



Fig. 2

of creatinine in 20 ml. water was run into the column. Two visible bands were formed, the lower of which was coloured dark reddish-brown (glycine) and the other yellowish-orange (creatinine). The column was then washed with water to remove anions present as impurities. Finally, 0.043 *M* ammonia solution was used as the displacement developer. A volume of 140 ml. of ammonia solution was passed into the column before the *pH* and resistance of the effluent changed from that of the distilled water used. The lower band of glycine then emerged from the column, followed by the next band (creatinine), the two bands overlapping as shown in the lower half of Fig. 2. Finally, the ammonia band emerged, the front overlapping with the tail of the creatinine band. In the figure the volume of effluent (abscissæ) is plotted against the concentration of solute (ordinates) from the time at which the first change in *pH* and resistance occurred. The concentration is expressed as a percentage of the expected concentration calculated from the retention isotherms. This concentration (the equilibrium concentration) is readily obtained by the graphical method of Claesson²; a straight line is drawn from the origin to the point on the isotherm of the developer, corresponding to a concentration of 0.043 *M*. The intersection of this straight line on the corresponding isotherms of glycine and creatinine then gives the concentration at which these components will emerge from the column.

The volume-concentration curves for the glycine, creatinine and ammonia fractions are plotted separately in the figure as histograms, the base of each rectangle representing the volume of the fraction taken for chemical analysis. In the upper half of the figure, the *pH* (mV.) and the resistance (in ohms $\times 10^4$) (ordinates) are plotted against the volume of effluent (abscissæ). It will be seen that these curves give a very clear indication of the actual concentration-changes in the effluent. Chemical analysis of the fractions showed that 87.5 per cent

of the total glycine and 73.0 per cent of the total creatinine were recovered pure. The total recovery of glycine and creatinine was respectively 98 and 103 per cent.

In the experiment described above, the solutes were displaced in order of their ϵ -values, glycine ($\epsilon = 1.81$) emerging first, followed by creatinine ($\epsilon = 2.20$) and ammonia ($\epsilon = 2.88$). Reference to the table, however, shows that this order is not the rule. The ϵ -values of the various bases or amino-acids are quoted at the equilibrium concentration at which they emerge when displaced with 0.10 *N* barium hydroxide.

RETENTION DATA OF A NUMBER OF BASES AND AMINO-ACIDS ON 'ZEO-KARB. 215'

Substance	Equilibrium concentration (<i>c</i>) (millimols/ml.)	ϵ	<i>pH</i> of emerging solution
$\frac{1}{2}$ Ba(OH) ₂	0.1	5.45	12.72
NaOH	0.071	3.87	12.85
NH ₄ OH	0.055	3.00	11.00
Anserine	0.035	1.91	8.27
Carnosine	0.035	1.91	8.17
Creatinine	0.041	2.23	8.17
Creatine	0.037	2.02	7.00
Glycine	0.033	1.80	5.97
Glutamic acid	0.0325	1.77	3.22
Aspartic acid	0.023	1.25	2.77

In the table, the bases are arranged in the order in which they displace one another, and the displacement is seen to be in ascending order of the *pH* values given by the emerging components. Thus, although creatinine and creatine have higher ϵ -values than anserine, the latter displaces them from the column. In the table the brackets include substances which do not separate completely on short columns.

Experiments carried out using longer columns and more complex mixtures have given encouraging results, and the technique shows promise as a method of general application for the isolation of amino-acids and bases.

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¹ Tiselius, A., *Ark. Kem. Min. Geol.*, **16** A, No. 18 (1943).

² Claesson, S., *Ark. Kem. Min. Geol.*, **23** A, No. 1 (1946).

CHEMICAL CARCINOGENESIS

THE discovery and development of cancer-producing chemical compounds represent a major achievement of cancer research in Britain, although many important contributions have been made in other countries, notably in Japan and in the United States. It is therefore peculiarly appropriate that the British Council should sponsor the publication of an excellent and comprehensive series of articles reviewing the whole field of chemical carcinogenesis*. There are papers by twenty authors from eleven different research centres, representing the main fields of cancer research activity in the United Kingdom. This symposium ranks in importance with, and supplements, the symposium on cancer research published in 1945 by the American Association for the Advancement of Science (see *Nature*, **158**, 217; 1946). The planning of the British Council's publication was carried out with the advice of Prof. Alexander Haddow, who has himself contributed three interesting articles, one of them in collaboration with Prof. G. A. R. Kon. "Its intention is not merely to provide

* This is the general title of a series of articles which comprise a special number of the *British Medical Bulletin* (**4**, Nos. 5-6; 1947).

a conspectus of our present knowledge, but to indicate also the probable trends of development for the years ahead."

The articles are classified under seven sub-headings; namely, nature of carcinogenic compounds; mechanism of carcinogenesis; metabolism of carcinogenic compounds; carcinogens of biological origin; remote carcinogenic action; occupational cancer; chemotherapy of cancer. They are based on research carried out with the support of the British Empire Cancer Campaign, to which acknowledgment is justly made as having achieved more than any other single body towards advancing the study of cancer in Britain. This in no way obscures the valuable part played by the Imperial Cancer Research Fund and many of the voluntary hospitals, or the generous financial support given to British research centres from American sources, such as the International Cancer Research Foundation, the Anna Fuller Fund, and the Jane Coffin Childs Memorial Fund.

There is little doubt that the greatest promise of a final solution to the social as well as the scientific problems of cancer lies in a full understanding of the nature and causes of malignant growth and of the conditions which promote it. So far as can be judged at present, there are two main avenues by which these objectives may be approached. One is concerned with the study of chemical carcinogenesis, and the other with the induction and transmission of tumours by viruses. It is interesting that whereas the discovery of chemical carcinogenesis was primarily a British achievement, the three major discoveries in connexion with virus tumours were made in the United States. These are concerned with the viruses of the Rous chicken sarcoma and the Shope papilloma of the cotton-tail rabbit, and the 'milk factor' in mammary carcinoma of mice, discovered by Bittner. The chemical and the virus methods of investigating the causation of cancer are complementary, and in his article on the mode of action of carcinogens Haddow has attempted a synthesis of the two. His speculations are based on recent advances in cell physiology which have emphasized the importance of the cytoplasm, as distinct from the cell nucleus, in cell growth and heredity.

The subject of chemical carcinogenesis may be said to have originated in the clinical observations of Percivall Pott, published in 1775, on chimney sweep's cancer. Pott was a surgeon at St. Bartholomew's Hospital, and his clear-sighted deductions as to the role of soot in the disease which he described had their final consummation in the researches carried out and inspired by E. L. Kennaway at the Royal Cancer Hospital, leading to the discovery of the carcinogenic properties of polycyclic aromatic hydrocarbons. By common consent, Sir Ernest Kennaway is acknowledged as the outstanding British cancer research worker of the present century, and to have been a member of his team is the greatest privilege that has fallen to the lot of the present writer. There is a certain fitness in the circumstance that Kennaway has gone to work, during his years of retirement, in the same hospital in which his distinguished prototype, Percivall Pott, did his pioneer work. The intimate association between the various forms of industrial cancer and the experimental cancer due to chemical compounds is recalled by three articles in the symposium under discussion. Dr. S. A. Henry gives a review, with illustrations and statistics, of occupational skin cancer; Dr. M. W. Goldblatt discusses occupational cancer of the bladder; and Dr. A. N.

Currie deals with the role of arsenic in industrial cancer. In regard to the latter, Kennaway (*Lancet*, ii, 769; 1942) has pointed out that the evidence for the carcinogenic action of arsenic is very slender.

One means of studying the mechanism of carcinogenic action is to determine the influence of various factors in promoting or retarding the production of tumours. Cocarcinogenic agents, such as croton resin, are discussed by Dr. I. Berenblum, and inhibitors of carcinogenesis by Mr. H. G. Crabtree, who gives an account of the effect of nutritional factors in inhibiting the induction of liver tumours. Another important factor, dealt with by Prof. F. Dickens, is the influence of the solvent which is used for the administration of a carcinogenic agent. The evidence for the presence of carcinogenic substances in human tissues is analysed by Dr. I. Hieger, and attention is directed by Dr. P. R. Peacock to the possible conversion of fats into carcinogens during cooking processes. These are all important aspects of chemical carcinogenesis, and represent some of the directions in which further efforts should be concentrated.

The upheaval of war has had its impact on the progress of cancer research, and there is now need for considerable intensification of effort. The present symposium would serve an invaluable purpose even if it did no more than provide an interesting and authoritative survey of the present state of knowledge in an important branch of cancer research for a new generation of scientific workers, of whom some may be attracted to work on this intriguing and elusive problem.

J. W. COOK

DIFFUSION OF DISSOLVED SUBSTANCES THROUGH THALLI AND LEAVES OF AQUATIC PLANTS

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SO far as I know, there is no information in the literature as to the rate of diffusion of dissolved substances through plant tissues. With animal tissues such investigations have been made, for example, by Krogh¹. Of course, botanists have been interested in the problem of diffusion, but it has been tackled differently. Instead, investigations have been made as to how the various substances enter the cells. It is the so-called permeability that has been determined. It is, however, impossible to obtain any values for the rate of diffusion through the cells by this method.

Diffusion is due to differences in concentration and follows the so-called Fick's law. If the concentration (mol./l.) in two layers at a distance of 1 cm. from each other is C_1 and C_2 ($C_2 > C_1$), there will be through A cm.² in t times 24 hr. a diffusion of an amount Q

$$(\text{in mols.}) = k \times \frac{C_2 - C_1}{l} \times A \times t \times 10^{-3}, \text{ where } k \text{ is}$$

a coefficient dependent on the substances and the temperature, the diffusion coefficient.

In what follows, the word 'diffusion' is used in a wider sense than commonly. For a substance like oxygen it is only to be kept in mind that the concentration gradient, because of the cytoplasmic membranes, is not even through the plant. When salts