

# Measuring milestones

## – the rise of the glucose meter



Glucose meters are one of the most important innovations in healthcare – offering life-changing benefits for millions of people with diabetes around the world. **Dr Richard Elliott** meets the pioneering scientist who played a vital role in their evolution

**R**egular monitoring of blood glucose levels is a vital part of diabetes management and appropriate testing 'kit' is part of everyday life for everyone who uses insulin, as well as for some with Type 2 diabetes who use other forms of glucose-lowering medication. But, this wasn't always the case. For many years, self-testing was regarded as unfeasible, or even dangerous, by doctors, and this only changed as the accuracy and user-friendliness of the process improved. In the 1920s, the very first at-home glucose tests involved a laborious 10-minute process that included mixing a sample of urine with a chemical provided by the doctor (Benedict's solution), heating the mixture in boiling water and watching for a colour change. Blue indicated no glucose, green meant there was a trace and red or orange signalled an excess. This approach was slowly, but steadily, improved on over the years – first with the introduction of Clinitest tablets in the 1940s (which didn't require a source of heat) and, again, in the 1950s and 1960s with paper test strips that could be used to measure glucose in the urine and, later, for more up-to-the-minute readings, the blood. However, these methods were limited because they relied on people's judgement of colour change to give an estimate of glucose levels, which was imprecise and could be misread, especially by those with poor eyesight.

The Ames Reflectance Meter was the first portable blood glucose meter. It also used test strips, but gave a more precise estimate of blood glucose by accurately measuring their change in

colour via the amount of light they reflected. Despite being large, expensive, heavy (at around 1kg), challenging to set up and use, and only available on prescription, the technology behind this meter was a success. Marketed to doctors, but often used by people with diabetes themselves, it was the start of over 45 years of tremendous progress that led to the wide variety of small, user-friendly meters that we know today.

### From setback to success

In the late 1970s and 1980s, the work of one scientist was absolutely key to the creation of a new kind of sensor that is now found in virtually all of the glucose meters that are used in routine diabetes management. Professor Anthony Turner began his career in the early days of biotechnology. His specialty is in linking biochemical reactions with the electronic

“We decided that improved glucose testing for people with diabetes was a major need”

create a biological fuel cell that would convert alcohol into electricity using biochemical reactions.

“We had some success,” he says. “But, one afternoon, I did a quick calculation to work out what size our fuel cell would need to be in order to

power an average household, and it turned out that it would have to be about the size of the living room!” Concerned that the fuel cell would never be a practical source of energy, Prof Turner was nevertheless interested

to see that the electricity generated by the cell increased whenever alcohol was added. “At that point,” he says, “I turned to my student and said: ‘This is perhaps not a very good power source, but it’s a damn good measurement device!’ We got very excited and went to the pub for a drink to celebrate our invention of what we called a biosensor. Of course, when we came back in on Monday morning and looked back through past research, we realised that this wasn’t a



Professor Turner presents his work to HRH Prince Charles in 1984 (left). In the lab at Cranfield University in 1981 (above)



new invention at all – an American scientist called Leland Clark had already thought of the idea in 1962.”

Dr Clark’s elegant idea, based on a sensor that could measure the amount of oxygen in a sample of blood or other liquid, had already been adapted for the measurement of glucose as part of the Yellow Springs Instrument Company’s ‘Blood Glucose Analyser’. The size of a microwave oven, this bulky device was, by the late 1970s, used by clinics and labs around the world, but was too large, too complicated and too expensive for use by people at home.

“We decided that improved glucose testing for people with diabetes was an important need and an ideal problem for us to tackle,” says Prof Turner. “We started work on new glucose sensors, and my plan was to look at a range of different ways of monitoring and managing diabetes, and to try to create a simple device that could be easily mass-produced and made less expensive as a result. However, we needed funding for our work and that’s what spurred me on to apply for support from Diabetes UK.”

### Diabetes UK and the first hand-held meter

In 1982, a five-year fellowship from the charity helped launch Prof Turner’s career in biosensors by giving him the freedom to focus on what was most important. During those five years, Prof Turner and his team at Cranfield University in Bedfordshire took their first steps to becoming one of the top biosensor laboratories in the world. Building on the work of Leland Clark,



Professor Turner at Linköping University in Sweden

they collaborated with Allen Hill, Tony Cass and Graham Davis at Oxford University to develop a new mediated electrochemical biosensor, which was simpler, cheaper and performed better than existing devices. In simple terms, the more glucose present in a sample of blood, the stronger the electrical signal produced by the sensor. The strength of the signal could then be interpreted to give a reading of blood glucose concentration. This small step forward turned out to be hugely important – enabling Prof Turner and his collaborators to create the first digital hand-held glucose meter, which was more sensitive, faster and required less blood than anything that had come before.

“We not only shrank the technology down to something the size of a calculator,” he says, “We also introduced new manufacturing processes that enabled us to ‘print’ biological materials for the first time, so that we could mass-produce key components and

bring their cost down to only a few pennies.”

It was a tricky process to begin with but, by 1987, Prof Turner and his colleagues were, with the company MediSense (now part of Abbott Diabetes Care), able to launch a pen-sized glucose meter called ExacTech, the great-grandfather of most meters on the market today – a market that’s now worth more than US\$13bn worldwide. The new technology wasn’t just important for diabetes and healthcare; it laid the foundations for a whole range of biosensors that are now used in everything from food safety to environmental monitoring.

### Future glucose meters

Despite the progress of glucose meters, tight diabetes management over the long term remains a challenging goal

“We’ve brought these devices from the size of a microwave down to the size of a pen”

and is an important focus for researchers. Prof Turner now leads the Centre for Biosensors and Bioelectronics, which he set up at Linköping University in Sweden in 2010, and is often called ‘Mr Biosensor’ because of the lasting influence of his work. Diabetes is

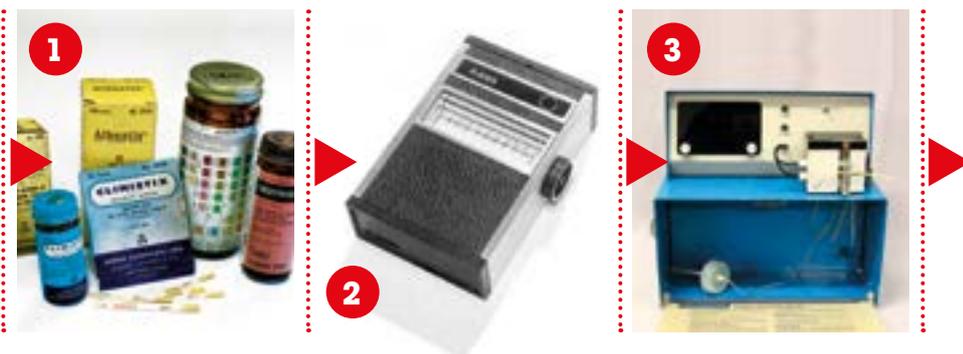
still an important part of what he does, and he’s confident that glucose meters will continue to advance as the technology behind them improves.

“We’ve brought these devices from the size of a microwave down to the size of a pen, and now we’re putting them on a piece of paper,” he says. “We’re

PHOTOS: ANTHONY TURNER/ABBOTT DIABETES CARE/ AMERICAN CHEMICAL SOCIETY AND BAYER HEALTHCARE LLC/ LELAND CLARK AND CHEMICAL HERITAGE FOUNDATION COLLECTIONS/ DAVID MENDOSA

## A BRIEF HISTORY OF GLUCOSE MONITORING...

How have the techniques and technology advanced over time to improve the management of diabetes?



working on technology that looks like a business card, but which has processors, circuits and a digital display, can make measurements and will send them to a smartphone via Bluetooth. Either you would apply a drop of blood, or wear it like a sticking plaster. You would stick it on and it would give you a glucose reading either with numbers or with colours, or by communicating with your smartphone or tablet. Trying to minimise the invasiveness of devices in a way that is comfortable, but still gives accurate readings, is the way we are pushing forward.”

Wearable devices might also include things like contact lenses, which were highlighted in the media by Google and Novartis in 2014, but are being worked on by scientists all around the world. It's likely that the next generation of meters will also incorporate many different kinds of sensor, allowing them to measure a range of different biological changes. They will also include complex computer code and connect to databases of expert knowledge to become more intelligent. As a result, they will be able to provide information and suggest actions tailored to the individual – instead of just numbers, allowing people to achieve better diabetes control than ever before.

Relying on slightly different technology to traditional meters, continuous glucose meters (like Medtronic's Guardian or the Dexcom

G4) provide greater insight into fluctuations in glucose levels over the course of a day and their possible causes. This, too, continues to improve, becoming less invasive, more affordable

and easier to calibrate and use. There are also hybrid devices like Abbott's Freestyle Libre, that combine the features of both fingerstick and continuous glucose testing. Such meters are likely to become

more widely available to ever more people with diabetes, again leading to improvements in diabetes management.

Self-monitoring empowers people to manage their diabetes, with significant benefits to health and quality of life.

“The next generation of meters will also incorporate different kinds of sensor”

Though his work has become more diverse over the years, Prof Turner hasn't forgotten its roots. “Diabetes is still very important to me,” he says. “My Diabetes UK fellowship brought me into contact with patients and carers, and that has stayed with me for my whole career. It put me in touch with real people and real people's needs and those lessons never left me. They help me to remember that it's all very well making a technically brilliant device, but if people can't use it or don't use it, what's the point? Science has to be useful.”

**i** **Diabetes UK relies on donations to fund research like Prof Turner's. If you would like to help, go to [www.diabetes.org.uk/donate](http://www.diabetes.org.uk/donate)**

CALLS MAY BE RECORDED FOR TRAINING AND QUALITY PURPOSES.

### Diabetes UK says...

**We believe that self-monitoring of blood glucose levels should be regarded as an integral part of treatment for everyone with diabetes treated with insulin and should not be restricted. Self-monitoring should also be available to people with Type 2 diabetes who are being treated with medications that put them at risk of hypos. Blanket policies to**

**restrict access to self-monitoring should be removed and replaced with individual assessment, where all options are explored in a joint decision-making process between the person with diabetes and their clinician to ensure resources are adequately used. Diabetes UK campaigns for all people with diabetes using insulin**

**or insulin-lowering medication to have the right number of test strips to help them manage their condition. People living with diabetes can download the charity's advocacy pack, which covers information about how to challenge test strip restrictions at [www.diabetes.org.uk/test-strip-advocacy-pack](http://www.diabetes.org.uk/test-strip-advocacy-pack) or call 0345 123 2399\*.**



- 1 1940s–1960s:** Tablets and test strips estimate glucose levels in urine or blood.
- 2 1969:** Ames Reflectance Meter – the first portable glucose meter.
- 3 1975:** Yellow Springs Instrument Company Blood Glucose Analyser – bulky, complex.

- 4 1987:** MediSense ExacTech – the first digital hand-held glucose meter.
- 5 2014:** Abbott Freestyle Libre combines continuous and fingerstick monitoring.
- 6 The future:** Maybe contact lens meters like those proposed by Google/Novartis?