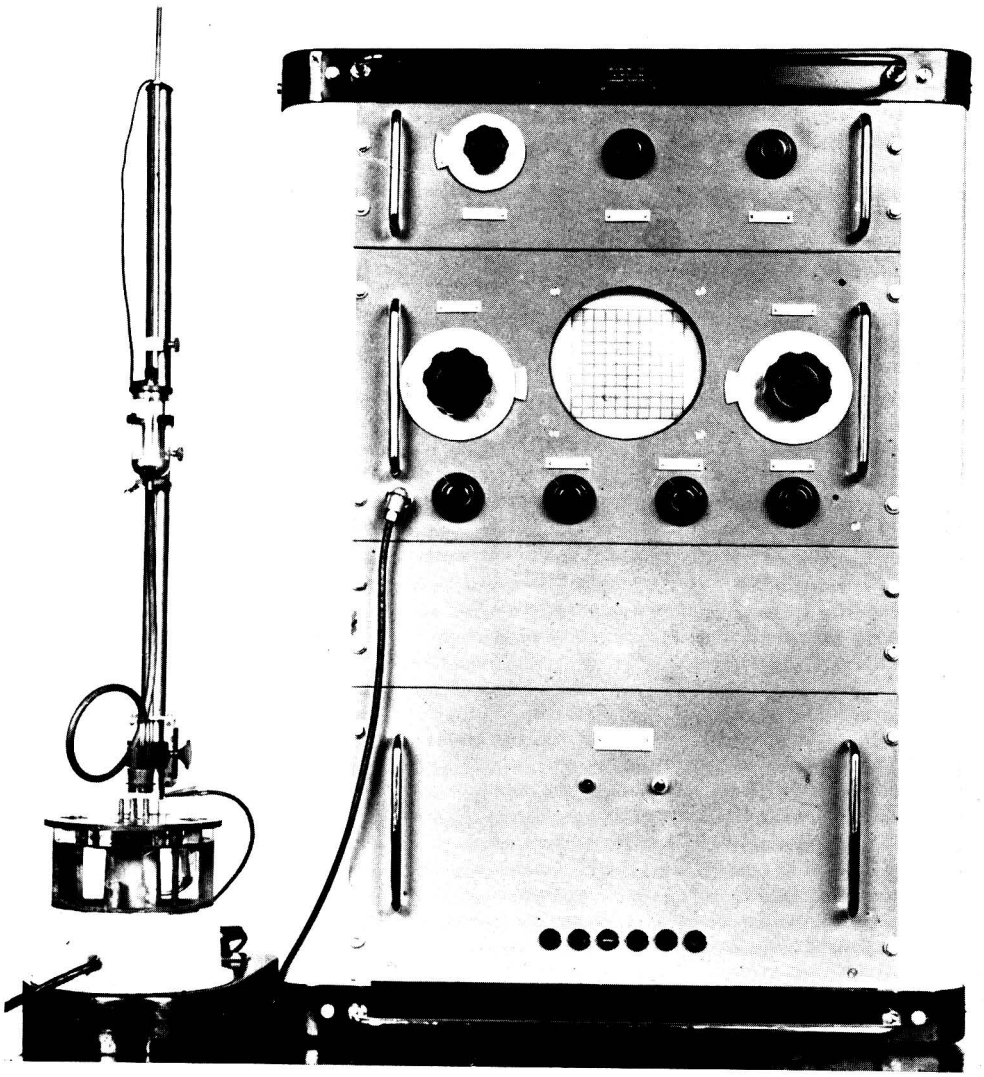

Fig. 1. The improved Randles-type cathode-ray polarograph

controlled by diffusion and gives an initial current greater than the limiting diffusion current. However, once the reducible ions in the immediate vicinity of the drop have been removed they are replaced by the usual process of diffusion, and the current falls to the limiting diffusion current. Since the amount of ion initially stripped from the solution is a function of concentration, so also is the height of the peak and, in practice, this is measured.

An equation relating the concentration of a reducible ion to the peak current has been worked out by Randles[2]—

$$i_{peak} = \frac{1{\cdot}24 \times 10^{-3}\ \mathrm{F}}{(0{\cdot}0018)^{1/2}}\ n^{\frac{1}{2}}\alpha^{\frac{1}{2}}\gamma^{\frac{2}{3}}D^{\frac{1}{2}}t_{peak}^{\frac{1}{2}}C \text{ amperes,}$$

where i_{peak} = peak value of current in amperes,
t_{peak} = time at which the peak occurs,
F = Faraday's constant,
n = number of electrons involved in the reduction of one ion,
α = rate of application of sweep voltage in volts per second,
γ = a constant depending on the rate of flow of mercury,
D = diffusion coefficient of the ion species being reduced in sq. cm per second,
and C = concentration of the ion species being reduced in moles per litre.

An alternative equation has been proposed by Sevcik,[10] but Delahay[4] has shown that these two equations can be reduced to an identical form, when they differ only in the numerical factor, and has indicated[11] that Randles' factor is more correct.

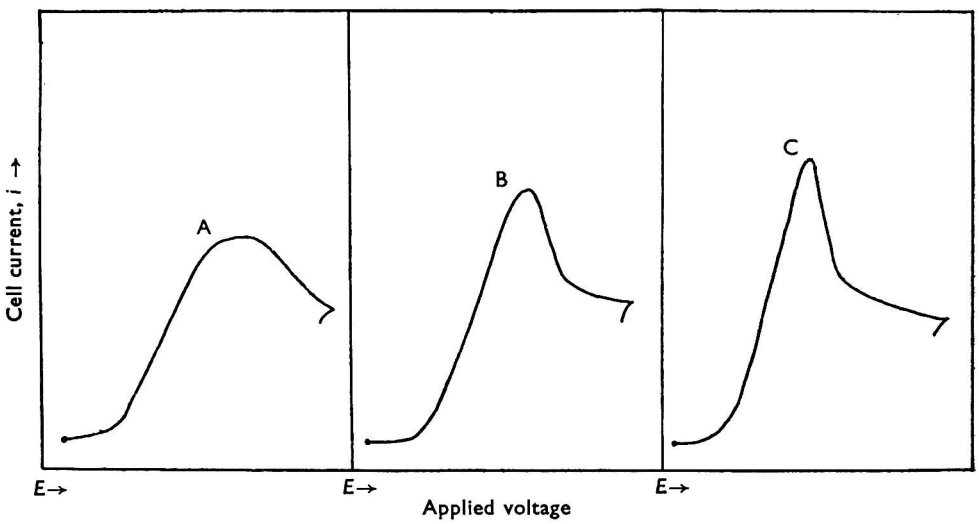

Fig. 2. Characteristic shapes of polarographic "steps." Curve A, thallium[I] in 0·1 *M* potassium chloride solution (1-electron reduction); curve B, cadmium in 0·1 *M* potassium chloride solution (2-electron reduction); curve C, aluminium in 0·1 *M* potassium chloride solution (3-electron reduction)

It is, of course, not practicable to use an equation of this complexity in normal work, and a simplified version has been made possible by virtue of the fact that many of the quantities in the equation are constants in our present instruments. The equation reduces to—

$$i = 1{\cdot}25 \times 10^{6}D^{\frac{1}{2}}m^{\frac{2}{3}}n^{\frac{1}{2}}C,$$

where i = peak height in microamperes,
and m = average mass of one mercury drop, in milligrams.

No terms relating either to drop time or to the time of drop growth appear in this equation. This is only valid if the surface area of the drop does not change appreciably during the application of the potential sweep. As already noted, this condition applies with the delay and drop times used in this instrument.

The shape of the step obtained does not lend itself to an accurate determination of half-wave potential, but the potential at which the peak occurs is constant for a given

reduction, and has been found to be about 0·05 volt more negative than the half-wave potential in the reduction concerned. The nature of the reduction step also renders the cathode-ray polarograph less useful in research work where the data required is contained in the shape of the step, *e.g.*, in the study of electron transfer and reversibility. The number of electrons per molecule involved in the reduction is indicated, however, by the sharpness of the peak; the sharpness increasing with increase of electrons transferred, as indicated in Fig. 2. The shape of the step may be modified by irreversibility. For example, with nickel in dilute chloride medium the peak is much reduced and the step is drawn out over 0·25 volt, as shown in Fig. 3. The peak height is, however, quantitatively related to ionic concentration, but the wave may interfere with the steps of other ion species that occur in the same region.

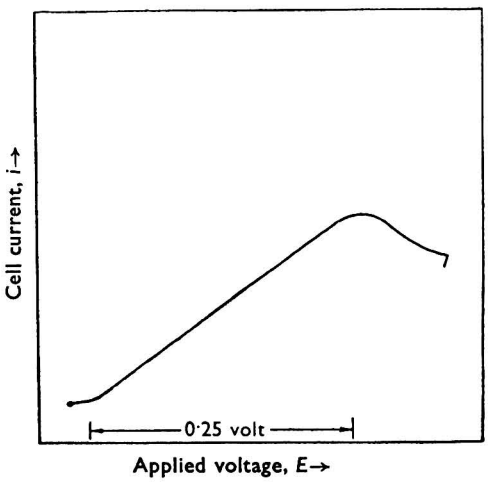

Fig. 3. Modification of step shape by irreversibility.
Nickel in 0·1 *M* potassium chloride solution

Maxima occur with the cathode-ray polarograph as with conventional instruments, but they are much less frequently met. The maximum is superimposed upon the peak of the reduction step, but the chances of failing to recognise the occurrence is remote, as the maximum peak is so sharp that no one who has seen both types would confuse them.

The advantages of the cathode-ray polarograph

The Randles-type cathode-ray polarograph is about equal to all conventional types in accuracy and reproducibility, since these factors are largely bound up with the conditions in the polarographic cell. In addition it has a number of advantages.

(1) Determinations can be made rapidly. The entire step is produced on the screen in less than 2 seconds, and a number of steps can therefore be measured in a fraction of the time required for a conventional polarogram. This renders the instrument especially suitable for routine analytical work and also for the study of kinetics.

(2) In its present form the instrument is about 100 times as sensitive as a photographic polarograph. This does not mean, however, that all solutions that are one hundred times more dilute can be handled, as conditions in the solution may preclude this. However, the extra sensitivity has enabled chemical concentration to be avoided on numerous occasions where it would otherwise have been essential.

(3) It has been found much easier to train inexperienced staff to use the cathode-ray polarograph than the photographic instrument. The reason for this is certainly because the step is under continuous observation as a whole, and the effect of changing a control setting is at once obvious. With a photographic recording instrument the effect must be inferred from the movement, over a period, of a spot of light on a scale, and is usually not fully appreciated until the polarogram has been developed.

(4) A somewhat better resolution of steps is obtained when they occur close together. This is an effect of step shape, and steps only 0·1 volt apart can be measured with the normal trace. However, a circuit has been incorporated in this polarograph that produces

a graph of di/dE against E on the screen instead of the usual i against E. In this way the steps are converted to relatively sharp peaks, as occurs with derivative circuits on conventional instruments. This is illustrated in Fig. 4. A loss of sensitivity is occasioned by the use of this circuit, but the peaks are much better resolved. The change of circuit is effected merely by the operation of a switch and adjustment of the sensitivity control.

(5) Grosser amounts of an ion species that reduces at a more positive potential than the one sought can be tolerated. For instance, cadmium can be determined in the presence of several hundred times its own concentration of lead.

(6) This type of polarograph is much less sensitive to external vibration.

In conclusion it should be pointed out that the Randles-type polarograph appears to have a number of advantages over other cathode-ray polarograph circuits. As has been stated by Delahay, the multi-sweep type of cathode-ray polarograph, in which the potential sweep is applied many times in the life of one drop (the maximum peak height being measured), is subject to errors that arise from the nature of the application of the sweep. The main

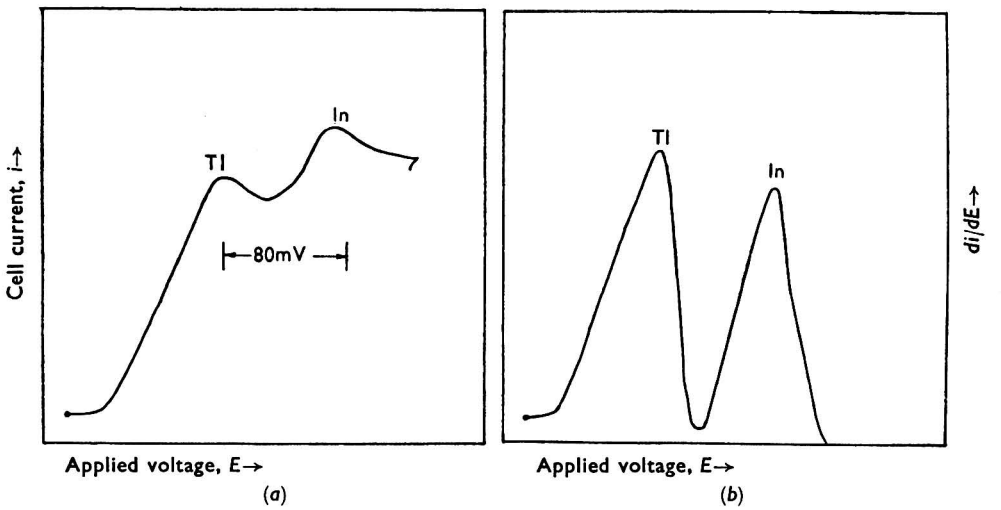

Fig. 4. Polaragrams of thallium and indium in 0·1 M potassium chloride solution. (*a*) Normal polarogram. (*b*) Derivative polarogram

cause of this appears to be that the depletion of the solution near the drop surface by a preceding sweep is not made good before the next sweep, and, hence, the peak height corresponding to maximum drop area may be depressed. The linear-sweep instrument does not suffer in this way, and is also less sensitive to minor variations in drop time.

Acknowledgment is made to the Chief Scientist, Ministry of Supply, for permission to publish this paper. The authors wish to thank Mr. A. S. Nickelson for his assistance and encouragement during the work and Dr. J. D. H. Strickland for his advice on some theoretical aspects.

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Chemical Inspectorate
Ministry of Supply
Royal Arsenal
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April 15*th*, 1952

(*After the presentation of the above paper, the instrument was demonstrated*)

Notes

DETERMINATION OF CARBON DIOXIDE AND SULPHUR DIOXIDE IN THE ORSAT APPARATUS

WHEN the well-known Orsat apparatus is used for flue-gas analysis, any sulphur dioxide present will be absorbed, together with carbon dioxide, in the first pipette containing potassium or sodium hydroxide. For most analyses, any small amount of sulphur dioxide that may be present, which will consequently be counted as carbon dioxide, is of no practical significance. In some metallurgical industries, however, gases from roasting, smelting or waste-heat boiler operations contain considerable amounts of sulphur dioxide. A rapid procedure to determine carbon dioxide in these gases in the presence of sulphur dioxide would be very desirable for industrial analyses.

Sulphur dioxide in gases is sometimes determined by absorption in an excess of standard iodine solution followed by titration of the excess of iodine with standard sodium thiosulphate solution. If the solubility of carbon dioxide in a slightly acidified iodine solution were sufficiently low it might be possible to determine carbon dioxide in the usual Orsat apparatus after prior quantitative removal of sulphur dioxide in the iodine solution.

We understand that this method is in use for routine work at certain smelters throughout the world. It is, however, inapplicable. We have found that the solubility of carbon dioxide in iodine solutions is far too high, being of the order of 0·40 volumes of carbon dioxide to one volume of 5 *N* iodine solution containing 4 per cent. of hydrochloric acid at 23° C, and appreciably higher for the more dilute iodine solution that would have to be used in practice.

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September 11th, 1952

THE PRESERVATION OF FERMENTING LIQUORS IN THE DETERMINATION OF REDUCING SUGARS

IN the course of an investigation of the factors influencing production of glycerin by fermentation of blackstrap molasses and raw sugar media by yeast in the presence of sulphite, it was necessary to preserve samples of the fermenting medium for periods of up to 24 hours before determining reducing sugars.

It was found that the method recommended for preservation of *Aerobacter aerogenes* fermenting liquors, in which neutral lead acetate was added,[1] did not completely inhibit yeast fermentations. Samples of these fermenting liquors in presence of the reagent suffered a considerable decrease in reducing-sugar content on prolonged standing at room temperature. With a molasses medium containing initially 15 g per 100 ml of total sugars (as invert sugar), di-sodium hydrogen phosphate and ammonium sulphate as yeast nutrients, and about 0·3 g per 100 ml of yeast (*Saccharomyces cerevisiae*), visible fermentation occurred in the presence of 2 to 5 per cent. of neutral lead acetate, and the initial rate of fermentation as determined by Slator's method[2] was about 40 per cent. of that when the reagent was absent (see Table I). Culture tests on agar plates showed that viable yeast cells were present after exposure for 48 hours to the lead acetate reagent.

TABLE I

FERMENTATION OF MOLASSES SULPHITE LIQUORS

Conditions	Fermentation tube test: length of column of gas at 18° C after fermentation for 3 hours, cm	8 hours, cm	24 hours, cm	Rate of fermentation by Slator's method, mg of CO_2 per minute*
Sample + equal volume of water (control)	Trace	1·2	6·5	3·0
Sample + equal volume of 10 per cent. neutral lead acetate solution	Trace	Trace	3·8	1·2

* Observations were made with 100 ml of solution at 35° C at 10-minute intervals for 1 hour. The solutions were vigorously shaken by hand at 2-minute intervals.

new edition easier to use as a work of reference than were previous editions, which, owing to repeated insertion of new matter, were beginning to show signs of a lack of cohesion and plan.

The enlargement takes, for the most part, the form of insertion of new methods and recent modifications of old ones. This new matter is scattered widely throughout the text and is of itself evidence of the careful revision that has taken place.

Important subjects that contain new writing are: bread and flour products, meat and meat products, eggs, soft drinks, preservatives and drugs. New sections deal with extraneous matter, food containers and wrappings, and with animal foods.

The notes on such legal information as is of more than transitory interest to practising analysts have been revised to the end of 1951.

In addition to the many analytical methods that are given in working detail, almost every page carries references to further information of proved worth. No paper of present importance that has appeared in *The Analyst* or *The Journal of the Association of Official Agricultural Chemists* during the past fifty years seems to have been overlooked. In this respect the book, as a whole, forms a very complete guide to the literature of food and drug chemistry.

In the preparation of this new text the author has drawn fully on his long experience of the chemistry of food and drugs and on his critical ability and gift for clear and concise exposition.

The preface to the first edition, which bore a disclaimer that this book is in any way intended to be a cram-book to the chemistry of food and drugs, is again reprinted, as in previous editions. This limitation of range is confirmed by the book's style and is indubitably true. Nevertheless, the many analysts who have disregarded this warning note and made a thorough mastery of its contents the basis of success in an examination may well be forgiven for having held a different opinion of this book's potentialities and value. F. L. OKELL

LES THÉORIES ÉLECTRONIQUES DE LA CHIMIE ORGANIQUE. By BERNARD PULLMAN, D.ès S., and ALBERTE PULLMAN, D.ès S. Pp. x + 665. Paris: Masson et Cie. 1952. Price 5800 fr.

This is stated to be the first book on its subject in the French language; as such, it must be admitted to be a lusty infant, despite its flimsy covering.

First there is a short description of the fundamentals of theoretical chemistry and then a brief survey of atomic structure. Next comes the study of the chemical bond, which is further developed with particular reference to conjugation. Resonance energy and its chief applications are discussed in some detail, then bond order and its relationship to various physico-chemical concepts. Other topics are dipole moments, electronic spectra and colour, chemical reactivity and, more briefly, diamagnetism of aromatic compounds. The whole subject is thus progressively developed from relatively simple beginnings.

At all stages the text is interspersed with many clear diagrams and illustrative tables; the references, up to late 1950, include not merely those relating to the textual matter, but also those that can be pursued for further study. This topic cannot be developed without mathematics in fair measure, but this has been kept to the minimum necessary for proper understanding and application. The book does not go beyond the confines of its title to describe the various experimental methods used in the investigation of physico-chemical properties. B. A. ELLIS

SAND AND WATER CULTURE METHODS USED IN THE STUDY OF PLANT NUTRITION. By E. J. HEWITT, B.Sc., Ph.D., A.K.C. Pp. x + 241. Farnham Royal, Bucks.: Commonwealth Agricultural Bureaux. 1952. Price 42s.

For well over a century plant physiologists have interested themselves in problems connected with the mineral requirements of plants in the spirit of fundamental scientific inquiry. It is only fairly recently that the economic aspects of mineral deficiencies in agricultural and horticultural crops have assumed their present importance, and the investigation of such deficiencies has demanded an experimental approach by a variety of methods. Few of the latter have yielded more valuable information and results than those of sand and water culture. Although such methods were first used by the older plant physiologists more than a hundred years ago, it is true to say that their full development in the study of both major and minor mineral elements in plant nutrition has been inspired by the need to solve problems of pressing economic importance affecting the growth of fruit, vegetable and agricultural crops. In this important field of plant physiology the contributions of the Long Ashton research workers have deservedly received world-wide recognition, and the present book, written by a distinguished worker under the inspiration of Professor Wallace of the Long Ashton Research Station, sets out to review the numerous sand and water culture techniques used in the study of fundamental and applied aspects of plant

nutrition. Although these methods have yet to attain a final state of perfection, Dr. Hewitt devotes a fair proportion of this book to a detailed description of the technique adopted at Long Ashton for large-scale pot sand cultures.

One of the most important discoveries of recent years has been the role in plant nutrition of the micronutrients manganese, copper, boron, zinc and molybdenum, which are required in amounts of less than 1 p.p.m. in solution. The various techniques involved in their evaluation as plant nutrients demand careful, indeed punctilious, attention in order to avoid possible sources of extraneous contamination, and this book not only provides a valuable compendium of information on the subject, but describes, with great attention to detail, the techniques evolved and perfected at Long Ashton for studying mineral aspects of plant nutrition. These details will be of great value to the newcomer in this field of applied research, especially in teaching him what errors to avoid. Analytical chemists, faced with a new and intricate determination, are always grateful to the author whose full technical descriptions with adequate explanations and reasons enable them to avoid pitfalls into which they might otherwise have fallen. In a similar manner, plant nutritionists working on mineral requirements of plants will be very grateful to Dr. Hewitt for his full and lucid description of the Long Ashton techniques, which no doubt have evolved by the long process of trial and error.

The book contains a bibliography and full author and subject indexes, suitably cross-referenced; a commendable feature is the extensive table of contents, making for easy reference to any desired section of the subject-matter covered. Altogether, Dr. Hewitt has made a most valuable contribution to plant nutrition by this extensive review of sand and water culture techniques. In such a field as this, where new knowledge is constantly accruing, no doubt even the techniques at present in use at Long Ashton will be modified and improved upon; which is a polite reminder to the author that further editions of such a useful work should not be indefinitely postponed.

A. EDEN

ANTIBIOTICS: A SURVEY OF THEIR PROPERTIES AND USES. Second Edition. Pp. ix + 290. London: The Pharmaceutical Press. 1952. Price 25s.

It is not surprising that this survey, being a second edition of "Penicillin: Its Properties, Uses and Preparations," should attempt to cover the wider field denoted in the title. It was pointed out in the preface to the first edition that no one person could hope to follow more than a fraction of all the work published on penicillin; to-day, six years later, this fraction must be far smaller, especially for the whole field of antibiotics.

When the first edition appeared in 1946 the Official Secrets Act hampered the publication of scientific information on the chemistry of penicillin, but the ban no longer applies and the chapter on Chemistry in the second edition admirably condenses that of penicillin into 11 pages, the remaining 12 being shared equally by streptomycin and the other antibiotics. The continuing progress in this field is strikingly emphasised by the publication, since this book has appeared, of structural formulae for both aureomycin and terramycin; these will no doubt find appropriate places in a future edition.

The chapter on Stability is inchoate and can be confusing to the casual reader; for instance, on page 59 solutions of penicillin containing 100,000 i.u. per ml are reported to have lost 52 to 82 per cent. of their activity in 2 days, yet on page 61 a solution of the same strength is reported as losing only 33 per cent. in 3 weeks. To resolve this inconsistency one has to turn to the original papers quoted. Again, on page 60, an account is given of the efficiency with which sodium citrate stabilises penicillin solutions, but not until page 209 is it pointed out that solutions so stabilised would be markedly hypertonic.

It is surprising to find no reference in this chapter to the incompatibility of penicillin and chlorocresol, although reference is made to it in the chapter on Pharmacy, where one also learns that *Guttae Penicillini* N.W.F. (containing chlorocresol) is still being prescribed.

It would appear that the other antibiotics are far less fastidious about their surroundings than is penicillin, for a mere 3 pages disposes of their stability troubles.

The chapter on Standards and Methods of Assay has been considerably enlarged and brought up to date; sterility testing methods are also included. The only mention of the ferric hydroxamate method for the determination of penicillin is in connection with the paper chromatographic technique of Baker, Dobson and Martin (*Analyst*, 1950, **75**, 651). Some 30 pages of this chapter are devoted to penicillin and 8 suffice for the other antibiotics, streptomycin occupying the major part.

In the chapters on Experimental Background and on Clinical Use there is one inconsistency; on page 136 the use of penethamate hydriodide (Estopen), the diethylaminoethyl ester hydriodide of benzylpenicillin, for treating respiratory infections is quoted, yet on page 161 no mention is made of its use in the treatment of diseases of the chest.

A chapter on Veterinary Practice has been included and appears to summarise the literature to the beginning of 1951 only: this no doubt accounts for the absence of any mention of the use of antibiotics in animal feeds. A summary of the legal aspects and a list of some 130 commercial preparations completes the survey, which will find a welcome place on many a shelf, if only for its references to the literature; these are now collected at the end of each chapter and number 841, compared with 331 in the first edition.

Typographical errors seem to be absent except for "chromotrophic acid" on page 104 and the use of the word "solution" on page 183 for a finely divided procaine penicillin preparation, when obviously "suspension" is intended.

Despite the slight flaws indicated by the criticisms made above, much useful information is given in this volume and there is little doubt that it will prove of value to a wide public.

D. C. M. ADAMSON

AN ADVANCED TREATISE ON PHYSICAL CHEMISTRY. Volume III. THE PROPERTIES OF SOLIDS. By J. R. PARTINGTON, M.B.E., D.Sc. Pp. lx + 639. London: Longmans, Green & Co., Ltd. 1952. Price 70s.

It is a pleasure to draw the attention of readers of *The Analyst* to the appearance of the third volume of Partington's "Advanced Treatise," the previous volumes of which have been very favourably received.

In this volume the author deals with the mechanical and thermal properties of solids, successive sections of the work being devoted to general properties; crystals; crystal lattices and space groups; isomorphism; density; elastic properties; tensile strength; hardness; surface energy; viscosity; thermal expansion; specific heat; theory of the solid state; thermal conductivity; fusion. The optical and electrical properties of solids are to be dealt with in Volume IV. In harmony with the author's definitely adopted policy, mathematical appendixes, occupying some 75 pages and dealing with vectors and tensors, the complex variable and the calculus of variations, conclude the volume. These sections should prove of much value to many chemists.

Although an individual reader, owing to his own particular interests or to the state of knowledge, will no doubt find certain sections less satisfying than others, the author has succeeded in maintaining the high standard of excellence already set by himself, an excellence shown not least, perhaps, in the sections dealing with crystals and crystal lattices.

For his comprehensive references to older as well as to more recent work and for his critical care in considering experimental data, one must be very grateful; and one should bear in mind his warning against considering the most recent work as likely to be the most accurate.

Lists of abbreviations and symbols are given at the beginning of the volume, as also are lists of errata for the first two volumes.

ALEX. FINDLAY

CHEMICAL INDICATORS. By O. TOMIČEK, Ph.D., translated by A. R. WEIR, R.Nat.Dr., B.Sc., A.R.I.C. Pp. x + 258. London: Butterworths Scientific Publications Ltd. 1951. Price 21s.

According to the translator's preface the book is intended for all students of chemistry. Chapter II caters for this by giving many illustrative examples, which, although useful for students, may be irksome to other readers. The plan has, in fact, been abandoned in succeeding chapters. The chapters dealing with acid - alkali neutralisation indicators and hydrogen-ion determination follow the well established lines. No mention is made of the recent adoption of a number of practical standards for pH determination, nor is there any explanation of the difficulty of applying theoretical considerations to accurate standardisation (pH scale, British Standard 1647 : 1950, and *Analyst*, 1952, **77**, 653). The buffer solutions recommended are those of Clark and Lubs and Sörensen, which do not quite agree with the new standards, and this may puzzle the student who has to deal with both the pH meter and buffer solutions. It would have been helpful if the translator had expressed some preference for the best colorimetric methods of pH determination, since some of those described, although interesting, are rarely, if ever, used. The student would be fortunate if he were able to repeat accurately the results, shown in Table XIII, due to Michaelis, since at high pH values the colour of phenolphthalein in solution fades appreciably. He would

also be equally lucky if he were able to repeat Table XVI, due to Kolthoff, unless he used an illuminant with a spectral distribution so favourable that the metamerism between the inorganic solutions and the indicators was not evident. Similarly, he would need better colour memory than the reviewer if he could judge pH to 0·1 unit by using the mixed indicators in Table XXIII*a* without the use of reference solutions (see *Analyst*, 1952, **77**, 742).

The most informative chapter is that dealing with oxidation - reduction indicators. The author has been at great pains to collect all the available information in a most convenient tabular form. Many of the indicators described are worthy of a wider application than they receive at present. The author has performed a useful service in giving so much information in this condensed form. The chapter on miscellaneous indicators includes some interesting and useful examples, amongst them sodium starch glycollate, which, in the reviewer's experience, is greatly superior to the soluble starch normally used to indicate the end-point in iodine titrations. The use of methyl orange is mentioned for bromate estimations, but not its use in the Cavett method for the determination of alcohol in blood and urine. The student will welcome the use of structural formulae throughout the book, particularly as the Schulz numbers are given for dyestuffs instead of the Rowe colour index numbers. The book is well printed, and the English used by the translator is clear and concise. Apart from one or two instances, such as "oxy" instead of "hydroxy" in Table XXVIII and the omission of a carbon atom in the structural formula of indigotin-5:5′-disulphonic acid, the book is reasonably free from typographical errors. J. KING

Publications Received

DISSOCIATION ENERGIES AND SPECTRA OF DIATOMIC MOLECULES. By A. G. GAYDON, D.Sc. Second Edition Revised. Pp. xiv + 261. London: Chapman & Hall Ltd. 1953. Price 35s.

FERROUS ANALYSIS. MODERN PRACTICE AND THEORY. By E. C. PIGOTT. Second Edition Revised. Pp. xxviii + 690. London: Chapman & Hall Ltd. 1953. Price 84s.

CALENDAR OF THE PHARMACEUTICAL SOCIETY OF GREAT BRITAIN, 1952–53. Pp. iv + 305. London: The Pharmaceutical Press. 1953. Price 12s. 6d.

GENERAL AND INORGANIC CHEMISTRY. By ALEXANDER FINDLAY, C.B.E., M.A., D.Sc., LL.D. Pp. xvi + 239. London: Methuen & Co. Ltd. 1953. Price 8s. 6d.

QUALITATIVE ANALYSIS AND ANALYTICAL CHEMICAL SEPARATIONS. By PHILIP W. WEST, Ph.D., MAURICE M. VICK, Ph.D., and ARTHUR L. LEROSEN, Ph.D. Pp. xii + 223. New York: The Macmillan Co. 1953. Price $3.75.

A HANDBOOK OF COLORIMETRIC CHEMICAL ANALYTICAL METHODS FOR INDUSTRIAL, RESEARCH AND CLINICAL LABORATORIES. DEVELOPED FOR USE WITH THE LOVIBOND COMPARATOR. Pp. xii + 119. Salisbury: The Tintometer Ltd. 1953. Price 15s.

CHEMICAL ANALYSIS. Volume VII. CHEMICAL ANALYSIS OF INDUSTRIAL SOLVENTS. By MORRIS B. JACOBS, Ph.D., and LEOPOLD SCHEFLAN, Ph.D. Pp. xxii + 501. New York and London: Interscience Publishers Inc. 1953. Price $10.00; 80s.

POLYSACCHARIDE CHEMISTRY. By ROY LESTER WHISTLER and CHARLES LOUIS SMART. Pp. xvi + 493. New York: Academic Press Inc. 1953. Price $10.80.

A TEXTBOOK OF PURE AND APPLIED CHEMISTRY. By JAMES E. GARSIDE, Ph.D., M.Sc.Tech., F.R.I.C., F.I.M., and R. F. PHILLIPS, M.A., B.Sc., Ph.D., F.R.I.C. Pp. x + 1044. London: Sir Isaac Pitman & Sons Ltd. 1953. Price 25s.

STARCH AND ITS DERIVATIVES. Volume I. By J. A. RADLEY, M.Sc., F.R.I.C. Third Edition Revised. Pp. xii + 510. London: Chapman & Hall Ltd. 1953. Price 65s.

THE DESIGN AND ANALYSIS OF EXPERIMENT. By M. H. QUENOUILLE, M.A., F.R.S.E. Pp. xiv + 356. London: Charles Griffin & Co. Ltd. 1953. Price 36s.

ELEMENTS OF FOOD ENGINEERING. Volume I. By MILTON E. PARKER, ELLERY H. HARVEY and E. S. STATELER. Pp. x + 386. New York: Reinhold Publishing Corp.; London: Chapman & Hall Ltd. 1952. Price 70s.; $8.75.

REPORT OF THE ANALYTICAL METHODS COMMITTEE

THE Interim Report of the Meat Extracts Sub-Committee, "Determination of Gelatin in Meat Extract and Meat Stocks," reprinted from *The Analyst*, March, 1953, **78**, 134–135, is now available from the Secretary of the Society, Miss D. V. Wilson, 7–8, Idol Lane, London, E.C.3; price to members 1s. 6d. and to non-members 2s. 6d. Reports of the Analytical Methods Committee are only obtainable direct from the Secretary (not through Trade Agents) and remittances must accompany orders.

A YOUNG GRADUATE with a chemical degree required as Technical Assistant to Chief Chemist of a Valve Development Laboratory to act as liaison with and introduce new processes to the Manufacturing Division of the Company. Previous experience in the radio valve industry will be considered an advantage, but is not essential for this post. Applications, stating age, full details of experienc and salary expected, should be addressed to the Managing Director, Box No. 3841, THE ANALYST, 47, Greshom Street, London, E.C.2

SENIOR ANALYTICAL CHEMIST required at chemical works in provinces. Principal duties involve research into new methods of analysis. Applicants should be of A.R.I.C. or honours degree standard, and should have had several years' experience in analytical chemistry. Starting salary £600–£800 per annum according to experience. Write stating age and full particulars of qualifications and experience, salary required, etc., to Box No. 3842, THE ANALYST, 47, Gresham Street, London, E.C.2.

ALBRIGHT & WILSON LTD. have a vacancy for a graduate chemist at the Company's factory at Oldbury. The work comprises analytical investigation and research into analytical methods concerning phosphorus compounds. The qualifications desired are a degree in chemistry together with knowledge of investigational methods and experience of analytical research. Those taking a degree in 1953 will be considered if possessing a genuine analytical interest. Age 23–28. Non-contributory pension scheme. Salary according to age, qualifications and experience. Apply to the Appointments Officer, Albright & Wilson Ltd., Oldbury, Birmingham.

EAST MALLING RESEARCH STATION

CHEMIST required for mineral analysis of plants. The post entails routine work, including microchemical procedures and supervision of assistants. Applicants for the appointment, which may be in the Experimental Officer grade, should have a pass degree or equivalent qualifications and substantial experience in routine chemical analysis. Superannuation under the Ministry of Agriculture Scheme. Further particulars and application form may be obtained from the Secretary, East Malling Research Station, near Maidstone, Kent, by whom applications should be received not later than 15th June.

ANALYTICAL CHEMIST graduate required for the Research Laboratories of British Insulated Callender's Cables Limited, 38, Wood Lane, W.12, with experience with inorganic chemical analysis and a good knowledge of instrumentation as applied to analytical work. Applications should be made in the first instance to the Staff Officer, B.I.C.C. Ltd., 21, Bloomsbury Street, London, W.C.1.

VACANCY in food laboratory in N.W. London area for laboratory assistant with Intermediate B.Sc. who is continuing studies for degree. Salary in the region of £300 p.a. depending on experience. Write Box No. 3843, THE ANALYST, 47, Gresham Street, London, E.C.2.

ARMSTRONG SIDDELEY MOTORS require urgently an experienced Analytical Chemist, preferably B.Sc. or A.R.I.C., to control analytical work of ferrous and non-ferrous alloys. Reply in detail to Reference ZR.1, Personnel Manager, Armstrong Siddeley Motors, Coventry.

ASSISTANT CHEMIST required for industrial establishment in Malaya, age 25–30, with good training in Metallurgical and Inorganic Analytical Chemistry and preferably some experience in an industrial laboratory. It is desirable, though not essential, that the applicant should be single. The salary will be Malayan dollars 770 per month (equivalent to £1,078 per annum) with annual increments of Malayan dollars 35 per month, cost of living allowance (at present single men £280 per annum and married men £490 per annum) and free housing. Write with full details age, qualifications and experience to Box No. 6725, c/o Charles Barker & Sons Ltd., 31, Budge Row, London, E.C.4.

TATE & LYLE LIMITED require a qualified male Analyst (A.R.I.C. or B.Sc.) for their Liverpool refinery. Applicants should be under 35 and have at least two years' varied experience; a knowledge of bacteriology would be an asset. Pension scheme. Canteen. Salary according to qualifications and experience. Full particulars should be sent to the Personnel Manager, Tate & Lyle Ltd., Love Lane, Liverpool, 3.

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