Near patient testing in general practice: a review

SEAN HILTON

SUMMARY. Until recently, technological advances in general practice have generally been thought of as the applications of microcomputers in practice organization and record keeping. Advances in miniaturization and versatility of diagnostic technology will have a similarly large impact on the way general practitioners practice medicine in the next decade. This article reviews some of the newer tests that are already available to general practitioners, particularly in diagnostic biochemistry and microbiology. Preliminary evaluative work and research studies in general practice are also described.

Introduction

THE government's consultative paper on the future of primary health care services[1] and the response to it by the Royal College of General Practitioners[2] have referred to the need to utilize and develop the technological advances of recent years. Progress in these areas has been given fresh and substantial impetus by the recent publication of the white paper on reform of the National Health Service.[3] The proposals to make general practitioners budget holders for a number of areas of care, including laboratory services, raise the possibility of diagnostic testing moving from the laboratories into primary care on a large scale for commercial rather than sound clinical reasons. Notwithstanding any such pressures imposed by the creation of a primary care 'market place', there will be major technological advances in the next decade which will undoubtedly influence the ways in which we practise medicine.

Most of the emphasis on new technology in primary care thus far has been placed on the introduction of microcomputers for patient data bases and practice organization. Diagnostic technology has been rather underutilized, although electrocardiography machines, usually at a cost exceeding £1000, have been used on site by many practices for a considerable time, and blood glucose meters are frequently used by practices as well as diabetic patients.

New tests for use in general practice are rapidly becoming available, and the speed of scientific development in this field means that desktop analysers will soon be able to perform a large proportion of the tests now carried out exclusively in laboratories. This article examines some of the diagnostic equipment already or soon to be available to general practitioners and reviews the evaluative work carried out in primary care in this country. The advantages and disadvantages of 'near patient testing' in general practice are considered.

Background

When hosting an international symposium on near patient testing in 1986, Professor Vincent Marks referred to the substantial advances that had been made utilizing solid phase (dry) chemistry, microprocessors and miniaturization.[4] Desktop analysers had become available to measure a number of parameters although they remained expensive and still limited in their scope. During the conference, Alberti reported an evaluation of near patient testing from an endocrinology outpatient clinic in Newcastle, where one in four patients were able to benefit from an immediate change in therapy. An American primary care physician reported on the common clinical conditions for which office testing can be used. These were: cardiovascular, principally cardiac failure, hypertension and cardiac arrhythmias, utilizing electrolyte estimations; diabetes mellitus, utilizing glucose and electrolyte estimations; and chronic lung disease, utilizing blood gas and electrolyte estimations.

In the field of bacteriology, Manek and Wise[5] have referred to the 'revival of sideroom technology'. Before the advent of comprehensive laboratory services in the 1950s sideroom testing in hospital and general practice was widespread, with doctors frequently performing microscopy on stool and urine specimens, and gram stains on clinical specimens. In recent years, with the development of rapid simple tests for accurate microbiological diagnosis, the pendulum has swung back.

Near patient testing, or office testing, is much more widespread in primary care in the USA and parts of Europe, notably West Germany, than in the UK, no doubt because of the differing systems of remuneration.[4] Under our present system, innovative practices investing in near patient testing equipment will incur considerable capital expenditure, and it will be some time before this becomes incorporated into the procedures for indirect reimbursement for expenses. There is a clear analogy with the introduction of computers into primary care, and if proposals now before the profession do not initiate change, it may require a large entrepreneurial scheme (such as the free microcomputer scheme for general practitioners set up by computer companies) to establish widespread use of near patient testing in general practice.

What tests are available?

Biochemistry

There are at least six desktop blood analysers available which will perform a range of biochemical (and in some cases haematological) tests. Most will measure glucose, cholesterol, uric acid, sodium and potassium, plus enzymes such as aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma glutamyl transpeptidase (GGT) and creatine kinase. Machines cost from £3000 to £15 000 while the cost of tests varies from around £1.50 to £2.00 each.

Some of the tests likely to be most useful to general practitioners are not yet available on this range of machines; these include thyroxine (T4), thyroid stimulating hormone (TSH), and in particular glycosylated haemoglobin.

The Reflotron (Boehringer Mannheim) is the most widely used blood analyser in general practice to date. It uses whole blood, which is a significant advantage in general practice, and does not require calibration, but problems have been reported with its accuracy and with quality control. It gives quick results, within one to two minutes, but will perform only one test at a time and does not give a printout of the result. Its reagents are relatively cheap and stable, so that they may be stored easily for a prolonged period. As with all 'dry' chemistry machines, potassium estimation is difficult and unreliable, and will not be generally available until at least 1990. The Reflotron costs approximately £3500.

S Hilton, MRCGP, senior lecturer, Department of General Practice, St George's Hospital Medical School, London.
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The Vision (Abbott) is the other machine currently available that uses whole blood. It has a built-in centrifuge to enable this. It offers a wide range of tests on fingerprick or venepuncture samples, and will run batches of up to 10 tests. Results are printed out in approximately eight minutes, or every three minutes on batches. For cholesterol testing, it will also estimate a risk for coronary heart disease, using other major risk factors from the patient's history if these have been entered into the machine. It is a more accurate and user friendly machine than the Reflotron, but this is reflected in the considerably greater cost (approximately £14 000). It also has more stringent quality control requirements. Another disadvantage is the need to refrigerate at 4 °C the bulky test kits, which have a shelf life of only 60 days.

The Ektachem DT60 (Kodak) is a sophisticated machine which is more suitable for laboratories than general practitioner surgeries. It will perform multiple tests on three separate units of equipment or 'modules' for electrolytes, enzymes, and drug level tests. Blood requires centrifugation and separation before loading. It costs approximately £10 000.

The Seralyser (Ames) is a simpler and less costly analyser which also requires serum or plasma samples and frequent calibration. It costs approximately £4000.

The Analyst (Dupont) performs up to 11 tests in 10 minutes. It has two modules, one an ion analyser for potassium and sodium which can use whole blood. For quality control it requires a daily control run, as well as calibration once per month. Like the Abbott Vision it has the facility to produce a coronary heart disease risk estimation along with cholesterol estimations. It is the most expensive of the desktop analysers at a cost in excess of £15 000. There are a number of 'stand alone' ion analysers similar to the Dupont module, such as the Nova 1 (Nova). These are fully automated and will perform sodium and potassium estimations on venous blood. They cost in the order of £2000–£3000. Other ion analysers further up the range will also measure chloride, bicarbonate, calcium and pH. A disadvantage is their size, more akin to a small refrigerator than a desktop instrument.

Easy ST (BDH) is the most recently marketed of the desktop analysers. It requires plasma or serum samples and most of the wide range of tests it offers are inappropriate to general practice use. It will carry out drug levels for 15 different drugs, but of these only phenytoin and theophylline might prove valuable to general practitioners on a regular basis. Kits for measuring drugs of abuse are under development. The Easy ST retails at £12 000.

Stratus, a recent development by the company Baxter, is an immunoassay system performing a wide range of endocrine, enzyme, and drug estimations, including thyroid function. As yet it is very expensive (approximately £30 000) and was not developed for the primary care market. It is time consuming to operate and is not easily portable. Nevertheless, its emergence is evidence of the speed of progress in this field. Manufacturers might well feel it worthwhile to seek reduction in initial costs if they see themselves as guaranteed a continuing income from the sale of tests to general practitioners (who would be unlikely to change equipment as frequently as a commercial laboratory).

Microbiology

General practitioners tend to use microbiology or public health laboratory services more heavily than they do other pathology services. A recent audit indicated that 16% of Public Health Laboratory Service specimens were ordered by general practitioners (Hilton S, unpublished data), compared with only 4% of the total tests for the clinical chemistry laboratory. These microbiology tests involved predominantly diagnosis of urinary tract infection, vaginal discharge and pharyngitis as well as pregnancy testing.

Of tests currently available, simple latex agglutination tests or 'dipstick tests' involving a colour change, are most appropriate for general practice since they can be obtained in the form of single-shot kits. Such kits are expensive and may become more so as current tests are replaced by more specific ones employing monoclonal antibodies. Monoclonal antibody tests, however, require 'labels' which are usually enzymes or fluorescent particles and are not widely available yet for near patient testing. Such monoclonal antibody tests as are available are said to 'require a high level of sophistication on the part of the individual performing them'.[6]

There are other new tools such as gene probes and biosensors, which involve considerable capital outlay and operator skill and are likely to remain unsuitable for general practice for the foreseeable future.

Group A streptococci. There are a number of tests available for rapid detection of group A streptococci. These are coagglutination, latex agglutination, or enzyme assay tests in which the streptococcal antigen attaches to antibody linked to a latex particle. The resultant macroscopic clumping of the particles gives a result in between 10 minutes to one hour.

An enzyme assay kit Test Pack Strep A (Abbott) is being marketed in this country. Each test kit costs around £4.00. It will not detect group C or B beta haemolytic streptococci, although these may also cause clinical problems. Under these circumstances, withholding antibiotics because of a negative test for group A streptococci could give rise to disseminated infection.

Urine. Nephur Test Plus Leuco (Boehringer Mannheim) and Multistix 8SG (Ames) are inexpensive and easily performed rapid tests on urine. As in standard dipstick tests, reagent patches which are attached to a plastic strip indicate the presence of leucocyte and nitrate-converting bacteria. Neither indicator is specific for bacterial infection, so the positive predictive value (specificity) of the test is low at 42–54%, but the use of the two tests together has a high negative predictive value (sensitivity) of greater than 90%. The test takes less than two minutes to perform and is therefore a potentially useful screening test for general practitioners to use.

Vaginal infections and sexually transmitted disease. Two of the commonest pathogens in vaginal infections are gardnerella and chlamydia species. A rapid diagnostic test for use in general practice is being developed for gardnerella by O'Dowd and colleagues (O'Dowd TC. The development of a diagnostic test for *Gardnerella vaginalis.* Presentation to annual scientific meeting of the Association of University Teachers in General Practice, 1987),[7] and is based on an azo dye test. For chlamydia, the Microtrak test (Syva) uses a monoclonal antibody. Currently this test requires a fluorescent microscope for completion, but work is continuing on a kit which will enable results to be quicker, easier and less expensive. Such a kit, Clearview Chlamydia (Unipath), will shortly be marketed. Abbott produces an enzyme linked immunosorbent assay (ELISA) test, Chlamydiazyme, which takes four hours to perform, and is no more reliable than Microtrak (Baselski V, McNeeley G, Robinson M. Comparison of two non cultural tests to culture for detection of *Chlamydia trachomatis* in obstetric patients. Presented at interscience conference on antimicrobial agents in chemotherapy, 1985).

An inferior method of testing for vaginal infection is to measure vaginal pH. A value of 5.0 or more indicates either non-

specific vaginitis owing to gardnerella, or trichomoniasis, both of which can be treated with metronidazole.[8]

For *Neisseria gonorrhoeae,* few general practitioners offer diagnostic testing in their surgeries, since referral to sexually transmitted disease clinics is generally considered to give a more efficient service in terms of diagnosis and case contact. The tried and trusted 'on site' gram stain of urethral discharge remains cheaper and more sensitive than any of the newer tests, including a bedside oxidase test, Gonodectin (Laporte), which gives a result in three minutes.[9]

Identification of herpes simplex virus is still best carried out in diagnostic laboratories using direct immunofluorescence studies of scrapings. A rapid latex agglutination test has been described which looks promising but is of low sensitivity.[6]

HIV antibodies. Dupont have recently developed a rapid test for human immunodeficiency virus (HIV) antibody status, HIVCHEK. The ELISA methods currently used by most centres require relatively sophisticated equipment and need approximately four hours to produce a result. HIVCHEK is a membrane test which uses a recombinant HIV protein and a protein-A-gold conjugate within a single kit to give a rapid (five minute) result. The test has been evaluated against the more established Wellcome ELISA test on 4000 prospective blood donors in Zaire (Spielberg FL. A review of HIV antibody detection assays. Paper presented to international congress on AIDS, Stockholm, June 1988) and showed a comparable reliability, that is, sensitivity greater than 98% and specificity greater than 99%. The test is available for use in practices, but ethical and legal issues make it impractical for general practitioners to take it up. It may be used only when ordered by a doctor, when there is a good clinical reason, and the clinician in charge has obtained informed consent from each patient. When there is a positive result the test must be repeated and samples sent for confirmation by other methods. Facilities for pre- and post-test counselling must be available. Without written confirmation of these principles the test cannot be supplied, except for bona fide research purposes. A number of other companies are developing similar tests, but to date Dupont is the leader, with the most rapid and reliable version. General practitioners may well become involved in HIV testing to a much greater degree in the future.

Pregnancy. Latex agglutination tests for pregnancy are already used widely, both in the National Health Service and over the counter at the pharmacist. Their sensitivity is acceptably high.

A new and related test is First Response, an ovulation prediction test marketed by Tambrands to improve the management of subfertility. It is an ELISA test which detects the surge of luteinizing hormone (LH) which occurs in the urine 24–48 hours before ovulation.[10] The test uses two monoclonal antibodies to form a complex with the LH from the urine. An intense blue colour reaction indicates the presence of increased LH. A small evaluation study on this test suggests it has a high specificity, and a greater sensitivity to the LH surge than basal body temperature measurement.[11] The test is commercially available at a cost of approximately £20.00 for a six day test pack. It may even have a commercial role as a contraceptive for those wishing to improve the safety of the 'rhythm method'.

Haematology

The prospect of miniaturized Coulter counters appearing in our surgeries seems less likely than for the biochemical analysers. Haematology instruments rely on the principle that as cells flow, single file, through apertures within the equipment they cause a rise in impedance to a current flowing between electrodes on either side of the apertures. This causes voltage spikes which allow quantitative measurements of number and size of cells to be made. Such machines are costly and time consuming to operate, since samples require preparation in different dilutions for red and white cells. Basic haematology models used in physicians' offices in the USA are the Hemo-W (Boehringer Mannheim), and the Quick Count +2 (Seragen). These measure haemoglobin, packed cell volume and red and white cell counts. More sophisticated machines also measure red cell indices, and one machine will carry out a white cell differential count.

Prothrombin time and haemoglobin measurements can be carried out by most of the biochemistry analysers described above, but they cannot give any red cell indices or white cell and platelet counts.

Quality control

Quality assurance is an important consideration for all machines. Recently a hazard notice was issued by the Department of Health as a result of a fatal error in interpretation of a blood glucose test by insufficiently trained nursing personnel. It would be possible for a 'package' of quality control training and back up to be provided by manufacturers to general practitioners, but for the moment, it is likely that both verification of test levels and staff training will involve local laboratories. Most potential non-laboratory trained users of near patient testing are likely to be unaware of the general concepts of quality control, and these will need to be instilled carefully during periods of training. As Marks has stated: 'like all new technologies its [near patient testing's] apparent simplicity often belies its complexity and the need for attention to detail in order to achieve optimum effects and avoid disasters'.[12] Nevertheless, the value of near patient testing lies in its ease of use by semi-skilled personnel after only a minimum of training, and general practitioners and their practice staff need have no fear when using sophisticated equipment as long as standard safety and quality control procedures are followed carefully.

Evaluation of near patient testing in primary care

Cholesterol measurements

Jones and colleagues have reported on a screening programme in their practice of 10 000 patients in Swansea.[13] Their aim was to screen all patients aged 25–55 years for identifiable risk factors for coronary heart disease. This included total plasma cholesterol estimations on fingerprick samples of whole blood using the Reflotron (Boehringer). Quality control was carried out by means of parallel testing, with split samples being tested at the local laboratory, and by using a commercial quality assurance serum. All patients with a raised cholesterol value (over 5.5 mM for men under 30 years or over 6.0 mM for men aged 30 years and over and women) were referred to a weekly cholesterol clinic. Of the 2353 patients screened, almost 10% had total cholesterol values in the high range (over 6.5 mM for men and over 7.0 mM for women), including 2% in the very high range (over 8.0 mM). The quality control programme of the Reflotron showed the mean result to be 108% of the mean of the laboratory results. With the low cut off points that Jones and colleagues selected for intervention, they felt that the probability of their missing patients with hypercholesterolaemia was slight.

Anggard and colleagues[14] have reported a large multi-centre screening model based in general practice, employing nurses to supervise a lifestyle management programme. The screening programme included cholesterol estimations performed on a fingerprick sample of whole blood using a Reflotron analyser. The investigators chose a cut off point of 7.0 mM for high cholesterol (15% of their population), and 9.0 mM for very high level

requiring referral to a doctor (2%). Microcomputers were used for data entry to enable central collation and analysis of data from all centres. Nineteen health centres throughout the country participated in the study, which was funded by a pharmaceutical company. When this funding ceased, more than half the practices involved elected to continue the programme at their own expense.

Gorman, in Edinburgh, carried out a follow up study in one of these practices to determine whether the collection of data and calculation of risk scores was accurate and repeatable.[15] At a follow up assessment, those found to be in the low risk group at the initial screening showed a significant increase in their calculated risk score, although repeat measurements in the original high risk group and in a control group did not show this change. Cholesterol measurements at follow up were carried out in a laboratory rather than with the Reflotron, and were significantly higher, even in those patients claiming to have made no lifestyle changes since their original screening two to four months before. When he carried out a parallel testing study on 50 samples in the practice using another Reflotron machine, Gorman again found a significant difference between mean laboratory values and mean Reflotron values. On this occasion the laboratory mean value was significantly lower (5.8 mM versus 6.2 mM). The study suggests that single estimations of cholesterol in the surgery should be interpreted with caution, as with single blood pressure readings, and the findings emphasize the importance of adhering to good quality control procedures.

Other authors have also questioned the reliability of results obtained from such community cholesterol screening programmes. Broughton and colleagues reported three quality control surveys of a number of community programmes which were using Reflotron machines to measure total cholesterol.[16] The programmes were largely based in occupational health services and general practices, and over the course of the three surveys there were 170 respondents. Each respondent received three specimens of serum for analysis, being asked to return results to the investigators. On average, half of the participants had results within 0.3 mM of the mean, but in 8.6% these differed seriously by 1.0 mM or more. Investigation showed the main causes of error to be poor technique and carelessness, such as the use of reagent strips that had passed their expiry date, rather than inherent unreliability of the machine. The authors have issued guidelines for the measurement of cholesterol outside the laboratory, and have instituted regular two monthly quality assessment surveys for cholesterol, using mainly fresh human sera. They have invited any non-laboratory user in the UK to join their scheme without charge.

Notwithstanding the problems of accurate and repeatable measurements, there is a current debate on the whole subject of population screening for cholesterol, and further research is needed to establish beyond question the benefits of such programmes.[17-19]

Beta haemolytic streptococci

Burke and colleagues have evaluated an enzyme assay kit tailored to identify group A haemolytic streptococci (Abbott Test Pack Strep A).[20] In a two stage study, the investigators aimed to describe general practice prescribing for sore throat, to assess the sensitivity and specificity of the new test compared with clinical assessment and to determine the effects of the availability of the test on general practitioners' prescribing. They surveyed the management of nearly 1200 episodes of sore throat reported by participating general practitioners and found an antibiotic prescribing rate of 64%. The rapid diagnostic test was then made available to seven group practices, where treatment room nurses were trained in its use. The nurses carried out diagnostic tests on 250 patients with sore throat. At the same time they took a throat swab for conventional culture in the laboratory. The general practitioner reviewed the patient and decided on treatment when the rapid test result was available. Of the 46 'laboratory positive' tests, only 29 were positive with the rapid test — a sensitivity of 63%. Of the 204 'laboratory negative' tests, 17 showed positive on the rapid test — a specificity of 92%. The sensitivity of the test as used did appear to increase as the study progressed, probably indicating a learning effect. The investigators found that the prescribing decisions of the general practitioners were rarely affected by the availability of the result; only 18% of the rapid tests were positive compared with an antibiotic prescribing rate in this group of 44%. A further 11% of swabs yielded other bacteria on culture, principally streptococci of other Lancefield groups. These findings, combined with the relatively low sensitivity of the test and the high unit cost (£4.00), led the authors to conclude that the time is not ripe for the introduction of this test on a wide scale in routine management of sore throats.

Implications of near patient testing

Introduction of near patient testing into general practice is likely to have far reaching effects. On the positive side, the availability of rapid test results should lead to greater convenience for patients, better monitoring of certain chronic conditions, and probably to more rational prescribing. For preventive work, the immediacy of results such as serum cholesterol levels should improve doctor–patient rapport and enhance the quality of any intervention. Indeed, in the case of cholesterol, this may be the most important contribution of near patient testing.

Possible disadvantages of near patient testing may be the temptation to over-investigate, to use the test because it is easily available rather than clinically necessary. The greater the number of tests performed, the more abnormal results of doubtful importance will be uncovered. One of the strengths of the present delay in obtaining results for certain tests is that it allows extra time for self-limiting conditions to resolve, or for 'unorganized illness' to evolve. The requirements of quality assurance should not perhaps be viewed as a disadvantage of near patient testing, but will certainly be a constraint to ease of use, if accuracy of results is to be safeguarded.

The economic implications of near patient testing are not yet clear, and they too will require careful evaluation in the light of changing laboratory facilities in the modified NHS. Costs will need to include patients' personal expenses, such as bus fares and time off work, as well as direct and indirect health service expenditure. Full scale cost-benefit analysis, where benefits are assigned a money value and weighed against costs, is difficult to achieve.[21] Cost-utility analysis, on the other hand, where benefits to patients are measured, but not expressed in money terms, may seem more relevant to general practitioners.

The evaluative work which is taking place in areas of high importance to general practice, cholesterol and beta haemolytic streptococcus testing, underlines the need for careful consideration of the advantages and disadvantages of near patient testing before it is widely adopted. The recent establishment of a general practitioner testing working group within the British Laboratory Ware Association is to be welcomed. The working group consists of members of several leading diagnostic and reagent manufacturers, together with representatives of general practice and the hospital pathology services. The group will be looking

at ways in which technology, in the form of near patient testing, can lead to better care of patients, and a closer integration of testing facilities (central and near patient) available to the general practitioner.

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Address for correspondence

Dr S Hilton, St George's Hospital Medical School, Jenner Wing, Level O, Block Gl, Cranmer Terrace, London SW17 0RE.