PROCEEDINGS OF THE LEADERS IN WOUND HEALING CONFERENCE

In May 2021, 38 leaders in the practice of wound care gathered in New Orleans for a one-day event to address unanswered questions in wound healing. The morning lectures set the stage for five afternoon sessions, each focusing on a selected topic. The topics were chosen by the planning committee with input from clinicians and interested parties in the wound-healing field. The sessions were led by a moderator and panel that reviewed the literature prior to the meeting. In addition, the clinicians in the audience contributed to the debate.

Session one: Design an improved cellular and/or tissue-based Product (CTP)

Moderator: Kerry Thibodeaux MD; Panel: Peter Moyer DPM, Gary Harmon MD, Terry Treadwell MD, James Vestile DPM; sponsored by Tides Medical

The moderator, briefly reviewed the extensive evidence for CTPs in promoting wound healing. In addition, he presented an overview of the classification of CTPs:

- Tissue based—animal derived
- Tissue based—human derived
- Human cells—xenogeneic collagen
- Human cells—synthetic substrate
- Synthetic matrices

The moderator reviewed the various pathways for U.S. Food and Drug Administration (FDA) approval of CTP products from 361 wound coverings to products with premarket approval (PMA). He also updated the group on the reimbursement structure for these products. The panel acknowledged that a detailed analysis of FDA approval and reimbursement strategies were beyond the scope of the meeting; however, there was unanimous agreement that clinical trial design must incorporate requirements for regulatory and reimbursement approvals.

Dr Treadwell led the conversation with his definition of the ideal CTP:

1. It would work every time
2. It would work on every wound
3. It would be easy to store and apply
4. It would be available to all patients
5. It would be inexpensive.

The panel stressed the importance of wound bed preparation prior to CTP application (e.g., aggressive debridement, effective offloading, appropriate moisture balance and reduction in bacterial burden). In a morning session Dr Aropallo, presenting on the MolecuLight consensus, suggested that clinicians avoid applying CTPs until the wound bed is free of bacterial fluorescence, indicating that the wound bed has less than 10^4 CFU/g. Dr Serena added that in the ongoing diabetic foot ulcer (DFU) clinical trial, evaluating the efficacy of dual-layer amniotic membrane, negative fluorescence in the wound bed is an inclusion criterion.

Building on Dr Treadwell's characteristics of the ideal CTP, the panel noted that a single CTP may not heal all wounds. They suggested designing CTPs to fit the needs of a wound at a given state. The initial CTP application, for example, might treat elevated bacterial levels and lower host proteases while the second stage would promote re-epithelialisation. Dr Driver, founder of the *Wound Care Collaborative Community,* stressed the importance of developing surrogate endpoints for clinical trials that evaluate staged procedures. In addition, members of the audience expressed the need for diagnostics and theranostics to guide the use of CTPs, particularly if staged applications are introduced.

Dr Harmon encouraged research into developing 'supercharged' CTPs. The panel and audience proposed several concepts:

- Increasing protection from bacterial infection by adding antimicrobials or increasing the expression of host defence peptides
- Enhancing growth factor delivery
- Adding mesenchymal stem cells protected by the CTP matrix.

Finally, the conference members advocated for

expanded use of CTPs. Not all patients who would benefit from this technology receive it. The reasons vary, ranging from lack of clinician education, evidenced-based guidelines on the timing of CTP use, to a lack of reimbursement for a large segment of the wounded population.

Session two: Guidelines for treating biofilms in chronic wounds

Moderator: Paul Glatt MD; Panel: Marcela Farrer DPM, Scott Johnson MD, Greg Schultz PhD; sponsored by Next Science

The moderator and panel members reviewed the importance of biofilms in chronic wound care. There is mounting evidence that wound bed preparation must focus on the treatment of biofilms, including aggressive and frequent debridement as well as topical antiseptics and antimicrobials that disrupt biofilms and kill bacteria. Summarising the recommendations of the leaders of the session, we introduced the concept of the six Ds:

- Diagnose: identifying bacteria in biofilm form is the key first step in biofilm-based wound care. Dr Schultz presented several new technologies aimed at rapid diagnosis of biofilm. In the morning sessions, Dr Cole described the use of the MolecuLight device to identify bacterial load, including biofilms.
- Debride: there was universal agreement among the conference attendees that aggressive debridement plays a crucial role in disrupting biofilms.
- Douse: applying topical antiseptics, the next step in biofilm treatment, reduces planktonic bacteria. In addition, antiseptics with a high osmolarity will disrupt biofilms. There is limited in vivo evidence for the use of antiseptics; however, a survey of the panel and audience confirmed that clinicians use antiseptics routinely. The panel recommended further research into the use of antiseptics in the treatment of biofilms.
- Deconstruct: In addition to debridement, there are topical antibiofilm agents that disrupt biofilms. In the morning session, Dr Al-Jalodi reviewed research on the use of the antibiofilm agent BLASTX (Next Science, Jacksonville, FL) to improve outcomes in patients receiving negative pressure wound therapy. This antibiofilm agent deconstructs the biofilm. Several commercially available agents use a surfactant to disrupt the biofilm. Dr Schultz presented several novel agents under study: dispersin B that pokes holes in the extrapolymeric substance (EPS) that forms a film, DNAses and quorum-sensing inhibitors that inhibit biofilm formation.
- Destroy: once the biofilm is disrupted, using debridement and topical antibiofilm agents, antimicrobials, topicals and dressings are applied to kill the bacteria.
- Defend: the final step is to modify the wound environment in ways that discourage biofilm reformation.

Session three: Guidelines for the use of topical oxygen in chronic wounds

Moderator: Bob Frykberg DPM; Panel: Matt Garoufalis, Keyur Patel DO, Charles Anderson MD, Munier Nazal; Morning lecture: David G Armstrong DPM; sponsored by Advanced Oxygen Therapy inc., E02, Inotec Inc.

This session inspired a consensus document included

in the current issue of the *Journal of Wound Care* using a Delphi approach.

Session four: Measuring perfusion and oxygenation in the wound care center

Moderator: Lee Rodgers DPM; Panel: AJ Applewhite MD, Jeff Niezgoda, Erik Lichtenberger MD, Munier Nazal MD; sponsored by Kent Imaging Inc.

The moderator, Lee Rodgers, started the session by differentiating between measuring perfusion and oxygenation in the wound clinic: perfusion is the arterial flow into the affected limb versus oxygenation, which is the amount of oxygen delivery to the area of skin breakdown. The consensus among the conference attendees was that in the assessment of the wound care patient, measuring both is important.

The panel led the discussion on the current technology to screen wound care patients for vascular disease. Dr Serena noted that screening on a patient's first visit to the centre is a commonly used quality metric. Ankle–brachial index (ABI), the most commonly used technology, is a proven screening technique; however, non-compressible vessels in diabetic and elderly patients are a major limitation of use in the wound care clinic. Some of the panel members have added toe–brachial index (TBI) in addition to ABI to address this limitation. Dr Nazzal mentioned that he also adds duplex examination to ABI/TBI. Less commonly employed technology includes skin perfusion pressure and pulse volume recording. Dr John Lantis remarked that there is an opportunity for new technology in screening patients. Ideally, the device would be easy to use, readily available in the wound clinic and permit rapid evaluation of patients.

The panel turned its attention to measuring oxygenation. Transcutaneous oxygen measurement (TCOM), the traditional technology for measuring oxygenation, has fallen from favour for several reasons: TCOMs are difficult to perform, the results are not consistent between technicians conducting the test, it takes up to an hour to complete and disposables are expensive. Dr Neizgoda shared his experience with near infrared spectroscopy (NIRS) (SnapShotNIRS, Kent Imaging, Alberta CA). The NIRS image solves many of the problems associated with TCOM: it rapidly captures an image map of tissue oxygen saturation, the measurements are reproducible and there are no disposables. Early research suggests that the NIRS and TCOM measurements are comparable.

The panel and audience made several suggestions concerning NIRS. First, the medical community needs to understand the difference between tests of perfusion and tests of oxygenation. There needs to be continued research into to the correlation between TCOM and NIRS with clinical trials aimed at correlating tissue oxygen saturation values and wound healing and level of amputation prediction. The panel suggested evaluating the relationship between NIRS values and the effectiveness of hyperbaric oxygen therapy. Additionally, there may be a role for NIRS in determining adequacy of wound debridement and proper timing of cellular and/or tissue-based product usage. Overall, the panel and audience were enthusiastic about a technology that solves many problems of peripheral arterial disease (PAD) diagnosis in the wound care centre.

Session five: Comparative effectiveness and combination clinical trials

Moderator: Elizabeth Faust CRNP; Panel: Naz Wahab MD, Thomas Serena MD, Luris DeCalero MD, Rachel Hamil MD; sponsored by Sanuwave Inc.

Liz Faust started the session with a discussion on the lack of comparative effectiveness research in wound healing. The audience complained about a lack of funding for comparative effectiveness research. The panel stressed the importance of an increase in government funding for comparative clinical trials.

Dr DeCalero commented that certain technologies go together like 'peas and carrots'; however, there is limited evidence supporting the use of products in combination. The panel divided combination trials into two categories: using products at the same time, such as the clinical trial presented earlier in the day by Dr Al-Jalodi on the use of antibiofilm agents and negative pressure wound therapy (NPWT); and the use of products and technologies in sequence. There are a number of technologies that are designed to prepare the wound care space for advanced wound care products. Unfortunately, the panel noted that there are few if any sequential trials anticipated or presently being conducted in the field. A discussion concerning potential sequential trials ensued. Dr Serena reviewed his trial design for an upcoming study evaluating the use of non-contact, non-thermal ultrasound followed by CTP application. ■

Tomas Serena

The SerenaGroup Research Foundation would like to thank the outstanding leaders who presented and participated in the conference. We look forward to next year's second Leadership in Wound Healing Conference. See you back in New Orleans.