Pure & Appl.Chem., Vol.54, No.11, pp.2031-2033, 1982.
Printed in Great Britain.

0033-4545/82/112031-03$03.00/0
Pergamon Press Ltd.

REPORT OF THE SYMPOSIUM ON SOLID PHASE CHEMISTRY

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Abstract - The symposium provided information on the performance of solid phase and a pre-packed reagent and instrument systems. It was proposed that these systems and further developments showed be used to review the organisation of testing both within the laboratory and at the patient side with a view to improving the cost effectiveness of the work of the laboratory.

The Chairman (Geary) introduced the symposium by proposing that careful consideration be given to reviewing the role of solid phase chemistry to obtain the maximum benefits from the advantages of these systems. He proposed that the pathology provided to patients in the various locations serviced by a laboratory be investigated to discover if it was possible for the existing workflow patterns to be modified to allow for patient side testing, extended discretionary requesting, and the wider use of a common technology for the determination of a range of analytes at present being performed in a number of areas within the laboratory.

The question of workflow patterns were discussed by reference to Fig. 1,2 and 3.

Analytical systems are available to allow the laboratory testing to be taken to the patient. They provide for the determination of glucose in Diabetic Clinics, blood gases in the Intensive Care Units and the need of Psychiatric Units for drug monitoring. This range of tests can be extended by the use of the Ames Seralyzer and other systems.

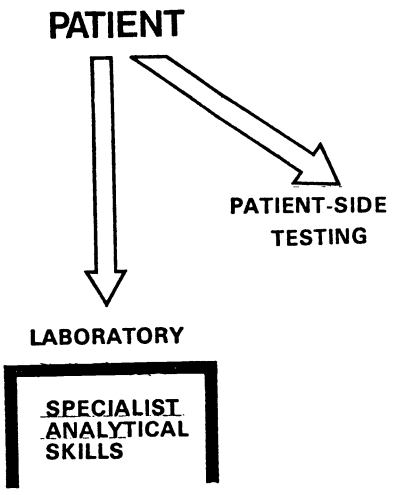

Fig. 1 Patient side testing and laboratory testing

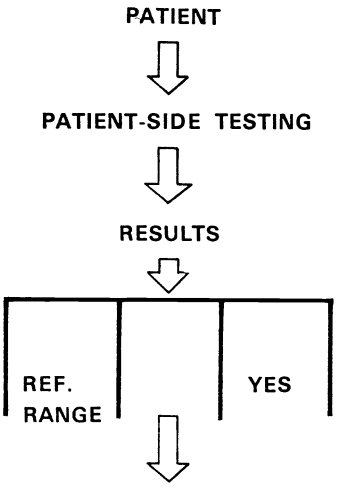

Fig. 2 Patient side testing

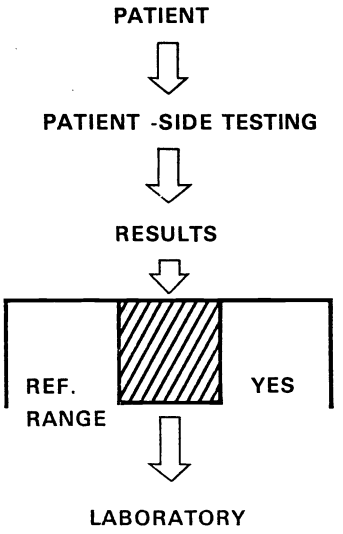

Fig. 3 Patient side testing

In some situations it may be possible to use methods which although not meeting the strict criteria needed in the laboratory provide results which are relevant clinically, enabling a clear separation of the positive disease state from the reference range (Fig. 2)

A system may still be used if it is possible to establish a well defined zone in which there is overlap between positive results and those within the reference range (Fig. 3). The choice in this case, where results fall into this zone, is for either the patient or the specimen to

be referred to the laboratory. Furthermore, the papers which followed showed that within the laboratory the use of the Kodak Ektachem, or, in the small workload situation, the Ames Seralyzer provides an additional means of handling an increased demand for discretionary testing. On the other hand the Dade system utilising radial separation, the I.D.T. FIAX and other such solid phase techniques enables the staff of the laboratory to perform many differing analysis on the same instrument using a common technology.

Dr. Giegel introduced the Dade radial separation technique which is a general approach to immunoassay utilizing the principle of radial chromatography to separate the bound from the free fraction. Antibody is immobilized in a defined area of a porous matrix such as glass fiber filter paper by using conventional double antibody techniques and allowing the two antibodies to react within the fibrous matrix.

High concentrations of primary antibody can be achieved using this technique. Sample, along with labelled antigen, is applied and allowed to react. The unbound antigen is washed from this area by applying a fluid to the centre of the area and removing the unbound fraction by circular chromatography. Two circular zones are produced, the inner zone containing the antibody bound fraction whilst the outer zone contains the unbound fraction.

In the case of enzyme immunoassay the wash fluid may be the substrate for the appropiate enzyme label, permitting the wash step and the initiation of enzyme activity to occur simultaneously. Enzyme activity may be monitored by measuring front surface fluorescence. Immunoassay may be conducted using the same basic system as enzyme immunoassay. This technique has been used using isotopically labelled antigens and a special gamma counter designed which counts only the centre area of the matrix. The system has proved to be simple to operate, and provides rapid reaction rates with considerable sensitivity. The methods available are for therapeutic drug assays but work is progressing on methods for the measurement of other analytes.

For general chemistries, single unit packaged dry reagents in combination with instrumentation designed to enable random access testing with minimal interventation of the operator have been available for some time. The new dry Syva technology presented by Dr. Miller provides immunoassay reagents in a similar form with the same speed of reconstitution and convenience of use. Upon addition of sample and water, the powder is dissolved completely following an inversion of the vial or if it is more convenient the tubes may be placed upon a rotator for fifteen seconds. The binding reaction and the enzyme reaction commence immediately upon reconstitution of the powder and the enzyme rate is measured over a period of 90 seconds. The homogeneous enzyme immunoassay reagents have been filled into unit test vials with an imprecision of less than one percent. The first application of this technique is in the qualitative measurement of drugs of abuse in serum or urine. In this system, the enzyme rate due to the sample is compared to the rate due to a known calibrator. The value obtained for the calibrator is taken as the cut-off level for the detection of the drug. The vial acts as cuvette and are measured simultaneously in a specially designed photometerFollowing a ninety second determination the enzyme rate in each vial is printed with a positive result being greater than that for the calibrator and a negative result being less. The system requires minimal operating skills and is suited to the prevision of an emergency toxicology service.

The Kodak Ektachem 400 Analyzer offers an unique approach to chemical chemistry analyses. All reagents are supplied in the form of dry reagents slides which obviate the need for preparation of reagents. Each test can be individually requested and only 10 μl of specimen are required making it ideal for use in a paedriatric laboratory. Dr. Hicks reported that at the Children's Hospital, Washington, the fifteen tests offered currently on the analyser were performed previously on a number of separate instruments which increased the cost to perform the tests. Using the College of American Pathologists Workload System, it has been possible to show a reduction in 1.3 full time equivalents of technical time in the Clinical Laboratory. This, together with the lower costs of a rental and purchase plan provided a cost saving of approximately nine thousand dollars a year in addition to decreasing staff. The system allowed for an alteration in the workflow pattern within the laboratory providing an improved turnaround time.

Dr. Raichwarg presented further evidence on the performance caracteristics of the Kodak system by presenting data obtained on an engineering model of the Kodak Ektachem. The methods for calcium and urate were evaluated using the protocol proposed by the National Committee for Clinical Laboratory Standards and Dr. Raichwarg concluded that the methods were both precise and accurate.

Manufacturers in Japan have developed various easily operated instruments employing a solid phase technique for precise and accurate bedside clinical testing and physicians are putting them to wide use. These include a system for the assay of glucose in blood from the Fuji Film company. It employs the same multi-layer film analytical element as the Kodak system except that it uses whole blood instead of serum. The reaction mechanism for glucose determination uses 4 aminoantipyrine as the color reagent and the glucose concentration is calculated from the intensity of reflection by a microcomputer. The effects of varying sample volumes between

7 to 11 microlitres and varying the haematocrit value from 10 to 50% is negligible. The within run coefficient of variation for whole blood was 2% and that for serum 1.5%. When the hexokinase reference method for glucose was compared to the Fuji Film method, the correlation of coefficient was found to be 0.989 and the regression line was calculated to be $y = 0.97x + 0.27$. A small instrument for ammonium testing has been developed by the Kyoto Dauchi Kagaku Company. The analytical element utilizes the multilayer solid phase technique approach. The optical measuring device includes a spherical integrator for measurement of reflected light. This system has been shown to have sufficient precision for clinical applications. When compared with the enzymatic method using glutamate dehydrogenase, the correlation coefficient was 0.95, and the regression line was $y = 1.06x + 2.1$. The small instruments for analyses using dry chemistry methods have advantages for they are simple to operate and so suitable for urgentdetermination, require a small sample, and little space for storage of reagents and at the same time are both accurate and precise. The thrust of development in Japan has been towards the production of simple instruments for clinical analyses which are suitable for both the developing and developed nations alike.

The Institute of Medical and Veterinary Science has provided, for Ames, data on the performance of the Seralyzer methods and as a consequence has considered the principle of locating Seralyzer units within hospital clinics and in associated small country laboratories. The concept is dependent upon the provision by the laboratory of patient data management sheets, patient handling information and a quality control programme. The performance of the Seralyzer is adequate for this purpose.

The traditional disciplines in clinical laboratory medicine and the manner in which the development of testing procedures has evolved have not allowed for the most effective use of techniques such as the IDT Fiax system which has a sample rate which could enable it to perform many of the tests for the presence of specific proteins analysed in Microbiology, Virology, Haematology and Clinical Chemistry laboratories. It should be possible to develop an analytical area around such a technique within the Clinical Laboratory such as that set aside for the analysers used for the determination of the commonly performed electrolyte and liver function tests. The number of systems which would allow this reorganisation to take place will be increased with the introduction of further fluorometric label techniques.

The presentations supported the suggestion made in the introduction that this are technologies available which will give staff the opportunity to reconsider laboratory organisation in order to improve the cost effectiveness and quality of service.