



Point of care testing: lateral flow technology and beyond

For the last 50 years the pathology industry has been centralised and built around a strong skills base in laboratory medicine. Over recent decades, that skills base has been diluted as advances in technology have seen automation takeover many laboratory-based functions. These changes have, perversely, been driven by advances in medical science. With advances in medicine has come the demand for more intervention (testing) and the concomitant economic pressure to reduce the real cost of pathology testing as access is expanded.

Linked to the economics of pathology testing and the ideal of real-time diagnosis have come the concepts of near patient and point of care testing (POCT). In the Australian context, POCT is not as developed as in other parts of the world. While in the foreseeable future laboratory based pathology testing will remain predominant, worldwide there is an irresistible progression towards POCT for selected conditions.

The largest POCT market is that for glucose monitoring, used in management of diabetes mellitus. Indeed, many of the technological advances that take place in POCT originate in the blood glucose monitoring sector and later flow on to other fields of POCT. For example, the latest technologies in non-invasive biochemical detection, implantable biosensors and salivary analyses are all being lead from the blood glucose-testing market.

Lateral flow technology

Lateral flow technology, also known as immunochromatography, involves the complexing of an antibody or antigen with a target analyte, which in turn is immobilised within a 'capture' zone after flowing up a membrane. The complex formed in samples containing the target



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analyte are visualised by use of particulates, such as colloidal gold, deposited with the analyte and reactants (Figure 1).

One of the most common applications of lateral flow technology can be seen in home pregnancy testing. Notwithstanding, lateral flow technology can be used in POCT to detect antibodies to specific agents of disease, antigens (e.g. malaria) and markers of organic disease. An advantage of these technologies is the capacity to design systems that can be used to detect analytes directly in specimens such as serum, saliva, whole blood and urine.

These assays are fast (results in between 5 and 20 minutes) and can be performed by personnel without specific technical training, but may not be as sensitive or specific as more conventional laboratory based immunoassays. Thus the target application must be defined and understood.

Next generation technologies

The ideal in POCT is to take the attributes of large and complex laboratory systems and put them into a miniature device. These small, integrated systems will exploit micro-engineering technology to

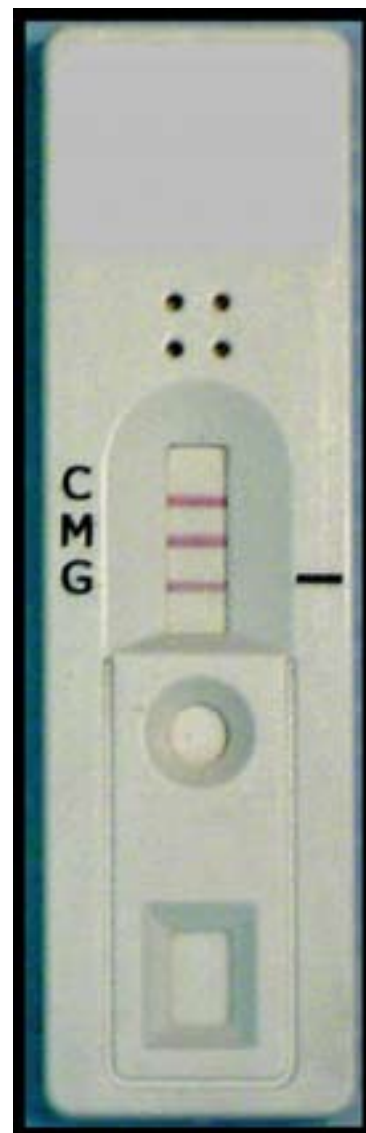


Figure 1. Example of a lateral flow assay used in the detection of antibodies, IgG (G) and IgM (M), in a person infected with a particular pathogen. The positive reactions (red lines) are formed by an antigen-antibody complex captured in a capture zone and visualised by colloidal gold bound to the antigen-antibody complex.



deliver the laboratory in small hand-held devices.

An example of developing technology in the field of POCT is biosensors. Biosensors are small electronic devices that are composed of a recognition element or sensor (antibody, enzyme or chemical receptor) coupled to a transducer, which converts a signal into electrical signals that can be displayed by a small computer. These are the key to the development of POCT for agents of infectious disease, clinical chemistry and haematology. As this technology matures it is expected that biosensors will be incorporated into the everyday delivery of patient care. Their advantage will be the ability to substantially reduce the cost of care while delivering quantitative data with an improved turnaround time.

Microfabrication techniques will be a core determinant in the success of biosensors. Microfabricated silicon chips are eliminating the advantages currently enjoyed by chemical strips and nitrocellulose based detection methods such as lateral flow. Using silicon microchips, the sample will be distributed to the test areas via microfluidic channels where test menus could include assays for infectious disease, electrolytes, metabolites, blood gases, glucose and hematocrit. There is also the potential for these systems to include micro real-time PCR.

The growth of global POCT

The POCT market is one of the fastest growing segments of the *in vitro* diagnostics (IVD) industry in the developed world, with a growth rate of the order of 15%. By way of comparison, the overall IVD market is experiencing growth of only 5%. The infectious disease-testing segment of the market is growing rapidly from a low base.

The growth in infectious disease POCT is expected to be above the market average at 17%. For reasons of timely diagnosis, POCT is very attractive. For example, a patient infected with HIV can be counselled and the implications of the infection discussed, reducing the risk that they do not return for treatment. Accurate POCT have a high degree of utility in diagnosis of enteric infections, giardia, malaria, HIV, hepatitis, influenza, Streptococcus A, Staphylococci, chlamydia, EBV, rubella, gonorrhoea, vaginitis, tuberculosis and anthrax. Influenza is by far the largest single disease target segment valued at over \$150 million. HIV testing is expected to grow at about 15% over the next 5 years.

The majority of infectious disease POCT are run in lateral flow format and are performed in the hospital or physicians office. While the strongest demand for POCT is in the developed world, in the developing world POCT can have advantages where laboratory systems are poorly developed or non-existent and

so uptake in these areas is increasing. In particular, use of rapid POCT for infectious diseases will continue to grow in developing countries in coming years. Increased spending on healthcare and diagnostics in concert with a lack of infrastructure and areas remote from clinical laboratories have stimulated a rapid uptake of POCT in Africa and Asia, particularly in response to infectious disease epidemics such as the spread HIV.

Regulatory hurdles in the future of POCT

A major barrier to entry for POCT is government mandated regulations. Internationally, regulatory bodies face the challenge of integrating POCT diagnostics into current regulatory frameworks. The issues of concern to regulators are quality, performance and appropriate interpretation of results. However, both the developers and manufactures of POCT and the regulatory bodies are addressing these issues. Ultimately, the demand for quality and accurate cost effective tests that have clinical utility in the near patient or point of care environment will drive the market.

Conclusion

As the technology underpinning POCT improves, it is expected that many of the assays for infectious disease will perform at levels exceeding that currently available on platforms such as ELISA.

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