Saving Lives at Birth: novel microarray patch to treat neonatal sepsis receives international funding

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Neonatal infections, including sepsis, are a significant cause of childhood mortality, accounting for an estimated 26-36% of the neonatal deaths that occur globally in low- to middle-income countries.[1,2] This is despite the fact that effective and curative treatments do exist. A major barrier to receipt of this treatment, however, is the requirement for hospitalisation – often inaccessible, unaffordable and unacceptable to parents in these low resource settings.

To help counteract this, the World Health Organization (WHO) has recommended a treatment regimen for outpatient care of neonates when referral is not feasible, including injected gentamicin, along with oral amoxicillin.[3] However, this regimen is not without its drawbacks. Both antibiotics require that the dose be calculated, based on the weight of the infant. Gentamicin must be delivered by intramuscular injection, meaning that healthcare providers must have access to safe injection supplies and sharps disposal. Amoxicillin for infants is provided either as a liquid suspension, which is not suitable for long-term storage or transport at high temperatures, or fast dissolving tablets, which require accurate reconstitution in clean drinking water. Although beneficial in many ways, this outpatient regimen still poses several impracticalities and barriers to effective treatment. To help address this issue, researchers at Queen's University Belfast have proposed a novel microarray patch to deliver the required antibiotics for treatment of neonatal sepsis.

The microarray patch proposed by our drug delivery team at the School of Pharmacy in Belfast is designed for application to the skin, offering a transdermal treatment option for neonatal sepsis. It consists of a large number of micron-scaled projections grouped together on a supporting base (**FIGURE 1**), which is then combined with a drug reservoir, containing amoxicillin and gentamicin. The tips of the micro-projections are sharp enough to penetrate the upper-most integument of the skin, the stratum corneum, but their short length ensures that there is no stimulation of dermal nerves or bleeding following insertion. This approach considerably enhances transdermal drug permeation as the stratum corneum, the principle barrier to drug delivery across the skin, is bypassed.

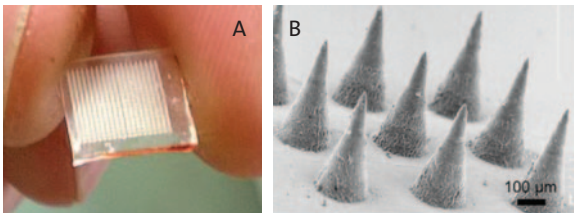

FIGURE 1 (A) A 1cm^2 hydrogel-forming microarray patch, and (B) a microscopic view of the microarray patch revealing the micro-projections.

The unique microarrays produced by our research group are composed of a polymeric, hydrogel-forming material, with the drug(s) of choice contained in a water-soluble reservoir, positioned to the reverse of the array (**FIGURE 2**). The micro-projections are hard when they are dry but following insertion into the skin, they rapidly draw in the interstitial fluid, which bathes the cells, and begin to swell. This creates an open, porous network, through which drugs can permeate. The drug reservoir begins to dissolve upon contact with the imbibed fluid, enabling drug diffusion through the hydrogel matrix and into the dermal layers of the skin, which are rich with blood vessels for systemic absorption. Previous work by our group has demonstrated the enhanced transdermal delivery of different compounds in this way with varying physicochemical properties and pharmacological doses, including ibuprofen, donepezil, theophylline and insulin.[4-6]

The potential of this microarray patch to offer an affordable, less-invasive and user-friendly treatment option for neonatal sepsis was recently recognised by the Saving Lives at Birth: A Grand Challenge for Development team in Washington DC. Funding of $250,000 was awarded for the development of the patch over a two-year period following the annual innovation event (**FIGURE 3**).

Saving Lives at Birth

The Saving Lives at Birth partnership was launched in 2011 with the aim of identifying novel, scalable and sustainable solutions to improve infant and maternal health during childbirth.[7] The partnership includes:

- the US Agency for International Development (USAID)
- the government of Norway
- the Bill and Melinda Gates Foundation
- Grand Challenges Canada (funded by the government of Canada)
- the UK's Department for International Development (DFID)
- the Korea International Cooperation Agency (KOICA).

Each year applications are invited for new, ground-breaking approaches to address the many problems associated with childbirth. Funding is provided for three different types of projects:

Seed funds to investigate the feasibility of innovative ideas and develop these ideas (seed funding was awarded for this microarray patch project).

Validation funds to help innovations reach proof-of-concept, following their introduction and validation.

Transition funds to assist with the scale-up of projects that have already demonstrated proof-of-concept.

Initial application for funding is via an online application platform, with comprehensive guidance notes provided by the funders. An expression of interest (maximum three pages) is submitted towards the end of February, which then undergoes a review process. Depending on the outcome of this, innovators may be invited to proceed to the next round and attend the DevelopmentXChange event held in Washington DC in July each year. At this meeting, approximately 50 innovators have the opportunity to promote and explain their research at an open marketplace event, as well as network with other innovators, potential stakeholders, funding agencies and the public. The event also involves interviews, pitch competitions, training and mentoring sessions, along with guest presentations. It culminates with an awards ceremony, where grant nominees are announced. Last year, 12 projects (seed and validation categories) received funding following the selection process, which involved more than 650 submissions from 78 countries.

The funding award

This microarray project falls under the category of science and technology, but applications are also sought with a service delivery focus and a demand-side innovation focus that empowers pregnant women, their communities and their families.

The microarray patch for the delivery of a combination of antibiotics for the treatment of neonatal sepsis was recognised as being an innovative and scalable method of addressing a huge problem in low resource settings. This patch offers the potential of home treatment of neonatal sepsis, when hospital treatment is not possible, while simultaneously avoiding the issues associated with injectable and oral therapies. Over the next two years, the funding awarded by Saving Lives at Birth will allow our team at Queen's University Belfast to work on developing the microarray patch technology to demonstrate the feasibility of combined amoxicillin and gentamicin delivery.

Initially the project focus will be on the technical development of the combined antibiotic microarray patch, investigating dosage, stability, safety and cost. Secondly, stakeholder needs will be assessed with information gathered from key partners in target low resource settings. Specifically, requirements related to antibiotic delivery for neonatal sepsis treatment, perceived advantages and challenges of the concept, desirable attributes, and potential price range will all be considered to further inform patch design and development.

The final component of the project will be to evaluate the usability of the patch, to ensure any product can be easily used as intended. For example, patches will be prepared with doses appropriate for different weight categories, negating the performance of complex dosage calculations. The simple and painless application of the patch to the neonate by the parents, without the requirement of a nurse or doctor, will be confirmed, which would offer massive benefit in improving access to the treatment.

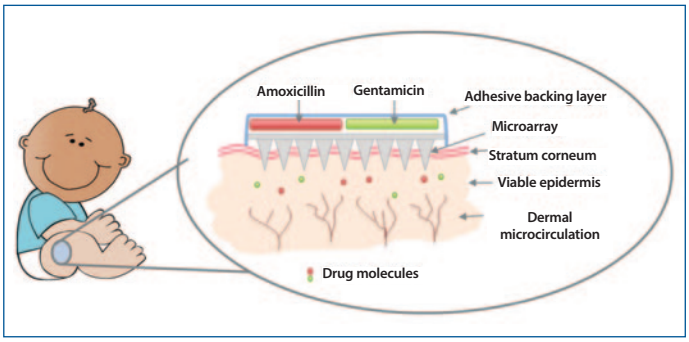

FIGURE 2 A schematic representation of a microarray patch containing amoxicillin and gentamicin for treatment of neonatal sepsis.

FIGURE 3 Mary-Carmel Kearney at the Development XChange innovation event in Washington DC, July 2016.

It is hoped that after two years, if technical development and subsequent clinical validation are successful, the technology will be poised for future pilot introduction in neonatal health programmes. The unique capability of this technology and the various advantages offered makes it potentially transformative in its impact for treatment of neonatal sepsis, particularly in low resource settings.

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