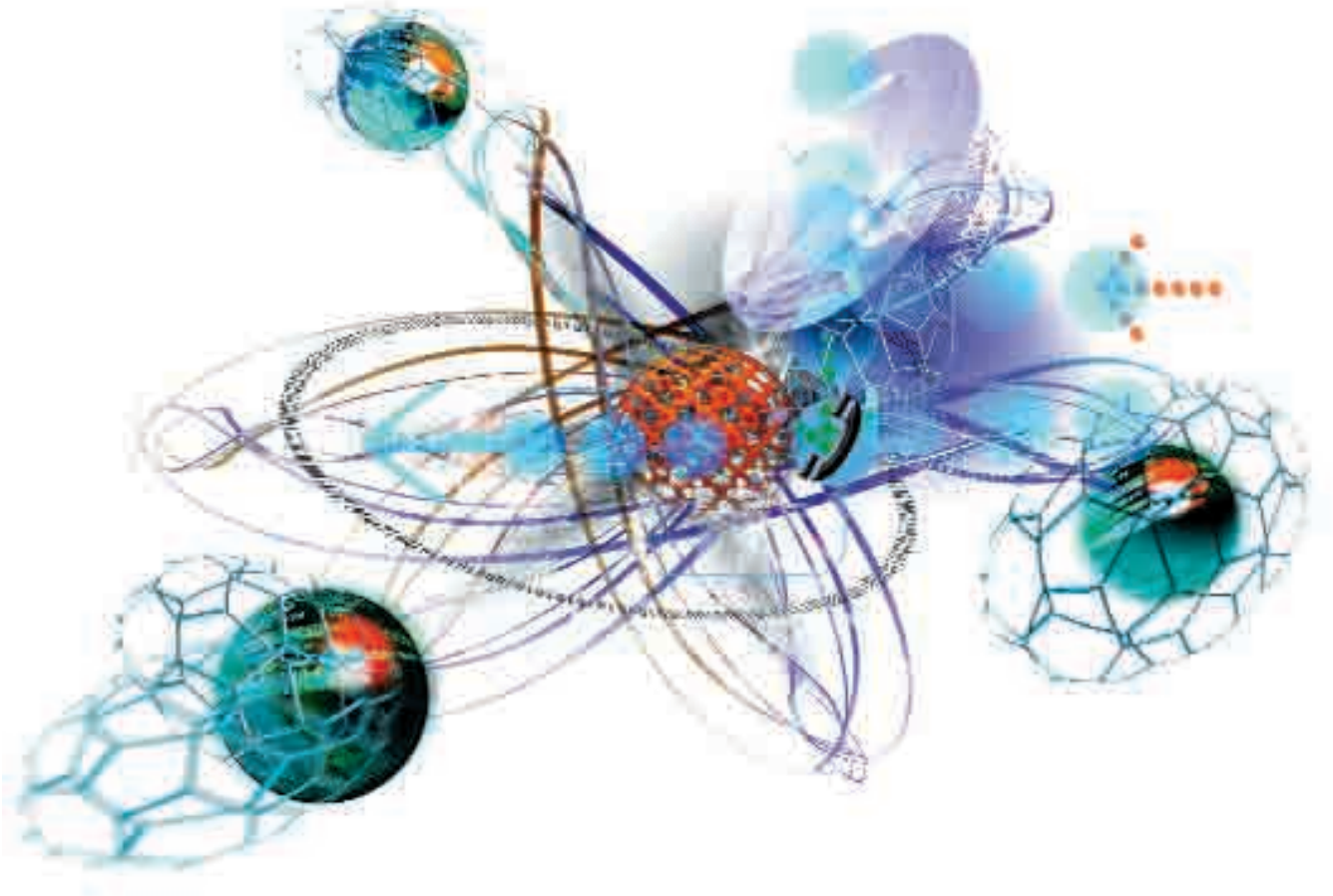

It's a small world after all

NANOTECHNOLOGY HAS THE POTENTIAL TO CHANGE THE WAY MANY PATHOLOGY TESTS ARE DONE. BUT IT ALSO BRINGS ISSUES THAT SOCIETY SHOULD NOT IGNORE. **TONY JAMES** REPORTS.

Imagine that a tourist with a severe upper respiratory tract infection visits her GP a day after returning from Vietnam, where an epidemic of SARS has re-emerged and human-to-human transmission of avian influenza is picking up pace.

Her doctor takes a finger-prick drop of blood, places it in a tiny well in a disposable credit card-sized carrier and 10 minutes later a desk-top analyser shows she has nothing more serious than the common cold. Nanotechnology puts this scenario within reach. However Dr Peter Garcia-Webb, head of the department of Chemical Pathology at Western Diagnostic Pathology in Perth says like all new forms of technology the application in the practice of medicine needs to be done with care. In particular there must be safeguards from a quality perspective and appropriate medical involvement.

"Nanotech" is a term that's easier to use than define. Many branches of science deal with concepts of the incomprehensibly small - students in school chemistry learn about reactions between atoms and molecules - but, so far, our machines have been built on a much larger scale.

"Nano" is a prefix for 10^{-9} (one-billionth) so a nanometre is a billionth of a metre or a millionth of a millimetre. The dots on the letter "i" on the pages of PathWay are squares with sides about 250,000 nanometres long. Red blood cells (of which there are five million or so in every cubic millimetre of blood) are about 7000 nanometres in diameter.

Applications of nanotech to pathology are likely to be evolutionary, rather than revolutionary, and involve close co-operation between pathologists, medical scientists, engineers, chemists and IT specialists. This mix is evident at AMBRI Limited (the Australian Membrane Biotechnology Research Institute), a Sydney-based company that evolved from a research group within the CSIRO that is a world-leader in biomedical nanotech research and development.

AMBRI holds patents for a device called an ion channel switch. Designed to mimic the function of a nerve cell membrane, the switch consists of a thin film of gold in which molecular ion

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channels are self-assembled during the manufacturing process.

One side of the membrane is coated with an antibody to a target substance. When the antibody and the target react, electrical conductivity through the underlying ion channels is disrupted, and the change can be measured to give an accurate assessment of the target's concentration.

For example, the membrane could be coated so it measured glycosylated haemoglobin (HbA1c, used as a marker of long-term blood sugar control in diabetes), or any of a large number of biological compounds.

Initial trials of the technology at Royal North Shore Hospital in Sydney, measuring HbA1c, confirmed it worked, but there is still some way to go before the process is commercially competitive with established laboratory methods, according to AMBRI general manager Russell Richards.

"The advantages we eventually hope to offer are a combination of portability, speed, the ability to perform a number of tests from a very small specimen, and cost-effectiveness," he says. "For example, when patients with diabetes visit their doctor, they could have their HbA1c result available to discuss by the end of the consultation."

Photographer: Richard Goodwin

Dr Peter Garcia-Webb, head of the department of Chemical Pathology at Western Diagnostic Pathology in Perth

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Meningococcal infection can be rapidly fatal, but the initial presentation is not always distinctive. Identifying the infection in its early stages or ruling it out would be a boon for worried GPs and their patients.

The ion switch channels are extraordinarily sensitive. AMBRI's chief scientist, Dr Bruce Cornell, has said they could detect a concentration equivalent to a sugar cube dissolved in Sydney Harbour.

AMBRI's research staff are now working on a microchip version of their device, measuring about 8x16 mm, which could conduct 16 different tests simultaneously. For example, a series of tests for respiratory infections could be used on our tourist from Asia.

Dr Garcia-Webb, says the slow uptake of nanotechnology in medicine has been surprising. "There are industrial companies in Australia already applying nanotech, for example in using new techniques to suspend particles in a paint product," he says. "We have yet to see a breakthrough in medicine where the technology has been integrated into routine practice."

The concept of smaller, faster, cheaper and more portable testing is inevitably linked with debate about "point of care" testing, Dr Garcia-Webb says. The archetype is a home pregnancy test, available over-the-counter from pharmacists for decades and providing a

Photographer: Paul Jones

AMBRI's chief scientist, Dr Bruce Cornell, left, and AMBRI general manager Russell Richards

result that is accurate enough for most purposes. Blood glucose monitors for home use are now established as an essential part of diabetes care, and there is a growing range of rapid tests available for use at the bedside in hospital or in the doctor's office. There has been a recent international laboratory standard developed on point of care testing and any development such as nanotechnology will need to be introduced in accordance with this standard.

"But what are the implications if it's a test for prostate-specific antigen, a marker of possible prostate cancer? Or a gene for Huntington's disease, a diagnosis that will be devastating for the individual and may have been inherited by their children?" Dr Garcia-Webb says.

Americans can already buy kits to test at home for a wide range of genes, including those associated with a high risk of breast and ovarian cancer (for $US585 to $US3,311). A cystic fibrosis test, at $US260, involves sending a simple cheek swab back to the laboratory, then receiving a "personalised report" by email and "expert support" - but not necessarily any face-to-face contact with a doctor to explain and interpret the results. It is important that a treating medical practitioner is involved in discussing these issues with patients and because of the complexity of some of these diagnostic test results consultations between treating doctors and pathologists, who specialise in understanding and interpreting such tests, will be vital.

"The importance of the patient-doctor interface varies with the type of test, and as a society we will need to sort out how best to deal with this potential explosion in personal medical information," Dr Garcia-Webb says.

Dr Debra Graves, Chief Executive Officer of the Royal College of Pathologist of Australasia said the College was very cognisant of the need to work through the implications of this potential explosion of medical information in the future and was looking at ways to ensure pathologists receive appropriate training to help manage and interpret what this information explosion would mean for individual patients.

Nanotechnology will also become an important part of diagnostic testing and targeted treatment. Dr Garcia-Webb says "nanotubes" can be made from a sheet of carbon that is one atom thick and then rolled, cannelloni-style, into a tube. They could be arranged as conductors, linked to targets in the blood, and transmit a signal detectable by a device outside the body.

"We already use subcutaneous devices that read blood sugar levels and then radio a signal to an insulin pump worn on a person's belt, so this technology is not as fantastic as it might seem," he says. "The growth of the technology can't and shouldn't be halted, but we will need to learn how to use it."