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Getting the right answers from blood

Errors in the results of blood tests can lead to mistaken treatment of disease. The avoidance and correction of errors are clearly helped if laboratory workers are aware of the causes. The procedures of standardization, internal quality control, and external quality assessment should be used in all haematology laboratories, and health workers should be able to assess the reliability of tests and their value in primary care and hospital practice.

In industry and commerce everybody recognizes the importance of having quality control so that the goods and services sold to the public are satisfactory. Quality assurance is no less important in the medical laboratory, where it ensures that tests are carried out reliably and that the results can be used with confidence by health workers.

Anaemia, the most prevalent health problem in the world, is diagnosed by measuring the concentration of haemoglobin in the blood. Unfortunately, some of the methods used may have an error of plus or minus 20% or more, and a result suggesting moderate anaemia is just as likely to occur either if the haemoglobin level is normal or if there is severe anaemia. When such error is compounded by poor technique the tests would seem to be hardly worth conducting. The management of patients may go seriously wrong if test results are strongly affected by measurement variation. This also applies to other parameters, e.g., blood sugar in comatose patients, and prothrombin in patients on anticoagulant therapy.

Poor laboratory performance may result in increased costs for patients and in strains on health facilities required to conduct additional tests and provide extended hospitalization. If a test wrongly indicates normality, the consequence may be chronic morbidity because of missed diagnosis. Incorrect data in population surveys may have a misleading influence on the organization of health services: in the United Kingdom, for example, methods used for lead assay gave results in an interlaboratory survey with such wide variation as to be of little use in reliably identifying individuals whose lead concentrations were unacceptably high.

The reliability of a test can be assessed by surveys in which various laboratories perform it on samples of the same specimen. A few atypical results will identify laboratories that have made errors, whereas a high degree of variation involving all the participants will indicate the test itself to be unsatisfactory.

In haematology the common laboratory tests involve a range of technologies—photometry for haemoglobin, flow cytometry for blood counts, biological
staining and microscopy for blood film morphology, visual interpretation of agglutination or haemolysis for serological determinations, and so on. Many potential sources of error exist but

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perhaps the gravest problem is that most haematological analyses relate to blood cells suspended either in plasma or in a diluent. Unless the suspensions are homogeneous and the measured aliquots are truly representative there will be inherent errors that may be greater than those due to the processes themselves.

The laboratory worker should be aware of the causes of errors (see box).

Avoiding and correcting errors

Knowing potential causes of error undoubtedly helps to prevent mistakes. But certain procedures should be used in all laboratories not only to avoid errors but also to recognize, as early as possible, when they occur and require correction. They are described below.

Standardization

This covers both material standards for the calibration of instruments, and the use of

Specimen errors

- Faulty collection from patient, perhaps due to poor veins, use of tourniquet, wet or contaminated syringe and needle
- Incorrect specimen tube
- Inadequate or excessive anticoagulant
- Delay in transit of specimen to laboratory
- Specimen left at high ambient temperatures before testing
- Specimen incorrectly labelled or confused with others in laboratory
- Inadequate resuspension of specimen resulting in unrepresentative sampling

Test errors

- Inaccurate dilution of sample
- Excessive or insufficient dilution
- Incorrect or deteriorated reagents
- Instrument fault
- Incorrect instrument calibration
- Standard or reference preparation not used
- Excessive inherent error
- Unconscious or conscious bias in reading results
- Wrong interpretation of observed results, reactions or morphological features

Documentation errors

- Calculation error
- Error in recording and reporting of results
- Failure of report to reach clinician
- Report illegible or unintelligible
specified methods and reagents. The World Health Organization has an important function in establishing international material standards. In haematology the standardization of methods is undertaken by the International Committee for Standardization in Haematology. Collaboration between the Organization and the Committee led to the development of an international haemoglobin standard (1). In 1980 the Organization issued guidelines on the determination of the haemoglobin concentration in blood (2). This allowed a marked improvement in the reliability of haemoglobinometry. Different laboratories now obtain virtually identical results.

Advances in the standardization of oral anticoagulant control have also been achieved (3). Thromboplastin standards are now available for assigning international sensitivity indices to manufactured thromboplastin reagents used for measuring prothrombin. Test results can thus be expressed in a constant way so that they are comparable between laboratories. This is of great benefit to travellers receiving anticoagulant therapy and to researchers conducting therapeutic trials of new drugs.

The Committee’s recommendations are published in medical journals and incorporated into the Organization’s guidelines and manuals, which are available through its regional offices to laboratories in all countries.

Internal quality control

Internal quality control comprises procedures undertaken by laboratory staffs with a view to deciding whether the results of tests are reliable enough to be released to clinicians. The main objective is to ensure day-to-day consistency of measurement. Consistency, or precision, is achieved by regular measurement of control samples alongside patients’ specimens, and duplicate testing of some specimens in each batch of tests. The results for the control materials are plotted so that any deviation in measurement, indicating a malfunction, can be seen easily and quickly. For this purpose the exact value measured on the control material is irrelevant; it is the constancy of the measurement which records the extent to which the laboratory can be relied on to get consistent and precise results. A good laboratory will have an established protocol for practising internal quality control, and all the workers involved should take an interest in the control charts, which should be placed on a wall where they can be readily inspected.

Precision does not mean accuracy in this context. For most clinical laboratory tests it is not easy to ensure accuracy as this requires comparison with a standard having a known true value. Weight, length, volume and time can be defined in this way but there are few clinical laboratory tests for which absolute standards are available, and biological standards are usually defined arbitrarily.

How important is it to obtain accurate quantitative measurement in blood tests?

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The clinician requires numerical results in order to know whether patients have normal or abnormal values, the degree of abnormality, and whether there has been
any change since the previous testing. In a laboratory working in isolation and having its own ranges of normal values, the control of precision internally would provide sufficient assurance of reliability for clinical purposes. However, laboratories do not function in this way. It is essential that all laboratories use similar reference values for distinguishing the normal from the abnormal, that clinicians can judge test results for a patient in perspective, and that data obtained in any laboratory can be used in a common pool for the advance of scientific knowledge and for public health analysis at the national and international levels. This requires interlaboratory harmonization, which is the function of external quality assessment.

**External quality assessment**

This is the objective checking of laboratory results by means of an external agency (4). A given laboratory’s performance of selected tests is compared with that of other laboratories. Since the checking is retrospective, sometimes with a delay of several weeks, the comparison will not influence the laboratory’s output of results on the day of the test. The main objective is not to bring about day-to-day consistency but to establish between-laboratory comparability, including between-instrument and between-method harmonization. Inconsistent results are identified and appropriate remedial action is taken. Identical specimens are sent to the participating laboratories, where they are measured, and the results are reported back to the scheme organizer who analyses and assesses the data; then either a general report is presented to all participants or an individual report with comments on performance is sent to each laboratory. The criterion of unsatisfactory performance may be statistical, e.g., results differing by more than two standard deviations from the mean, it may be the likely effect of an erroneous result in a clinical situation, or it may comprise results obtained by selected referees.

In the United Kingdom, data collated by the National External Quality Assessment Scheme for Haematology enable individual laboratories to assess their own performances in successive trials and to see when a specific fault requires attention, while the organizer of the Scheme is able to identify “state of the art” problems. Thus, for example, when several laboratories failed to obtain the correct positive result in a sickle-cell screening test, a fault in one type of commercial kit was indicated. This kit was withdrawn and an improved one was introduced. Participants, too, can judge from survey results whether a method is less satisfactory than or superior to others. Thus the most commonly used technique for fibrinogen assay used to be that of the thrombin titre; relatively few participants used the slightly more elaborate Clauss technique. Surveys showed the greater reliability of the latter, with the result that it is now favoured by a much larger number of participants. It was noted, however, that some laboratories continued to use unsatisfactory methods; this indicated the need for a technical publication and other ways of disseminating recommendations.

External quality assessment may be organized nationally, regionally, or even at
Organization of the United Kingdom National External Quality Assessment Scheme for Haematology

Department of Health and Social Security

Advisory Committee on Assessment of Laboratory Standards

National External Quality Assessment Scheme

Organizer

Steering committee

Advisory panel on performance

Professional bodies

Workshops, guidelines

WHO 881020

Reports on state of art

Contact with persistent poor performers

Advice to participants

district level; for a scheme to be viable there should be at least 20 participants. The first national scheme in haematology, together with clinical chemistry and microbiology, was organized in the early 1960s in the USA by the College of American Pathologists. Over 8500 laboratories are now enrolled in their haematology surveys and an equal number participate in clinical chemistry surveys; smaller schemes are organized by the Centers for Disease Control and the American Association of Bioanalysts, and there are specialist schemes, e.g., for drug monitoring and hepatitis B antigen testing. There are also national external quality assessment schemes in Canada, Australia, and several countries of Western Europe in addition to the United Kingdom. Altogether, it appears that such schemes have so far been organized in 30–40 countries.

The schemes are essentially educative, having the aim of improving laboratory standards. Some of the schemes have been organized as a result of legislation obliging clinical laboratories to carry out quality control and to take part in external quality assessment programmes. The schemes thus provide information that is used for accreditation or licensing and for imposing legal, financial or professional sanctions on laboratories showing poor performance. In some countries, only laboratories that take part in an external quality assessment programme and whose performance is satisfactory have the right to charge fees or to make claims on health insurance agencies for the service provided. In the United Kingdom there is no such legal obligation but almost every pathology laboratory participates voluntarily. The range of assays is very wide, covering all the specialities of
laboratory medicine. Funding is provided by the Department of Health and Social Security. What is perhaps unique in the United Kingdom is the organization of the programme (see figure). For each speciality there is a steering committee, membership of which includes technical experts and clinicians; their role is to advise the organizer on its overall operation, which type of tests to use, how results should be analysed, and how data should be presented. The committees are not concerned with the performance of individual participants; indeed, participation is on a confidential basis, the laboratories being identified by code numbers known only to themselves and the organizer. How the laboratories perform is the concern of an advisory panel whose members are nominated by the appropriate professional associations and whose work is coordinated by the Royal College of Pathologists.

When a participant’s results are unsatisfactory the organizer of the Scheme tries to resolve the problem by direct contact with the laboratory. If this fails and the laboratory continues to perform badly in subsequent surveys, the chairman of the advisory panel writes to its director to offer assistance. The letter is passed on by the organizer, the only person who knows the laboratory’s identity. If there is no response and unsatisfactory performance continues, the identity of the participant is revealed by the organizer to the chairman of the advisory panel, who then pursues the matter. This formal procedure is required only rarely, and most problems are resolved by the laboratory with or without the help of the organizer. The fact that the Scheme is considered educational and not punitive means that there is little incentive for laboratories to manipulate their results to indicate an improved performance, and the offer of help is usually welcomed and appreciated.

The results of surveys may demonstrate that a test itself is unreliable or that the participants have used a faulty kit or an inaccurate calibrator. In such cases the organizer or the advisory panel informs the authorities whose function it is to evaluate and control manufactured kits and reagents. When there is evidence of a poor “state of the art” and the use of an unreliable test, the professional bodies organize workshops for unsatisfactory performers and publish technical reports and guidelines on recommended techniques.

In a few countries, schemes have been organized following regional and interregional workshops of the World Health Organization. In Indonesia, for example, a feasibility study was carried out with six laboratories, each receiving lysed blood samples for the measurement of haemoglobin. A scheme was then set up with the agreement and support of the Indonesian Ministry of Health; there were 70 participants, most of them government laboratories. The Organization’s Collaborating Centre for Quality Assurance was invited to serve as a referee, and survey samples were also sent to its laboratory in London. Analysis of the results showed a generally high standard of performance, with relatively small variations in results between the participating laboratories. It is intended to have two or three distributions a year in the first instance and to add other tests progressively; the most recent survey included the taking of blood films for reticulocyte counts, reflecting the importance of the latter for diagnosing haemolysis and for assessing bone marrow function and response to treatment for anaemia. Serious difficulties are presented by the long distances between outlying laboratories and the Centre in Jakarta, as well as by unfavourable climatic conditions. Delays result and specimens deteriorate before they reach the participating
laboratories. Under such circumstances it may be helpful to have a number of reference centres in different regions of the country, each being responsible for its own distribution but all being linked by the national external quality assessment scheme.

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In those countries where national external quality assessment schemes are established the impact on laboratory medicine and the improvement in the service provided are readily seen. Regrettably, not enough countries are operating schemes, because of shortages of time, staff, funds and facilities. In the background, perhaps, is a failure of administrators and governments to appreciate the importance of quality assurance. It is essential for governments to be made aware of the need to provide the relatively modest funding required for improvement of their laboratory services, and it should be made clear to laboratory directors that no tests can be undertaken with confidence in the absence of an adequate quality assurance programme.

Health workers should be able to assess the reliability of laboratory tests and their value in primary care and hospital practice, i.e., whether they are being used to define and screen for health, to identify ill health, to diagnose conditions requiring further investigation, or to make definitive diagnoses. It is necessary to learn which laboratory tests are relevant, what equipment is appropriate for performing them, and why quality assurance is important for all tests.

Reliable data are required so that patients can be properly cared for and so that administrators can assess what care to provide. There should be regular participation in quality assurance programmes, including national external quality assessment schemes, by all laboratories as well as by health centres, even if only the simplest screening tests are undertaken. The procedures clearly take time and money but doctors, laboratory staff, and health administrators cannot afford to do without them.

**References**


