Contemporary Themes

Analytical investigations closer to the patient

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Summary and conclusions

Do-it-yourself bioanalytical equipment that requires no analytical skill to operate is currently available for use in intensive care units, operating suites, side wards, health centres, clinics, general practitioners' surgeries, etc. Agreement is needed between the laboratory consultant and doctors and others using laboratory-type equipment and reagents in near-bedside analyses for diagnosis, clinical management, or health screening of their patients. Choice and safety of method procedure, operator training and accountability, quality control and assessment, maintenance, safety and future development of do-it-yourself equipment must be considered.

Introduction

In Britain most tests with a diagnostic or health screening purpose are carried out in a laboratory by people either technologically or professionally trained in a branch of laboratory medicine. A few of the simpler tests are performed outside the approved or recognised laboratory—usually though not invariably by a member of the medical or nursing professions. In other countries, notably France and Russia, these latter tests are done in a side ward by pharmacists. Is it in the best interests either of the community or the patient to have all tests performed in a recognised laboratory? There is obvious advantage in that the occasional do-it-yourself test may provide faster diagnosis and management. There are also some problems; not least of which is that of quality assurance. Can the do-it-yourself test be made sufficiently precise and accurate to ensure that incorrect crucial clinical decisions do not stem from wrong results?¹

Table I shows some tests that may currently be made close to the patient. These are done in various ways ranging from visual colour observations on dip-sticks to performing simple manipulations with advanced equipment which offers almost instant read-out of one or more analytes.

Table II lists some currently available analytical machines from industry. They are designed to be robust in construction and versatile in performance so that they can function in a side room when operated by any suitably instructed member of staff.

We need to recognise a tendency for certain investigations (usually those euphemistically termed "routine" tests) to be moved away from the professionally staffed clinical laboratory. Here the desirability and implications of bedside or near-bedside analyses are considered and some recommendations made.

Need for non-laboratory based diagnostic equipment

The desire for stand-alone do-it-yourself analytical equipment generally reflects the difficulties laboratories have in providing from one generic laboratory a 24-hour service (especially the evening and night-time service). During the past decade there has been much politicoeconomic pressure to centralise where possible the health care facilities for patients. Laboratory services have *pari passu* become more and more concentrated following earlier government policy to close many of the smaller satellite laboratories.² At the same time, expensive computerised multichannel analysers once installed can cope with many times their initial work load for little increase in cost. Contrary to a

TABLE I—Some analytical tests usefully performed in the vicinity of the patient

Clinical environment	Investigation
Accident and emergency department	Alcohol in whole blood. Sugar in peripheral blood (test strips "stix" and meters)
Diabetic clinic/wards	Sugar analysis in venous heparinised blood. Sugar in peripheral blood (test strips "stix" and meters)
Intensive care units	Blood gases PO_2 , PCO_2 , pH.
Obstetric wards	Urine osmolality Fetal blood gases. Amniotic fluid optical density for fetal lung maturity.
Paediatric clinic/wards	Urine pus cells (microscopy) Sweat chloride ions or conductivity screen for cystic fibrosis
Special-care baby unit	Bilirubin in heparinised plasma
General practice surgery/health clinic/pharmacy	Haemoglobin and erythrocyte sedimentation rate estimations. "Stix" for ketones, glucose, proteins, etc. Dip-sticks for significant bacteriuria. Pregnancy tests on early morning urine. Faeces occult blood

widely held view these big analysers do not in themselves reduce labour or material costs³ but only begin to show cost-effectiveness when serving large populations (probably more than that of the average district). The pressure to use only one central (or even peripheral) site for carrying out diagnostic tests is thus reinforced while in turn those at a distance from the chosen site tend to look more favourably on an alternative rapid diagnostic service close to the patient.

Today district laboratory departments are rarely on the same sites as all the units that may need their services urgently—for instance, cardiac catheterisation units, special-care baby units, and intensive care units. Sometimes more could be done to reduce this difficulty by employing an efficient transport system primarily responsible to the laboratory—whether of vans or motorcycle drivers or carrier pigeons. But in any case a tendency towards decentralising some parts of the analytical service and bringing it back to the wards is encouraged.

Clearly the laboratory has many calls on its services, and continued clinical and scientific developments still lead to an increasing number of tests. Sometimes, therefore, a laboratory may have insufficient staff and equipment to cope with an

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unforeseen demand or to cover the one-off need. On other occasions, extension of acute services provided by units has been allowed by AHAs before extra laboratory staff have been granted, appointed, and trained. In my own region, for example, a new district obstetric and gynaecology department is being built which provides for an increase in obstetric beds from 118 to 144 while the same district's identical number of laboratory

TABLE II—Mechanised analyses available for use outside the laboratory—for the immediate management of patients

Analysis	Equipment	Supplier	Basic cost
<i>Quantitative</i>			
Bilirubin in neonatal serum or plasma	Bilirubinometer AO Unistat*	American Optical Co	£1000
	Advanced bilirubinometer Spectrophotometer* Nova 2	Fisons Scientific apparatus	£1230
Calcium ions in heparinised whole blood		American Hospital Supply	£4800
Chloride ions in sweat	Skin chloride electrode system Orion 417	Fisons Scientific Apparatus	£784
Glucose in whole blood	GM5 oxidase analyser	Analox Instruments	£2245
	YSI 23 AM enzyme glucose analyser	Clandon Scientific	£2345
Osmolality of urine and serum	Advanced osmometer clinical	Fisons Scientific Apparatus	£1767
	Osmometer, digital BG II	Camlab	£1500
pH, PCO ₂ , base, PO ₂ in whole blood heparinised	Corning 175 IL 613	Technicon	£11 858
		Corning-Eel Instrumentation Laboratory	£9358
Sodium and potassium ions in heparinised whole blood or urine	Micro Bloodgas Analyser	Sandoz	£10 050
	Radiometer ABL2 Nova 1	V A Howe	£8795
	Spacestat 30	American Hospital Supply	£4370
		Fisons Scientific Apparatus	£4700
<i>Semi-quantitative</i>			
Alcohol in blood	Alcolmeter AEDI	Lion Labs	£654
Glucose in whole blood	Eyestone	Ames	£225
	Reflomat	Boehringer	£265
	Glucochek	Medistron	£91
	Hypocount	Hypoguard	£75
Haemoglobin in blood	AO-Spencer haemoglobinometer	A R Horwell	£99

*Additional equipment, that is, a centrifuge is also necessary.

and emergency wards situated some distance from an inaccessible recognised laboratory may find it advantageous to have on-the-spot facilities to perform blood-gas and acid-base analyses. Since most poisons that impair consciousness also depress respiration, patients in hospital for acute poisoning and in grade IV coma (unconscious with no response to stimuli) should have their blood pH, PCO₂, and base excess measured to ensure rapid diagnosis and treatment. In such cases when analytical results are essential to the immediate management of the patient and cannot be provided by the laboratory fast enough, bedside clinical chemistry equipment may be the answer.

Cost considerations of ward analytical tests

CAPITAL COSTS

The capital cost of the semi-automatic type of equipment now available is often in the minor capital range (table II). When such apparatus is purchased for non-laboratory use, it clearly reduces the amount of finance for the purchase of laboratory equipment. Laboratory-type equipment based in the ward or clinic can be expensive in terms of the time it lies idle. In the laboratory the same equipment may be used for requests both from other sources and for other tests. For example, glucose analysers may be used to perform tests by related methods, such as those for urate or cholesterol. Thus the capital cost may be less efficiently used when equipment is sited other than in the laboratory.

RUNNING COSTS

Costs arising from reagents alone can be from three to ten times that of the usual laboratory cost per test (table III) so that revenue consequences accruing from the use of do-it-yourself equipment for non-urgent assays can be considerable. Additional and unnecessary costs will accrue if the equipment is neglected; experience has shown that it is often abused and poorly maintained when sited outside an NHS laboratory. Visits by service

TABLE III—A comparison of some urgent test costs (£)

Manner of analysis performance	Equipment	Blood glucose	Serum urea	Serum aspartate transaminase	Serum calcium	Neonatal bilirubin
Manual (semi-quantitative)		0.31 (L) Test Glycemic Boehringer	0.35 (L) Azostix (Ames)			
Work-simplified		0.23 (L)	0.32 (L) (Roche kit)			0.51 (N)
Mechanised batches (single channel)	AA1 or ChemLab Inst LKB reaction rate analyser	0.28 (D)	0.10-1.03 (L)	0.49 (N) 0.72 (W)	0.52 (W)	0.55 (W)
Multiple* channel	Centrifugal analyser Technicon SMA-2 Vickers M300	0.10-1.03 (L)	0.10-0.90 (W)	0.10-1.03 (L) 0.10-0.90 (W)	0.10-0.90 (W)	
Stand-alone machine	Du Pont analyser	0.81 (N)	0.77 (N)	0.91 (N)	0.73 (N)	0.77 (N)

Costs according to procedure HN(76)29 for determining test costs in pathology laboratories; costs adjusted to 1980 prices and excluding collection and initial handling.

L = A D Lewis, University College Hospital, London, 1980.

N = George Elliot Hospital, Nuneaton, 1976.

W = G W Willing and K Caldwell, East Berkshire, 1980.

D = A Clark, Withybusch Hospital, Dyfed, 1977.

*Higher figure given for these procedures is that for one or up to 12 analytes per specimen; lower figure is average cost per test when 10-12 analytes are done together.

staff are being rehoused in buildings with considerable contraction in their working area. In such conditions, laboratory equipment purchased for use in non-laboratory areas by clinical staff appear to provide an answer.

It may be claimed that a specialised instrument in a ward allows a clinician to monitor a patient more frequently than if he had to rely on the laboratory. Whether or not there is a real need will depend on geographical and other circumstances.

For example, special-care neonatal units require facilities for immediate measurement of blood PO₂ to help steer between the dangers of cerebral hypoxia and retrolental fibroplasia. Accident

engineers can be expensive. In laboratories preventative maintenance treatment is carried out, and if there is damage or misuse it is usually easy to identify the person concerned.

EMERGENCY COSTS

The cost of small equipment—say, less than £500 used for urgent clinical tests—can soon be recuperated by the savings made on the emergency rota payment to laboratory staff for unsocial duty hours, travelling time, and special portage or

transport, or both, of the sample to a laboratory on another site. It should not be forgotten, however, that laboratory staff undertake emergency work voluntarily; they do so partly because of their sense of duty and partly for the financial reward. As use of equipment outside the laboratory becomes more popular a time will come when laboratory staff consider that participation in emergency duty is no longer either their responsibility, or financially worth while.

EQUIPMENT FAILURE COSTS

Equipment failure costs are transfer costs provided for the service to continue when the ward-based equipment breaks down. Tests will usually be referred to the laboratory, often without prior notification. If suitable equipment is available most laboratories will carry out tests under such circumstances for the benefit of the patients. Since they are not usually equipped or staffed for this extra work, however, this clearly imposes a strain on resources.

Choice of test procedure, equipment, and reporting procedure

In the light of the above it cannot be too strongly recommended that the clinician and the laboratory consultant should agree before acting to devolve work away from the recognised laboratory. This would seem advisable even before purchasing inexpensive aids such as glucose meters. Any request for equipment to be operated by ward staff might best be considered on its merits by a small working party including the head of the scientific department normally responsible for providing the diagnostic data. This group would assess the volume of the work, alternative ways of meeting the demand, the most suitable method available, the capital, running, and maintenance costs, the method of funding, and the staff necessary to maintain the service. Senior staff in the appropriate department (clinical biochemistry, haematology, medical microbiology) would give appropriate advice as to the most suitable equipment for the job.

Sometimes independent evaluation of diagnostic equipment gives incorrect results when non-ideal specimens are tested. Thus considerable errors may occur when a bilirubinometer is used to analyse a haemolysed specimen.⁴ Many drug in-vitro interferences occur with assays, an important factor to be considered when interpreting a read-out figure on a ward instrument. In supportive tests for cystic fibrosis only the sweat Cl⁻ test using pilocarpine iontophoresis and an ion specific electrode placed on the skin is worth doing outside the laboratory. There is, however, a danger of falsely high concentrations being recorded in a small group of children who do not produce adequate amounts of sweat.⁵ Equipment may differ in methodology from that used in the laboratory, it may also use serum instead of blood or vice versa, or it may express results in different units, which may cause problems in comparing results and reference ranges—for instance, bilirubin on neonates expressed in $\mu\text{mol/l}$ and $\text{mg}/100\text{ ml}$.

Choice of equipment may even depend on future staff availability. In my own district some eight years ago our obstetrics department bought an acid-base analyser PHM 71 (Radiometer) for fetal scalp blood pH. This worked fine when a particular registrar used it. When he left it proved too complicated for his successor, who was not technically minded. It is to be expected, however, that further simplification of diagnostic machinery will come. Industry will continue to develop more easily operable instruments, which will be especially appropriate for use in developing countries where large laboratories can never hope to provide all the services required.

Safety aspects

Safety aspects of do-it-yourself equipment and testing outside the laboratory have to be considered. There are instances of equipment being bought against the advice given in *Hospital Equipment Information* (DHSS). Potential hazards exist. Thus tonometer water and buffer solutions have been reported as a source of *Pseudomonas cepacia* and *P. aeruginosa* infection in an intensive care unit.⁶

Departments of medical microbiology take extra special precautions against risk of infection with organisms in category B1 (Howie Code of Practice)⁷ and clearly no tests should be attempted in side wards on specimens about which there is a reasonably strong suspicion that they may contain B1 organisms.

In a communication to the Association of Clinical Biochemists a DHSS committee (Interim Advisory Committee on Safety in Clinical Laboratories) offers the following suggestions for the safe conduct of work to be undertaken on wards or clinic premises.

(1) Tests should be carried out only in suitably designated rooms. When this is not possible the work should be restricted to an area that is set aside solely for the purpose. It must be remembered that the Howie Code of Practice will apply; no eating, drinking, smoking, or applying cosmetics is allowed in the area.

(2) All work, including the disposal of waste, should be carried out according to written instructions. The instructions should be the considered outcome of local discussion between the control of infection committee and other appropriate safety committees and the groups of staff at risk.

(3) Tests should only be performed by staff who are trained to perform them safely.

After implementation of the Howie Code of Practice, the person nominated to assume overall responsibility for safety in units outside laboratories must make periodic safety audits on the functioning of equipment and on procedures, and keep records of these.

Training and accountability of operators

At an early stage in the inauguration of a local analytical service the clinical unit should appoint a suitable senior and relatively permanent member of staff to be responsible for operating and cleaning the apparatus and maintaining reagent supplies. Not all staff already have or desire to acquire the necessary technical ability to manage certain instrumentation and at any time the lack of a suitable operator on-site will require either a temporary withdrawal of, or an appeal to, the laboratory for service. Operators of quantitative assay machines listed in table II will not only need adequate training, but some check on their competence should be accepted before carrying out tests on patients.

Competence by an operator demands the following: (1) a sufficient knowledge about the mechanised method to use it intelligently and safely; (2) an understanding of the importance of checking machine performance and doing control tests; and (3) acceptance of responsibility for keeping the instrument continually fit for use.

Simple practical training for those responsible at ward level may well be best achieved when both a specialist from the industrial company and a senior member of the laboratory staff are available. The laboratory department will be obliged to provide continual retraining as unit staff come and go, and untrained people should not attempt to carry out tests on patients.

Industrial companies favour the obligatory use of quality-control procedures. Regrettably, instructions for using equipment are often inadequate, and the most frequent omission is how to use essential quality-control procedures. Currently, simple straightforward instructions for doing these mechanised

analyses should be requested from the district laboratory. Other written instructions as listed below are suggested as the minimum needed for the smooth and safe running of a ward or unit service by non-laboratory staff.

ESSENTIAL DOCUMENTATION TO HELP THOSE WHO "DO-IT-YOURSELF"

- (1) A diagram of the instrument(s) to facilitate telephone discussion about the method.
- (2) A method sheet listing in numbered steps how to prepare the patient and the samples, and briefly how to use the equipment and how to obtain and check the results.
- (3) How to dispose of specimens and waste safely.
- (4) A quality monitor sheet—on which a high and a low concentration recovery is to be recorded each day (or occasion) the equipment is used.
- (5) A list of potential instrument errors, sample care, how to spot reagent deterioration, known interferences to the analyses—for instance, paracetamol may cause serious error to certain mechanical blood glucose tests.
- (6) The telephone numbers of staff able to offer advice on the method.
- (7) What to do in the event of complete breakdown of equipment.

Maintenance of equipment and reagents

Calculation from a personal survey suggests that in the UK more than £0.5m of expensive equipment (mainly blood-gas analysers) is lying around in clinical units in an unserviceable state or is a recurring problem to laboratory staff asked to salvage a wreck and restore it to working order. In addition, manufacturers have been known to complain about the excessive frequency of calls to their service engineers for repairs caused by misuse or ignorance. Undoubtedly cleaning the past generation of blood-gas analysers has often been neglected. It must be accepted that technical disciplines that include such things as cleaning up, topping up, removing electric plugs, reordering reagents after use, are often found most irksome and demanding. Nevertheless, the essentiality of all this must be agreed by the clinical unit and accountability in this connection clearly defined. Additionally to routine maintenance, a regular equipment-servicing scheme needs to be agreed, and this may take the form of a contract with the company providing the equipment or be undertaken by a member of the laboratory staff.

It is strongly urged that formal agreement with a laboratory department on the planned use and maintenance of analytical equipment in a ward accompany any application for its purchase by the district management team or regional committee.

Quality control, quality assessment, and reporting procedures

All pathology laboratories in the UK use control serum in each batch of tests to ensure reliable results (internal quality control). In addition at intervals of two to four weeks all laboratories that are directed by consultants analyse control sera and record results in subscription to one or more national monitoring schemes.⁸ These—external quality assessment schemes—are mainly used to detect any deterioration in performance of individual analytes and to show overall trends in results produced by different types of method and equipment used.

Outside the pathology laboratories uncontrolled analyses on patients are often made. Such tests may have been inaugurated without agreement or even the knowledge of the laboratory. This may happen when representatives of firms who manu-

facture do-it-yourself instruments and reagents approach non-laboratory staff directly, such as general practitioners, clinical specialists, hospital pharmacists, and emphasise the simplicity and "foolproof" nature of their instruments. Long experience in the laboratory, however, has shown that equipment that is simple to use often needs frequent and careful attention to maintain it in a state where it gives reliable results. It is naive to assume that because a result is stable or repeatable it must therefore be correct. In the past the justification for laboratory equipment on wards has been that results affecting clinical care must be obtained rapidly. If these tests are so essential to managing the patient clearly they should also be accurate and reliable. Quality control is the means of ensuring that reagents and equipment are each functioning correctly when the patient's sample is introduced. Quality-control procedures have therefore to be used for all tests and adequate records of it need to be kept.

At least one quality-control sample and preferably two of known values should be supplied by the laboratory and stored near the unit or ward instrument. These quality-control samples should be of different concentrations, preferably with one close to that which would, if found, bring about urgent clinical action. These samples will be analysed on each occasion that patient samples are analysed. The results obtained should be documented and compared with previous results to assess bias (deviation from target value) and precision (reproducibility). Several ways of doing this are available, such as quality-control charts; mean and SD of quality-control specimens; and cumulative sum (cusum) technique. The most appropriate has to be chosen, bearing in mind the objective is to get the result right without spending too much time calculating.

It is possible for results produced by two different instruments not to be directly comparable. Thus an apparent rise in value when two specimens are analysed, the first specimen by ward staff and the subsequent one by laboratory staff, may be simply due to a difference in the two instruments. Recently a quality-control exercise has shown this to be particularly true of oxygen measurements. Oxygen electrodes may respond to the presence of nitrous oxide in different ways. Thus where duplicated services are provided consultation is essential so that the same or similar instruments are used.

Future trends

Doubtless, new devices capable of giving biochemical, physiological, and microbiological data to all comers will continue to be developed. The initiative for all this comes not from the NHS but from the world health agency laboratory and the industrial laboratory, which today are the sites of much new expertise needed to identify ill health or to produce results needed by clinicians for immediate patient management. One important advance, the culture of permanently switched-on selected "hybridoma" cells, is capable of producing indefinite quantities of antibody completely specific for a single antigenic determinant.⁹ This has enormous potential for simple and supersensitive measurement of complex substances. Recent advances being made eliminate the need for complex liquid reagents and for manipulative analytical technology. They permit many commonly run metabolites and enzymes to be analysed at the bedside with sufficient accuracy and precision. One uses 0.03 ml diluted serum on a resin strip that is then manipulated by an inexpensive microcomputer-controlled instrument (Ames Co). Another uses "solid phase" chemistry in a cartridge of film slides.¹⁰ Other innovations, such as the use of calorimetry in the presence of fixed enzymes, may solve the occasional need to analyse at the bedside for even more clinically valuable analytes—for example, urea, creatinine, as well as glucose.

All this leads one to accept that there is, in principle, no reason why the most complex blood, urine, or saliva test could not be designed to be executed by any responsible member of

the health care staff. Currently, however, the health equipment industry is against the concept of supplying sophisticated equipment to, for example, intensive care units or other near-bedside users who do not have technical support from laboratory doctors.

Whether or not the industry does devise the necessarily foolproof ways of doing the more routine tests close to the patient, the performance of a laboratory will continue to be judged by the range and quality of the service it offers to the clinician in particular and to the community in general in diagnosing and preventing disease.

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Lesson of the Week

Fetal subdural haemorrhages presenting as hydrocephalus

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Ultrasonic measurement of fetal biparietal diameter and abdominal circumference is now widely used to assess gestational age. A discrepancy between head size and abdominal girth may suggest hydrocephalus. We report on a fetus with a large head caused by subdural haemorrhages born to a woman taking an anticoagulant.

Case report

An 18-year-old woman had been taking warfarin since mitral valve replacement at the age of 16 years. She was first seen at 32 weeks by dates into her second pregnancy. Hydramnios was noted, and ultrasound examination showed a fetal biparietal diameter of 10.4 cm (normal values 8.6 ± 0.4 cm, mean $\pm$ SEM). Fetal abdominal circumference was 31.3 cm (normal 28.5 ± 2.5 cm). Repeat examination the following week gave the same measurements, and spontaneous labour and delivery occurred shortly afterwards. The infant weighed 2700 g, gestational age was assessed at 34 weeks, and head circumference was 35 cm. There was extreme pallor, tachycardia, and hepatomegaly. The infant died three hours later and necropsy showed large bilateral subdural haemorrhages.

A large head on a fetus may indicate intracranial haemorrhage secondary to anticoagulant treatment of the mother.

Comment

The risk to the fetus of bleeding or possible malformation when the mother is taking anticoagulants is weighed against the risk to the mother of thromboembolism if anticoagulants are withdrawn. A change in treatment from oral anticoagulants to heparin is usually recommended to avoid maternal or fetal bleeding at delivery. Opinions differ about when this change-over should be made: at the end of the first trimester,¹ at the onset of labour,² or at other times.^{3,4} If a woman is receiving treatment with oral anticoagulants the possibility of subdural haemorrhage should be considered in the differential diagnosis of a large fetal head, and this should be investigated by detailed ultrasound studies.

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