

BOOK REVIEW

MICRO-DIFFUSION ANALYSIS AND VOLUMETRIC ERROR

By Edward J. Conway, M.B., D.Sc.

(Crosby, Lockwood and Son, Ltd. London. 1947. Pp. 357. 55 illus. Price 21s.)

One of the most important advances in biochemical analysis in the past fifteen years has been the development of the so-called "ultramicro" or "drop-scale" methods. These make it possible to work with weights of a few microgrammes of material and with volumes of a few cubic millimetres. Prof. Conway, who has been a prominent worker in this field, presents in his book an important aspect of it. The microdiffusion method developed by him is both elegant and simple. A gaseous reaction product is allowed to diffuse (usually at room temperature) from an annular space into an inner chamber charged with a suitable absorbent. It can then be determined by any method, volumetric, colorimetric, or gravimetric, which can be adapted to the ultramicro scale. In theory at least, any reaction producing a reactive gaseous product could be followed by microdiffusion methods. The simplicity and accuracy of the Conway methods are outstanding, while the range of utility of the technique can be gauged by the methods at present available. These comprise ammonia and aliphatic amines (including ultramicro Kjeldahl methods), urea, adenine compounds, nitrates, amides, halogens and halides, acetone, lactic acid, ethyl alcohol, the amino acid threonine, carbon monoxide, carbon dioxide, and glucose. A recent addition, which may be of considerable importance in the future, is a vapour pressure determination on the ultramicro scale.

The book is divided into three sections. The first deals with the general theory of micro-diffusion analyses,

both from the theoretical and experimental aspects. It provides a secure foundation for the analytical methods described, with full experimental details in the second section. Although the greater part of this section is devoted to the Conway methods, microdiffusion techniques of other workers are also given in detail. The third section provides an admirable discussion of error in volumetric analysis. The emphasis throughout is on statistical methods of evaluation of error, and the whole section is a most valuable contribution to the theory of analytical chemistry. It stands in vivid contrast to the vague generalities current in many text-books of analysis.

Major points of criticism are few. The symbols χ and μg are used interchangeably for the microgramme, apparently at random. The chapter on micro-burettes does not mention the micrometer syringe, which many workers prefer to any of the apparatus described. It is stated rather dogmatically (p. 68) that "the Lambert-Beer law . . . is not valid on the presence of proteins." This is certainly not true; many dyes obey the Lambert-Beer law over a wide concentration range in the presence of serum proteins. The term "monochromatic radiation" is somewhat loosely applied to the relatively wide wave bands isolated by filters, and it is not made clear that the Lambert-Beer law is only strictly valid for monochromatic light in the physical sense. The principles governing the choice of light filters are given very slight treatment. Many would feel that, in view of the almost universal use of photoelectric absorptiometers today, the space given to visual instruments is disproportionately large. Misprints are few and none is misleading.

This book is the first, to the reviewer's knowledge, to give a detailed account of ultramicro methods, and it is to be hoped that it will introduce the techniques and the principles behind them to many who will find them of use in their own problems. C. J. O. R. M.

BRITISH AND FOREIGN OFFICIAL PUBLICATIONS

THE ROAD BACK TO HEALTH : THE STORY OF MEDICAL REHABILITATION

(H.M.S.O. 1947. Pp. 28. Price 6d.)

Whatever one's reactions to blasts of propaganda, there can be few more popular ports of call for the occasional visitor to London than the Retail Department of H.M. Stationery Office in Kingsway, and it would indeed be a hardened sales-resistant misanthrope who left without the attractive sixpennyworth of excellently reproduced press photographs entitled *The Road Back to Health* (S.O. Code No. 32-371) presented in a sky-blue cover with the subtitle *The Story of Medical Rehabilitation*. It will be to the hypersensitive alone that the first three words, *The Road Back*, are slightly reminiscent of *Der Weg Zuruck*, but the subtitle is open to more serious criticism, for the frontispiece is a full-page illustration of

a patient in the inevitable dressing gown, toying with basket work reposing on the beginnings of a rug, over a caption which can only mean that he is in the process of recovery from pneumonectomy. Thereafter the volume is devoted to surgical rehabilitation as opposed to medical rehabilitation, though reference is made to the uses of physiotherapy in bronchitis, asthma, and pneumonia.

In his foreword the Minister points out that the book is intended for hospital authorities, family doctors, welfare workers, Trade Union officials, and voluntary bodies, and expresses the hope that members of the public who read this book will realize what is being done and also what is to follow.

The story of surgical rehabilitation is well told and the relationship of physiotherapy, remedial exercise, occupational and "diversional" therapy, is clearly presented, as is also the role of the almoner and welfare worker.

More could possibly be said, even in a brief résumé, confining its attention to schemes sponsored by the Ministry of Health, about the development of industry round special sub-standard communities, as exemplified for instance by village settlements; in this connexion it is particularly necessary to keep in view the relationship between diversional therapy and true rehabilitation, with its economic as well as remedial implications.

L. B. Stott.

THE EFFECTS OF ALIPHATIC NITROUS AND NITRIC ACID ESTERS ON THE PHYSIOLOGICAL FUNCTIONS WITH SPECIAL REFERENCE TO THEIR CHEMICAL CONSTITUTION

W. F. Von Oettingen. *National Institute of Health Bulletin*, No. 186. Washington. 1946. Pp. 66. Refs. 228

The pharmacological and toxicological actions of aliphatic nitrous acid esters (alkyl nitrites) are characterized by a fall of the blood pressure due to peripheral vasodilatation, acceleration of the pulse rate, and, if exposure is sufficient, by the formation of methæmoglobin. The fall of the blood pressure is due to peripheral vasodilatation, which is bound to the grouping R-ONO. The properties of ethyl nitrite and amyl nitrite are described in detail.

Aliphatic nitric acid esters are explosive and the properties of methyl nitrate, ethyl nitrate, ethylene glycol mononitrate, ethylene glycol dinitrate, glycerol dinitrate, glycerol trinitrate, erythritol tetranitrate, pentærythritol tetranitrate, mannitol hexanitrate, mannitol pentanitrate, 1, 4, 3, 6-dianhydromannitol-2, 5-dinitrate are reviewed. All cause lowering of the blood pressure and methæmoglobinæmia.

The mechanism of the circulatory changes has only been closely studied for amyl nitrite and glycerol trinitrate. An extensive review of pharmacological literature is given. Both cause an increase in pulse rate and lowering of blood pressure. Small doses which do not affect the blood pressure increase the cardiac output. The pressure on the pulmonary artery increases (and may lead to pulmonary oedema). The coronary arteries are dilated. Little information is available about the effects of continued exposure.

Methæmoglobin resulting from the action of aliphatic nitrous and nitric acid esters is of importance in the acute toxicity of these compounds, especially of those—such as ethylene glycol dihydrate—with which this effect is marked. This methæmoglobinæmia may lead to an anoxic condition in vital organs, especially the brain and the heart muscle.

T. A. Lloyd Davies.

THE TOXICITY AND POTENTIAL DANGERS OF METHYL BROMIDE WITH SPECIAL REFERENCE TO ITS USE IN THE CHEMICAL INDUSTRY, IN FIRE EXTINGUISHERS, AND IN FUMIGATION

W. F. Von Oettingen. *National Institute of Health Bulletin*, No. 185. Washington. 1946. Pp. 37. Refs. 54.

Methyl bromide (monobromomethane CH_3Br) is a colourless gas which solidifies at -93°C . and boils at 4.5°C . On a large scale methyl bromide is made by heating sodium bromide, methanol, and sulphuric acid to 130°C . in a closed process. Methyl bromide-air mixtures are incapable of ignition but at raised temperatures decompose to carbon dioxide and carbon monoxide,

hydrogen bromide and bromine, and in some circumstances to carbon oxybromide. The halide lamp is unreliable for detection of methyl bromide below 50 parts per million. Reliable chemical methods of estimation are described.

Methyl bromide is used as a methylating agent, in fire extinguishers, as a fumigant and insecticide. Absorption is nearly always through the lung but may, if swallowed, be through the gastrointestinal tract. The amount absorbed through the skin is disputed. Methyl bromide is distributed throughout the body and stored in tissues rich in lipid material. Excretion, which is slow, is through the lungs and kidneys. Its toxicity for animals has been widely studied, and in general the symptomatology and pathology are similar to that in man. Deaths from acute poisoning result from its irritant effect on the lungs and from chronic poisoning from changes in the central nervous system. Published reports of experimental findings in dogs, cats, rabbits, mice, rats, guinea pigs, and monkeys are reviewed.

Since 1899, 28 cases of fatal methyl bromide poisoning in the human subject have been reported. Fourteen occurred in chemical or filling operations, 4 from the use of methyl bromide as a fumigant, 10 from the use of fire extinguishers. In addition, 150 cases of non-fatal poisoning, including 6 of systemic poisoning with skin injury, have been recorded. In addition, 32 instances of skin injury have been reported. The literature is reviewed in detail, and a complete list of authors and references given. The fatal cases resulted from exposure to relatively high concentrations (varying from 8,600 to 60,000 parts per million). In general, the onset of toxic symptoms is delayed: the latent period is usually from 4 to 6 hours but may be as short as 2 hours or as long as 48. Early symptoms of fatal poisoning are headache, visual disturbance, nausea, vomiting. Other symptoms, such as smarting of the eyes, skin irritation, listlessness, vertigo, and tremor, may occur first. Tremors and twitching develop into epileptiform convulsions; and, rarely, convulsions or unconsciousness may be the first sign. Cyanosis results from pulmonary oedema; fever is frequent, and heart failure supervenes. In view of the rapid progress clinical studies are rare, but inconsistent signs are met with in the central nervous system. The serum bromide is markedly raised. The most significant changes are found in the respiratory tract: the trachea and bronchi are inflamed with blood-stained or purulent exudate, the lungs are hyperæmic and oedematous. The meninges and brain are hyperæmic, and the latter may show petechial hæmorrhages. The brain is frequently oedematous, with ganglionic changes characterized by fatty degeneration, shrinkage, and pyknosis.

The immediate cause of death is the pulmonary injury associated with circulatory failure; whereas the cerebral changes, though significant for the clinical picture, are less extensive.

The clinical picture of non-fatal poisoning shows great variation. Symptoms have followed exposure to between 100 and 500 of methyl bromide parts per million. Fatigue, blurred or double vision, nausea, and vomiting, are frequent. Inco-ordination with tremors and convulsions are common; the patellar reflexes are exaggerated, clonus is present, and Babinski's sign is positive. Nearly every type of nervous disturbance has been reported. In contrast with fatal cases, the pulmonary symptoms are comparatively slight. Even moderate poisoning may lead to prolonged illness or permanent injury, commonly characterized by sensory disturbances, weakness, paresthesial and blurred vision. Occasionally