





"Slippery sheets and dressings that glow in the dark"

Dr Amber Young and the Clinical Burn Research Team

Children's Burns Centre, UHBristol, Clinical Lead, Scar Free Foundation Centre for Children's Burns Research Senior Research Fellow, University of Bristol



Children's Burns Research Centre

UHBristol Research and Innovation Day, 2016



"Our mission is to develop a UK research centre of worldleading excellence crossing clinical and academic boundaries for real patient benefit, to prevent burns and improve the outlook of children with burn injuries."





Clinical Burn Research Theme

To lead networks for pragmatic clinical research into burn care co-developed with patients to improve clinical decision-making and healthcare outcomes.



ASITISA

Health Research







http://scarfree.org.uk/research

"There has never been a better time to embark on the pursuit of scar free healing. With the right leadership, collaboration and support new therapies are within reach.

The UK is well placed to lead and The Scar Free Foundation is the right organisation to make this happen. Scar Free healing in a generation is a challenge but I believe we can get there".

> Professor Sir John Gurdon Joint Winner of the Nobel Prize for Medicine 2012



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SECTION 1: CLINICAL RESEARCH STRATEGY

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Diagnosis and investigations

"Early diagnosis and investigation remains a challenge. For example, early diagnosis of 'clinically relevant' infection in burns is necessary for targeted management and to promote wound healing. Similarly, the differentiation of infection (colonisation and true wound infection) and sepsis is extremely difficult."



Diagnosis of wound infection?

Isambard: 32% scald from hot tea

Amy: 22% scald from hot tea Both treated with adherent dressings.

Both had signs of infection day 2-3.









Isambard was lucky – no permanent scarring.

Amy was not so lucky – lifelong scarring, increased hospital stay, increased NHS costs.





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Neither child had infection.....



Clinically-Relevant Burn Wound Infection

Difficult to diagnose / differentiate from inflammation Delays healing, increases scarring, prolongs hospital stay, increases personal and NHS costs

Signs of infection common, true infection rare (~10%).

We cannot diagnose wound infection at point of care. Over-use of unnecessary antibiotics increasing bacterial resistance.





Article in Press

Variations in guideline use and practice relating to diagnosis and management of infection in paediatric burns services in England and Wales: A national survey

Anna Davies 🖾, Francesca Spickett-Jones 🖾, Paula Brock 🖾, Karen Coy 🖾, Amber Young 🗹 🖾

DOI: http://dx.doi.org/10.1016/j.burns.2016.07.032

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E Article Info





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Clinical Dilemma

- Treat sepsis early: *Surviving Sepsis*
- Antibiotic stewardship

Clinical signs of infection identical to systemic inflammatory response

Only difference is presence of bacteria at *critical* level.



NICE National Institute for Health and Care Excellence



Antimicrobial stewardship: systems and processes for effective antimicrobial medicine use

NICE guideline Published: 18 August 2015 nice.org.uk/guidance/ng15





Post-burn illness





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The **MISTIC** Study

<u>M</u>orbidity In <u>S</u>mall <u>T</u>hermal Injury in <u>C</u>hildren: A prospective multicentre observational cohort study

Aim: To describe the typical physiological response to small burn injury in pre-school children



Recruitment: Jan 2014 to July 2015

- 625 children
- < 5 years of age</p>
- within 48 hours of injury
- Burn < 10% TBSA





Data Collection

- Clinical details
- All physical observations & blood tests
- Parental questionnaires
- Home temperature diaries

llan

in hospital

la hospital

4.00pm

3.30pm 36.3°

4.15pm 36.2"



Nesearch Centre

Seems

Results

- 22% re-presented for medical review with unexpected post-burn symptoms:
 - 10% unplanned re-admission
 - 80% reported high temperature as a symptom
 - Median day for re-presentation was post burn day 3
 - 2 % body area identified as a cut-off for increased risk of re-presentation.









- A physiological response suggestive of an inflammatory response to injury is seen in burns of ≥2% body area.
- 2. Peak for the physiological response and representation with symptoms is post-burn day 3.

Some cases of re-presentation with febrile illness are likely to be attributable to an inflammatory response in the absence of infection.





MRC DPFS funding:

University of Bath, University of Brighton, Healing Foundation Children's Burns Research Centre, Queen Victoria Hospital, Chelsea and Westminster, Industry (Hartmann), Regulatory and IP expertise.

Development of a novel dressing to detect toxic bacteria – with a simple colour change







A problem in sensing:

Can we detect that a wound is infected?

- Can we do this at an early stage?
- Can we do this before systemic infection / sepsis takes hold?
- Can we do this cheaply, easily and quickly?

Model release profile from a surface reservoir of drug X:







Concept of detection

Triggered release of dyes from liposomes





Patterned Hydrogels: response to toxins



0 min

2 min

10 min

20 min

1 h







Patient Information

EVIDEnT

Study Title: Ex-Vivo study to investigate the sensitivity and specificity of a smart dressing to detect clinically relevant wound infection

We would like to ask if you to participate in this research study. Before you decide, you need to understand why the research is being done and what it will involve.

Please take time to read the following information carefully.

> Version Number: 1.0 Date: 01/06/2016 Short Title: EVIDEnT: Ev-Vivo study to investigate the sensitivity and specificity of a smart dressing to detect clinically relevant wound infection.

> > Ethics Reference Number: 16/LO/1414 UHBristol R&D No: CH/2016/6025





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Point of care detection of 'clinically relevant' burn wound infection

- Define 'clinically-important' infection.
 Determined in retrospect.
- Replicate trial in lab using patient samples to determine sensitivity and specificity. Lab blind to condition.
- Validate with test for genetic potential for bacterial toxin production qPCR.



The smart bandage that turns yellow to provide an early warning of infections

- The bandage can give an early warning of injuries going septic
- This could have the potential of preventing overuse of antibiotics
- Trials across the UK will establish how sensitive the bandages are to infections, and how specifically they react to different infections



Infection consensus statement

What is "clinically relevant burn wound infection"?

- BBA supported consensus statement through research sub-committee
- Systematic review

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Delphi process for maximum engagement with final consensus meeting











Research at UWE:

bacteria have characteristic "smells" due to VOCs (Volatile Organic Compounds).

Aim: Identify a library of VOC 'fingerprints' for different bacteria using SIFT - Mass Spectrometry to analyse the air (headspace) around discarded wound dressings and compare to wound swab results.

Technology could be developed into bedside electronic nose device to identify bacterial infection in wounds at POC.









Wound infection "replicating organisms within the wound bed and surrounding soft tissue causing a subsequent host response that leads to a delay in wound healing" Microbial populations produce destructive virulence factors Granulation tissue

formation

Re-epithelialization



Non-invasive point of care detection of infection using bacterial 'volatiles':

- Joint UWE / BCH PhD funded April 2016
- Second pilot study using wound dressings



Mass charge peaks detected at levels significantly greater (p<0.05) than control levels from dressing material inoculated with P. aeruginosa **PA2** (pale grey), E. coli **EC2** (dark grey) or S. aureus **SA3** (black).

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AIM: specific diagnosis of infection at point of care to allow targeted treatment and reduction in unnecessary antibiotic use





Can skin grafting success rates in burn patients be improved by using a low friction environment – a feasibility study?

- 2nd NIHR grant for research into clinical burn care
- Multicentre study comparing skin grafting success using low friction nursing package with a retrospective cohort of patients prior to the use of Parafricta[™] sheeting
- Aim to recruit 150 patients over 3 services currently @ 120
- No safety issues
- Applying for HTA grant







Permissive Hypovolaemia in Paediatric Burns

Is a reduced fluid resuscitation regime safe in terms of patients staying well hydrated based on biochemical markers?

- **Patients**: 6 months 16 years, 10-19 % surface area
- 2 groups: Reduced fluid & traditional
- Sampling: Routine bloods and urine
- Parameters (baseline & 24 hrs): Sodium, Urea, Creatinine, Urine output, Skin grafting



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Results

PH = Permissive hypovolaemia (reduced fluid) - N = 13TR = Traditional resuscitation - N = 18

TR patients received mean 656 mL [IQR: 344-852]; p=0.01 PH patients received mean 200 mL (IQR: 161-377) iv fluids





Results



- Biochemical markers urea and creatinine more likely within normal reference range for patients on reduced fluids compared to those on traditional volumes.
- PH patients remain well hydrated with no adverse effects
- Evidence of over-resuscitation in TR group



Permissive Hypovolaemia in burns patients

Health Technology Assessment Programme

NHS National Institute for Health Research

HTA no 16/109

Reduced fluid resuscitation regimen for burn injuries

Introduction

The aim of the HTA Programme is to ensure that high quality research information on the effectiveness, costs and broader impact of health technology is produced in the most efficient way for

- HTA grant application Feb 2017 led by Bristol
- Supported by BBA, BAPRAS, RSTN and I&E NIHR
- All burn services involved in grant application
- Oxford CTU involved



Optimising evidence-based decision-making for young people with burns by the development of a core outcome set and identification of outcome measurement tools: COSBy

NIHR Doctoral Research Fellowship ~ £500, 000

October 2016 to September 2020

Supervised by Professor Jane Blazeby

Supported by British Burn Association, Journal editor (*Burns*) and medical director specialised commissioning



Core Outcome Set











Core Outcome Set Development



Roald Dahl Marvellous Charity

A road less travelled: mapping children's and families emotional journey following moderate to severe burn injury.



Karen Coy Kate Beckett Shirin Pomeroy Julia Cadogan Paula Brock





Children's Burns Research Centre University Hospitals Bristol

- 25 30 patients admitted each year with severe burns.
- Little known about parent and child perspectives on psychological journey.
- Aim:
 - to map the psychological and emotional journey following burn injury
 - to develop a short film for staff to inform practice and allow targeted supportive information

"This was our first nurse led research project which captured patient/family and staff experiences of burn care and mapped the psychological and emotional journey following significant burn injury and to assess patient and family needs, current support and identify areas for service improvement."





Results

- 6 key themes: normality, catastrophe, dawning reality, riding the emotional rollercoaster, aftershocks, adjusting to a new normal
- Similarities between parents and health professionals
- A Co-design family event February 2016:
 - Focus event for 'A Road Less Travelled'
 - 10 parents, 10 children and 8 health professionals attended to view the film and encourage collaboration between service users and service providers.



University of Bristol Student Projects (eSSC) Investigating the static and dynamic coefficient of friction of hospital fabrics and dressings. Joanna Miles

- Friction can lead to skin graft failure
- Levels of friction between different bedding types and dressing covers used to cover skin grafts. Both static and dynamic coefficients of friction measured.
- Results for Parafricta sheets promising





University of Bristol Student Projects (eSSC) Hyperspectral imaging and burn depth assessment Jack Whiting

- Burn depth assessment is a challenge.
- Clinical evaluation inaccurate.

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• HSI has potential to assess burn depth in real-time.



Spectral responses of single, randomly chosen pixels from burns of different durations

Impact?

- Research networks enabling multicentre trials to solve true clinical problems for patients
- Translational research and innovation
- National profile for burns research: NIHR Portfolio
- Evidence synthesis: core research outcomes
- Medical student impact
- Patient and public involvement



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n's Burns





Acknowledgements THE FREE FOUNDATION

MAKING A WORLD WITHOUT SCARS A REALITY









Bristol Royal Hospital
For Children



University of the West of England



Children's Burns Research Centre University Hospitals Bristol

"The need to standardise care. This ranges from the need for agreement about diagnosis, definitions and interventions, to protocols for standardised care pathways and the development and routine use of standardised clinical and patient reported outcomes."

"...to achieve a cultural shift towards greater research participation, development of larger clinical cohorts with associated methodological opportunities and therefore better quality research outcomes."

"Translational studies: planning and gradual implementation of a program of translational studies leading to standardisation of care across main speciality areas, as outlined above."







Design

A qualitative study using structured around The Kings Fund *Experience Based Co-Design* toolkit.

- In depth semi structured filmed interviews with parents of children following burn injury (of >10% TBSA)
- Audio recorded interviews with a range of service providers from the South West UK Children's Burn Centre
- Parent and staff interviews evaluated and validated to identify key themes and 'touch points' in the patients journey.
- Filmed interviews edited using the key themes, to produce a short film.
- Co-Design Event- film shown to parents and staff.



University of Bristol Student Projects (eSSC) How do we swab? vs How should we swab? Ines Clement

Conclusions:

- Clean the wound with sterile saline before taking the swab sample
- The Essen technique of swabbing is shown to detect the most clinically relevant bacteria
- Wide variation in swab techniques observed
- Opportunity for production of an evidence based burn specific wound swabbing guideline to standardise practice
- Potential for auditing this process





Graph of different motions of swabbing observed in each hospital



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MOTION OF SWABBING OBSERVED DURING SURVEY

Results



NO DIFFERENCE AT ADMISSION

(P>0.05 for all measures)

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The Burns

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Success? Team work 😳







Triggers for detecting infection



Secondary

Immune system response: Cytokines, macrophage, proteases

Local Temperature change;

pH change



pH \uparrow or \downarrow ; Skin T > 36°C

Tertiary



MISTIC: Cohort

 Recruited:
 625 children

 Median Age:
 1y 7m
 [IQR: 1.15 to 2.45]

 Median % TBSA:
 1.00
 [IQR: 0.30 to 2.50]

 Burn Type:

Other 3 % Contact Scald 42 % Scald 55 %

Follow-up:

Medical notes data **100%** Post-injury follow-up **76%**

SIRS and Sepsis

Sepsis = "SIRS in the presence of, or as a result of, suspected or proven infection " (2005)

Sepsis = "a life-threatening organ dysfunction caused by a dysregulated host response to infection" (2016)



Children's Burns Research Centre Goldstein 2005, Singer 2016

Systemic responses following burn injury



Smartwound[™]

To create a wound dressing that provides an early indication of wound infection at point of care.



(a). Final dressing design for small scale production of the dressing.

(b). Establish toxicology of dressing.

(c). Establish sensitivity and specificity of the diagnostic wound dressing: in vitro study of burn patients with suspected infections.

(d). License technology to industrial partners for pilot scale production







Recent Patient and Public Involvement



Public Advisory Group, University of Bristol 23rd September 2016

Two of the clinical team Research Nurses presented the EVIDEnT study and asked for feedback on a potential NIHR HTA application on fluid resuscitation in burns.

Burns Research Involvement Group

We have a database of parents, patients and members of the public for those who want to be involved in research



