Correlazione Tessuto-Essudato

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EXUDATE

«Liquid Biopsy»

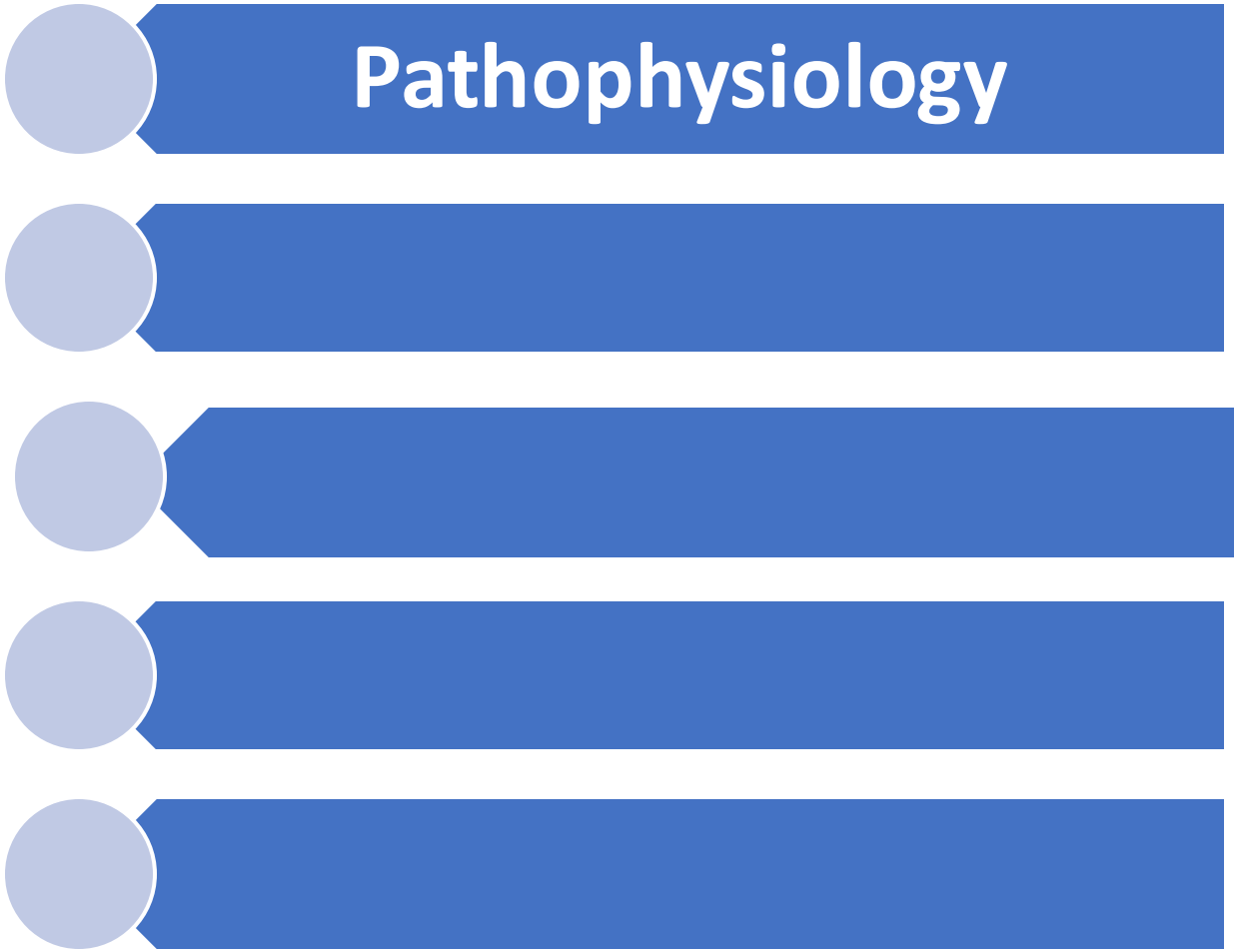
- ✓ Reflects the metabolic condition of the wound
- ✓ Containes soluble factors which may influence cellular functions
- ✓ Useful in identifying factors involved in skin repair or its failure

Moor,A.N.;Vachon,D.J.;Gould,L.J.Proteolyticactivityinwound fluids and tissues derived from chronic venous leg ulcers. *Wound Repair Regen.* **2009**, *17* (6), 832–839.

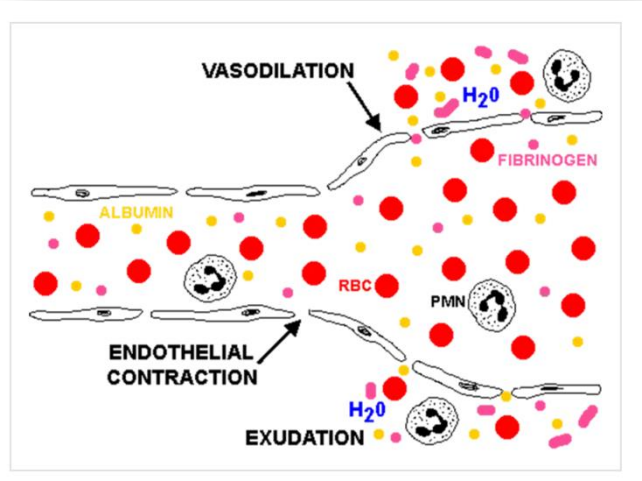
Chronic Wound Exudate

- Pathophysiology
- Collection and Assessment
- Composition
- Consequences
- Wound State Biomarker

Chronic Wound Exudate



Wound Exudate Pathophysiology

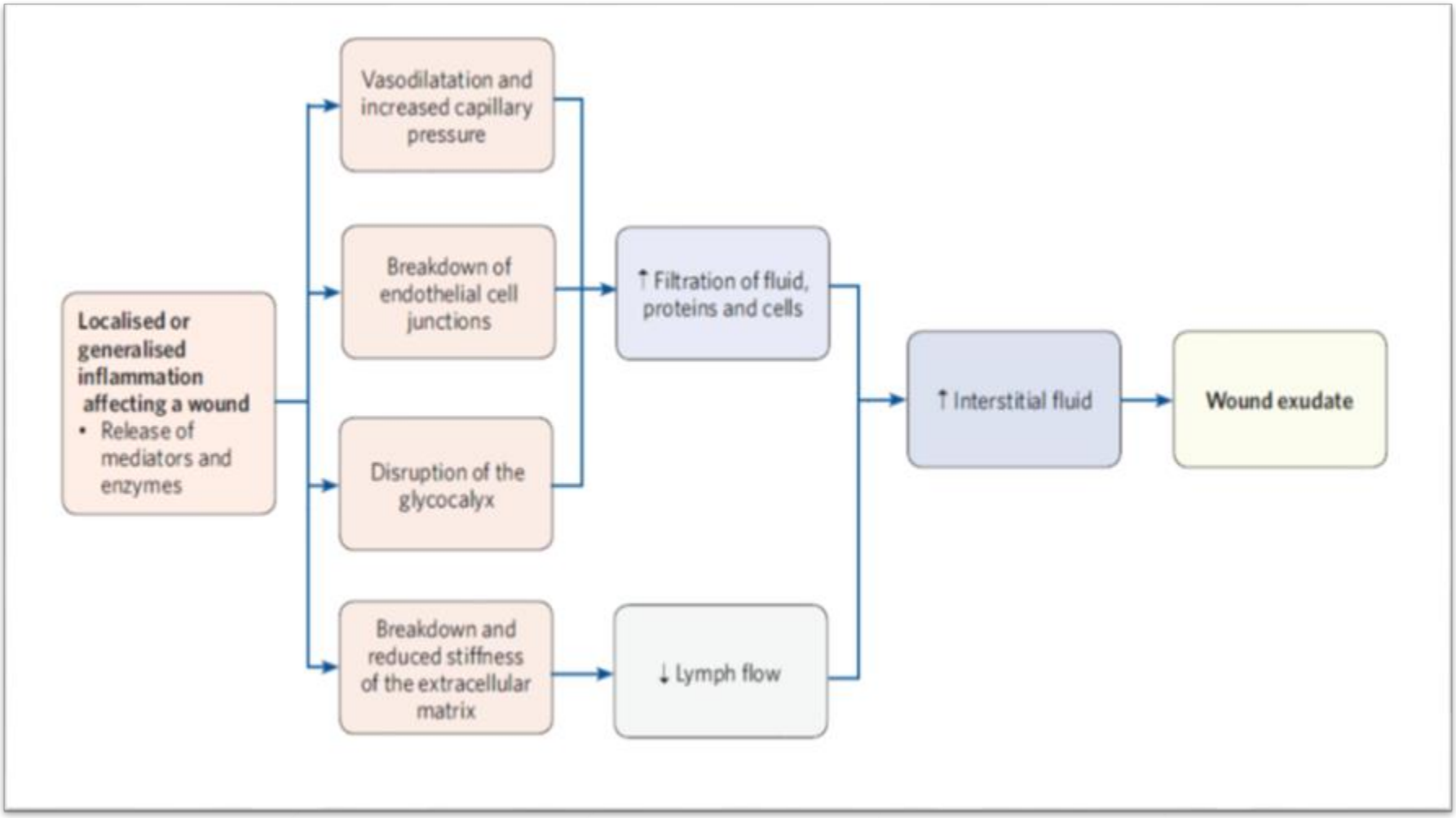


Injury/Inflammation

Increased permeability of the blood vessel

Leakage or Secretion of fluid from vessels into the tissue

The release of exudate is an essential step in the process of wound healing



Role of inflammation in exudate production (Scallan et al, 2010)

DEFINITIONS

- Exudate

- Fluid that is secreted or leaked from the blood vessels in the adjoining tissue as a result of injury or inflammation
- >> Protein and cells
- >> High amount of LDH

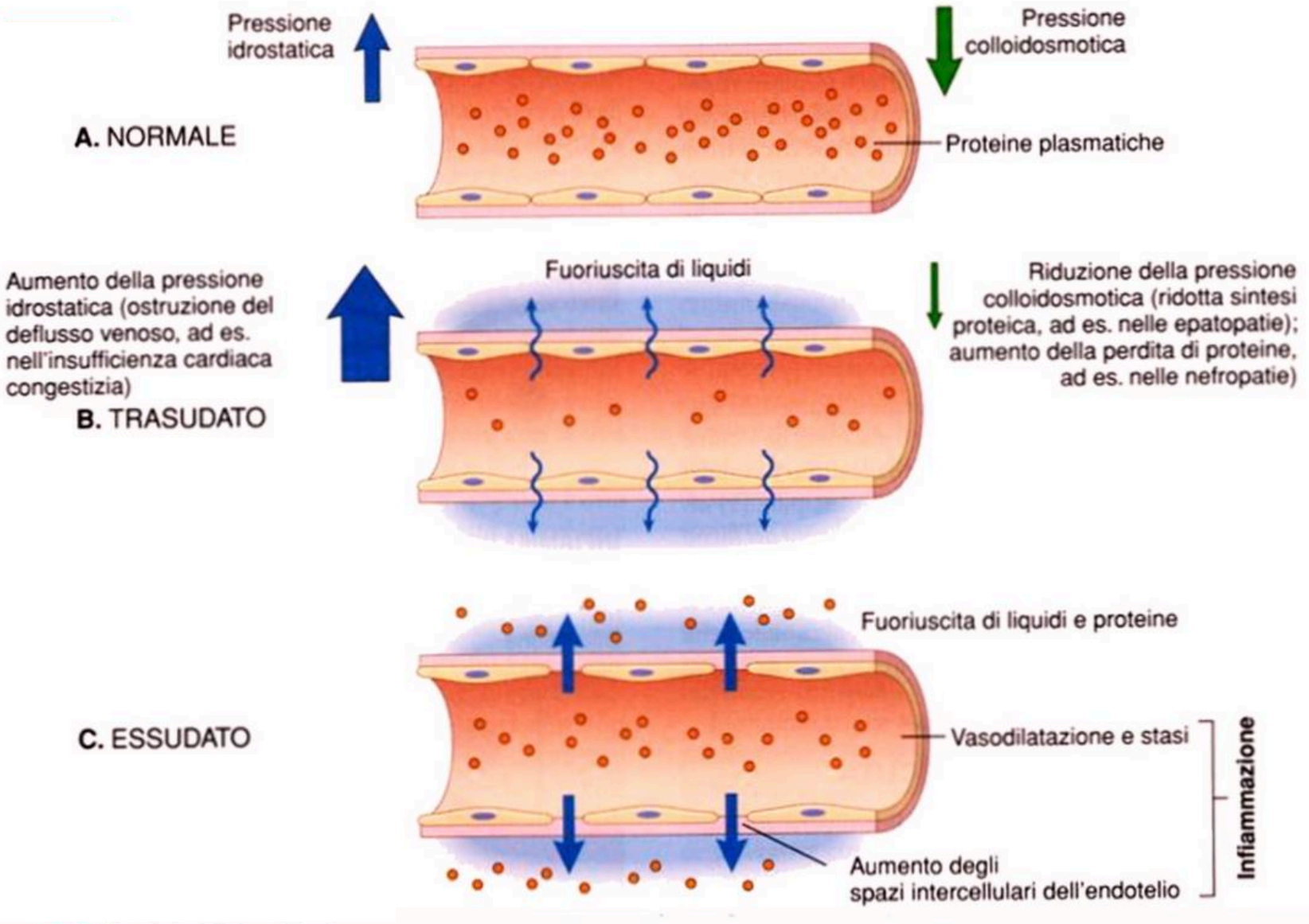
- Transudate

- Ultrafiltered fluid secreted or leaked from the circulatory system due to underlying medical conditions:

  1 Increased capillary hydrostatic pressure, e.g. due to venous stasis

  2 Decreased capillary oncotic pressure, e.g. due to low serum protein from malnutrition

- << Protein and cells


Pressione idrostatica
Pressione colloidosmotica
A. NORMALE
Proteine plasmatiche
Aumento della pressione idrostatica (ostruzione del deflusso venoso, ad es. nell'insufficienza cardiaca congestizia)
Fuoriuscita di liquidi
Riduzione della pressione colloidosmotica (ridotta sintesi proteica, ad es. nelle epatopatie); aumento della perdita di proteine, ad es. nelle nefropatie)
B. TRASUDATO
Fuoriuscita di liquidi e proteine
C. ESSUDATO
Vasodilatazione e stasi
Aumento degli spazi intercellulari dell'endotelio
Infiammazione

Understanding that wound drainage can comprise exudate and transudate can help clinicians determine reasons for any increase in wound drainage and so identify and implement appropriate management

Chronic Wound Exudate

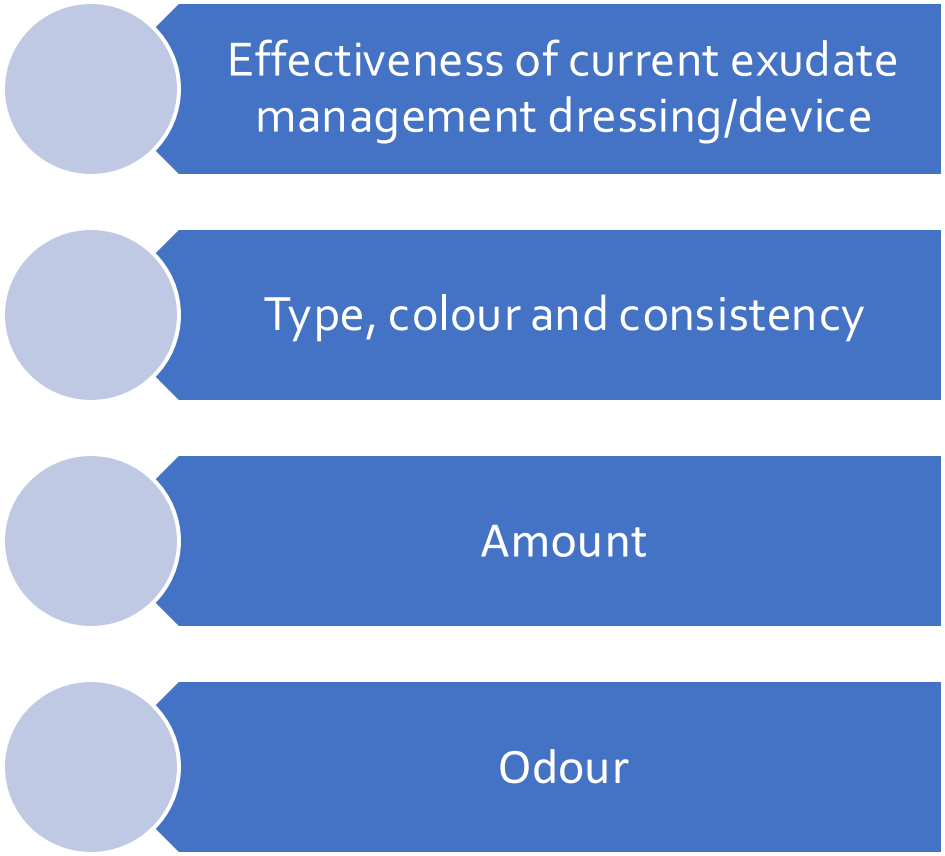
Wound Exudate Collection and Assessment

Published exudate production rates		
Wound type	**Method of exudate production measurement**	**Rate of exudate production (g/cm^2/24 hours)**
Leg ulcers	Dressing weight (Dealey et al, 2006)	**0.17–0.21**
	Dressing weight (Thomas et al, 1996)	**0.43–0.63**
Various	Negative pressure wound therapy canister collection (Dealey et al, 2006)	**1.3***
Granulating wounds	Vapour pressure gradient (evaporative water loss) (Lamke et al, 1977)	**0.51**
Skin donor sites	Vapour pressure gradient (evaporative water loss) (Lamke et al, 1977)	**0.42**
Partial-thickness burns	Evaporimeter (Ferguson et al, 1991)	**0.42-0.86**
	Vapour pressure gradient (evaporative water loss) (Lamke et al, 1977)	**0.43**
Full-thickness burns	Vapour pressure gradient (evaporative water loss) (Lamke et al, 1977)	**0.34**

Exudate collection device

- Exudate collection by using negative pressure therapy without interface filler
- Timing : 2 hours for each patient

Wound Exudate Assessement



Wound Exudate Assessment: TYPES

Type of exudate	Consistency & Colour	Medical implication
Serous exudate	Watery, thin, translucent, clear, straw-colored	Clear fluid from the wound or the Normal wound exudate
Fibrinous exudate	Thin, presence of strands of fibrin, cloudy	Normal wound healing exudate
Serosanguinous exudate	Clear, pink-colored, thin, watery	Normal wound exudate
Sanguineous exudate	Red-colored, thin, watery	Exudate from a wounded, bleeding blood vessel
Seropurulent	Yellow, tan, opaque, cloudy, thick	Infectious wound
Purulent exudate or pus exudate	Thick, Green, Grey, or yellow drainage from the wound	Bacterial infection of the wound with heavy inflammation
Hemopurulent or bloody exudate	Red, dark, blood-stained, thick, highly viscous	Inflammatory cells with a bacterial infection
Hemorrhagic	Thick red-colored	Indicative of fragile blood capillaries/ trauma/ Infection

Wound Exudate Assessment: AMOUNT

Clinical methods of assessment of wound exudate production				
Method	**Details**			
Wound Exudate Score (Falanga, 2000)*	**Wound exudate score**	**Extent of control**	**Exudate amount**	
	1	Full	None/minimal	No absorptive dressings required. If clinically, feasible dressing could stay on for up to a week
	2	Partial	Moderate amount	Dressing changes required every 2–3 days
	3	Uncontrolled	Very exudative wound	Absorptive dressing changes required at least daily

Exudate amount element of Bates- Jensen Wound Assessment Tool (Bates-Jensen, 2001)	**Exudate amount**	**Indicators**
	None	Wound tissues dry
	Scant	Wound tissues moist; no measurable exudate
	Small	Wound tissues wet; moisture evenly distributed in wound; drainage involves ≤25% dressing
	Moderate	Wound tissues saturated; drainage may or may not be evenly distributed in wound; drainage involves >25% to ≤75% dressing
	Large	Wound tissues bathed in fluid; drainage freely expressed; may or may not be evenly distributed in wound; drainage involves >75% of dressing

Clinical methods of assessment of wound exudate production

Method	Details	
Dressing: exudate interaction (WUWHS, 2007)	**Status**	**Indicators**
	Dry	Wound bed is dry; there is no visible moisture and the primary dressing is unmarked; dressing may be adherent to wound
	Moist	Small amounts of fluid are visible when the dressing is removed; the primary dressing may be lightly marked; dressing change frequency is appropriate for dressing type
	Wet	Small amounts of fluid are visible when the dressing is removed; the primary dressing is extensively marked, but strikethrough is not occurring; dressing change frequency is appropriate for dressing type
	Saturated	Primary dressing is wet and strikethrough is occurring; dressing change is required more frequently than usual for the dressing type; periwound skin may be macerated
	Leaking	Dressings are saturated and exudate is escaping from primary and secondary dressings onto clothes or beyond; dressing change is required much more frequently than usual for dressing type
Others (Gray, 2005; Fletcher, 2010)	■ Low, medium, high ■ None, scant, moderate, high ■ None, low, moderate, high, very high ■ Dry/none; slight (weekly dressing change); moderate (2–3 times weekly dressing change; copious (daily or more frequent changes) ■ +; ++; +++	

Assessment of odour

Odour characteristic	Approaches to assessment
Strength	■ When the odour is noticeable – e.g. on proximity to the patient, before dressing/ device removal, after dressing/device removal and whether the odour remains once the dressing/device has been removed for a short while; an example of this approach has been formalised in the TELER system (Table 9) ■ Absent, faint, moderate or strong (Nix, 2016) ■ Visual analogue scale, e.g. 0 = no smell to 10 = worst smell imaginable (Gethin et al, 2014)
Nature	■ Malodourous, pungent, foul ■ A smell of ammonia may indicate infection with Proteus species of bacteria (Bates-Jensen et al, 2012)
Impact	■ Psychological and social impact on the patient and carers
Interventions	■ Measures currently in place to deal with odour – e.g. topical treatments to the wound and environmental approaches

The severity and nature of the wound determine the composition and the amount of the exudate released

The amount of exudate produced by a wound is dependent on:

- Wound aetiology – some wound types are more prone to high or low exudate levels

- Wound healing phase – the amount of exudate produced by a wound usually diminishes as healing progresses (Wounds UK, 2013)

- Wound size, depth and position – larger and deeper wounds may produce higher levels of exudate, as can wounds in dependent parts of the body, e.g. the lower leg (Dowsett, 2012)

- Comorbidities, complications and other factors – there are many other reasons for increased or decreased exudate production

Exudate Causes

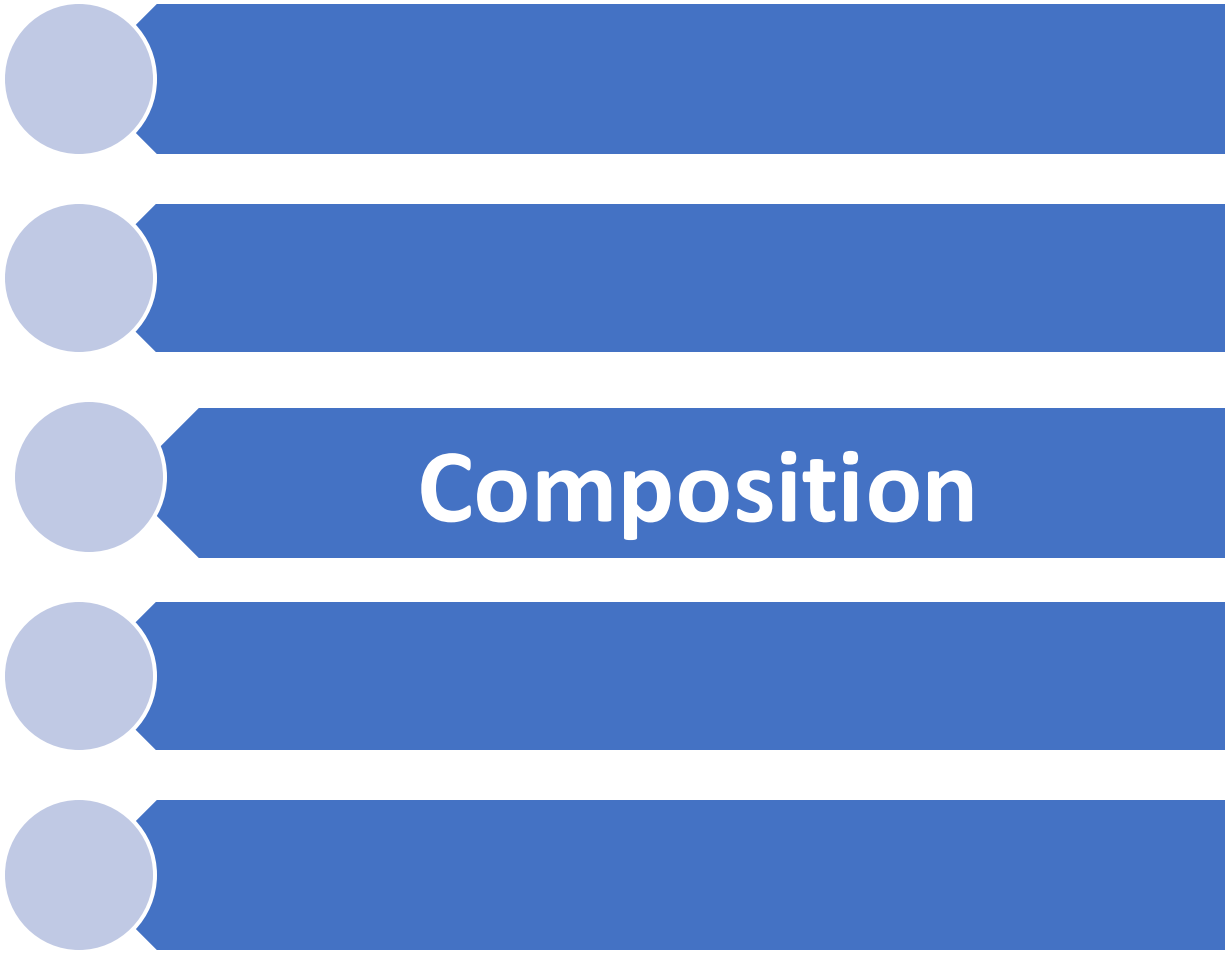
Local

- Inflammation
- Infection
- Necrosis
- Allergies

Systemic

- Venous Stasis
- Lymphatic Stasis
- Systemic diseases

Chronic Wound Exudate



Exudate is an essential step in the process of wound healing

- Providing a moist wound environment
- Enabling the diffusion of immune mediators and growth factors across the wound bed
- Acting as a medium for the migration of tissue-repairing cells across the wound bed
- Supplying essential nutrients for cell metabolism
- Promoting the separation of dead or damaged tissue (autolysis) (Cutting, 2003; WUWHS, 2007).

Wounds with a moist environment heal more quickly than those that dry out and form scab (Winter, 1962). In fact, moist wounds heal 2–3 times faster than dry wounds (Swezey, 2014).

Acute Vs Chronic Environment

Healing wounds

High mitogenic potential

Rapid cellular migration

Balanced inflammatory cytokines

Low proteases

Cells responsive to growth factors

Chronic ulcers

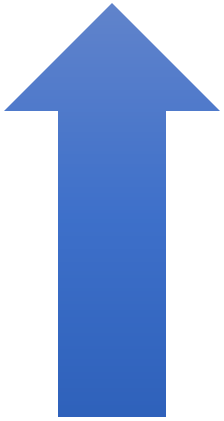
Low mitogenic and migratory potential

High inflammatory cytokines

High proteases

Senescent cells

unresponsive to growth factors



Chronic Wound Exudate composition

Plasma components

Inflammatory Cells

Proteins (from the inflammatory response)

Bacteria

Components of Biofilm matrix

High viscosity

High Protein > 30 g/L

Exudate in chronic wounds

- ↑ level of Tumor Necrosis Factor alpha (TNF-α).

  Tarnuzzer R Wound Rep Regen 1996; 4:321-25

- ↓ level of IL-1, IL-6 e TNF-α in healing wounds

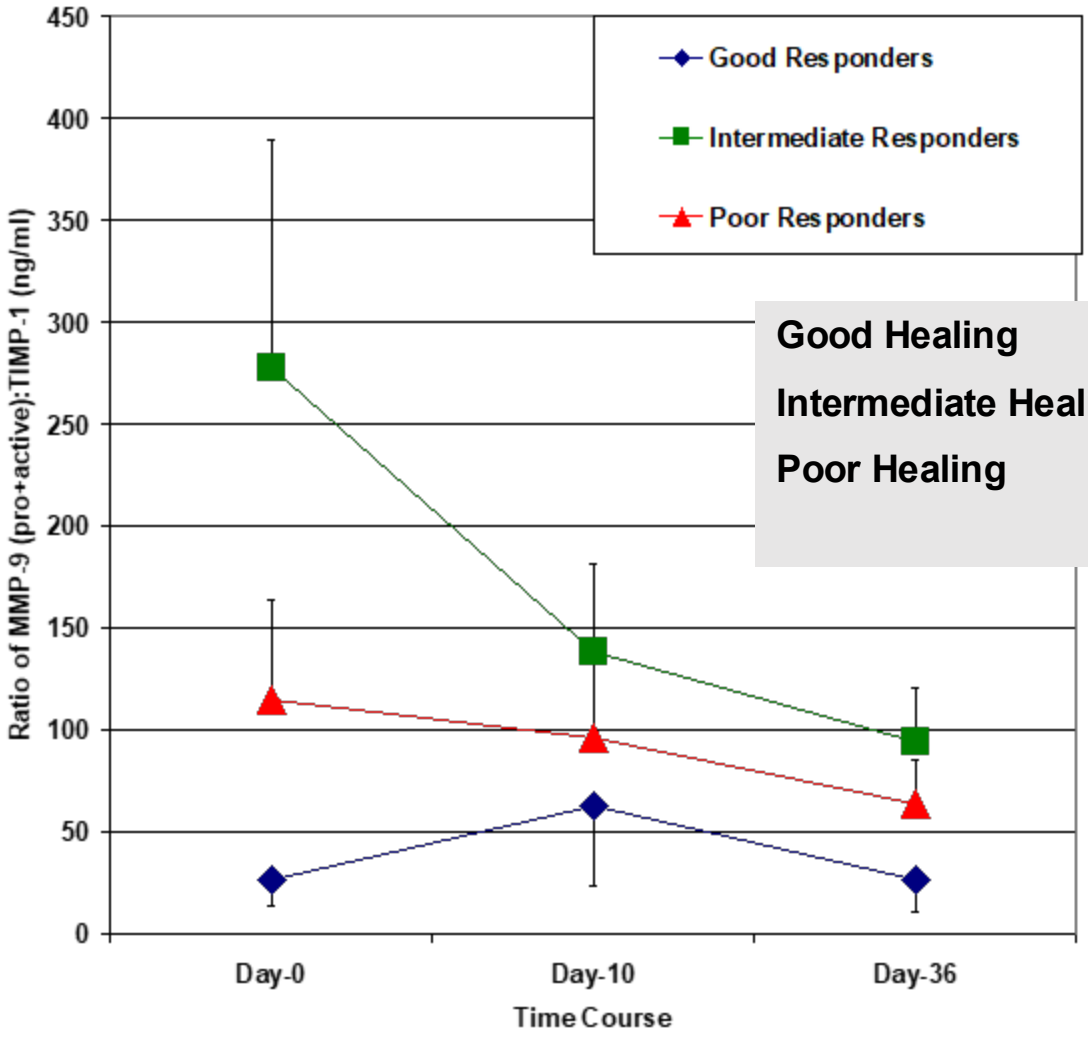
  Wallace HJ, J Invest Dermatol 1998;110:292-6

- ↑ level of MMPs

  Agren M, J Invest Dermatol 1999

- Prolonged inflammatory phase

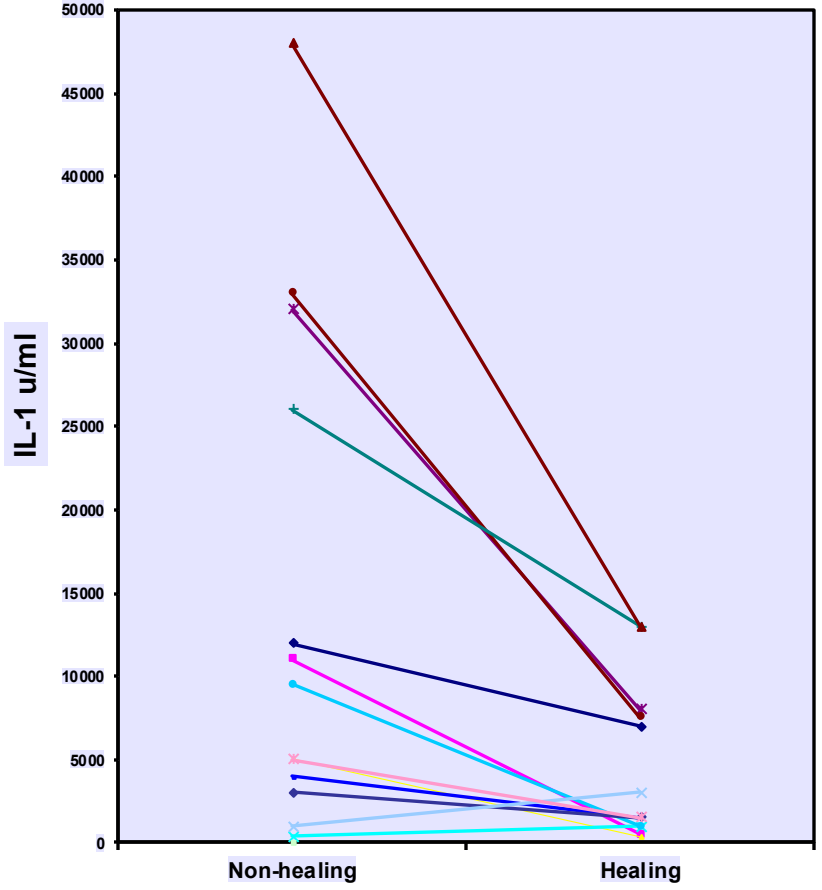
Healing of Pressure Ulcers is Predicted by Protease Activity in Wound Fluids

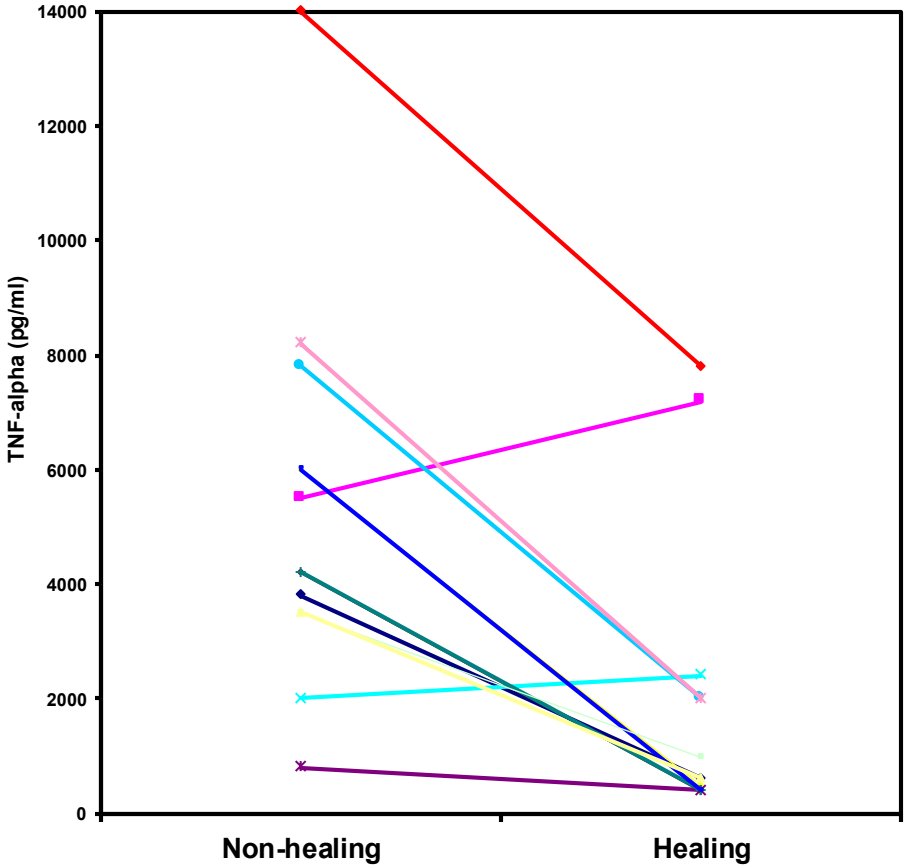


Good Healing	**>95% area healed; n=12**
Intermediate Healing	**<95% but >65% area healed; n=36**
Poor Healing	**<65% area healed; n=8**

Ladwig, Robson, Liu, Kuhn, Muir, Schultz. Wound Repair Reg 10:26-37, 2002

High Levels Of IL-1 and TNFα In Fluids From Chronic Venous Ulcers Decrease With Healing





Trengove, Stacey, Macauley, Bennett, Gibson, Burslem, Murphey, Schultz. Wound Rep Reg 7:442-452, 1999

international wound journal

International Wound Journal ISSN 1742-4801

ORIGINAL ARTICLE

Acute and chronic wound fluids influence keratinocyte function differently

Oliver C Thamm[1,2,†], Paola Koenen[1,2,†], Nicola Bader[1,2], Alina Schneider[1,2], Sebastian Wutzler[2,3], Edmund AM Neugebauer[2] & Timo A Spanholtz[2,4]

1 Clinic of Plastic and Reconstructive Surgery, Handsurgery, Burn Care Center, University of Witten/Herdecke, Cologne-Merheim Medical Center, Cologne, Germany
2 Institute for Research in Operative Medicine, University of Witten/Herdecke, Cologne, Germany
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4 Department of Handsurgery, Plastic and Aesthetic Surgery, Ludwig-Maximilians-University, Munich, Germany

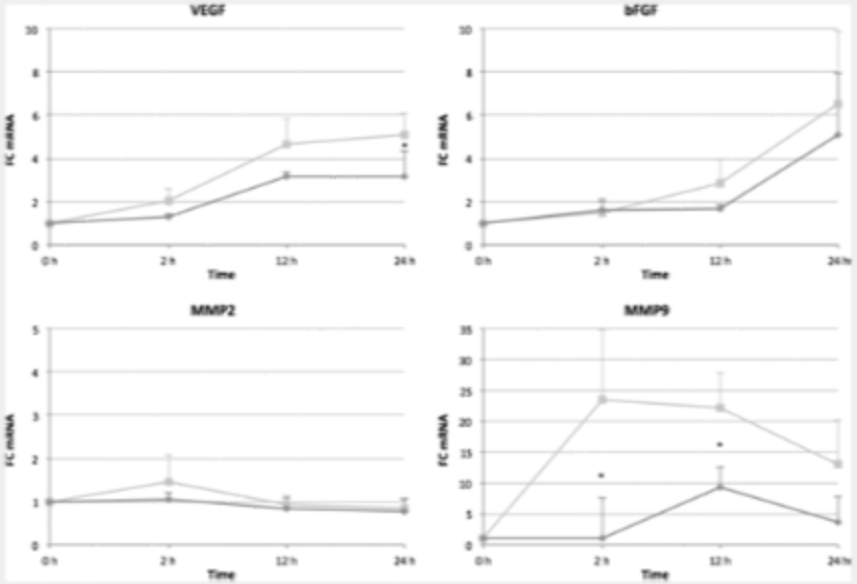
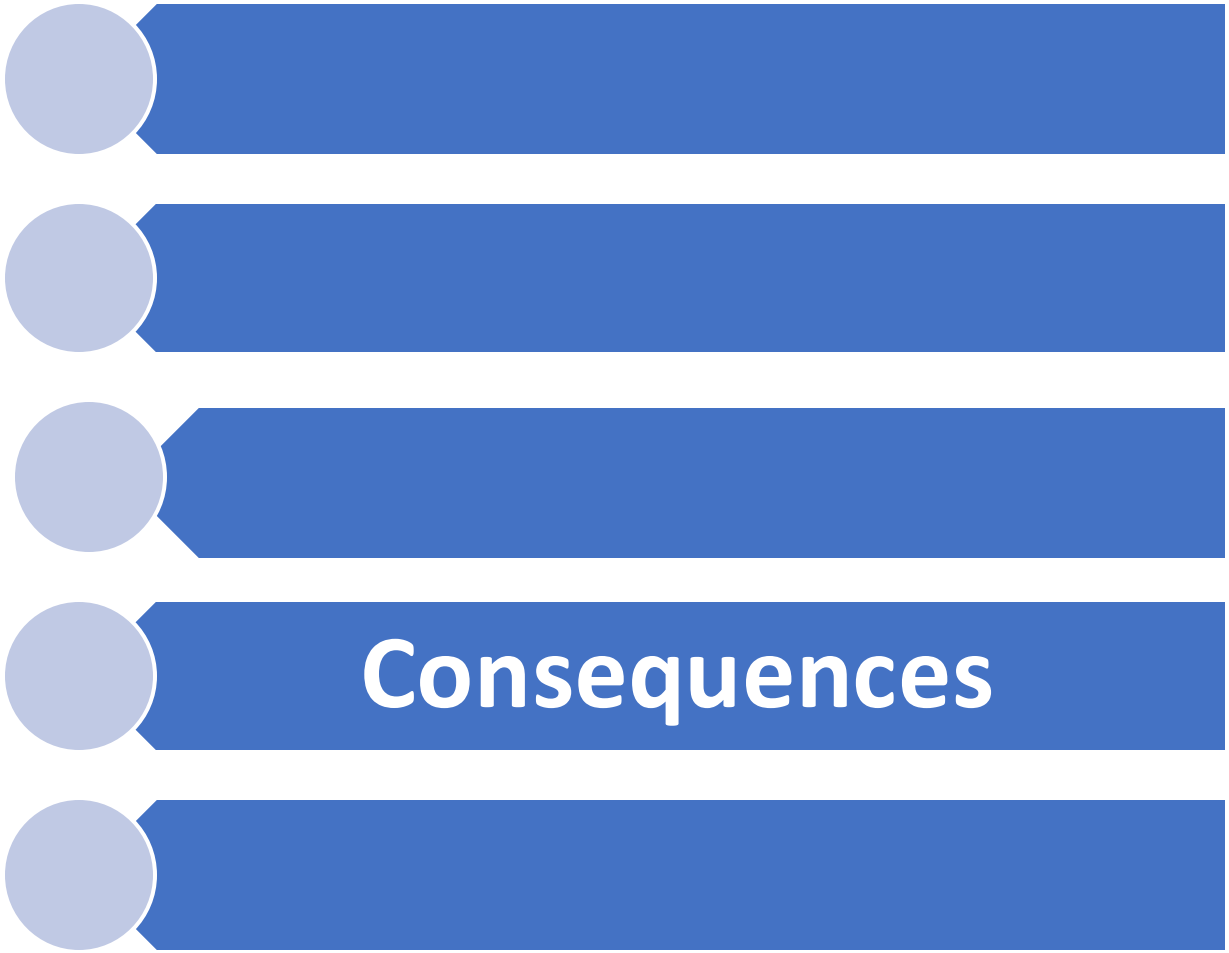
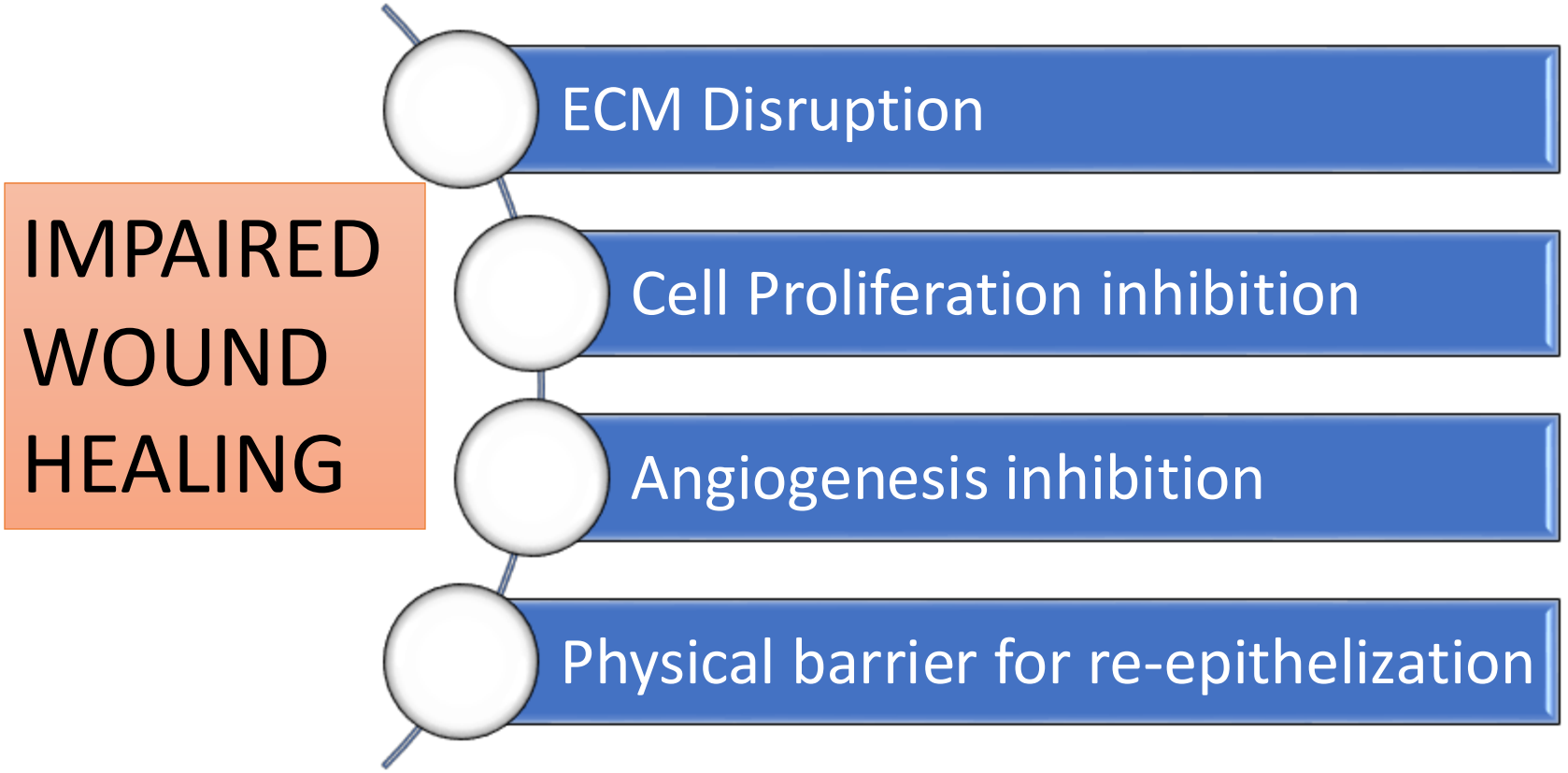


Figure 3 Gene expression changes by acute wound fluid (AWF) and chronic wound fluid (CWF). Keratinocytes were treated with 2% AWF (dark grey lines) or 2% CWF (light black lines) for 2, 12 and 24 hours or left untreated. Fold-changes of gene expression were analysed by qRT-PCR and plotted as mean ± SD. Asterisks indicate significant differences in gene expression between AWF and CWF with $P \leq 0.05$ ($n = 3$).

Chronic Wound Exudate



Chronic Wound Exudate Consequences



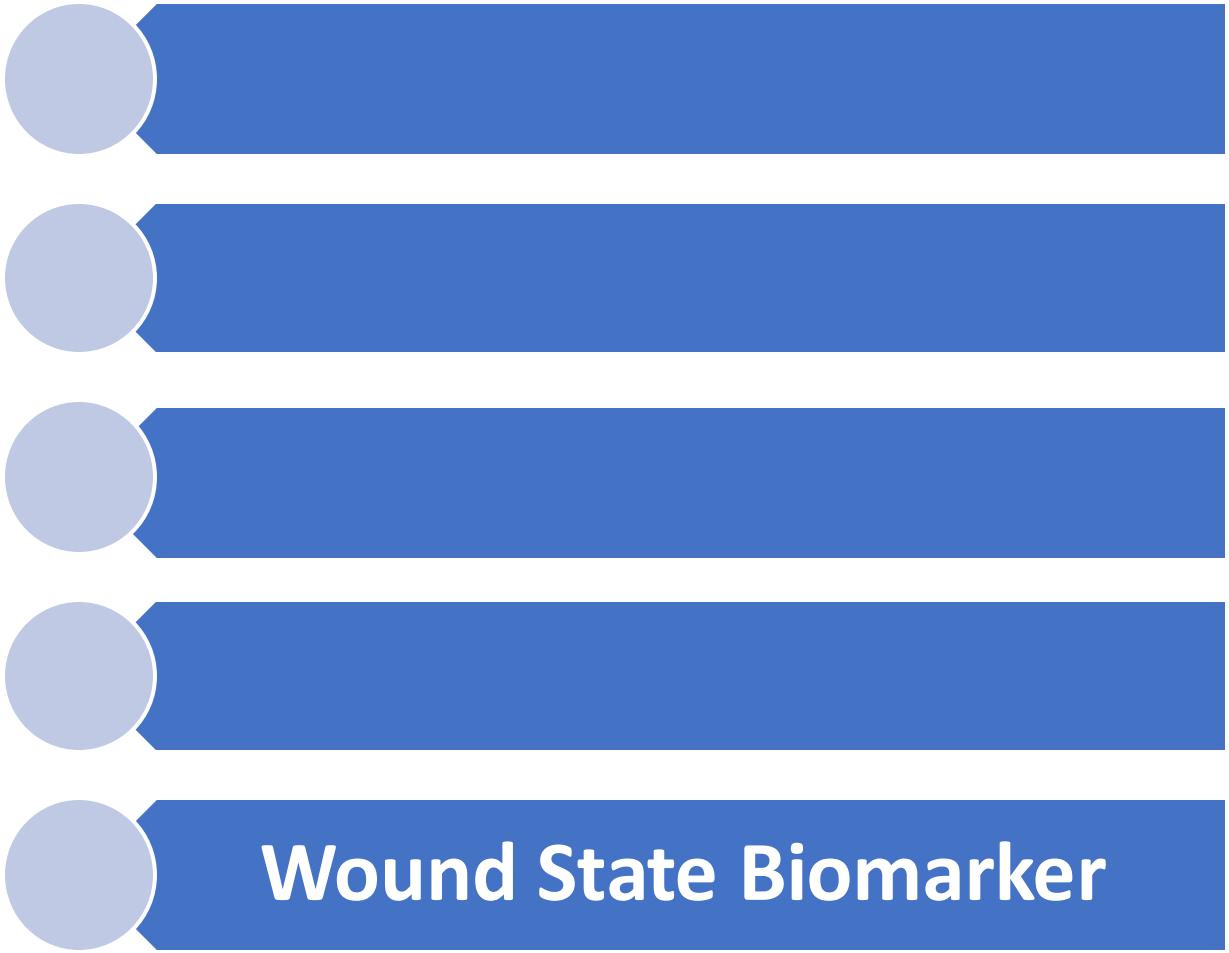
Exudate complications

- Colonization
- Proteins and electrolites decrease
- Maceration
- Impair wound healing/wound expansion
- Discomfort/pain

White Maceration

Red Maceration

Chronic Wound Exudate



Wound Repair and Regeneration

PERSPECTIVE ARTICLE

Chronic wound fluid—thinking outside the box

Alan David Widgerow, MBBCh, FCS (Plast), MMed (Wits)[1,2]

1. Emeritus Professor Plastic Surgery Department, University of the Witwatersrand, Johannesburg, South Africa, and
2. Adar Science, Irvine, California

Figure 1. Chronic wound fluid perpetuates continued tissue destruction via MMPs and bacteria. It is suggested that control of these components of CWF could interrupt this inflammatory cycle and initiate healing. PMNs, polymorphonuclear leukocytes; MMPs, matrixmetalloproteinases; inflamm., inflammatory; NCS, nanocrystalline silver.

Chronic Wound fluid :

Needs to be controlled and treated

Needs to be modified (quantity and quality)

Needs to be transformed from chronic to acute

Interaction between
MMP9 and Bacteria activity

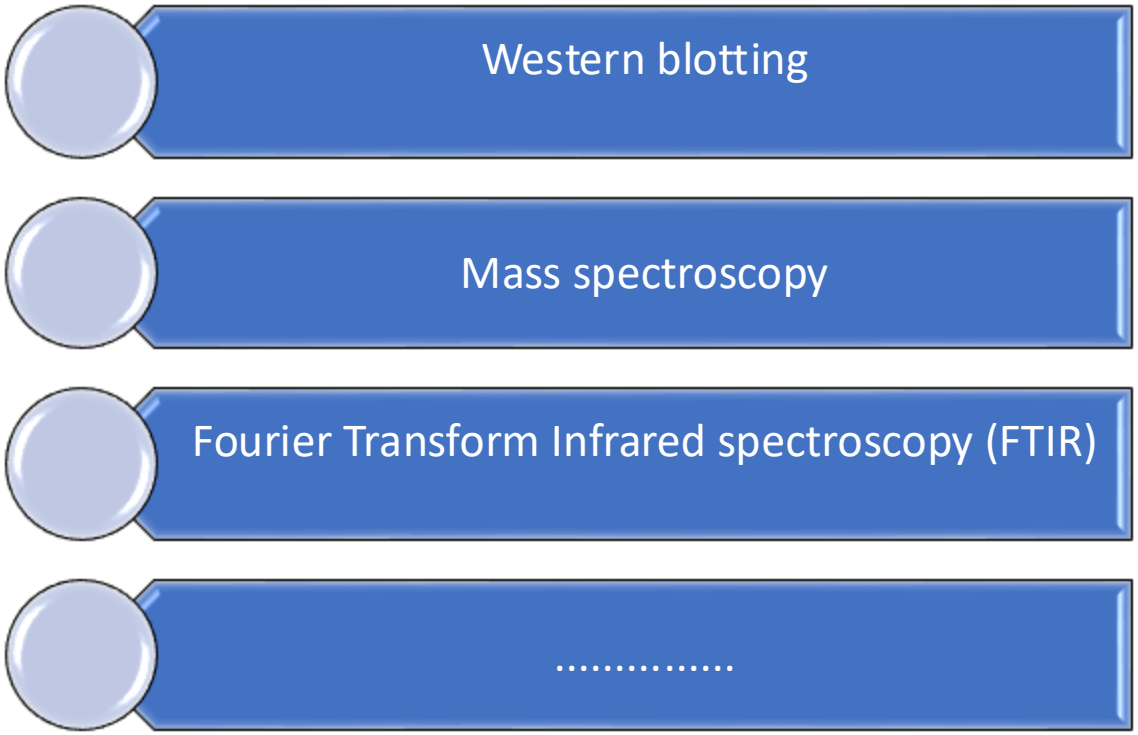
Wound exudate composition

Wound state indicator

Reflects wound biochemical processes

Allows the identification of prognosis / diagnostic markers

Wound Exudate Analysis Methods



Cerusico J et al Analyst 2018

research articles Journal of proteome research

Differential Proteomic Analysis Distinguishes Tissue Repair Biomarker Signatures in Wound Exudates Obtained from Normal Healing and Chronic Wounds

Sabine A. Eming,[*,†] Manuel Koch,[‡,∥,⊥] Andreas Krieger,[†] Bent Brachvogel,[⊥] Sandra Kreft,[⊥] Leena Bruckner-Tuderman,[#,▽] Thomas Krieg,[†,‡,§] John D. Shannon,[○] and Jay W. Fox[○]

Department of Dermatology, Center for Molecular Medicine Cologne (CMMC), Cologne Excellence Cluster on Cellular Stress Responses in Aging-Associated Diseases (CECAD), Institute for Oral and Musculoskeletal Biology, and Center for Biochemistry, University of Cologne, Cologne, Germany, Department of Dermatology, University Medical Center Freiburg, Germany, Freiburg Institute of Advanced Studies, School of Life Sciences-LifeNet, Germany, and Department of Microbiology, University of Virginia, Charlottesville, Virginia

Received May 14, 2010

The identification of biomarkers that predict a healing response would represent a milestone in the understanding of the tissue repair pathology and potentially point to novel therapies for chronic wounds.

Proteome Analysis of Wound exudate

« A Proteomic window» on wound bed status

Eming S. et al J of Proteome Res 2010

Healing Wounds

ECM: **Collagen Family (I-III)**
(granulation tissue formation)

Tetranectin (6 fold increase)
(plasminogen.-activation)

Serine proteinase thrombin
SERPINs (1and 3)
SERPINF 1 (3,4 fold increase)
(antiangiogenesis)
Dermcidin

Non - Healing Wounds

ECM : Fibronectina
Fibrinogen
Vitronectin
a2-HS -glycoprotein
olfactomedin-4

(components of provisional ECM)

MMP9
Leucocytes elastase
Proteinase 3
SERPIND 1 (inhibits thrombin)
Immunomodulatory molecules:
Lactotransferrin
ANXA1
S100A9

Take Home Messages

- Wound exudate reflects wound status and may influence cellular functions
- The analysis of exudate is a highly promising approach to gain a better understanding of the complex mechanisms underlying pathologic phenomena
- …and to develop novel target therapy for chronic wound

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Wound Games

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