held in the closed fist rather than by the fingers, to obtain as even as possible an application of heat to the tube, keeping sufficient clear view of the meniscus to pick up the first drop of melt with the capillary; the intention is to permit sufficient heat energy from the hand to penetrate the plastics tube only to melt the outer surface of the ice mass. The dehydrated solute lying at the interface of ice mass and tube is redissolved in the small quantity of water which is permitted to result.

Methods for Measuring Serum Gentamicin Concentrations

In two papers (*J. clin. Path.*, 1974, 27, 447-451, 452-456) Phillips *et al* and Ten Krooden and Darrell have compared three methods for measuring serum gentamicin concentrations. Both state that the urease method (Noone, Pattison, and Samson, 1971; Noone, Pattison, and Slack, 1972) is less accurate than either the 18-hour plate assay or the adenylase method of Smith, Van Otto, and Smith (1972). It was insufficiently emphasized that this inaccuracy is not an intrinsic feature of the urease method *per se* but probably the result of inexperience with the method.

Although we too have compared the three methods, we have not sought to publish the results because we consider that, since we do not have equivalent experience and expertise with all three methods, there could not be a valid comparison. Surely the only way to compare these methods for their intrinsic accuracy and reproducibility is by comparing the results obtained by workers equally experienced in the use of the individual methods. We have had a great deal of experience with the urease method and have elucidated its mode of action (Pattison *et al*, 1974).

Our own evaluation of the urease

The technique has been in use in this laboratory for two years and has given excellent results, comparable with osmotic methods of concentration with apparently less denaturation. In this connexion it is interesting to note that we have not seen the 'tau' fraction on csf electrophoresis using this means of concentration,² although comparison of serum before and after dilution and reconcentration sometimes indicates diminution in β -globulin levels.

method (in press) shows that it can produce results as consistently accurate as the best performed plate assays (table). From the data of Ten Krooden and Darrell, it is apparent that our results are on the whole better than the adenylase method in their hands (table). In this study the urease assays were performed by two junior technicians and one qualified technician (each doing eight assays at each nominal concentration). None of them had had more than six months' experience with the method.

Ten Krooden and Darrell correctly stress the necessity of obtaining results rapidly in order to provide the data required for accurately controlling gentamicin therapy in seriously ill patients. However, both these workers and Phillips *et al* have used a plate diffusion assay involving 18 hours of incubation in their comparisons. We know of no data that are available to compare the urease and 'rapid' plate assay method (incubation period four to six hours). Nor do we know of any extensive statistical comparison between rapid plate assays and overnight plate assays.

Therefore, it would seem that the only methods which will provide results rapidly enough for clinical use and which have been subjected to some statistical validation are the urease and adenylase methods.

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- ¹Smith, A. U. (1961). *Biological Effects of Freezing and Supercooling*, Ch. 11. Arnold, London.
- ²Henry, R. J., *et al* (1974). *Clinical Chemistry, Principles and Techniques*, 2nd ed., p. 445. Harper and Row, New York and London.

Since both methods can be of equivalent accuracy the decision as to which method to use must be based on other factors. The urease assay is more rapid and less expensive than the adenylase method; and the salt-free variation (Noone *et al*, 1972) requires only 0.3 ml of serum. The only technical skill required is that of pipetting. Because of the small volumes involved this must be accurate. We have found that Oxford and Epanorff automatic pipettes are satisfactory providing care is taken to use them properly (in particular to avoid bubbles in the tip).

The only expense is the need for a pH meter, reading to two decimal places (about £200-£250). That used by Phillips *et al* is stated as reading to one decimal place only, which greatly reduces the potential for accuracy.

The urease method can be organized easily in routine, clinical laboratory practice. Assay tubes, containing urea medium and gentamicin standards only, are made up on Monday morning to provide sufficient sets for a week's tests. This will take about one hour at the most. The sets are stored at 4°C or frozen until needed when (after thawing) test and pool serum and the proteus inoculum are added. This takes five to 10 minutes at the most. The proteus is subcultured each day into fresh Todd Hewitt broth

Expected Concentration	Number of Assays	Mean	Mean Percentage Error	Standard Deviation	Mean + 2 SD of Percentage Error
<i>Ten Krooden and Darrell</i>					
3.0	8	2.7	10.0	0.47	45.0
5.0	8	4.97	0.6	0.71	29.2
6.5	8	7.30	12.0	0.51	26.0
12.0	8	11.61	3.0	0.72	15.4
<i>Noone, Pattison, and Garfield Davies</i>					
4.0	24	4.17	4.0	0.43	24.6
8.0	24	8.18	2.0	0.66	18.2
12.0	24	12.00	0	0.99	17.0

Table

with a CLED purity plate. In all, little technical time is involved and a 24-hour service can be provided giving results in less than two hours of the taking of the specimen. This rapidity and ease of execution are important advantages in clinical laboratory practice. The fact that most technicians can become proficient in the use of this method facilitates on-call arrangements and is an important advantage over the adenylase method, which requires greater skill, constant attention during performance, and the handling of radioactive material. A method that can only be performed by a few key persons inevitably runs into problems during weekends, holidays, and sickness. In addition, the adenylase method requires the use of expensive isotopes and purchase of a liquid scintillation spectrometer (£5,000 or more) which virtually excludes its use outside of teaching hospital laboratories. Even in most of the latter such expensive equipment will have to be shared with other departments to justify such expenditure and this may impede access for emergency assays.

The rapid plate assay is performed by many laboratories and if properly done is better than no assay service at all. Nevertheless it takes considerably longer to perform and can only just be fitted into a normal laboratory working day. Where the danger of initial undertreatment of septicaemia is the problem, six hours is too long a time to wait for a result. Most technicians find plate assays at least as time consuming and no easier to perform than the urease assay.

The urease method is currently being used successfully in over a dozen laboratories to our knowledge. If there are microbiology technical or medical staff who wish to try the method or are having problems with it then they should contact Dr Noone at the Microbiology Department, Royal Free Hospital. Arrangements can be made for a visit to the department to learn the technique or sort out difficulties.

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Book reviews

Host Environment Interactions in the Etiology of Cancer in Man: Proceedings of a meeting held at Primosten, Yugoslavia, 27 August to 2 September, 1972

IARC Scientific Publications No. 7). Edited by R. Doll and I. Vodopija. (Pp. xix + 464; illustrated. Sw.fr. 100.-.) Lyon: International Agency for Research on Cancer. 1973. Distributed for IARC by the World Health Organization, Geneva. Available through HMSO, London.

Organizers sometimes seem to overstrain themselves in dreaming up titles for conferences which, in reality, cover a not unusual range of topics. This book records the proceedings of a week-long meeting which took place in Yugoslavia in the autumn of 1972 and at which 140 participants discussed certain epidemiological, endocrinological, immunological, and metabolic aspects of cancer. Among the more interesting points to emerge was the description of statistical methods suitable for testing whether the apparent space-time clusters of cases of Hodgkin's disease described by Vianna and his colleagues are chance phenomena or support the hypothesis that it is a communicable disease. There is, also, Sir Richard Doll's conclusion that the shape of the age-incidence curve for any form of cancer is seemingly not dependent on any 'aging' process other than might be secondary to the duration and degree of exposure to environmental carcinogens. Female laboratory rats fed *ad libitum* tend to become adipose and experience a

high age-standardized incidence of mammary cancer, and dietary restriction reduces the incidence of mammary cancer. According to de Waard, lean ladies in Holland, São Paulo, and the United Kingdom have a lower age-specific incidence of breast cancer than do fatter ones. Later in the book, Higginson rightly states that nutrition 'is one of the most important and yet neglected aspects of carcinogenesis in man'. McLean, however, in a systematic review of the modifying effects of diet in carcinogenesis, fails to deal specifically with what might be regarded as 'overnutrition'. But Bras, on the last page of the book, makes up for this deficiency where he writes '... we know from extensive work ... that different intakes of protein, carbohydrate, fat and/or calories will cause profound differences in the activity of enzyme and in the incidence of both benign and malignant tumours. Unless, therefore, the dietary intake of experimental and control animals is made identical, we may easily misinterpret the outcome of our experiments. . . .'

The book is well produced and has much of interest in it. The editors are to be congratulated in their decision to reproduce, in a chapter by Paffenbarger, three cartoons by the American cartoonist Charles M. Schulz. On the other hand, it is to be hoped that the inclusion of 'funny pages' is not destined to become a feature of future IARC or other publications on cancer.

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Notice

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