FAKULTNÍ NEMOCNICE U SV. ANNY V BRNĚ

Wound healing in dermatology

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Definition

- **Wound** - a defect of skin integrity

- - *acute*

  - *chronic* – secondary healing wound without tendency to heal after 6-9 weeks

Chronic wounds

- leg ulcers
- pressure ulcers
- burns
- malignant tumours
- surgical wounds with secondary healing
- ulcers after radioth

Leg ulcers

- **prevalence** : 1% of adults
- **incidence**: in population over 50
  - 0,3 to 1000 inhabitants
- **chronic disease** : - 60 % of ulcers heal more than 6 months,
  - 33 % heal more than 1 year
- **impact on quality of life**
- **reccurences – 2/3** of healed leg ulcers

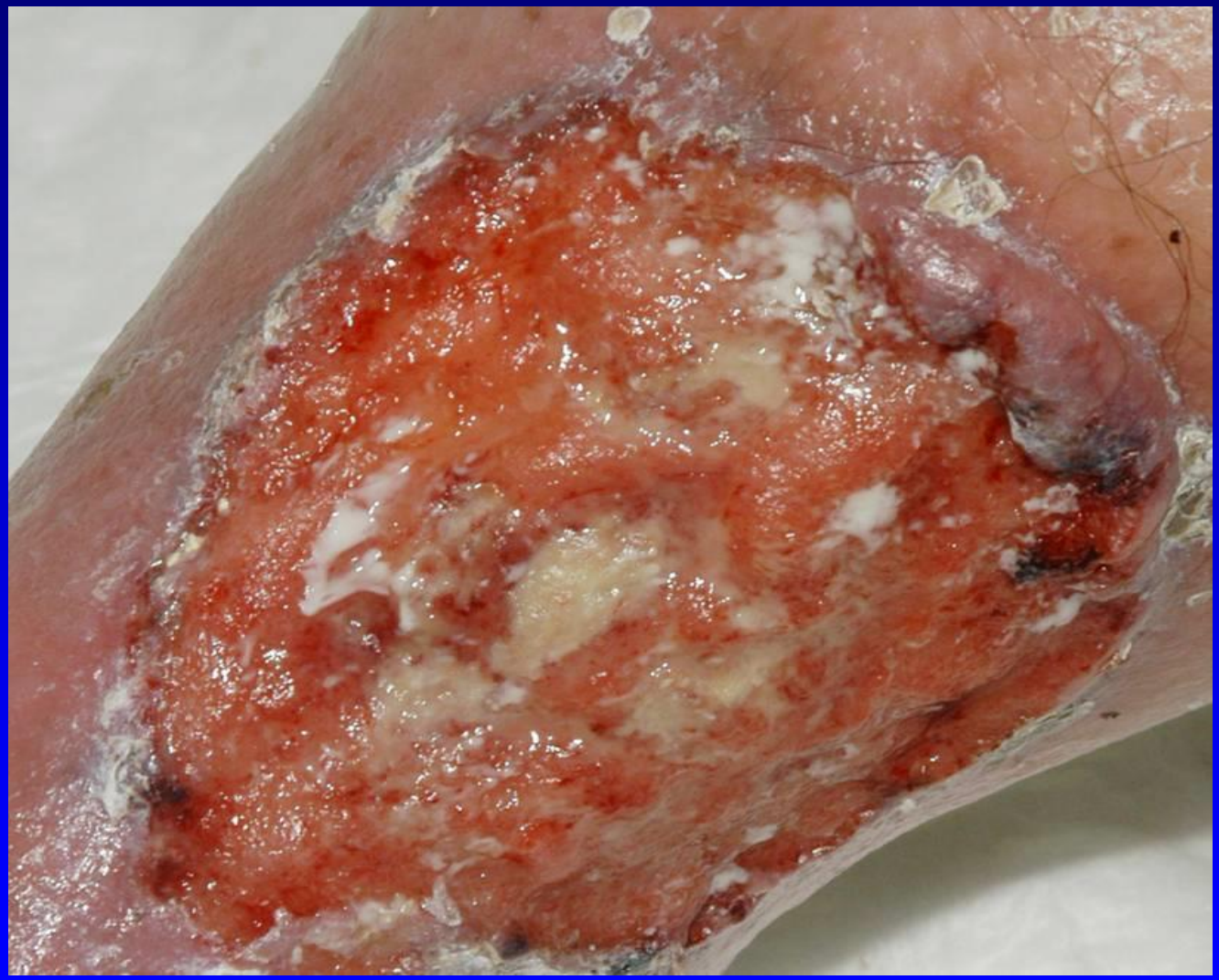
Etiology of leg ulcers

- 75% venous
- 15% arterial
- 10% other

Ulcus cruris infectiosum - bullous erysipelas

Basal cell carcinoma

Squamous cell carcinoma



Pyoderma gangrenosum – AI disease

Lymphatic ulcers

Venous leg ulcers

- 75% of all leg ulcers
- pathogenesis – valvular insufficiency
- 2 types:
- 1) **ulcus cruris varicosum** – due to primary varicose veins
- 2) **ulcus cruris posttromboticum** – due to deep vein thrombosis

CEAP classification

- Classification and grading of **chronic venous disease (CVD)** on the basis of:

- **C** – clinical manifestations
- **E** –etiologic factors
- **A** – anatomic distribution of involvement
- **P** – pathophysiologic findings

CEAP classification of CVD

C 0 – no visible or palpable signs of CVD

C 1 – telangiectases and reticular veins

C 2 – varicose veins

C 3 - edema

C 4 – skin changes: pigmentation, eczema, lipodermatosclerosis, atrophia blanche

C 5 - skin changes + healed ulcer

C 6 **– skin changes + leg ulcer**

Chronic venous disease

- **Vein Consult Program (2012)**
- epidemiologic study in Europe, Asia, Latin America, 90 000 persons
- CVD – **global problem**
- **prevalence**:
- **84%** - including stage C0s (symptomatic patients without clinical signs of the disease)
- **64%** - from stage C1

Chronic venous disease

- in the Czech republic - **prevalence - 70%**
- progressive disease
- treatment costs: 350 milion Kč
- prevalence of leg ulcers – 1-2%

- ***Czech Vein Program***,*Prakt.flebol.2012;21:1-28*

C4 - pigmentation

Atrophia blanche + leg ulcers

Treatment of venous leg ulcers

- **surgical**

- **conservative**:
  - local treatment
  - compression
  - pharmacological treatment

Wound healing - TIME

- **A structured wound assessment tool in the form of acronym**

- **T** – tissue management
- **I** – inflammation, infection control
- **M** – moisture balance
- **E** – epithelization advancement

TIME – T - tissue

- debridement, wound bed preparation

Debridement

- treatment of wound bed and wound edges
- necessary for wound healing
- reduces odour, exudation
- improves quality of life

Debridement

- autolytic
- enzymatic
- biosurgical
- mechanical
- surgical
- hydrosurgical - Versajet
- UZ
- TNP (topical negative pressure)

Autolytic debridement

- **the most often used method**
- **semi-occlusive dressings** – film dressings
  - hydrocolloids
  - hydrogels
- create a moist wound-dressing interface which enhances the activity of endogenous proteolytic enzymes within the wound
- separation of necrotic tissue from healthy tissue

Autolytic debridement

- **advantage** : - selective
  - painless

- **disadvantage** : - slow
  - maceration
  - odour

Enzymatic debridement

- **highly selective**
- **enzymatic agents** derived from
- proteolytic enzymes extracted from bovine plasma or pancreas, fruit and plants such as papain from papaya or bromelain from pineapple
- or bacterial collagenase derived from Clostridium histolyticum

Enzymatic debridement

- **Iruxol mono - bacterial collagenase**
  derived from Clostridium histolyticum
  (tzv. clostridiopeptidasis)
- cleaves triple helix of collagen
- selective debridement of necrotic tissue
- painless
- minimal risk of bleeding

Biosurgical debridement

- **larval therapy (Maggot)**
- fast and very effective method
- application of sterile fly larvae **(Lucilia sericata)** to the wound
- dressing change in 2-4 days

Biosurgical debridement

- **complex mechanism of action**
- mechanic movement of larvae
- production of proteolytic enzymes (collagenase, trypsin) and bactericid substances
- ingestion of bacteria
- increase th pH of the wound – inhibitory effect on bacterial growth

Mechanical debridement

- mechanical removement of necrotic tissue
- disadvantage –pain, traumatisation of healthy tissue
- advantage –quick method

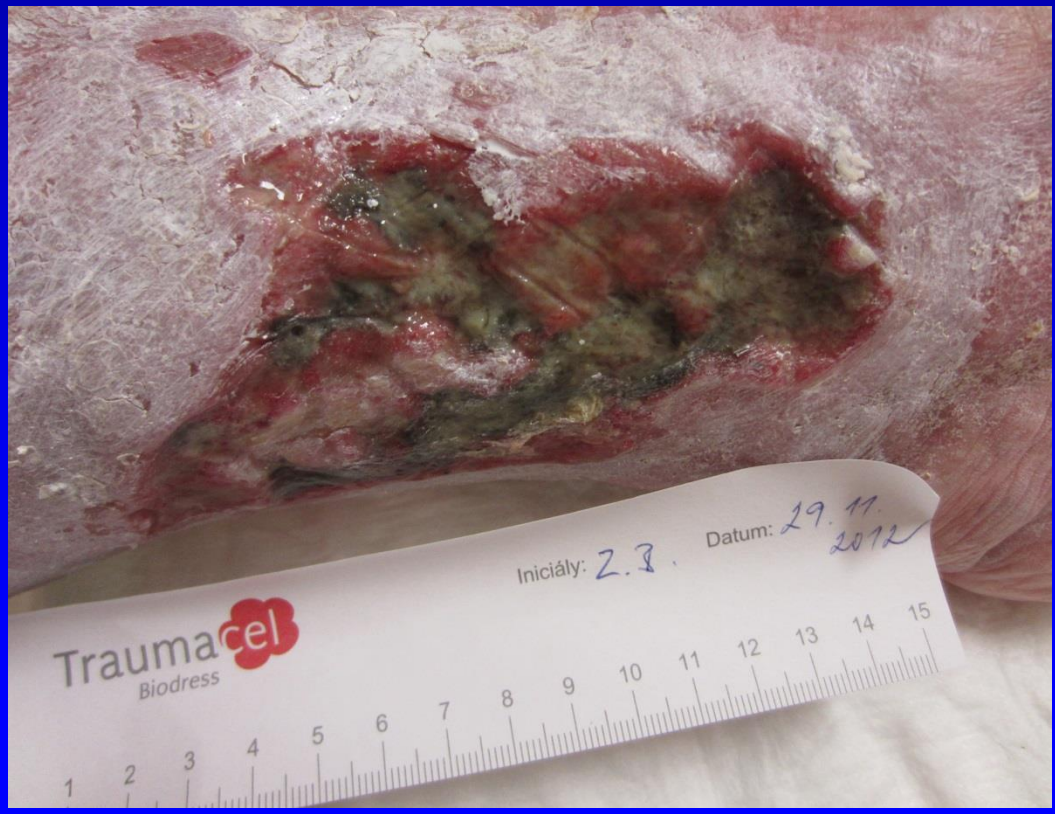
- **sharp debridement**
- **debridement wet-to-dry** – gause – painful

Hydrosurgical debridement

- **Versajet**
- pressurised water or saline
- the pressure is controlled via a handset
- the jet of fluid both cut and removes tissue while irrigating the wound
- advantage: quick
- Disadvantage: - expenssive
  - painful

TIME – I (infection)

- infection, inflammation control
- antiseptics



Antiseptics

- synthetic antimicrobial drugs
- they kill or inhibit microorganisms
- they are not toxic for keratinocytes
- **they act non selective**
- **broad antimicrobial spectrum**
- resistance – not often

Antiseptics

- silver
- iodine
- chlorhexidin
- honey
- polihexanid

Silver dressings

- **A broad antimicrobial spectrum:**
- Staphylococcus aureus, including MRSA, VRE (vancomycin-resistent enterococci), Streptococcus pyogenes, Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae
- viruses, yeasts

Silver dressings

- A variety of antimicrobial dressings containing silver
- A silver contect and physical and chemical properties vary greatly
- Available in various formulations:
- - flat sheets
- - combined with hydrogels, alginates, hydrofibres
- Resistance - rare

Silver

- International consensus - 2012
- „**Appropriate use of silver dressings in wounds**
- www.woundsinternational.com
- Effectivity, safety, cost-effectiveness

Iodine dressings

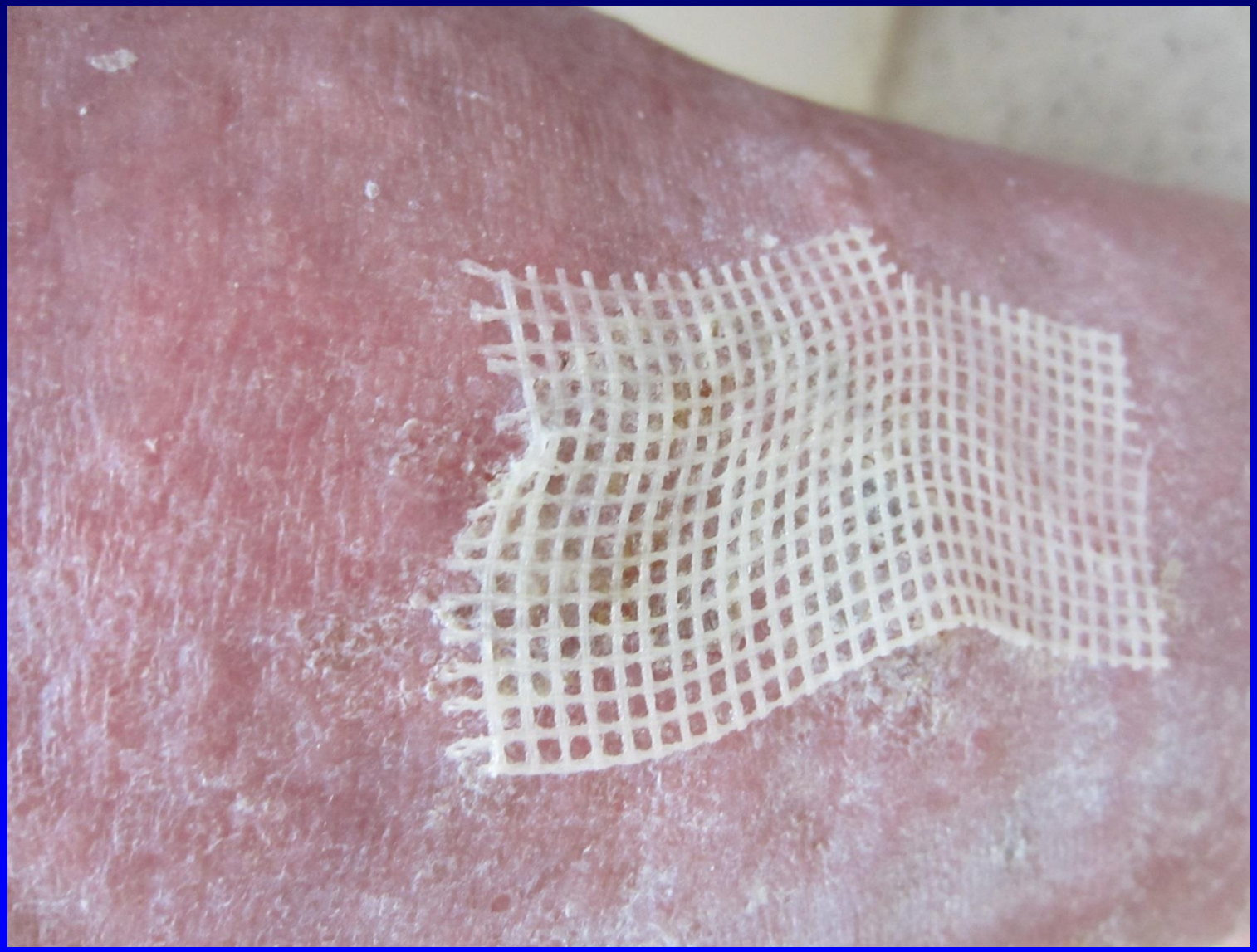
- **a broad antimicrobial spectrum:**
- G+, G- bacteria, viruses, fungi
- resistence – 0
- iodine is slowly released to the wound
- 2 forms: cadexomer iodine
  povidone iodine

Iodine dressings

- **contraindication**:
  - known sensitivity to iodine
  - thyroid disease
- do not exceed 3 months continuous use – risk of systemic absorption
- available in **various forms**:
  - ointment
  - paste
  - flat sheets

Chlorhexidin dressings

- **a broad antimicrobial spectrum:**
- G+, G- bacteria, viruses, fungi
- resistence can occur



Honey dressings

- first used in ancient Egypt - 4000 years ago
- medical-grade honey dressings developed in the late 1990s
- a broad antimicrobial spectrum, including MRSA and VRE
- the ability of honey to **produce low levels of hydrogen peroxide** in the wound
- the provision of an **acidic wound environment (pH 3)**

Honey dressings

- reduce wound odour
- promote autolytic debridement
- available in various formulations:
- flat sheets
- paste
- ointment

Honey dressings

- **Contraindication:**
- patients with known allergy to bee stings
- highly exudating wound – risk of maceration
- may cause stinging sensation

Polihexanid

- **Polyhexamethylene biguanide (PHMB)**
- a broad antimicrobial spectrum, including MRSA
- used in healthcare and cosmetics for many years
- no reports of bacterial resistance to date
- no allergy

Polihexanid

- well tolerated
- contraindication:

  - pregnancy – first 4 months
  - dry wounds

- Prontosan – PHMB + betain

TIME – M -moisture

- moisture – management od exudate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Moist wound healing

- **moist wound necessary for optimal healing**
- optimal hydration of the wound
- **copious exudate –** causes leakage, maceration, odour, infection
- **minimal exudate** delays autolytic debridement, inhibits epithelialisation and causes pain on dressing removal

Moist wound healing

- **dry wounds:** hydrogels

- **highly exudating wounds:**
  - alginates
  - hydrofibres
  - polyurethan foams

Hydrogels

- **amorphous gels**
- **flat sheets -gel compresses** (hydrogel + polyurethan layer)
- a high water content (30-90%)
- rehydrates dry tissue
- promote autolytic debridement
- have a cooling effect
- are easily removed
- are comfortable and flexible

Hydrogels

- may cause eczema or irritation
- they need secondary dressing
- may be combined with:

  - silver
  - hyaluronic acid

Hydrofibers

- nonadherent dressings
- ability to **absorb high levels of wound exudate**
- composed of sodium **carboxymethylcellulose**
- form non-adherent gel in exuding wounds
- create a moist wound-dressing interface

Hydrofibers

- promote autolytic debridement
- available in varius formulations:
  - flat sheets
  - packing rope for cavities
  - combined with silver – antimicrobial activity

- contraindication: dry wounds

Polyurethane foam dressings

- **semipermeable**
- low adherent, soft, highly absorbent
- outer semipermeable membrane – allows fluid to pass into the insulating foam
- waterproof
- gas/water vapour permeable
- impermeable to bacteria
- **create a moist wound-dressing interface**

Polyurethane foam dressings

- available in various formulations:
- adhesive/non-adhesive
- shaped cavity devices for cavity wounds
- shaped sacral or heel dressings
- thin
- combined with silver or PHMB – antimicrobial activity
- combined with charcoal – reduce odour

- contraindication: dry wounds

Polyurethane foam dressings

Silicone dressings

- **silicone –** inert material
- atraumatic dressings
- painless dressing change

- **non-adherent sheets**
- **polyurethane fom dressings with silicone**

Alginate dressings

- **Obtained from seaweed**
- **High absorbents**
- Derived from calcium/sodium salts of alginic acid
- On contact with wound fluid, sodium salts in the exudate exchange with tha calcium in the alginate dressing to form a soft gel which maintains a moist environment

Alginate dressings

- should be cut to the shape of the wound
- **hemostatic properties**
- may provide pain relief
- available in various forms:
- flat sheets
- packing rope for cavities
- combined with silver or charcoal

Charcoal dressings

- active charcoal
- reduction of odour
- absorption of microorganisms and exudate

TIME – E - epithelialisation

Bioactive dressings

- indication: **hard-to-heal ulcers**
- 20% of leg ulcers
- bad prognosis – leg ulcers larger than 10 cm2 and lasting more than 6 months

Bioactive dressings

- protease modulating dressings
- hyaluronic acid dressings
- collagen dressings
- growth factors
- skin substitutes

Matrix metalloproteinases (MMPs)

- **group of zinc-dependent endopeptidases**
- produced by **granulocytes, keratinocytes and fibroblasts**

- **elevated protease activity in chronic wounds**
- **decreased levels of TIMPs** (tissue inhibitors of MMPs)

Protease modulating dressings

- composed of **collagen and ORC – oxidised regenerated cellulose**
- act by absorbing wound fluid and trapping proteases within their structure to render them inactive
- form a non-adherent gel which binds with growth factors protecting them from degradation by MMPs

Oxidized celullose

Hyaluronic acid

- main part of extracellular matrix
- glucosaminoglycan
- hygroscopic – skin hydration
- antioxidant

Hyaluronic acid

- accelerates wound healing (acute and chronic wounds)
- reduces scarring

Growth factors

- **Regranex** - recombinant PDGF in form of gel
- indication: diabetic ulcers

Skin substitutes

- Integra
- Dermagraft
- Apligraf
- Cultured epidermal keratinocytes

Skin substitutes

- **Integra** - acellular dermis composed of bovine collagen and glycosaminoglycan matrix on a silicone layer
- **Dermagraft** - dermis replacement, composed of cultured allogeneic fibroblasts applied on a biodegradable sheet

Apligraf

- Biosynthetic product composed of 2 layers
- **inner dermal layer** – cultured human fibroblasts in bovine collagen type 1
- **outer epidermal layer** – cultured epidermal keratinocytes
- similar to human skin

Cultured epidermal keratinocytes

- **allografts or autografts**
- **native, cryopreserved or lyophilized**

- stimulate migration and proliferation of host keratinocytes from wound edges and from skin adnex

Dressing change

Dressing change

Dressing change

Dressing change

Dressing change

Dressing change

Compression

- Basic treatment of venous leg ulcers

Compression

- Basic treatment of venous leg ulcers
- Compression leads to healing of 70% of venous leg ulcers smaller than 10 cm2 in 3-6 months
- More than 50% of patients have wrong compression

Multilayer bandage

Multilayer bandage

Multilayer bandage

Multilayer bandage

Compressive stocking for leg ulcers

- system of 2 stockings

Contraindication of compression

- PAOD – ABI less than 0,5
- Acute erysipelas
- Acute eczema
- Heart failure

Compressive systems

Inteligent compression

Inteligent compression

After a week

Classification of compression bandages

- elastic
- inelastic
- stiffness

- **Classification of compression bandages:practical aspects**
- **Partsch H. et al, Dermatol Surg 2008;34:600-609**

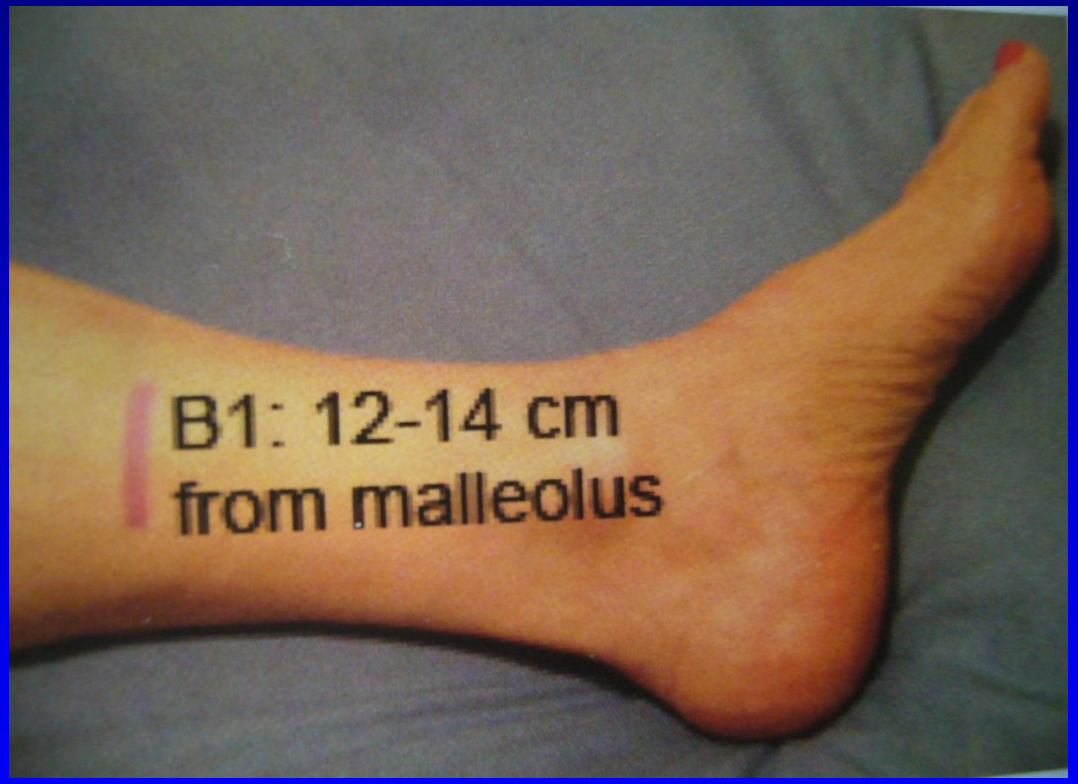
Compressive bandage

- 4 main features: **P-LA-C-E**

- **P**ressure
- **LA**yers
- **C**omponents
- **E**lastic properties

P - pressure

- **Sub-bandage pressure**
- **Measured in B1**



Picopress

Compression

- mild : under 20 mm Hg
- moderate: 20-40 mm Hg
- severe: 40-60 mm Hg
- very severe: nad 60 mm Hg

Compressive garments

Circaid

Circaid

Circaid

Circaid


PLACE VELCRO® OVER CALF
CIRCUMFERENCE MEASUREMENT
60
CIRCAID
circaid® juxtacures® leg
31 – 35 cm
ankle circumference
23 – 25 cm
ankle circumference
19 – 22 cm
ankle circumference
36 – 42 cm
ankle circumference
20
30
40
50
mmHg

Circaid


CALF
PLACE VELCRO® OVER CALF
CIRCUMFERENCE MEASUREMENT
60
Circaid
Juxtacures Tec

Circaid

Circaid

- **adequate sub-bandage pressure**
- easy application by patient himself
- better compliance
- improvement of quality of life

Pain

- main factor decreasing quality of life

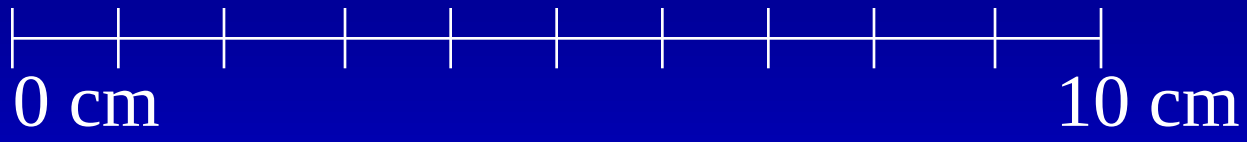
- **venous** ulcers – 60-80% pacients (20% - extreme pain)
- **arterial** ulcers – 83%
- **diabetic** ulcers – 48%
- pain results in **delayed wound healing**

Pain

- **nociceptive** – in tissue damage – stimulation of intact afferent nerve endings
- **neuropathic** – damage of peripheral nerves
- **psychogenic** – fear of the patient

Pain intensity

- **VAS = visual analogue scale**



score ≤ 3,0 cm … mild pain

score 3,0-5,4 cm … moderate pain

score ≥ 5,5 cm … severe pain

- **NRS = numerical rating scale**

□ □ □ □ □ □ □ □ □ □ □

0 1 2 3 4 5 6 7 8 9 10

Pain at dressing change

- Very often
- For 40% of patients the worst moment of their life
- Necessity of **atraumatic dressing changes**