

Schiller Saal

17.30–19.00

V 8

Proteases and Antiproteases in wound healing

Proteasen und Antiproteasen in der Wundheilung

V 8-1

Matrix metalloproteinase function in epithelial injury and repair

J. Mc Guire

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Matrix Metalloproteinases (MMP) are a family of structurally related enzymes that cleave a variety of matrix and other extracellular proteins, and work in our laboratory focuses on understanding MMP function in tissue injury and repair. Using transgenic mice deficient in individual members of the MMP family, we have identified critical roles for specific MMP in epithelial responses to injury in the lung, kidney, and gastrointestinal tract. These findings provide new insights into MMP substrates and functions in different tissues.

V 8-2

Dysregulation of matrix-metalloproteinases in impaired tissue repair

M. Agren

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The matrix metalloproteinase (MMP) enzyme family comprises 24 known zinc-dependent endopeptidases. The obligatory role of MMP in normal wound healing and specifically in epithelialization has been shown with the use of synthetic broad-spectrum MMP inhibitors. The importance of individual MMP in the epithelialization process has not been delineated fully. The gelatinase MMP-9 (92-kDa gelatinase) is consistently expressed in the advancing epithelium of acute wounds although wound healing is normal in mice lacking functional MMP-9 gene. Conversely, in chronic wounds MMP-9 is absent in wound epithelium but concentrated in the inflammatory cell infiltrate indicating a disproportionate MMP-9 distribution in chronic wounds. Commonly many MMP-9 positive neutrophils are observed in close proximity to the negative MMP-9 epithelium. Excess MMP-9 in the

ulcer may deprive the keratinocytes of signals by ECM molecules. In addition, MMP-9 can degrade a1-proteinase inhibitor, which can result in elevated neutrophil elastase activity. Thus, MMP-9 can contribute to unfavorable conditions in several ways leading to delayed epithelialization in chronic skin wounds. In this talk, the role of MMP in normal wound healing will first be briefly presented followed by summation of pathogenic mechanisms in chronic wounds related to MMP expression.

V 8-3

Regulation of matrix metalloproteinases and TIMPs in tissue repair and tumor invasion

C. Mauch

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Tissue repair and tumor invasion require degradation of connective tissue a process which is regulated by cytokines and growth factors released by various cell types including inflammatory cells. While in healing wounds inflammation is usually self-limiting, in tumors the inflammatory reaction is dysregulated leading to abnormalities and finally to pathogenesis. Tumor cell proliferation is sustained by a microenvironment which is rich in inflammatory cells, growth factors, activated stroma that support the growth of the tumors. In this sense, tumors act as wounds that fail to heal.

In addition, tumor cells produce large amounts of cytokines and chemokines which are mitogenic and serve as chemoattractants for inflammatory cells, fibroblasts and endothelial cells. In addition, activated fibroblasts and infiltrating inflammatory cells secrete proteolytic enzymes, cytokines and chemokines which are mitogenic for tumor cells, for fibroblasts and endothelial cells leading to enhanced tumor-associated angiogenesis and lymphangiogenesis.

Beside growth factors, cytokines and chemokines released by inflammatory cells modulating proliferation, migration and gene expression of the various cell types, interactions between epithelial or tumor cells and stromal fibroblasts has become increasingly important in both wound healing and in tumor progression. Epithelial cells and fibroblasts engage in a reciprocal dialo-

gue by the release of stimulatory and inhibitory factors to facilitate wound healing. Once the wound is healed the reciprocal signalling subsides. In contrast, in cancer, the stimulation of the peritumoral stroma is continued resulting in an ongoing activation of the stroma.

To obtain insight into the cellular changes induced by tumor-stroma cross-talk, we analyzed the gene expression profile of high and low invasive melanoma cell lines and fibroblasts cocultured with both melanoma cell lines. We could identify key proteins for tumor progression expressed by both, tumor and

stromal cells, as a result of their interaction and emphasize the role of the microenvironment in tumor invasion and metastasis. In addition we could show that high but not low invasive melanoma cells induce synthesis of distinct matrix metalloproteinases in fibroblasts which facilitates degradation of the extracellular matrix and tumor invasion suggesting that development of drugs which specifically interfere with tumor-stroma cross-talk will be useful in the treatment of cancer.

Donnerstag, 15.09.05

Freie Vorträge V 31

ETRS

Hall Köln, Bonn, Hamburg

17.30–19.00

V 31

Stem Cells

Stammzellen

V 31-1

Stem cell participation in the wound repair process

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Stem cells and progenitor cells provide a renewable resource for the repair of epithelial and mesenchymal tissues. While there is strong evidence for the role of resident stem cells in the epidermis and other epithelial tissues, the source of progenitors in blood vessels and connective tissue is not clear. In 1997, initial evidence was presented to suggest that endothelial progenitor cells (EPC), which were derived from bone marrow precursors, were an important contribution to the process of vasculogenesis during wound healing. Further characterization and isolation of EPC has revealed that they are recruited to sites of neovascularization by factors such as VEGF and SDF-1, possibly under the influence of local tissue hypoxia. Such cells have shown potential for therapeutic angiogenesis to restore microcirculation in damaged tissues. As early as the 1950's, primitive marrow stromal cells (MSC) with mesenchymal characteristics were suggested to be the precursors of a mesenchymal cell lineage, and more recent investigations have shown the MSC to be a pluripotential cell with prospects for tissue engineering in hard

and soft connective tissue. Other studies have identified a CD34+/CD14+ population of fibrocytes that arise in bone marrow and enter wounds during the inflammatory phase. Using adoptive bone marrow transfer from transgenic mice bearing a fibroblast-specific collagen promoter, the MSC contribution to wound repair was evaluated. These cells enter wounds from the circulation and expand their activity during granulation tissue formation, reaching a peak of collagen expression more than 3 weeks after injury in the experimental wound model of sponge implantation. More importantly, more than 30 % of the fibroblast population at that point in repair is derived from bone marrow sources. Stem cells can thus make a significant contribution to the healing process, and they may be particularly relevant to conditions of reduced healing such as diabetes, ischemia, and aging.

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V 31-2

Effects of HA-1077 on differentiation of bone marrow mesenchymal stem cells into epidermic cells

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Aim: To investigate the effects of Rho inhibitor HA-1077 (fasudil) on the differentiation of bone marrow mesenchymal stem cells (MSCs) into epidermal cells and conditioned culture medium in vitro.

Methods: Bone MSCs were separated from human bone marrow using Ficoll-Paque lymphocyte separation medium and proliferated in vitro. The surface antigens were detected with flow cytometer technology. The cells were divided into four groups randomly, control group cultured in DMEM containing 10 % FBS; induced group with condition broth contain 70 % DMEM with 10 % FBS, 30 % supernatant from fibroblasts cultured medium and EGF (10 ng/ml); HA-1077 group cultured with DMEM containing 10 % FBS and HA-1077; HA-1077 induced group cultured with 70 % DMEM containing 10 % FBS, 30 % fibroblasts supernatant, EGF (10 ng/ml), and HA-1077 (10 μmol/L). Cytokeratin 5/8, 10/13 and 19 expressed in MSCs were detected by immunocytochemistry and flow cytometer.

Results: Bone MSCs proliferated in culture medium for 15 generations were harvested. The cultured MSCs were uniformly expressed CD29 and CD44, but negatively expressed for CD34 and CD45. After treated with induction medium in HA-1077 induced group, Cytokeratin 5/8, 10/13 and 19 in MSCs could be detected after two to seven days. More MSCs differentiated into epidermal cells were also observed. The rates of positive cells expressed cytoke-
 ratin 5/8, 10/13 and 19 in HA-1077 induced group were higher than those of other groups ($P < 0.01$).

Discussion: Differentiation of MSC into epidermal cells was increased by HA-1077 through Rho-ROCK signal transduction pathway. Activation of RHO-dependent protein kinase might play an important role in the differentiation of bone marrow MSCs into epidermal cells.

V 31-3

High lactate in wounds may initiate vasculogenesis via stem cell homingR. Aslam¹, S. Becker², H. Scheuenstuhl¹,
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Introduction: Accumulation of lactate, a characteristic of healing wounds, is not due to hypoxia but is largely a result of aerobic glycolysis by inflammatory cells. We have shown that lactate al-

ne induces neovascularization in vivo. Increasing evidence suggests that post-natal neovascularization involves angiogenesis and vasculogenesis. Hematopoietic stem cells (HSC) are multipotent, capable of self-renewal, give rise to all formed blood elements and are the best characterized source of endothelial precursor cells (EPC). We asked: does lactate induce stem cell mediated vasculogenesis in wounds?

Methods: In vivo, Matrigel (solubilized basement membrane) implant assay: Female Swiss Webster mice (n=20) received subcutaneous injections of 1 cc matrigel supplemented with 30 mgs crushed polylactate (Poly DL-lactide-co-glycolide) to achieve a sustained concentration of lactate at 170 percent of control. Control implants were 1 cc unsupplemented matrigel. The matrigel implants were harvested after 9 and 11 days, formalin fixed, paraffin embedded and sectioned for H & E and histochemical staining. HSC's were identified by antibody labeling of the cell surface marker CD117/c-kit. Anti-CD31 antibody staining identified mature endothelial cells.

Results: In addition to increased vasculature, the number of HSC's in polylactated (PL) implants was 10 times greater than controls at day 9. Day 9 PL implants also showed blood islands and mature endothelial cells. No HSC's were identified 2 days later (day 11) when implants showed mature endothelial cell-lined blood vessels.

Conclusions: Lactate induces neovascularization, part of which seems due to stem cell-mediated vasculogenesis. Our future studies will regard the potential of lactate in therapeutic neovascularization.

V 31-4

Autologous bone marrow transplantation as a therapy of the angioneuropathic foot syndrome: First experiences**Autologe Knochenmarkstransplantation als Therapie des angioneuropathischen Fußsyndroms: Erste Erfahrungen**C. Luedemann¹, B. Amann¹, M. Stumm²,
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Introduction: Only 60 % of all patients with an angio-
 pathic diabetic foot syndrome (dfs) can be revascularised surgically or by intervention. The number of amputations are increased tenfold compared to the neuropathic diabetic foot syndrome. The induction of angiogenesis and arteriogenesis by autologous bone marrow transplantation may be a new therapeutic method to prevent major amputation.

Methods: In three patients with angio-
 pathic dfs and clinical signs of critical limb ischemia including relapsing bypass occlusions, autologous bone marrow transplantation was performed

after all established therapies as radiological intervention or repeated vascular surgery had failed. Therefore approx. 400 ml of bone marrow was collected, the monocytic cell fraction extracted and after purification injected deeply into the muscle of the ischemic limb at about 40 sites. Investigation of clinical parameters and non-invasive measurement of arterial perfusion were performed one and two month after bone marrow transplantation. Follow up investigations were done for five month after therapy.

Results: In each case uncomplicated collection of bone marrow and reinjection. Transcutaneous oxygen pressure before start of therapy (foot) 0 / 0 / 12 mmHg, 1 month post injectionem 0 / 30 / 24 mmHg, 2 month post injectionem 14 / 30 / 22 mmHg. Ankle brachial index before therapy 0.30 / 0.00 / 0.80, 2 month after start of therapy 0.60 / 0.40 / 0.80. Requirement of analgesics after 1 month 70 %, after 2 month 30 % of initial dose. Approximately 6 weeks after therapy onset of granulation, in one patient complete wound healing after 4 month. After 5 month of observation no major amputation. Within follow up time no bone marrow transplantation derived complication.

Conclusions: Autologous bone marrow transplantation is a therapy that is easy to perform and low in complication. On the strength of past experience bone marrow transplantation can help to prevent major amputation in critical ischemic limbs.

Ziel: Nur etwa 60 % der Patienten mit einem angiopathischen diabetischen Fußsyndrom (DFS) können operativ oder interventionell revaskularisiert werden. Die Amputationsrate ist etwa zehnmal höher als beim neuropathischen DFS. Die Induktion der Angiogenese durch autologe Knochenmarkstammzellen könnte eine neue therapeutische Methode zum Extremitäten-erhalt darstellen.

Methode: Bei bisher drei Patienten mit angiopathischem DFS und kritischer Extremitätenischämie wurde nach Ausschöpfung aller konservativen, interventionell-radiologischen und operativen Maßnahmen bzw. nach mehrfachen Bypassverschlüssen als ultima ratio die Indikation zur Knochenmarkstransplantation gestellt. Es wurden jeweils ca. 400 ml Knochenmark entnommen, die monozytäre Zellfraktion gewonnen und nach Aufarbeitung tief intramuskulär an ungefähr 40 Injektionsstellen in die ischämische Muskulatur injiziert. Klinische und apparative Perfusionsparameter wurden im Verlauf von fünf Monaten erfasst.

Ergebnisse: Jeweils komplikationsloser Verlauf von Knochenmarks-Entnahme und Reinjektion. Transkutaner Sauerstoffpartialdruck vor Therapie (Fuß) 0 / 0 / 12 mmHg, 1 Monat post injectionem 0 / 30 / 24 mmHg, 2 Monate post injectionem 14 / 30 / 22 mmHg. Knöchel-Arm-Index vor Therapie jeweils .30 / 0.00 / 0.80, 2 Monate nach Therapie 0.60 / 0.40 / 0.80. Analgetikabedarf nach 1 Monat 70 %, nach 2 Monaten 30 % der Ausgangsdosis. Etwa 6 Wochen nach Therapie beginnende Granulation, bei einem Patienten Wundverschluss 4 Monate post injectionem. Nach 5 Monaten Nachbeobachtung keine Majoramputation. Auch im weiteren Verlauf keine auf die Knochenmarkstransplantation zurückzuführende Komplikationen.

Schlussfolgerung: Die autologe Knochenmarkstransplantation ist eine einfach durchzuführende und komplikationsarme Therapie. Nach unseren bisherigen Erfahrungen kann die Knochenmarkstransplantation helfen, bei bedrohter Extremität Majoramputationen abzuwenden.

V 31-5

Investigation of cellular phenotype conversion during human mesenchymal stem cells cocultured with human sweat gland cells in vitro

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Aim: To investigate the cellular phenotype conversion during human mesenchymal stem cells (hMSCs) cocultured with injured human sweat gland cells (hSGCs) in vitro.

Methods: hMSCs and hSGCs were isolated, cultured, expanded and identified respectively. hMSCs were labeled with 5-bromo-2'-deoxyuridine (BrdU), then cocultured BrdU-labeled hMSCs with heat-shocked confluence hSGCs. The cocultures were observed by inverted phase contrast microscopy and detected by immunoenzymatic double staining, taking BrdU and CEA/CK7/CK14 as primary antibodies.

Results: The cultured hMSCs and hSGCs were clonogenic growth. hMSCs were positive for CD29, CD44 and CD105 and negative for CD34. BrdU stains nucleus of hMSCs. The positive rate of CD44 in hMSCs is 89.64 % while CD34 is 0.11 % by flow cytometry. Cell cycle studies revealed that a small fraction of hMSCs are actively engaged in proliferation (approximately 10 % at S + G2 + M), the vast majority of cells are standing at the Go/G1 phase. hSGCs were positive for CK7, CK8, CK14, CK19 and CEA. 2 weeks after cocultured, there were BrdU-labeled cells (nuclear-black purple) incorporated into sweat gland cell, which were indistinguishable from hSGCs under inverted phase contrast microscopy. Some cocultures had been stained with two different colors in single cell, while some stained only with one color. Interestingly, some cocultures had more than two nuclei which stained with different colors.

Discussion: hMSCs could differentiate into hSGCs under injured microenvironment in vitro. The mechanisms of which may be that hMSCs differentiate into hSGCs directly or by cell fusion, even nucleus fusion.

V 31-6

Kinetics of grafted-human mesenchymal stem cells in cutaneous wound healing

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Bone marrow derived cells such as the human mesenchymal stem cells (hMSCs) successfully accelerate cutaneous healing; however, there are little data on how and when the cells contribute to this event. As the hMSCs may be able to differentiate to mesenchymal lineage in each specific condition, "non-mesenchymal lineage rege-

neration" to cutaneous wound healing when the cells are grafted. In order to elucidate the cell kinetics, proliferation and differentiation, the hMSCs transfected with Green Fluorescent Protein (GFP) DNA plasmid (pIRES-EGFP) further kinetics were investigated. GFP-transfected hMSCs were grafted with artificial skin substitute (porcine tendon-derived, Pelnac®) in the dorsum of nude rats. The defects were healed in the grafted GFP-transfected hMSCs by 7 days post-operatively in accordance to the previous experiment, which was identical to that of without GFP-transfection but hMSCs grafting. Superficial layer at day 7 demonstrated the strong immu-

noreactivities of both GFP and STRO-1, which binds to bone marrow precursor cells and depicts the immature mesenchymal-origin cells, with the cell nuclear antigens of 6-Diamidino-phenylindole, Dihydrochloride (DAPI). In the deeper layer just above the muscle layers, the STRO-1 expressions were also demonstrated. On the other hand, human Pan-Cytokeratin expressions, which are specific to human origin antigen, were thoroughly expressed. Therefore, the grafted cells were located in either superficial or deeper layer and the re-epithelialization was more diffusely differentiated.

V 32

Quality of life for patients with chronic wounds

Lebensqualität von Patienten mit chronischen Wunden

V 32-1

Quality of life in leg ulcer patients: Significant improvement by short stretch compression treatment

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Background: To investigate the impact of "disease" and treatment on quality of life in patients with venous leg ulcers.

Patients, material, methods: 65 patients with venous leg ulcers were treated with short-stretch bandages. At study entry and exit or complete wound closure, whichever occurred first, each patient was assessed with the SF-36 Quality of Life Questionnaire which includes the following measures: Physical Functioning, Role Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role Emotional, Mental Health and Health Transition. Data analysis investigated the study population as whole and differences between healed and unhealed patients. Health domain means for all patients were compared with 'age equivalent norms' (AEN) at entry and exit.

Results: All 65 patients had a statistical improvement in the SF-36 domains of Bodily Pain, Health Transition, Mental Health and Social Functioning. Patients whose ulcers healed during the treatment period had statistical improvements in five domains

i.e. Bodily Pain, Health Transition, Mental Health, Social Functioning and Vitality. Patients whose ulcers did not heal during the treatment period had statistical improvements in Bodily Pain and Health Transition. At entry all SF-36 values except the General Health concept were less than AENs. On exit Bodily Pain, General Health and Mental Health were comparable to the AENs. Remaining 5 concepts had increased from entry to exit values.

Conclusions: Good wound management and effective compression therapy with short-stretch bandages can improve quality of life in patients with venous leg ulceration whether the leg ulcer is healed or not during a given treatment period.

V 32-2

Improvement of the management of venous leg ulcer patients by clinical pathways

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Introduction: A clinical pathway was developed, validated and implemented, with the aim to improve quality of the treatment

process for patients with venous leg ulcers. The assumption is that implementation of this tool will improve clinical efficacy of treatment for this patient category.

Methods: The clinical pathway and selected products* were evidence based and tested by using case ascertainment. Identified patients from two centers were clinically examined to determine general condition, associated factors, wound type, stage, wound evolution, quality of life aspects, efficacy of treatment and costs. (N = 20) Patients were recruited to the clinical evaluation. Clinical examination was performed, depending on wound type, upon initial and at 2 week intervals for a period of 12 weeks. The patients were then followed until ulcer closure. The outcome of the study was compared to the results of a random selected patient group (N = 20) at the centers before implementing the clinical pathway.

Results: After implementation of the clinical pathway and the selected products, a shorter period for ulcer closure was demonstrated (64 % vs. 72 % in 12 weeks), when compared to previous treatment. An improvement of quality of care was noted, as well as cost savings. As an extra the level of knowledge and communication of the clinicians were reported to be improved.

Conclusions: Communal knowledge and effort can be tuned to the interest of patients, institutions and commercial parties. Clinical pathways applied throughout the complete care chain, support improvement of quality of treatment, making effective use of resources and materials.

*Rosidal® sys, Suprasorb® A, Suprasorb® P and Suprasorb® C are products of Lohmann & Rauscher GmbH.

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V 32-3

Management of the peri-wound skin – a review

Management der Wundumgebung – eine Übersicht

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Introduction: Skin care is well developed in the literature, but in wound care often the carers lose sight of the peri-wound skin condition. Additionally the skin surrounding ulcers have typical pathological disorders or have to withstand external extraordinary strains. To take care for the peri-wound skin is an important part of wound management. This lecture intends to give an overview of the relevant symptoms of the skin surrounding ulcers and proposes adequate actions.

Methods: The different symptoms of the peri-wound skin are demonstrated with clinical pictures. Particularly maceration caused by wound exudate will be discussed, also similar but different symptoms. A composition of preventive, covering and nurturing measures, a list of open questions and recommendations follows.

Results: In chronic wound care carers are confronted with maceration, skin irritation, skin dryness or fragile skin. In the epithelialization phase the white gentle epithelium margin in moist wound care should not be taken for harmful maceration. To avoid maceration preventive measures are used: a functional compression bandage, a high absorbent dressing, early dressing change. As a barrier between moisture and epidermis: fluid barrier film, zinc crèmes. Fat ointments or zinc paste are not beneficial. To rebuilt the physiological epidermal barrier mainly use skin care products with lipid and moisture.

Discussion: Chronic wounds need a specific treatment, also the peri-wound skin of ulcers. It needs a specific treatment and the management of the surrounding skin is an important point in wound management. We can distinguish groups of care activities: preventive, covering, nurturing. The existing literature allows a recommendation in general.

Ziel: Hautpflege ist im Bereich der Pflegeliteratur ein gut abgehandeltes Thema. Im Rahmen der Wundversorgung wird die umliegende Haut jedoch oft nicht in das Behandlungsregime mit einbezogen. Hinzu kommt der Umstand, dass die wundumgebende Haut bei chronischen Wunden wie Dekubitus, Ulcus cruris oder diabetisches Fußulkus spezifische pathologische Veränderungen aufweist oder besonderen externen Belastungen ausgesetzt ist. Die Berücksichtigung der Wundumgebung ist ein wichtiger Bestandteil der Wundbehandlung. Der Vortrag beabsichtigt die übersichtliche Darstellung relevanter Erscheinungsbilder hinsichtlich der Wundumgebung und diesbezügliche Maßnahmen.

Methode: Es werden die verschiedenartigen pathologischen Hautphänomene im Zusammenhang mit der Versorgung chronischer Wunden vorgestellt. Insbesondere die Hautmazeration durch Wundexsudat und deren Abgrenzungen wird betrachtet. Es folgt eine Aufstellung präventiver, schützender und pflegender Maßnahmen. Die noch offenen Fragen zur Thematik sowie allgemeine Empfehlungen schließen den Vortrag ab.

Ergebnisse: Neben der Mazeration durch Wundexsudat wird der Wundbehandler mit trockener Haut, Hautirritationen oder fragilen Hautzuständen konfrontiert. Als wünschenswertes Erscheinungsbild darf der schmale Epithelsaum granulierender oder epithelisierender Wunden bei feuchter Wundversorgung nicht mit schädigender Mazeration verwechselt werden. Zur Vermeidung dieser wirkt präventiv: ein suffizienter Kompressionsverband, ein hohes Aufnahmevermögen der Wundaufgabe, ein frühzeitige Verbandwechsel. Eine Hautreizung aufgrund klebender Wundverbände kann vermieden werden durch den Einsatz eines Hautschutzfilmes oder der Meidung klebender Wundaufgaben. Als Barrierschutz zwischen mazerierenden Flüssigkeiten und der Epidermis fungieren z. B. Zinkcremes oder Hautschutzfilme. Fettsalben oder Zinkpasten bergen Nachteile. Zur Wiederherstellung der physiologischen Barrierefunktion der Haut sollten bevorzugt Hautpflegeprodukte mit Lipiden und Feuchthaltefaktoren Verwendung finden.

Diskussion: In gleicher Weise wie die chronische Wunde eine spezifische Behandlung benötigt, ist auch die umliegende Haut auf Grund der pathologischen Gegebenheiten in das Behandlungsregime mit einzubeziehen. Die unterschiedlichen Phänomene bedingen eine differenzierte Betrachtung hinsichtlich der Hautpflegemaßnahmen. Diese lassen sich den Gruppen „Prävention“, „Schutz“ und „Pflege“ zuordnen und erlauben die Vorstellung einer allgemeinen Empfehlung. Offene Fragen bedürfen der weiteren wissenschaftlichen Klärung.

V 32-4

**Gelebter Pflegestandard Nr. 3
– Umgang mit MRSA am Beispiel einer
mit MRSA besiedelten Wunde**

L. Sejdic

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MRSA, ein immer häufiger auftretendes Problem – auch im Alten- und Pflegeheim. Erste Konfrontation schon 1998, seither versuche ich als Pflegedienstleitung zusammen mit meinem Pflegeteam kontinuierlich diesem Problem auch in der Altenpflege professionell zu begegnen. Durch Optimierung in unserem Haus hat man einen gut gelebten Standard dazu gewonnen. Dieser beinhaltet das hauseigene Wundmanagement, regelmäßigen Hygienevisiten, interne und externe Schnittstellen und macht somit die Fachkompetenz unseres Pflegepersonals immer wieder sichtbar. Unsere bisherigen Ergebnisse zur Wundheilung geben uns recht (Ein Beispiel dazu in der Power Point Präsentation auf CD). Mit meiner Präsentation möchte ich deshalb auf dieses brisante Thema aufmerksam machen, unseren Beitrag dazu Anderen zur Verfügung stellen und auf Verdichtung aller Beteiligten zu appellieren.

V 32-5

**Erfolg und Misserfolg bei der Therapie
chronischer Wunden – Fallbeispiele**

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Einleitung: Die Behandlung chronischer Wunden erfordert ein spezielles Wundmanagement und eine langfristige und interdisziplinäre Patientenbetreuung. Die Lokalbehandlung kann nur erfolgreich sein, wenn Risikofaktoren für Wundheilungsstörungen erkannt und therapiert werden.

Patienten: Wir behandeln u. a. Patienten mit postoperativen und posttraumatischen Wundheilungsstörungen, chronischen Wunden nach Strahlentherapie oder Chemotherapie, chronischen Ulzera bei chronisch venöser Insuffizienz oder arterieller Verschlusskrankheit stationär und ambulant im Rahmen unserer Wundsprechstunde.

Methode/Ergebnisse: An Hand von Patientenbeispielen sollen Erfolge durch die Anwendung spezieller Behandlungsmethoden (Madentherapie, Ultraschall, Skin-Stretching) und Verbandstechniken (Vakuumverband, Schaumverband, Hydrokolloidverband) gezeigt werden. Diesen werden Patienten gegenübergestellt, bei denen diese modernen Methoden nicht zum Erfolg geführt haben. Die Risikofaktoren für Wundheilungsstörungen konnten nicht adäquat behandelt werden oder nach der

Krankenhausentlassung wurde das moderne Behandlungskonzept nicht fortgeführt.

Diskussion: Nur wenn Missfolge diskutiert und die Patienten nicht „fallen gelassen“ werden, können Behandlungsstrategien weiter entwickelt werden. Es gibt allerdings Patienten, bei denen trotz modernem Wundmanagement eine Wundheilung oder Befundbesserung nicht erzielt werden können. Dann muss man sich nach interdisziplinärer Fachkonferenz und Ausschöpfung aller Behandlungsmöglichkeiten manchmal doch zu einer Amputation entschließen.

V 32-6

**Anpressdruck und Tragekomfort eines
Kurzzug-Kompressionssystems
(Rosidal[®] sys) und eines Langzug-
Zweilagenerbandsystems
(ProGuide[®]) bei gesunden Probanden
im Vergleich über 7 Tage**

K. Sippel, H. Haase, M. Jünger

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Kompressionsmittel vermitteln ihre Wirkung auf die Hämodynamik der Beinvenen über den Anpressdruck, den sie auf die Haut ausüben. Ziel der Studie war die Überprüfung von Anpressdruck sowie Trageverhalten des Kurzzug-Kompressionssystems (Rosidal[®] sys, Lohmann&Rauscher) über 7 Tage im Vergleich zu dem Langzug-Zweilagenerbandsystem (ProGuide[®], Smith & Nephew) an 31 Probanden.

Methoden: Messung des Anpressdruckes über ELCAT-Druckkissen-Sensoren (Messprinzip nach Blackek, B1-Position, Ruheanpressdruck sitzend, Arbeitsanpressdruck sitzend mit Dorsalexension) an jeweils einem VQ 2000 Multifunktionsgerät mit digitaler Datenauswertung. Die Probanden trugen an einem Bein das Kurzzug-Kompressionssystem an anderen Bein das Langzug-Zweilagenerbandsystem. Zur Vergleichbarkeit beider Systeme wurde der anfängliche Ruheanpressdruck bei Rosidal[®] sys auf max. 40 mmHg (niedriger Anpressdruck = "low pressure bandaging") mit Hilfe des Druckmessgeräts Kikuhime[®] eingestellt, bei ProGuide[®] mit Hilfe des aufgedruckten Dehnungsindikators. Ausgewertet wurden neben dem Anpressdruck auch die Verträglichkeit mittels Fragebogen und klinischer Inspektion.

Ergebnisse: Der Ruheanpressdruck von Rosidal[®] sys fiel im zeitlichen Verlauf ab (32,3 ± 9,4 mmHg auf 22 ± 6,5 mmHg). Der Arbeitsanpressdruck blieb im therapeutischen Bereich (56,5 ± 15,4 mmHg auf 42,5 ± 12,4 mmHg). Der Quotient Arbeitsanpressdruck/Ruheanpressdruck stieg von 1,8 auf 2,0 an, d. h. der Einfluß des Arbeitsanpressdruckes nahm im Vergleich zum Ruheanpressdruck zu. Unter Anwendung von ProGuide[®] verringerte sich der Ruheanpressdruck nur geringfügig (37,2 ± 11,1 mmHg auf 35,1 ± 13,1 mmHg ab), der Quotient blieb mit 2,10 zu 2,05 weitgehend gleich. Der Ruheanpressdruckabfall bei Rosidal[®] sys wurde von den Probanden als angenehm empfunden. Der

vergleichsweise hohe Ruheanpressdruck bei ProGuide® führte bei einigen Probanden zu unerwünschten Ereignissen insbesondere zu Schmerzen und Hautirritation. Rosidal®sys zeigte beim Tragekomfort (z. B. bei den Parametern Einschnürungen, Engegefühl, Schmerzen, Bewegungsfreiheit) weniger Beschwerden als ProGuide®.

Folgerung: Das Kurzzug-Kompressionssystem Rosidal®sys sorgt für einen gut verträglichen Ruheanpressdruck. Selbst bei der hier bewusst mit niedrigem Ruheanpressdruck durchge-

führter Kompression wurde über 7 Tage ein therapeutisch ausreichender Arbeitsanpressdruck mit gewünschtem Massageeffekt ("natural dynamic compression") erzielt. Rosidal®sys zeichnet sich in dieser Studie durch eine höhere Compliance und einen besseren Tragekomfort im Vergleich zu ProGuide® aus.

V 33

Dressings

Verbände

V 33-1

Randomized controlled study of silver dressing effects on partial-thickness burn outcomes

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Introduction: Silver sulfadiazine 1 % cream (SSD)* remains the gold standard for managing partial-thickness burn wounds. A dressing (AQ)** comprised of Hydrofiber®*** technology and 1.2 % ionic silver sustains antimicrobial activity in the dressing and at the wound interface. This research compared cost effectiveness, healing, pain and burn care-related resource use for patients with partial-thickness burns managed with protocols including SSD or AQ dressings.

Methods: A Phase III, prospective, randomized, multi-center study, involving eight United States centers, randomly assigned 82 subjects with partial-thickness burns to management for up to 21 days with a regimen including either SSD changed at least once daily according to package insert instructions (n = 40) or AQ changed at the clinician's discretion (n = 42). Assessment visits in the clinic were required every 2 to 3 days.

Results: The Incremental Cost-effectiveness Ratio was -\$1019.21 favoring AQ. It cost \$ 559 less to heal each burn in the AQ group than to heal each burn in the SSD group. During 21 days, 73.8 % of subjects in the AQ group healed and 60.0 % healed in the SSD group (p = 0.22). Patients managed with the AQ regimen reported significantly less pain (p = 0.002) and anxiety (p = 0.009) during dressing changes, with fewer procedural opiate medications required (p = 0.022) and fewer overall types of procedural medications (p = 0.018). AQ-dressed burns required fewer dressing changes (p < 0.001), requiring less nursing time per dressing change (p < 0.001) than the SSD group. Safety results were similar for both groups.

Conclusions: A regimen of burn care using AQ was cost effective and was associated with less pain during dressing changes in partial-thickness burn patients with fewer dressing changes, each consuming less nursing time, compared with SSD. Based on these results a protocol of care using AQ is an effective solution for management of partial-thickness burns.

Product Notations: * Silvadene® Cream 1%, Monarch Pharmaceuticals, Bristol, TN **AQUACEL® Ag silver dressing with Hydrofiber® technology, ConvaTec, a Bristol-Myers Squibb company. AQUACEL and Hydrofiber are registered trademarks of E. R. Squibb & Sons, L. L.C.

V 33-2

How is research evidence used in advertisements for wound care products?

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Advertisements for pharmaceutical products are found in many of the journals read by health care professionals and such advertisements cite research to support their claims to varying degrees. The International Committee of Medical Journal Editors' (ICMJE) requirements [1] outlines appropriate practice with regard pharmaceutical advertising, for example by stipulating that the "juxtaposition of editorial and advertising material on the same products or subjects should be avoided." We sought to examine the use of research in wound care product advertising, and the extent to which ICMJE guidance was followed.

Methods: We identified all advertisements for wound care products in 2002 and 2003 printed volumes of one British and one U.S. wound care journal. Relevant data were extracted from each advertisement including: product type, product claims made, the number and type of cited references, and placement of the article vis à vis relevant journal content.

Results: We identified 603 individual advertisements from 2 years of 2 wound care journals. This number reflected 217 different adverts, of which 195 (90 %) made one or more product claim. Only 70 (36 %) of advertisements cited any data to support claims made: 26 (37 %) referenced unpublished company data only, 4 (6 %) referenced conference abstracts only and 37 (53 %) referenced at least one journal article. In total, only 15 (8 %) of advertisements making claims referred to a published randomised controlled trial. There were 85 cases (14 %) where individual advertisements were placed near to articles, including editorials, about the product itself or a related product.

Conclusions: A wide range of claims regarding wound care products are made in advertisements, however, good quality research is rarely appropriately used to support claims and advertisements are often placed in proximity to relevant editorial material.

References

1. **International Committee of Medical Journal Editors. Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication, Updated October 2004.**
<http://www.icmje.org/index.html#publish>

V 33-4

Randomized controlled study of diabetic foot ulcers dressed with hydrofiber® containing ionic silver or calcium alginate dressingsE. Jude¹, J. Apelqvist², M. Spraul³, J. Martini⁴¹Department of Diabetic Medicine, Ashton-Under-Lyne, United Kingdom²Dept. of Endocrinology, Malmo University Hospital, Malmo, Sweden,³Mathias Hospital, Rheine, Germany,⁴Hopital Diabetologie & Endocrinologie, Cedex, France

Introduction: Diabetic foot ulcers (DFU) risk infection and impaired healing, placing patients at risk of lower extremity amputation. Debridement and dressings are required for DFU care. Hydrofiber® dressings retain more absorbed wound fluid and bacteria than alginate dressings and with ionic silver, persistently kill local pathogens. A prospective, multi-center study compared clinical efficacy and safety of AQUACEL® Hydrofiber® dressings containing ionic silver (AQ*) to those of calcium alginate (CA**) dressings used within regimens to manage out-patients with Type 1 or 2 diabetes and neuropathic or neuro-ischaemic Wagner Grade 1 or 2 DFU.

Methods: Patients were randomly assigned to similar protocols including off-loading, AQ or CA primary dressings and secondary foam dressings for 8 weeks or until healing. Assignment was stratified by baseline antibiotic use (Antibiotic) or non-use for the study ulcer, reflecting baseline clinical ulcer-related infection or its risk. Primary efficacy measures were healing outcomes. Safety was measured as adverse events.

Results: AQ and CA groups were comparable at baseline. Both groups improved on all ulcer healing outcomes. The time to healing was 53 days for AQ ulcers and 58 days for CA ulcers. AQ ulcers reduced in depth nearly twice as much as CA ulcers did (2.5 mm versus 1.3 mm; $p = 0.04$). AQ subjects also experienced more overall ulcer improvement and less deterioration ($p = 0.06$), accentuated in the Antibiotic subset ($p = 0.02$). The safety profiles of both groups were similar.

Conclusions: A regimen including AQ significantly outperformed one using CA on ulcer depth reduction. This study reports the first significant clinical effects of a primary wound dressing containing silver on DFU healing.

Product Notations: *AQ, AQUACEL® Hydrofiber® dressing with 1.2% ionic silver (AQUACEL and Hydrofiber are registered trademarks of E. R. Squibb & Sons, L.L.C., Princeton, NJ, USA) **CA, Algosterile™ calcium alginate dressing (Algosterile is a trademark of Les Laboratoires Brothier, S.A., Paris-Nanterre, France); DFU, Diabetic foot ulcers;

V 33-5

The selection of honey and development of dressing materials and protocols to get best healing of problem wounds**P. Molan¹, J. Betts²**¹University of Waikato, Hamilton, New Zealand,²Waikato District Health Board, Hamilton, New Zealand

Introduction: Honey has been in use as a wound dressing for more than four thousand years, but in more recent times the ancient wisdom has been forgotten, of using selected honeys and formulations to keep the honey in place on the wound. Laboratory research over the past decade has shown that manuka (*Leptospermum scoparium*) honey has an outstanding broad-spectrum antibacterial activity. Clinical trials of this honey on infected or heavily colonised wounds not responding to other treatments revealed some practical challenges in keeping the honey on the wounds, especially on some problem wounds that were difficult to manage with any form of dressing.

Methods: By close collaboration between scientist and clinician it has been possible to deduce what has been wrong with dressing procedures being used, and to take a scientific approach devise dressing materials and protocols to improve the procedures and get better results.

Results: It has been found that honey does not easily soak into cellulose fibre dressings, so is often squeezed out from under these. If the dressings are impregnated with the honey, the honey can still be lost from the wound by it being flushed away by wound exudate. This loss can be decreased by the use of alginate fibre dressings, which convert to a gel when they absorb exudate. Gelling honey with sodium alginate gives a rubbery material which will absorb large volumes of exudate by swelling and softening but will still keep honey on highly exudative wounds. Sinuses could be healed rapidly by filling them with honey, via a catheter where the opening was narrow. Deep wounds were best treated by packing with honey-impregnated alginate fibre dressing. With the honey in a primary dressing keeping it on the wound, any form of secondary dressing could be used. With occlusive dressings the osmotic action of honey prevented maceration of skin around wounds.

Conclusions: The two-way communication, of ideas from laboratory work to the clinician, and of practical problems from the clinician to the scientist, has led to a very successful means of treating wounds not responding to any other modern treatments.

V 33-6

Randomized multi-center study comparing open surgical wound outcomes using silver or iodine dressings**T. Dugre¹, F. Jurczak², T. Offori³, B. Turnbull⁴, D. Hollander⁵**¹Centre Hospitalier Camille Guerin, Chatellerault, France,²Polyclinique de l'Océan, Saint Nazaire, France,³Barnsley District General Hospital, Barnsley, United Kingdom,⁴CareStat, Inc., Newton, United States of America,⁵Technical University Aachen, Aachen, Germany

Managing open surgical and traumatic wounds requires support of wound healing, exudate management and prevention/management of infection. Commonly used povidone iodine-impregnated gauze (PG)* has limitations, including incomplete exudate handling, painful, traumatic dressing changes and wound adherence. Advanced materials such as Hydrofiber[®] provide a non-adherent wound contact layer and good exudate absorption. Ionic silver incorporated into the Hydrofiber dressing (AQS)** adds antimicrobial properties. This study compared wound pain, comfort and other wound-associated parameters in open wounds managed with AQS or PG. Patients with surgical or traumatic wounds healing by secondary intent were randomly assigned to a regimen including AQS or PG dressings applied for two weeks. Pain, comfort, healing, ease of removal, and exudate management were assessed weekly. At final study evaluation, the AQS regimen was associated with less overall pain ($p < 0.001$) and greater comfort while the dressing was in place and during dressing changes compared with PG ($p < 0.001$). AQS managed exudate better than PG ($p < 0.001$) and was associated with easier dressing removal ($p < 0.001$) and less wound-bed trauma ($p = 0.001$) on dressing removal. Safety was similar with both treatment regimens. Protocols of care involving AQS silver-containing Hydrofiber[®] dressing offer an important option in the management of open surgical wounds.

Product Notations: * Povidone iodine 10% solution in gauze dressings.

**AQUACEL[®] Ag with Hydrofiber[®], ConvaTec, Princeton, NJ, USA. AQUACEL and Hydrofiber are registered trademarks of E. R. Squibb & Sons, L. L. C.

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