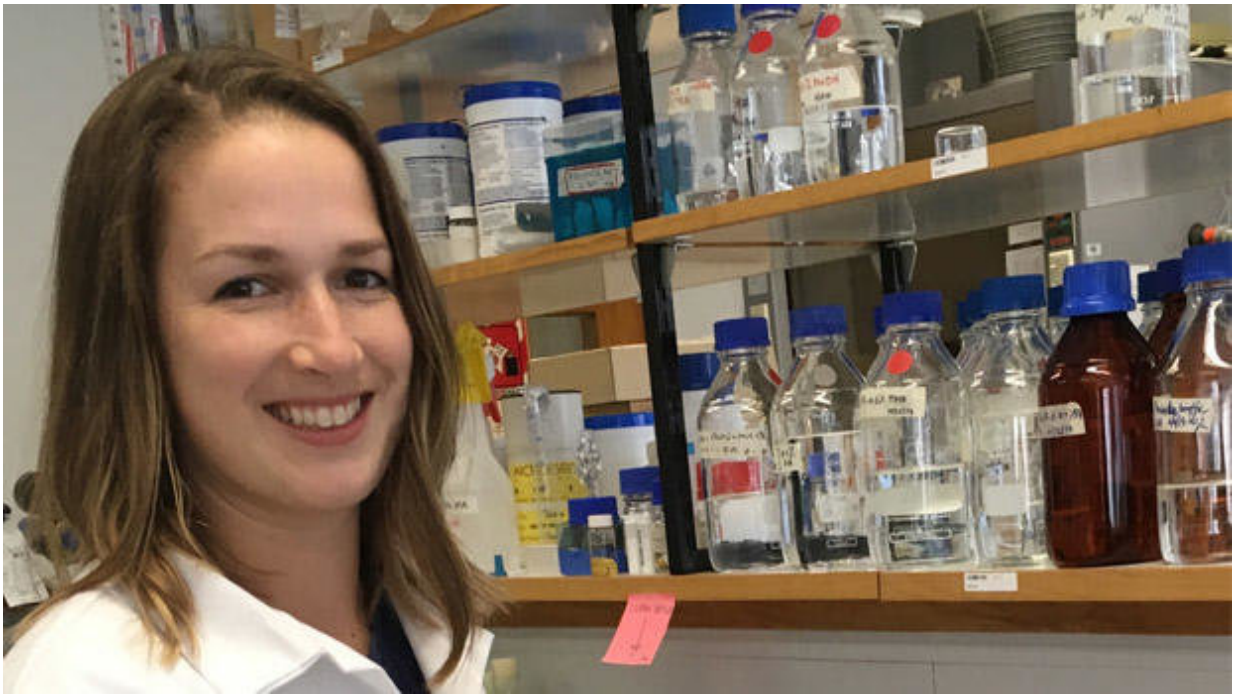
Making chemotherapy kinder for childhood leukaemia

September 14 2018, by Dr Rosanna Jackson



Dr Rosanna Jackson. Credit: Cancer Research UK

Chemotherapy often gets a bad reputation – mainly down to the side effects it can cause.

This bad reputation can be hard to shake off. And it often stops people hearing the vast improvements that have been made in how chemotherapy is used.

I can remember first learning about chemotherapy in my undergraduate pharmacology degree. I couldn't believe how much research has gone into making it better for patients. And although this research rarely hits the headlines, a small change in how a patient is treated can make a real difference to both their chance of survival and quality of life.

So when it came to choosing what to research for my Ph.D., I chose a project aiming to improve existing treatments.

I was fortunate enough to be offered a Cancer Research UK-funded Ph.D. position at Newcastle University, looking at ways to personalise the use of drugs for a type of blood cancer often diagnosed in children, called acute lymphoblastic leukaemia (ALL).

Throughout my Ph.D., I've had the privilege of learning from world renowned cancer researchers. In this post, I'm going to cover some of the progress these researchers have made in treating children with ALL with chemotherapy.

Why childhood ALL?

Childhood ALL is a shining example of the progress researchers have made in how we use chemotherapy. In the early 1970s, only around 3 in 10 children with ALL were cancer free 5 years after treatment. Today, this figure has risen to nearly 9 in 10 children.

But a large part of this improvement has been because doctors have used higher doses of drugs. Over time, this increased intensity has led to an increase in children experiencing side effects from their treatment, many of which are permanent.

The focus now is to find ways to make chemotherapy kinder to children with ALL, and also cure the small number of children that still aren't

today.

Getting personal

As with all cancer types, things are often more complicated with ALL than they seem. The disease can vary significantly from one patient to another and form many sub groups. These sub groups are usually defined by differences in the DNA inside the cancer cells. And these DNA changes can dramatically affect how the cells behave, and how sensitive they are to chemotherapy.

It's these genetic differences that are helping doctors to tailor treatment to individual patients.

This means that from the outset, we can give patients the right treatment intensity for their particular type of ALL.

Now, instead of giving all patients enough chemotherapy to cure the most aggressive types of ALL, which brings with it the possibility of more side effects, we can use genetics to identify the children with less aggressive disease and only give them the treatment they need.

An adaptive treatment plan

Scientists are also continuing to improve techniques to measure how many cancer cells have survived treatment.

Hospitals and research labs like mine work together to test patients' samples for ALL cells. We do this by detecting differences in tiny features of the cells. By using these new techniques, we can now identify less than one ALL cell in 10,000 normal cells .

This can help doctors to adapt the dose of chemotherapy based on how a child is responding to treatment, avoiding unnecessary side effects.

Scientists have found that counting the number of ALL cells in a blood sample after 28 days of treatment is the best way to predict how well a patient will do compared to other patients with the same type of ALL.

And UK researchers found that if a child has small numbers of cancer cells in their blood after 28 days of chemotherapy, they could be given less treatment from that point onwards and still have the same good chance of survival.

Now, treatment of children with ALL in the UK is adapted based on this initial response to therapy.

And we're continuously looking for more ways to improve therapy. During my Ph.D. I was involved in looking at whether a change in the way a drug called dexamethasone is given could help reduce side effects.

Dexamethasone is a crucial anti-leukaemia drug given to children at the start of their treatment, but it can cause side effects like increased risk of infection, altered sugar processing and long-term damage to bones.

Right now, children are given a course of dexamethasone for 28 days. Because side effects can sometimes happen when dexamethasone is taken for long periods of time, scientists predicted that giving higher doses for fewer days would decrease side effects, but still have the same effect on the cancer cells.

To test this, we compared giving a higher dose for 14 days to the standard way of giving dexamethasone over 28 days. I measured the levels of dexamethasone in patient's blood to compare the two groups.

Unfortunately, the shorter dose didn't reduce side effects, so doctors are continuing to give the standard dose. But interestingly, my results showed that although children on each dose were given the same amount of dexamethasone for their size, the concentration in their bodies varied dramatically.

It suggests that children are processing the drug differently, which may help to explain why no difference was seen between the two doses.

Although this part of the trial didn't help to reduce side effects, it helped us to better understand how dexamethasone works in ALL treatment. This is important for any future changes researchers make to therapy. And it's just one of the adaptions scientists are testing to try and lower the chance of children having side effects in a current UK trial.

The future

The fine-tuning of treatment over the decades has dramatically improved survival for patients. And new treatments are providing options for the small number of children whose cancer doesn't respond to current therapies. In August this year, NHS England announced that a personalised cancer immunotherapy will be offered to some children and young adults with ALL.

Now we're working to improve the quality of life for patients as they grow up and continue their lives. The importance of this should never be underestimated.

Unfortunately, this same progress hasn't yet been possible for all cancers. Our aim is to continue to develop established chemotherapy medicines alongside the use of new targeted therapies, to give all cancer patients the best chance of survival, and make those saved years the best they can be.

Medical Xpress

Provided by Cancer Research UK

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