THE FUTURE OF DRUG DELIVERY

With an eye on the current trends and range of innovations in the sector, particularly data and connectivity technology, Uri Baruch, Head of Drug Delivery, Cambridge Design Partnership, looks back on how far injectable drug delivery has come in the past thirty years, and forward to what the future may hold.

Cast your mind back 20-30 years and an autoinjector would have been a rare sight – a real novel approach to drug delivery. It was the time when these devices started to come onto the market due to conditions which allowed for, or even demanded, patients to self-inject a drug as part of a specific treatment regimen. Most people were uneasy about using syringes and needles, and unfamiliar with them unless they were suffering from diabetes. And even diabetes patients had to cope without the sophisticated next-generation insulin pens we now take for granted.

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Autoinjectors were originally developed for the military – for the rapid administration of nerve gas antidotes. The first EpiPen was invented in the mid-1970s and took its design cues from these military requirements, eventually being introduced into the general patient market in the 1980s. But patients would, of course, first need to be fully diagnosed, a process that often took weeks. A blood sample or biopsy would usually need to be sent away for analysis as only a handful of leading hospitals had the in-house facilities to enable a complete and timely diagnosis.

Fast forward to today and self-injection is commonplace in managing chronic diseases. Patients are becoming more informed "consumers" and demanding autoinjectors in preference to prefilled syringes and exposed needles. Therapies are also becoming more complex and can be targeted to specific indications rather than whole diseases. This in turn leads to much more targeted diagnostic tests and treatment delivery solutions, as well as new disease management tools.

Advancements in multiple areas are pushing the boundaries of what we deem possible today, all whilst developments in material science, electronics and software are happening at an ever faster pace and making inroads into pharmacotherapy. This is opening up vast new opportunities in healthcare management. We can track and monitor our activities and the "state" of our bodies more closely and frequently than ever before. But we are currently unsure of what to do with the sea of data we can collect – and what it actually means. Are we being enabled? Or will we drown if we do not carefully address why we are obtaining this data and how we can "translate" it into actionable information?

What does the future hold if we fast forward another 30 years?

A VISION OF THE FUTURE

Even with today's understanding we could imagine a future where, when feeling ill, you would have an instant video chat with a doctor located anywhere in the world who has access to all your medical records. You would take readings of simple metrics such as temperature and blood pressure using a bespoke "tricorder" unit which could measure everything in real time and upload the data to your health records. The online physician could then consult an artificial intelligence software package to diagnose your specific symptoms and perhaps prescribe further tests which could be delivered to your door in a matter of hours or minutes using an Amazon-style drone service – anything from an ECG monitor to full blood-works could be delivered to your door and the data streamed instantly to your physician to help them make a diagnosis and prescribe treatment.

However, this is a reactive system where we are waiting for external indicators to signal that something has gone wrong before we take any action or even consult a physician. If we look at the total cost of

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healthcare, as well as the cost of treatment, we have to include the impact on the patient themselves – their quality of life, for example, the number of work days missed and any support that may be required long term as a result of a debilitating condition. It soon becomes clear that a reactive healthcare system is far less cost effective in the long run. In the same way that you would rather not wait for your car's timing belt to snap before fixing it, to avoid expensive collateral engine damage, we should not have to wait for symptoms to be apparent before taking any action with our health. It would be far better to diagnose and treat any issue before it becomes a much bigger problem.

Envisage a fully integrated healthcare system, combining constant monitoring and instant diagnostics to provide a full picture of any healthcare issues and person-specific attributes. Your DNA could be sequenced to understand specific indicators suggesting you are more likely to suffer from certain health issues which could be specifically monitored for. Once any disease or first indicative symptom is detected, it could be analysed to understand its genetic make-up and then a targeted therapy could be specifically manufactured and delivered to you either in hospital or at home. This would mean very low-volume drug manufacturing and administration – potentially even just a single dose.

The same monitoring and diagnostic systems could continuously monitor your health and wellbeing. Further to this, it could potentially also regulate your diet to ensure your body has all the nutrients and vitamins it needs, without needing to overdose just in case of a specific deficiency. It could also monitor chronic conditions where regular therapy is required – using a combination of physical attribute monitoring as well as diagnostics, not only monitoring how well the therapy is working to treat the condition but also how your overall wellbeing is affected. Slow release/ultra-long-acting formulations would be able to stay in the body for extended periods (think weeks, not days) and continuously release drugs at therapeutic levels, with the release being triggered by disease indicators within the body; it would be effectively a self-regulating therapeutic system.

CAN IT BE DONE?

This may seem far-fetched at the moment, instant diagnostics, person-specific medication with low-volume manufacturing and at-home delivery, but the building blocks for these ideas are already in the works today. But how will these things connect? Do we have the understanding and tools to realise them? Is the desire there from patients?

There are already huge advances in diagnostics – from faster, more accurate tests at the point of care to personal diagnostic tools, such as a breath analyser to detect several different diseases, as well as continuous monitoring and analysis of several key physiological indicators. As costs and "time to result" are reduced, these diagnostic tools will become much more commonplace. Considered alongside an ever-reducing cost and time requirement to sequence an individual's DNA, coupled with the understanding we are currently gaining about the meaning and impact of different genetic markers, and the possibility arises that we may soon see these tools being implemented as standard care for all patients.

The thinking around disease management and the approach to identifying a treatment/cure are being challenged today with initiatives such as the approved CAR-T therapy from Novartis and Roche's innovative Personalised Healthcare, which uses liquid biopsy to identify specific biomarkers that shed light on the molecular root cause of a disease and then developing patient (group) specific therapies. Add a greater understanding of these biomarkers and continued iteration of the process and you can see how, in the near future, we will be seeing personalised medicine as the norm.

The drive to patient-specific therapy, as enabled by diagnostics, is putting pressure on manufacturing methods to enable these advances, current high-volume bulk manufacturing is no longer appropriate as each patient may need a personalised version of the same therapy. We are seeing existing pharma and large contract manufacturing organisations exploring new manufacturing methods which will enable this change – looking to take in-lab "development" processes and industrialise them into a personalised low-volume, low-cost manufacturing method.

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Combine all these current developments and you can start to see how we are enabling this vision of tomorrow. So how can we make use of this vision of the future to inform our activities today? Let's look at the challenges/issues still to be addressed.

THE CHALLENGES AHEAD

With low-volume manufacturing and personalised delivery, a certain kind of device will be needed. The physical qualities of any given therapy will vary and be highly dependent on person-specific attributes, as well as the disease, and may even need to change as part of the course of treatment. This is compounded when this variation is not just indication dependent but also patient specific, and will thus require a new family of devices to be developed that can be as flexible and programmable as the therapy itself – as these devices will have to contend with (in the case of injection) volume, viscosity, needle depth and many other variables which may be wildly different from patient to patient, even within the same disease space.

The building blocks to address these challenges may already exist, but we are yet to put them together and see whether they will address all the issues. We need to come up with a long-term strategy to develop the devices that will one day be used to deliver these therapies. I'm not suggesting we aim for our vision of 2050 – but we should look to see which halfway points we can target to further our understanding, and so be ready for the next challenges that will surely arise.