UNIVERSITY OF LIVERPOOL

THE FINE LINE

BETWEEN

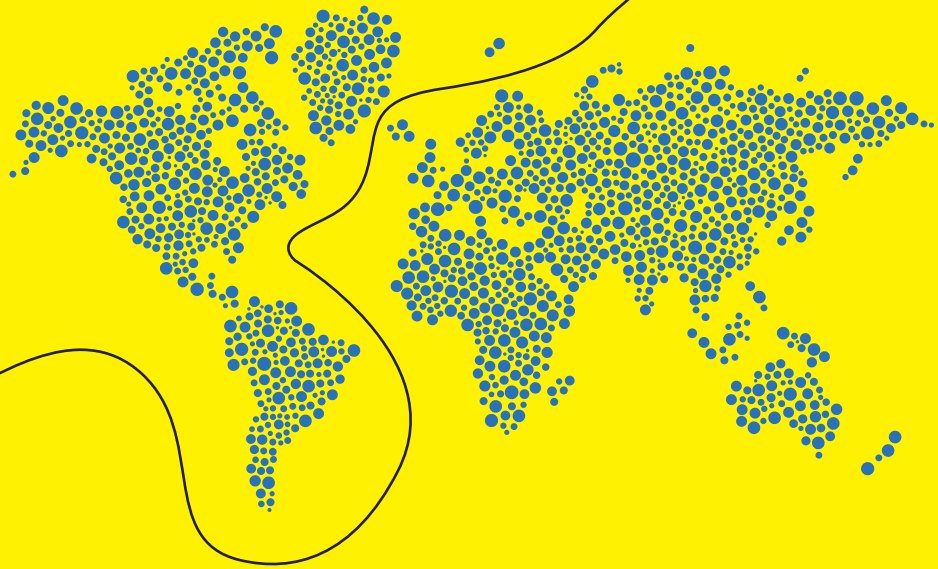
HELP & HARM

PROTECTION & INFECTION

LIFE & DEATH

THE PROBLEM

Children around the world are dying from HIV. Without treatment, 33 per cent of children infected with HIV die before their first birthday. Fifty per cent die before their second birthday, while 80 per cent die before they reach the age of five.

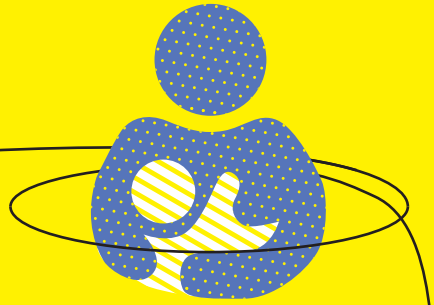


Every week, 34,000 people are infected with HIV.* More than 3,000 of those are children. In fact, of the estimated 38 million people living with HIV globally, at least two million are in this demographic.

For a virus so often associated with exchange of bodily fluids, though, how is it that so many children are getting infected?

The answer lies in mother-to-child-transmission (MTCT). It is rare for a baby to become infected in utero, even if the mother is HIV-positive; the placenta acts as an effective barrier. When the mother is fully surpressed on therapy, infection is also unlikely during childbirth. Where the majority of transmission happens is through breastfeeding.

*Source: Avert.org



Oral transmission of HIV is not normal. In the case of an immature gut ingesting repeated volumes of breast milk containing the virus on a daily basis, though, there's a high likelihood of transmission at one point or another.

The situation is a catch-22. Breastfeeding is essential in low- and middle-income countries where nutrition of children is a matter of survival, irrespective of HIV – and yet it is precisely these countries that bear the overwhelming burden of the virus in the first place.

The problem is amplified when considering treatment. The overwhelming majority of antiretroviral drugs approved for children by the World Health Organization are poorly soluble and so must be dosed in liquid form. The solution? Alcohol. At present, the most widely used paediatric antiretroviral therapy is an ethanol propylene-glycol solution – in lay terms, vodka and antifreeze.

We know the effects of routine consumption of alcohol in adults. Dosing children with alcohol is not safe. While the therapy is helping them, the alcohol is harming them.

More still, while all drugs are associated with their own safety considerations, the current therapy has been associated with gastro-intestinal problems, anxiety disorders, sleep disturbance, nausea – a plethora of toxicological side effects unrelated to alcohol. It's also unstable, particularly so in high temperatures.

In short, children as young as three weeks old in low- and middle-income countries are being dosed twice daily with an unstable alcoholic solution to treat a virus they have contracted through a basic means of survival. Should they survive childhood – and the majority won't – they'll become members of the adult HIV-positive population.

THE SOLUTION

The University of Liverpool is on the cusp of changing paediatric HIV therapy around the world. We have the potential to create a safer therapy that can reach more children – with the greatest impact felt in countries with a high HIV prevalence.

Andrew Owen is a Professor in the Department of Molecular and Clinical Pharmacology at the University of Liverpool. Steve Rannard is a Professor in the University's Department of Chemistry, with a background in industry as a materials chemist. Together, they have pioneered a very small solution to the HIV therapy crisis: an antiretroviral therapy based on nanomedicine.

FOR CONTEXT, DRAW A LINE BETWEEN THE TWO POINTS BELOW.

Your line is about 0.8 millimetres, or 800,000 nanometres, wide.

Andrew and Steve's work is within the 200-600 nanometre range – more than 1,300 times smaller. At this size, their drug particles enable drugs to pass through the gut and into the blood more effectively than current drug particles.

Pen width
0.8 millimetres
=
800,000 nanometres

Adult clinical trials of two medicines the pair are working on are currently proving the fact. With them, less of the drug is being wasted by not being absorbed – about 50 per cent less.

The benefits of this are manifold. The supply chain is being unburdened while the toxicological side effects of current therapy – many of which are connected with non-absorption of drugs – are being mitigated.

THE REQUIREMENT

Andrew and Steve have received UK and US government funding to follow their oral dose adult therapies. The one element that hasn't come through is funding to follow the paediatric therapy – the therapy through which they hope to end the daily dosing of children with alcohol and inadequate drugs.

More still, Andrew and Steve's work in nanomedicine and infectious disease has led them to develop a long-acting prophylaxis which erases the precarious issue of daily dosing. If administered before infection, it can even prevent HIV being contracted in the first place.

But what does this mean for children currently living with the virus? The scale at which Andrew and Steve are working has enabled them to develop free-flowing powders that can be dispersed in water or milk at the point of use. Instead of using ethanol-propylene glycol to dissolve a poorly soluble particle, nanotechnology is being used to suspend it in less-volatile liquids. Dosing children in this manner delivers the same blood-drug concentration as the alcoholic solution.

Clinical trials for the adult therapies are verifying everything Andrew and Steve had modelled. They are also now working with the US government and commercial partners to develop their long-acting prophylaxis, which could prove critical to diminishing the epidemic.

Clinical trials for children, however, are technically, ethically and financially challenging. What's more, funding tends to be awarded where the most impact can be made, and in the case of HIV that's treating the majority – the 36 million adults living with the virus.

What Andrew and Steve want to do is make sure that the two million children living with it aren't forgotten. Like their adult counterparts, they should be able to grow up and lead long, meaningful lives – and they should be able to do so without suffering complications that have been created by the very therapies given to them to help them live in the first place.

To help bring Andrew and Steve's paediatric therapy through clinical trials and closer to the market, they need to raise £400,000. Half of this amount needs to be secured by the end of the year. If achieved, the eventual outcomes will be given away to those who need it most – the work is entirely not-for-profit.

Crucially, the therapy works. It's already been successfully trialled in adults. The £400,000 Andrew and Steve need is to allow them to repeat those same trials in children, after which they could create a programme where their therapy is available for children within the next two to three years.

Too many children are victims of the HIV epidemic because they don't have access to therapy or because the therapy they have access to is not fit for purpose. With your help, the University of Liverpool can change that. Together, we can make the difference between help and harm, between protection and infection, between life and death.

£400,000

WHILE YOUR PEN'S HANDY ...

Every donation Andrew and Steve receive takes them closer to improving the lives of children living with HIV across the world. If you'd like to help, please fill in the tear-off form and pop it in the post.

Alternatively donate online at: www.liverpool.ac.uk/giving/donate

▶ Steve (front, centre) and Andrew (front, right) with their award-winning nanomedicine team.

“What about the children? We can’t just forget about the children being dosed daily with ethanol and propylene glycol”

THE TEAM

Professor Andrew Owen

Andrew Owen’s attention was first drawn to HIV when, as a child, he watched adverts of tombstones emblazoned with the words, ‘AIDS – Don’t Die of Ignorance’, being knocked down, or human skittles being bowled over by the Grim Reaper. They had a significant impact on him – enough to motivate him to pursue a career in infectious disease.

“What we’re aiming to do is help to diminish the HIV epidemic through new therapies. The fact that we’ve secured funding to follow our adult dose therapies but not the paediatric angle is disappointing but understandable. If you think about the scale of the problem you’ve got an estimated 38 million adults and 2 million children suffering from HIV. The focus is on impacting the 38 million; that’s where everyone feels they can make the biggest bang with their buck. But what about the children? We can’t just forget about the children being dosed daily with ethanol and propylene glycol.”

Professor Steve Rannard

Steve Rannard recalls the story of a friend visiting a hospital in sub-Saharan Africa in the 1990s. His friend was shown through ward after ward of patients before coming to a stand-alone ward – a non-HIV ward. It was the only ward of its kind in the hospital. The rest housed exclusively HIV-positive patients. Today, up to 30 per cent of the adult population of the countries worst affected by the epidemic are HIV positive – and that figure doesn’t take into account the prevalence of HIV amongst child populations.

“There are too many children dying before the age of five because they don’t have access to safe therapy. If we hit the £400,000 target, we’ll be able to run the paediatric trials. The formulations are there already; we just need funding to do the trials to show that our therapy is bioequivalent to the therapy already out there for adults. We’re not looking to make money out of this; we’re just trying to improve the therapy of children with HIV.”

UNIVERSITY OF LIVERPOOL

CONTRIBUTE TO THE IMPACT OF THE UNIVERSITY'S PAEDIATRIC HIV THERAPY

Thank you. Your gift will bring Andrew and Steve closer to getting their paediatric therapy through clinical trials and onto the market on a not-for-profit basis.

PERSONAL DETAILS

Name

Address

City Postcode

Country

Telephone

Email

(Please provide either a telephone number or email so that the University may contact you regarding your gift)

☐ I would like my gift to remain anonymous ☐ I would like to receive information on leaving a legacy

PAYMENT INSTRUCTIONS

I would like to give a single gift of £

☐ I enclose a cheque payable to **University of Liverpool**

☐ I enclose a Charities Aid Foundation Voucher

☐ I would like to pay by credit/debit card over the phone*

*A member of the team will call you on the telephone number you have provided above to process your gift.

DONATE ONLINE

You can also donate securely online - simply visit: www.liverpool.ac.uk/giving/donate

giftaid it

Please turn over to complete the Gift Aid section before detaching this form and inserting it into the enclosed pre-paid reply envelope.

GIFT AID DECLARATION - MAKING THE MOST OF YOUR GIFT

The University of Liverpool may reclaim basic rate tax on all gifts (25p for every £1 donated). Gift Aid is reclaimed by the University from the tax you pay for the current tax year. Your address is needed to identify you as a current UK taxpayer. I am a UK taxpayer and understand that if I pay less Income Tax and/or Capital Gains Tax than the amount of Gift Aid claimed on all my donations in that tax year it is my responsibility to pay any difference.

If you pay Income Tax at the higher or additional rate and want to receive the additional tax relief due to you, you must include all your Gift Aid donations on your Self-Assessment tax return or ask HM Revenue and Customs to adjust your tax code. Please notify us if you want to cancel this declaration, change your name or home address, or no longer pay sufficient tax on your income and/or capital gains

I want to Gift Aid my donation and any donations I make in the future or have made in the past 4 years to the University of Liverpool ☐

Signature Date

RETURNING THIS FORM

Please detach this form from the leaflet and return to us using the enclosed pre-paid reply envelope, or by sending it to: FREEPOST RTJU-KZAH-KBJH, Development & Alumni Relations, University of Liverpool, Victoria Building, Ashton Street, LIVERPOOL, L69 3DR.

thank you!

The Development and Alumni Relations Team (DART) supports the University of Liverpool through contact with alumni, students and supporters of the University. Our alumni and supporters are very important to us and we are committed to protecting your data. We use data to provide benefits such as access to academic, social and networking events and publications, providing services such as library and journal access and employment advice. We provide opportunities to attend events and reunions, learn about volunteering and fundraising and access to exclusive benefits and discounts. We process your data in accordance with our legitimate interest in these areas and you will always have the right to opt out. We may contact you by mail, email, telephone and social media. All data is held securely and in accordance with the Data Protection Act 1998. Our full Privacy Notice is available here: www.liverpool.ac.uk/alumni/privacy. We aim to keep your data up to date; you can send us your updates by email or tell us you don't want to hear from us by contacting: alumni@liverpool.ac.uk.

Registered with FUNDRAISING REGULATOR