Institution: University of Bath

Unit of Assessment:8: Chemistry

Title of case study:
Changing Clinical Approaches for Treatment of Burns in Children

1. Summary of the impact

Half of all burn injuries occur in children and around 10% of children who are burnt become infected by disease-causing bacteria that can increase the likelihood of scarring and in some cases cause death. Novel wound dressing prototypes have been developed using responsive smart sensing chemistry. These provide clinical solutions and commercial opportunities, have led to the founding of the charity Healing Foundation Children's Burns Research Centre with £1.5M of funding, have influenced the work of other charities and altered attitudes and practice in clinical paediatric burn treatment. The impact has been achieved by development of the novel chemistry in partnership with clinicians and practitioners, and through extensive engagement with health professionals, well beyond normal academic reach, parents and the wider public.

2. Underpinning research

The research, carried out in the group of Dr Toby Jenkins in the Department of Chemistry at the University of Bath, maps onto the Sensing & Healthcare theme in Bath Chemistry. It targets improved human health by cutting the risk of microbial infection in burns, wounds and damaged skin, especially in clinical environments, and by speeding diagnosis of infection. Burn infection can be especially difficult to diagnose since the primary method of determining infection, raised body temperature, has limited utility in burn patients due to resetting of the bodies thermal regulatory system post burn. Typically the only way to diagnose infection is to expose the wound to allow examination by swabbing and microbiological analysis; this process takes time (typically 24 hours) and dramatically increases the danger of severe infection, scarring, and the consequent, potentially fatal, side effects, such as sepsis and toxic shock syndrome (especially in children). The research, carried out since 2007, targets this vital clinical issue, by developing responsive wound dressings for burn victims, particularly children.

The research uses phospholipid vesicles dispersed in a composite hydrogel matrix, which retain some characteristics of eukaryotic cell membranes. The vesicles encapsulate a self-quenched non-toxic dye (fluorescein), which is released following the degradation of the lipid vesicles by bacterial virulence factors including Phenol Soluble Modulins (PSMs) from *S. aureus* and rhamnolipids from *P. aeruginosa*, which are key infection agents. Release of the dye into the surrounding matrix causes fluorescence 'switch on', clearly observable by eye and a key paper has been published which focuses on the sensor detection / response chemistry underpinning the developments being implemented [1].

In the development phase building on this initial sensor chemistry, laboratory scale prototype dressings have been developed with vesicle compositions that optimise stability and toxin sensitivity; the vesicles are stable in wound exudate taken from patients in clinical environments, and at the pH range and temperature range expected in the burn environment [2]. The dressings therefore give a clear visible indication of infection *in situ* without need to remove the dressing and this is key to its benefits in the clinical environment.

An essential component of this research programme is an absolute focus on clinical need, and manufacturability, and this has been supported by direct industrial and translation funding [3]. A range of working prototypes are available for *in-vivo* studies on murine and porcine models, while manufacturing partners are engaged with small scale, GMP compliant production. The research is also being targeted at better understanding of mechanisms of bacterial toxicity, with a particular focus on infection within paediatric burns, as noted below.

Timeframe: Research commenced in 2007, with initial key publication in 2010 and subsequently developed in partnership with clinicians at Frenchay Hospital in Bristol and the South-West Children's Burns Centre, and clinical charity research partners.

Key Researchers
Dr Toby Jenkins (Lecturer, now Reader; Bath since 2000; anti-microbials, functional wound dressing development; lead academic)
Dr J. Mercer-Chalmers (Bath 1998-2012; PDRA and Research Manager; research translation)
Dr N.T Thet (2008-2013; PhD then PDRA); S Hong (2010-2013; PhD).

3. References to the research

[1] J. Zhou, A. L. Loftus, G. Mulley, A. T. A. Jenkins (2010), *J. Amer. Chem. Soc*., **132**, 6566–6570. [DOI: 10.1021/ja101554a]. *A Thin Film Detection / Response System for Pathogenic Bacteria*

[2] J Zhou, T N Tun, S H Hong, J D Mercer-Chalmers, M Laabei, A E R Young, A T A Jenkins (2011). *Biosens Bioelectronics*, **30**, 67-72 [DOI: 10.1016/j.bios.2011.08.028]. *Development of a prototype wound dressing technology which can detect and report colonization by pathogenic bacteria*

[3] Direct industrial / translation funding
Total of £1489k including: (a) Knowledge Transfer Account Award (with SWUK Children's Burns Centre) 2010 (£78k), (b) EU FP7 grant Bacteriosafe, 2010-2014 (£731k); (c) EPSRC Delivery funding 2011 (£40k) and (d) EPSRC Healthcare Partnership (with AmpliPhi Biosciences) £640k; (e) Funding for a **clinical research nurse** (James Tudor charity; Young & Jenkins), a **clinical surgical PhD** (Healing Foundation & KOALA international network) directly charitably funded to pursue the clinical elements of this research.

4. Details of the impact

Impacts from this work: founding and influencing the work of charities, public awareness and attitudes, use of research findings by clinical practitioners

- Enhanced public awareness of a health risk (**Outreach and engagement with parents & public directly, through the NHS Trust and through the media**)
- The awareness, attitudes and understanding of (sections of) the public have been informed, and their ability to make informed decisions on issues improved, by engaging them with research (**as above**)
- Practitioners have used research findings in the conduct of their work (**influencing approach taken by clinicians**)
- The work of an charitable organisation has been influenced by the research (**including foundation of a charity, with £1.5M funding**)

The need
Half of all burn injuries occur in children under 16 years old, mostly by scalds from hot tea, coffee and bath water. In 2010-2011 the South West UK Children's Burn Centre at Frenchay Hospital in Bristol (an NHS Regional Centre with a 10 million population catchment area), the main clinical partner in this study, treated more than 700 children for serious burn injuries. Around 10% of children who are burned become infected, which increases the likelihood of scarring and disfigurement and in some cases can even cause death. The problem is obtaining clarity in diagnosis, and the dressing being developed at Bath provides quick evidence of infection without need to remove the dressing, informing clinical decision making.

Engaging and Influencing Clinicians and Clinical Research
The development of responsive wound dressings suitable for implementation in the clinical environment is a partnership with the clinical community. The key direct clinical collaborator is Dr Amber Young, Consultant Paediatric Anaesthetist, lead for South-West Burns Unit at Frenchay Hospital, but the impact of the work has also been manifest in the reach into the mainstream clinical practice community. The concept of using such responsive sensors, based on technology being patented by Bath Chemistry [A] has also led to substantial influence and attitude changing in the broader clinical community. Jenkins is a regular speaker at clinical forums, and is a passionate advocate for the role of these advanced chemistry solutions in saving lives of vulnerable patients.

It is extremely unusual for core chemists to be invited into such forums, but Jenkins is now a regular invited participant at high profile and influential clinical events, for example, the only chemistry plenary speaker at the International Society for Burns Injuries in September 2012, a large forum of 1250+ practising nurses and doctors investigating the latest methods of clinical practice. The high degree of awareness raising that Jenkins has managed to achieve is emphasised by his impact at such events, where "*his work had a real "eye-opening" effect in challenging current clinical practice and offering alternative solutions*" [B]. This is augmented by ongoing interactions with healthcare professionals in the British Burns Association and elsewhere. This raising of awareness and changing attitudes towards the potential of a system that would aid clarity of diagnosis and ease of treatment, has engaged clinicians in this debate.

The research has also made a major contribution to the founding of a charity, the Healing Foundation Children's Burns Research Centre [C; Jenkins lead academic in the "Clinical Management" theme]. **The Bath research has been used directly to secure at least £1.5M charitable funding for the new Centre** [B].

Prototype testing and clinical development

The development of prototype dressings has been carried out through initial *ex vivo* porcine testing and pre-clinical trials at the Blonde-McIndoe Research Foundation, one of the leading charities funding clinical work in the remediation of burns injuries, who quote that "A real need therefore exists to develop novel ways to detect and treat burn wound infections, and we are working with collaborators at the University of Bath and South West Children's Burns Centre, Frenchay Hospital, Bristol to develop innovative ways of monitoring infection" [D]. The manufacturing of prototype wound dressings has also been established with industry partners (Mölnycke AB Healthcare (Sweden), Hartmann AG (Germany) and Altrika Ltd (UK)), translating the research into a viable candidate technology. In addition to prototyping, the group are pursuing follow-on implementation studies, with publication in clinical journals, establishing a high degree of clinical involvement and 'buy in' at this early stage, to ensure rapid clinical take up of the product when manufactured [E]. Initial **direct clinical use has also been demonstrated** – having been adopted within an NIHR portfolio project [C], an initial cohort of six patients has been recruited and used for research-led clinical trials of the effect of burn and blister exudates on the Bath-developed prototype wound dressings. This was carried out by a charity-funded clinical research nurse whose funding resulted from the Bath Chemistry research, providing vital clinical information towards wider trialling.

Community and Media, Raising Awareness and Changing Behaviour

The Bath research has been instrumental in raising the profile of this area. By offering a potentially radical solution to many of the issues of diagnosis, it has focused wide attention on the issue of children's burns in the region, impacting on education, awareness and attitude changing amongst the directly concerned community – the patients, represented by parents and carers of infant burns victims or potential burns victims and amongst clinical practitioners: "*it is no exaggeration to say that exposure to this research has changed the way in which I think about the considerable clinical issues in this challenging area*" [B]. In partnership with the South West Children's Burns Centre and the Healing Foundation Children's Burns Research Centre, Jenkins and his work have been effectively used as a vehicle for publicising the risks of apparently innocuous, small volumes of hot liquids to small children [F]. This has enabled the development of an **educated community** of hundreds of adults, and of **educating children in the risks**, through programmes of school visits.

The patients involved represent a group whose injuries stir strong emotions and sympathy in the general public. Through a concerted effort led by Jenkins and Young, a "star patient" (Isambard, who fortunately made a full recovery from his dreadful burns injuries) has been used as an immediately identifiable vehicle for education, awareness-raising and to motivate researchers, clinicians and fund-raisers, through his clinical case study:

Isambard was a 2 year old child who knocked a cup of hot tea over himself, causing 32% total body surface area burns (partial thickness). He was airlifted to Frenchay hospital and treated. Two days post burn he became very pyrexic and non-specifically unwell. Infection was suspected and he was brought into the OR. In the OR a 'lively' discussion between the clinicians took place: should he be treated aggressively, removing his dressings – potentially saving his life but

guaranteeing life-long scarring, or treated conservatively, leave dressings on and watch and wait. In the event the latter approach was used – with a very good outcome, but the decision was not informed by clinical knowledge

The work has had impact far beyond the usual dissemination and has a very strong outreach element [G]. This has included articles in magazines such as New Scientist, and still more widespread reach and impact in mass media, on television and radio, and in national newspapers and news outlets (e.g. the Daily Mail and BBC). In addition the BBC recently filmed in Jenkins' laboratory, as part of a major piece in the popular, wide reach television programme "Bang Goes the Theory" [H], which regularly attracts total audiences of around 4 million, on the dangers of hot drinks, children's burns and newly developed treatments for those injured in this way.

5. Sources to corroborate the impact

[A] *IP/patents*

WO 2013104876 A1, A T A Jenkins, N T Thet, J Mercer-Chalmers, "Wound Dressing", January 2012 (PCT/GB2012/000625)
http://worldwide.espacenet.com/publicationDetails/biblio?DB=EPODOC&II=12&ND=3&adjacent=true&locale=en_EP&FT=D&date=20130718&CC=WO&NR=2013104876A1&KC=A1

[B] *Clinical Reference*:

Letter of Evidence from Consultant Pediatric Anaesthetist, South West UK Children's Burn Centre, Frenchay Hospital, Bristol

[C] *Healing Foundation Children's Burns Research Centre*

http://www.bristol.ac.uk/social-community-medicine/childrens-burns/

Jenkins is lead academic in the "Clinical Management" strand of the Foundation
http://www.bristol.ac.uk/social-community-medicine/childrens-burns/people/

http://public.ukcrn.org.uk/Search/StudyDetail.aspx?StudyID=13232 (NIHR portfolio clinical study)

[D] *Blond McIndoe Medical Research Charity*

Wound Assessment Tools

http://www.blondmcindoe.org/wound-assessment-tools.html

[E] *Follow-on clinical development studies*

A T A Jenkins and A Young (2010). *Expert Reviews of Anti-Infection Therapies*, **8**, 1063-1065 [DOI: 10.1586/eri.10.98]. *Smart dressings for the prevention of infection in paediatric burns patients*

M Laabei, AER Young, ATA Jenkins (2012). *Pediatric Infectious Disease Journal*, **31**, E73-E77 [DOI: 10.1097/INF.0b013e3182493b21]. *In Vitro Studies of Toxic Shock Toxin-1-secreting Staphylococcus aureus and Implications for Burn Care in Children*

[F-H] Broader Publicity, Awareness raising, Behaviour influencing

[F] North Bristol NHS Trust: Focuses on the collaboration between Jenkins and clinician Young

http://www.nbt.nhs.uk/news-media/latest-news/revolutionary-burns-dressing-could-save-young-lives
http://www.nbt.nhs.uk/news-media/video-gallery/childrens-burns-research

[G] Popular and mass media coverage
http://www.newscientist.com/article/dn19158-nanoparticle-bandages-could-detect-and-treat-infection.html – *9 July 2010*
http://www.dailymail.co.uk/sciencetech/article-1293052/Smart-bandage-fights-infection-using-tiny-glowing-capsules-antibiotics.html
http://www.bbc.co.uk/news/10550239
8 July 2010 – "Bath Uni developing new bandage to help fight infection"; Isambard as a case study

[H] BBC TV film, "Bang Goes the Theory", March 2013