Automated clinical chemistry

By T. P. WHITEHEAD, *Queen Elizabeth Hospital, Edgbaston, Birmingham*

The workload of the clinical chemistry laboratory doubles every 4 or 5 years. This increase occurs in teaching and non-teaching hospital laboratories in this country and in many other countries abroad. Such increases have forced new approaches in laboratory techniques and laboratory organization. In the Department of Biochemistry at the Queen Elizabeth Hospital, Birmingham, work study of the systems identified three 'bottle-necks'. These were first, the transport 'bottle-neck', that is, getting specimens from the ward to the laboratory and the report back from the laboratory to the ward. Second, the analytical technique 'bottle-neck' and thirdly, the data-processing 'bottle-neck'. New transport systems can only be introduced with prohibitive capital outlay. The analytical technique 'bottle-neck' has been intensively studied and the AutoAnalyzer is in very common use in hospital laboratories.

During the last years, attention has been focused upon data processing and the introduction of on-line computer facilities in many laboratories has already taken place or is about to take place. The computer in the clinical chemistry laboratory performs tasks which can be conveniently divided into two: first, acquiring data from the analytical equipment, calculating the result and associating it with patient identification; second, data-processing results, particularly with regard to quality control and other management techniques. Experience with computer work has shown that it can save clerical work by scientific staff but, what is more important, it is capable of providing information which was previously hidden, e.g., on-line monitoring of the AutoAnalyzer has shown that much more information can be obtained from the analogue signal normally transferred to a chart recorder. Blockages can be detected earlier and other defects in the system can be identified more precisely. In addition, data processing of results can lead to a much greater appreciation of the use of laboratory results in patient care. Several examples of the use of the computer in quality control have been published (see Whitehead, 1968; Whitehead, Becker & Peters, 1968; Whitehead & Carmalt, 1969). The computer is now an integral part of the clinical chemistry laboratory.

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The maintenance of analytical quality in the automated laboratory

By S. C. FRAZER, *Department of Chemical Pathology, University of Aberdeen, Foresterhill, Aberdeen*

The ways in which a laboratory's analytical work can be monitored are basically similar, whether or not the analytical processes are manual, or assisted in varying

degrees by machines. True automation requires not only that the analytical procedure, from sampling and sample identification right through to calculation and recording of results, should take place without human participation, but also that the system will detect and correct its own errors. Although some present-day computer-assisted analytical systems are programmed to detect and compensate automatically for certain faults such as instrument drift, most deviations from optimum performance in the mechanized laboratory still have to be detected and corrected by human agency, and continuing programmes of quality control are necessary if even moderate standards of analytical accuracy and precision are to be consistently attained. But, whereas human analysts may consciously or subconsciously resent any external assessment of the quality of their work, and introduce some degree of bias into such assessments, e.g. by specially careful handling of samples thought to be connected with the quality control process, the machine is independent of any implied criticism, and bias is only introduced if the operator plays a part, e.g. in reading results from a chart.

The control of quality in a mechanized laboratory should start before the first analytical machine is purchased, by finding out what the proposed instrument can in fact do, in terms of repeatability of results in duplicate or multiple analyses of the same sample within a single batch, in day-to-day reproducibility, linearity of calibration over stated ranges of concentration, zero and sensitivity drift over stated periods, and so on. Few manufacturers will commit themselves in such matters, and unless one can obtain a truly objective assessment from an earlier purchaser, one is likely to find that the reality does not match up to the implied promises in the glossy brochure. An extended trial in one's own laboratory before purchase is not unreasonable when the cost of the machine is many hundreds, if not several thousands, of pounds, and ought to be the rule rather than the exception.

The second important pre-purchase step is to ensure that the machine's rate of working is adequate. Stated rates of working usually count blanks, calibration standards and drift standards as if they were test samples, but in addition to these one must allow for the requirements of the quality control system and for the occasional but inevitable re-running of batches when the control programme has revealed a fault and this has been located and corrected. When a machine is working to near capacity, control samples and drift standards tend to be edged out, and a blind eye is turned to deteriorating performance, if only because of the backlog of samples which would build up if the dictates of proper quality control were rigidly enforced. The remedy is to start with ample spare capacity, knowing that it will not be spare for long if high standards are required.

The primary purpose of a quality control system is to allow the calculation of analytical confidence limits for a single result when the analytical process is working properly, and to detect when this standard is not being achieved. It is also possible, though less frequently done, to test repeatedly for specificity and for freedom from interference by extraneous substances, though this should not normally be necessary if the method has been adequately tested before introduction.

The secondary purpose of a quality control system is to provide a recurring

stimulus of dissatisfaction, leading to improved techniques and machines (and, incidentally, providing an excellent yardstick of present performance against which alleged improvements can be compared). Mechanization has a tendency to induce complacency and 'freeze' techniques, and active quality control programmes are an important counter-measure.

For repeated tests of reproducibility, one or more pools of test material are required. This should be as similar as possible to the material normally analysed; if, for example, blood plasma is the material normally analysed, simple aqueous solutions are not satisfactory as control materials, although they may be adequate as calibration standards (Whitby, Mitchell & Moss, 1967). The pool of test material must be stable for long periods, and if this is unattainable some compromise may be required, e.g. use of aqueous control solutions as well as standards, coupled with re-analysis, in each batch, of a number of samples which were analysed in the previous batch. It is absolutely essential that the control material be homogeneous, otherwise one is testing for overall reproducibility of both the sampling and the analysing steps, and (in biological materials especially) these are really separate problems which should be kept under separate but simultaneous review.

The day-to-day operation of the quality control system should be the responsibility of one person, of sufficient seniority and self-confidence to stop the operation of the laboratory when the control data warrant it, and able to direct the tracing and correction of whatever fault caused the control data to fall outside the permissible limits. In the mechanized laboratory, the machine operator should not also be the quality controller, but the latter must be continuously available and must deal with the results of the control analyses promptly. Control systems which generate data which are not promptly appraised, and acted on immediately when necessary, are both expensive and futile. Computer assistance should both simplify and speed up the whole process of control of analytical quality, but it is far from being a *sine qua non*, even in the extensively mechanized laboratory.

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Recent advances in amino acid analysis

By ALAN J. THOMAS, *Department of Biochemistry, Imperial College, London, SW 7*

The great interest in the nutritional and metabolic interrelationships of the amino acids has been stimulated by the increasing ease of separating and estimating them. Yet most available methods are still inadequate to provide the extent of information needed to sufficiently interpret the processes of digestion, absorption and conservation of protein in the animal. This is particularly true when one realizes that the really meaningful criterion in metabolic studies is turnover rather than static con-