White Rose
Health Innovation Partnership

TECHNOLOGY bulletin

## *White Rose HIP Health Technology Bulletins*

The White Rose Health Innovation Partnership (WRHIP) aims to accelerate new health-related technologies by facilitating interactions between academia, industry and the NHS using an *open innovation* approach.

The new projects funded as part of this initiative are built upon a foundation of excellence in health innovation by the Partnership's members. This series of Health Technology Bulletins offer an introduction to this research excellence and cover a broad range of clinical and technology areas.

Each bulletin is written to give a general introduction to the topic area along with short case studies of clinical applications of new knowledge. Information is also presented on where to learn more about these new technologies and health challenges, and how to access the network of health innovation professionals established by the Partnership.

# Advances in woundcare: a clinical overview

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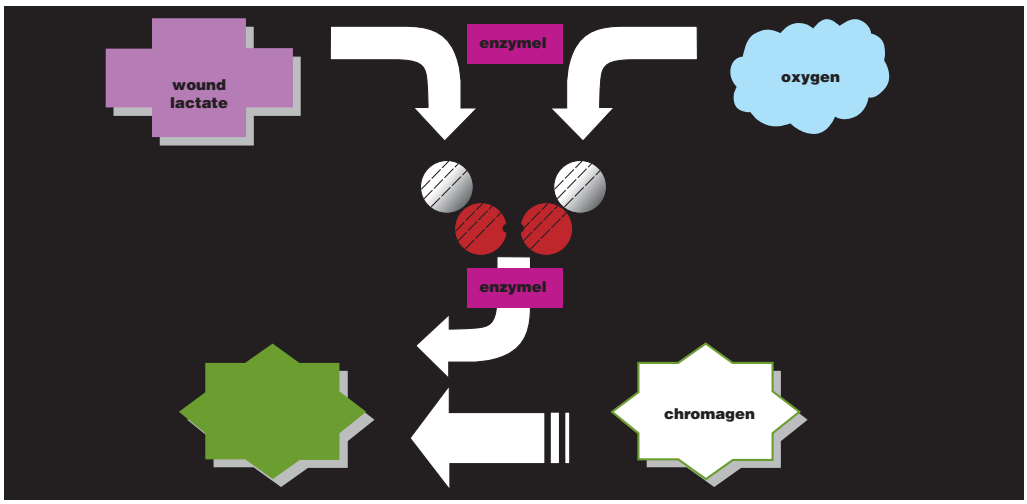
Our skin acts as an interface between a habitat that supports cell processes and a hostile and hazardous environment. When the body surface tissues are damaged, there is a breach in this natural protective barrier, and the delicate cell population is put in jeopardy. The injured tissues embark on a journey of repair and renovation, following a set itinerary aimed at restoring normal form and function. The repair process is an intense performance with high maintenance needs, during which the skin cells must be served with glucose, nutrients and oxygen and cosseted in an environment that supports their complex internal biochemistry and enables proliferation and tissue re-growth. Not all wounds follow a normal programme of repair; whilst an acute wound normally resolves within a couple of weeks, some wounds fail to heal within 8 weeks and are classed as a chronic wound. This increasingly common ailment mainly affects the elderly and those with multiple health problems such as vascular disease or diabetes. The chronic wound is persistent, recurrent and intractable, imposing severe effects on the health and well-being of the patient.

## The economics of woundcare

The financial impact of chronic wound care is enormous; in the U.S. alone, $2.8 billion is spent annually on treating nearly 5 million cases. Chronic wounds are growing in incidence at around 7% cases per annum due to the growing age of the population, increasing awareness amongst healthcare professionals and improved diagnosis. In the UK the primary care sector spends £1500 in products and resources in treating a venous ulcer. The total US market for advanced wound care was estimated at more than $1.7 billion in 2003 and is expected to rise at an average annual growth rate (AAGR) of 10.2% to $2.8 billion. The faster growth in sales is for wound healing devices and therapies, with AAGR of 15%. Woundcare management has been identified as a driving force behind economic growth in the Yorkshire and Humber region, represented by Global market leaders Smith & Nephew (York) and Johnson& Johnson (Gargrave).



# Concepts driving advances in

## Meeting the Clinical demand

The average treatment time in the UK is 16-52 weeks; unfortunately for some patients a timely positive healing outcome can not be achieved. Woundcare professionals are addressing these issues with higher levels of training and with audits aimed at monitoring patterns in the population chronic wound whilst targeting NHS expenditure to fit. This new science of Tissue Viability is driving the demand for devices, dressings and therapies selectively tailored to each manifestation of the chronic wound. The overall consensus is this: by partnering clinical experience with academic knowledge together with industrial know-how, we can invest in a specialist Tissue Viability service to provide the best evidence-based care supported by affordable and effective resources.

The pressure for new technologies in woundcare is being driven by our growing understanding of the fundamental failure to follow a natural healing timeline. Despite the availability of new 'Smart' dressings many wounds are treated still sub-optimally. Of the 5.5 million patients with pressure ulcers per year worldwide, many are treated with low-tech wound care products designed to simply cover and absorb the liquid exudates.

## *Hypoxia*

The trauma of an acute injury reduces the blood supply to the area, cutting out the supply of oxygen and tilting the cells' biochemistry into emergency mode; cells manage 'tick-over' on a very limited oxygen supply. The cell chemistry shifts to production of lactate, a beacon that creates chemical signals to recruit other cells key to the wound healing process. Lactate drives the formation of fresh blood vessels and activates the skin cells into building the collagen scaffold that fills the breach in the wound. As time progresses and the wound heals, the lactate beacon dims. But in some patients, systemic disease results in sluggish blood flow to the extremities – the medical term is 'hypoperfusion'. Impoverished oxygenation or 'hypoxia' leads to lactate overproduction, triggering a cascade process that seeds the wound with toxic biochemicals termed 'reactive oxidant species' (ROS). The ROS scatter like shrapnel, distorting the chemical signals by which cells are recruited and co-ordinated in healing events and corrupting their activities. One target is the freshly sprouting blood vessels which become strangled by choking 'cuffs' of collagen; this exacerbates the hypoperfusion. The change in wound chemistry results in a change of the acid balance or 'pH' of the wound which strays away from safe, normal pH conditions into extremes with the consequence of downgrading the activity of skin protease enzymes that help remodel the wound structure.

When there is a breach in the skin's defences, opportune invaders infect the wound, releasing toxins that stall the staged healing processes A further problem is that low oxygen conditions encourage dangerous pathogens to thrive and feast on tissue. Without rapid clinical intervention, that part of the patient will decay – the outcome of this 'necrosis' is too frequently literally carving out the dead tissue to save the patient, justifying amputation of digits and limbs. Tissue hypoxia is linked to a poor healing profile and high incidence of infection. The risk of lower limb amputation is excessive, and around 52% of ulcers related to hypoxia fail to heal completely.

## *Available technology*

Tissue viability practitioners have to make the majority of their therapeutic decisions based only on visual inspections of the wound. The choice of a dressing or therapy is largely subjective or practice-based. A practitioner may advocate oxygen therapy to rebalance the hypoxic wound environment, but is currently restricted to expensive equipment for topical oxygen delivery or specialist centres that can commission and support hyperbaric oxygen chambers. The more advanced 'intelligent' dressings such as Promogran and Biostep are engineered for particular wound pathologies- they are valuable resources but extremely costly if they are not correctly matched to the patient's treatment needs.

Currently there is no point-of-care technology for quantitative guidance on the impact of an intervention on the wound biochemistry. Practical diagnostic methods to specifically assess wound lactate, pH and oxygen levels may be an excellent way of monitoring the state of healing and the competency of oxygenated blood supply to the tissue thus enabling a more effective, cohesive and proactive treatment regimen.

# chronic wound healing

## *Case Studies*

## Advances in diagnosis of wound healing status

In order to address this, academics from the University of Bradford have joined with scientists from local bioscience enterprise AGT Sciences and healthcare professionals based at Bradford Royal Infirmary to push their innovative scientific concepts into viable and validated technology, delivering therapeutic solutions to the patient and the professional. The group has been exploring the relationship between high, persistent wound lactate levels and the patient's poor healing status. The Bradford studies suggest a strong link to the disordered glucose metabolism and elevated lactate found in diabetic patients. The 9% increase in referrals for diabetic ulcers alone is outpacing growth in the new therapies capable of reducing the incidence of wounds by healing. The balance has to be redressed by scientists and clinicians working together to advance understanding and push new technologies through to the bedside. The Bradford group have invented a simple to use point-of-care lactate dipstick, LactostixTM,. The technology incorporates enzyme-based chemical sensors into a novel polymer that wicks up the wound fluid and produces a trio of colour responses. Within 30 seconds, the traffic-light changes and the operator has answer to the lactate status of the patient literally at their fingertips. With HiP funding, extensive trials are underway to test the performance of the device in patients with diabetic ulcers or with poor oxygen profile.

## Developing a pH theragnostic for informed woundcare

The management of chronic wounds is increasingly complicated by the choices in products and strategies available. The consensus of health-care professionals is the need for a 'theragnostic' – a diagnostic device that allows objective therapeutic intervention and enhances the healing outcome. Prof. Vowden is working with HiP partners at AGT Sciences, Bradford on a novel patented hydrogel co-polymer formulation that has proved ideal for creating a miniature gel-bound chemistry lab.

By incorporating a cohort of chemicals they have produced a flexible carrier with huge potential for use in analytical applications. The research and development activities of AGT Sciences are currently focused upon developing of range of diagnostic dressings with the capability to inform physicians and nurses as to the status of the wound biochemistry. The current emphasis is an innovative point-of-care that rapidly informs the user of wound exudate pH. This would empower the clinician to make positive informed choices in specialist wound care products and redress any pH imbalance that is compromising tissue viability and so instigate accelerated healing.

## Targeting hypoxia in the chronic wound

An important aspect in chronic wound pathology is the clinical fact that vascular disease, smoking and tissue swelling can act to cut off the vital oxygen pipeline to the wound. By improving the patient's oxygen profile the high oxygen demand of tissue repair can be sustained. Dr. Chedly Tizaoui of the Department of Engineering at University of Bradford has been working with Bradford trust NHS partners to develop innovative technology for local delivery of active oxygen to the wound surface. The miniscule active oxygen molecule can readily penetrate the deepest wound, making the blood vessels bloom and knocking the hypoxia into touch. Additional advantages come from the ability of active oxygen to recruit the blood-borne immune cells and by an intrinsic antibacterial action that 'scrubs' the wound of the microbial burden of infection. Cells refreshed with active oxygen may generate essential growth and repair promoters and resume coordination of healing events. By mopping up the damaging ROS and the production of lactate should be countered and pH balance could be restored. The evaluation and appraisal of the clinical performance of active oxygen therapy can be ideally supported by quantitative information provided by the lactate and pH diagnostic devices rather than by subjective visual methods alone.

*Founding partners in the Programme include:*

University of Leeds

University of Sheffield

University of York

University of Bradford

Medipex

Medilink Yorkshire & the Humber

The Leeds Teaching Hospitals NHS Trust

Sheffield Teaching Hospitals NHS Foundation Trust

Bradford Teaching Hospitals NHS Foundation Trust

Yorkshire Forward

Health Technologies Knowledge Transfer Network

New Jersey Biotechnology Life Science Coalition

Rutgers University

University of Medicine and Dentistry of New Jersey

New Jersey Institute of Technology

Princeton University

International ARI Institute, University of Toledo, Ohio

Polymer Centre for Industrial Collaboration

Biomaterials and Tissue Engineering Centre for Industrial Collaboration

Pharmaceutical Innovation Centre for Industrial Collaboration

Wireless Technologies Centre for Industrial Collaboration

Particles Centre for Industrial Collaboration

# Regional Centres of Expertise

The **Yorkshire Forward Regional Development Agency** recently named healthcare technology at Bradford as an industrial 'cluster' in the region. Innovation in woundcare management is a growth sector of particular importance in the Yorkshire and Humber regions.

For this reason the Bradford focus groups represent a showcase for healthcare innovation that invests in the benefits of managed multidisciplinary collaborations to develop new woundcare technology partnered with practical and affordable theragnostic tools that can support and enhance these interventions.

**Yorkshire Association of Innovation in Wound Management (YAIWM)** promotes partnerships that will facilitate exchange of knowledge and best practice. The association manages connections between academics, healthcare companies, business support agencies and healthcare professionals. This robust approach to meeting clinical demand with new technology in woundcare is aimed at supporting the testing and validation process and informing strategies for funding and investment.

**The Medical and Healthcare Technology Research Centre** at the Department of Engineering, University of Bradford, is a multidisciplinary cluster dedicated to the application of engineering principles and techniques within the medical and healthcare sector. It combines engineering, biological and clinical expertise to solve medical problems and improve the wellbeing of patients. It is unique in that it has collaborative links both within the University (with the Medical Biosciences team in the School of Life Science) and close collaborative links with regional hospitals, the NHS, and industry. As such, members of the Centre frequently work with industrial partners in woundcare such as Smith and Nephew Plc and DePuy International Ltd.

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**The Medical Biosciences Team** in the School of Life sciences, University of Bradford includes members involved in pure research into wound healing and larval wound biotherapy. Their work progresses to proof of concept studies for technology transfer and commercialisation of woundcare theragnostics and advanced wound dressings for woundcare.

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**AGT Sciences,** the University of Bradford spin-out company, carries out innovative research in woundcare and polymeric drug delivery. Their patented advanced hydrogel technology provides a flexible platform with novel applications. Their product range features diagnostic dressings with the capability to inform physicians and nurses as to the status of the wound with respect to pH of the wound bed, the presence of enzymes and level of bacterial infection.

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**Prof. Peter Vowden,** a Consultant Vascular Surgeon and **Kathryn Vowden,** Nurse Consultant Acute and Chronic Wound Care, Bradford Royal Infirmary, Bradford Teaching Hospitals NHS Foundation Trust are regarded as world leaders in woundcare and tissue viability. As active researchers and clinical practitioners their team collaborates with industry and academia in validation of devices performance and shaping therapeutic strategies for woundcare treatment.

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**The Hull and East Riding Institute of Wound Care** was established in 2006 as a centre of excellence for wound care treatment, research and education. The Institute works with Acute and Primary Care Trusts and Smith and Nephew plc as well as the Post Graduate Medical Institute at the University of Hull. The aim is to provide a multi-disciplinary, multi-agency wound care service involving healthcare professionals whilst integrating research on new advanced products and programmes for wound treatment.

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