

Cryosurgery Overview

Holistic Medical Centre, HKSAR



What will you do...

- If u see this painful foot?



- Or the lump on the penis?



Or, if her face has this spot



Options

- Keep observe, send them away
- Refer them to other specialties
- Chemical ablation
- Cauterisation
- Surgical excision
- Laser
- Cryosurgery



	Advantage	Disadvantage
Chemical Ablation	Cheap	Scar imprecise
Cauterisation	Cheap	Need diathermy Scar Very Painful
Surgical Excision	Tissue for pathological exam	Expertise Expensive Surgical risk, scar...
Laser	Posh Precision	Very expensive Painful Bulky and not portable
Cryosurgery	Cheap Anaesthetic Excellent scar if any	Bulky equipments Tedious arrangement imprecise

Indication



Type of leison

- Benign
- Premalignant
- Malignant



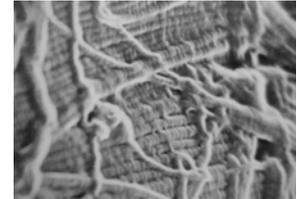
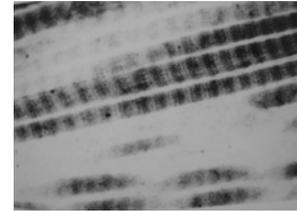


What if you cauterise with the vein underneath the wart?



Why so impressive, no scar?

- Differential sensitivity of tissue
 - Virus, collagen (least sensitive)
 - Blood vessel endothelium
 - Neural connective tissue
 - Fibroblast
 - Keratinocyte
 - Basal cell
 - Melanocyte (most sensitive)
- Cryosurgery can preserve tissue scaffolding
 - Kill cells without scar formation** (might have hypo-pigmentation)



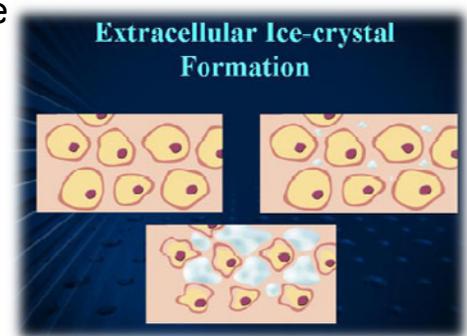
Mode of ablation

- Slow freezing
 - Dehydration with toxic elements concentration
 - Mitochondria, endoplasmic reticulum destruction
 - Vascular stasis at capillary level due to microthrombi
- Rapid freezing
 - Intracellular ice crystals with disrupted cell member
 - Late immunologic response has been reported



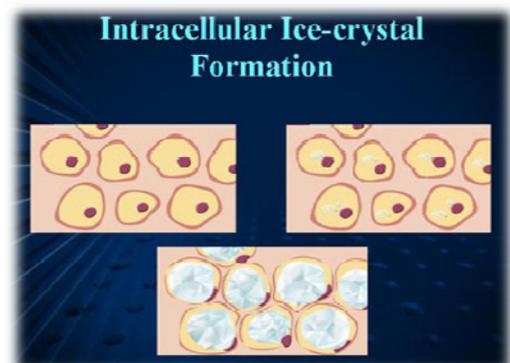
Early phase of rapid freezing

- Extracellular ice formation
 - occurs at $-7\text{ }^{\circ}\text{C}$
- Less effective extracellular fluid volume with unchanged amount of solute
 - dehydrates the extracellular space
- By osmosis
 - Dehydrate the intracellular space
- Dehydration
 - destroys or severely injures the organelle
 - Toxic metabolite concentration
 - apoptosis



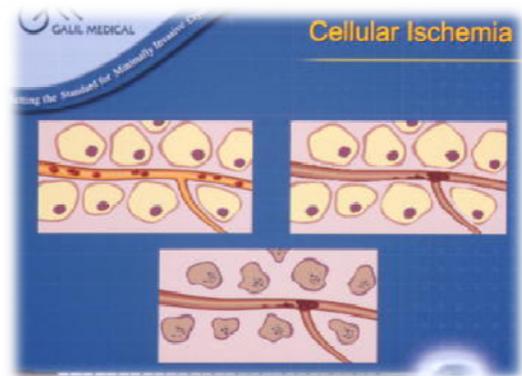
Middle phase of rapid freezing

- Intracellular ice formation
 - occurs at $-15\text{ }^{\circ}\text{C}$
 - disrupt and explode
 - the cell membrane and
 - organelle membrane
- K^+ and Ca^{2+} induced apoptosis



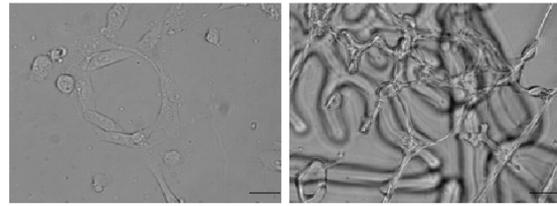
Late phase of rapid freezing

- Frozen and disrupted thrombocyte
 - intrinsic pathway triggered
- Capillary vasospasm
- Microthrombi formation
- Micro-embolism
- Capillary stasis
- Cut off blood supply
- Cell necrosis



Factors determining success

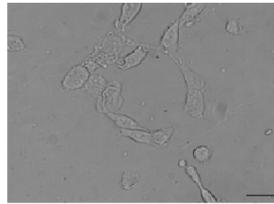
- Absolute temperature at cellular level
- Rate of lowering to such temperature



(a)

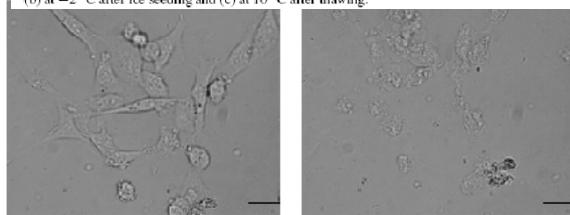
(b)

-2°C



(c)

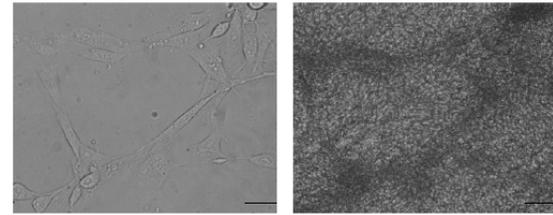
Figure 2. The morphological change of the tube structure during freezing and thawing with the end temperature -2°C (ice seeded at -2°C) (scale bar: $100\ \mu\text{m}$): (a) at -2°C before ice seeding, (b) at -2°C after ice seeding and (c) at 10°C after thawing.



(a)

(b)

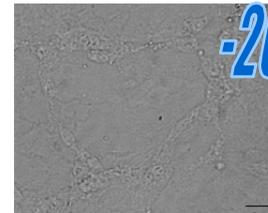
Figure 3. The morphological change of the tube structure during freezing and thawing with end temperature 20°C (ice seeded at 2°C) (scale bar: $100\ \mu\text{m}$): (a) at 2°C before ice seeding and (b) at 10°C after freezing and thawing.



(a)

(b)

-20°C, rapid



(c)

Figure 4. The morphological change of the tube structure during freezing and thawing with end temperature -20°C but without ice seeding (scale bar: $100\ \mu\text{m}$): (a) -2°C before ice seeding, (b) at -13.4°C and (c) after thawing.

-20°C, slow



Temperature – why cell not die?

- Cellular sensitivity to temperature
- Momentary exposure to sub-zero but above -7°C **will not** cause cell death
- All cells die at -27°C (unless ultra-rapid freezing)



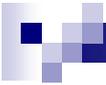
Different rate of freezing

- **Slow freezing** (e.g. Q-tip with liquid nitrogen, Histofreezer etc)
 - Osmosis infers a protective shift of fluid out of the cell
 - **Can leading to cell preservation** although with significant damage
- **Rapid freezing** (e.g. direct spray of liquid nitrogen, CryopenIc)
 - Early formation of intracellular ice crystals (together with extracellular ice)
 - **Re-crystallises in thawing**
 - Large crystal is particularly lethal in disrupting cell membrane
 - Late immunologic response has only been reported in rapid freezing
- **Ultra-rapid freezing** (e.g. Cryopreservation)
 - Instead of crystallising, water turns into amorphous ice (vitrification)



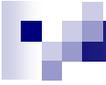
Options for cryosurgical tools





Are they the same?

- Absolute temperature at cellular level
 - Surface attainable temperature
 - Thermal conductivity
 - Depth of the targetted cell
 - Time of cryogen application
- Rate of freezing
 - Total latent heat capacity
 - Effectiveness of thermal conduction
 - Temperature gradient
 - All three factors related to **Direct / Indirect application**



Direct application

- Much higher TOTAL latent heat capacity
- Higher thermal conductivity (no icing front)
- More consistent
 - Temperature gradient
 - Shape of cryolesion (ice ball)
 - Intra-lesional temperature
- Translate into more consistent clinical result





Minor factors?

- User friendly
- Reliability
- Cost
- Portability



Cellular temperature

- Surface attainable temperature
 - Cryogen
 - Direct / Indirect application
- Thermal conductivity
 - Direct / Indirect application
- Depth of the targetted cell
 - Shape of Cryo-lesion
- Time of cryogen application
 - Direct / Indirect application



Surface attainable temperature

- Various refrigerants (Cryogen)

Ice	0°C
Salt ice	-20°C
CO ₂ slush	-20°C
Liquid nitrogen (swab)	-20°C
dimethyletherpropane (wartner)	-57°C??
Nitrous oxide (Cryopen c)	-89°C
CO ₂ solid	-79°C
Liquid nitrogen (spray)	-196°C

Thermal conductivity

- Water better than ice

- Rapid

- Lower surface temperature
- Constant surface temperature

- Slow

- Ice will hamper heat exchange and progression
- Therefore slow freezing will cause surrounding icing and prevent deep penetration

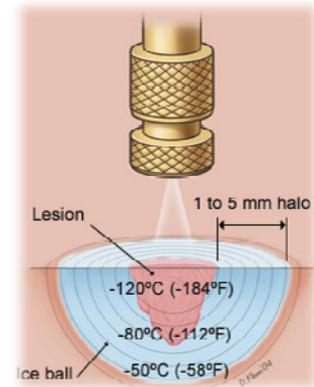
- Connective tissue worst

- Thickness of dermatological pathology

- Need to file a wart before application of cryogen

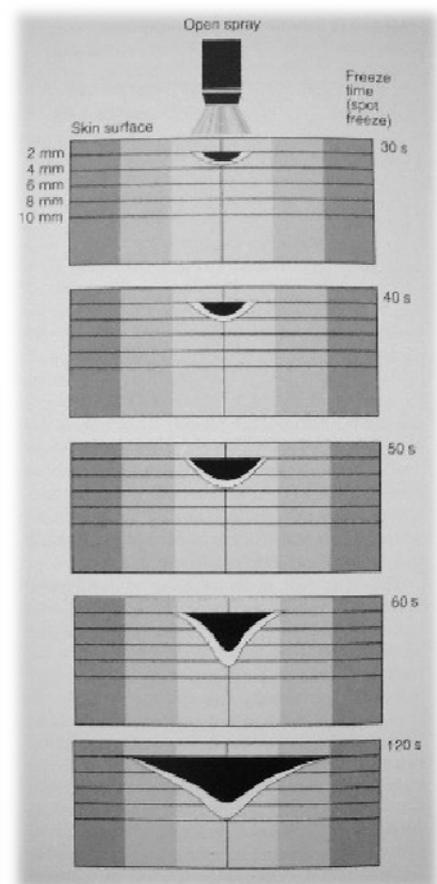
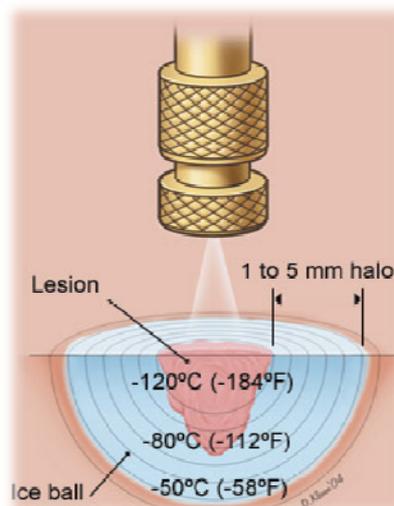
Shape of cryoleison (ice ball)

- Theoretically it is hemispherical **BUT**
- Surface attainable temperature
- Thermal Conductivity
- Circulation
- Contact time



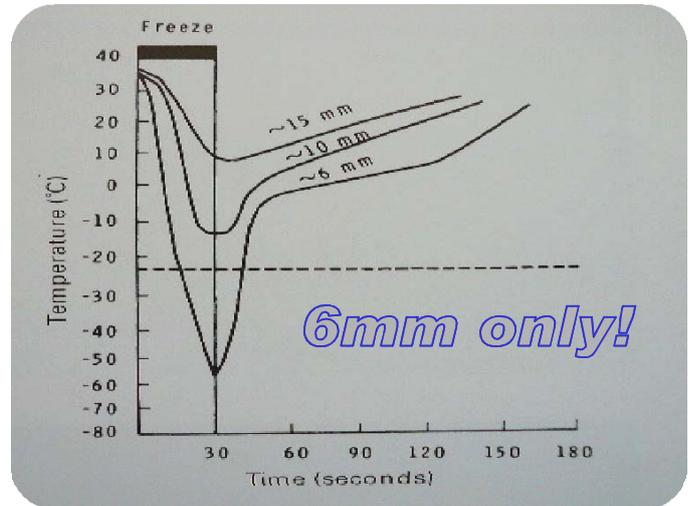
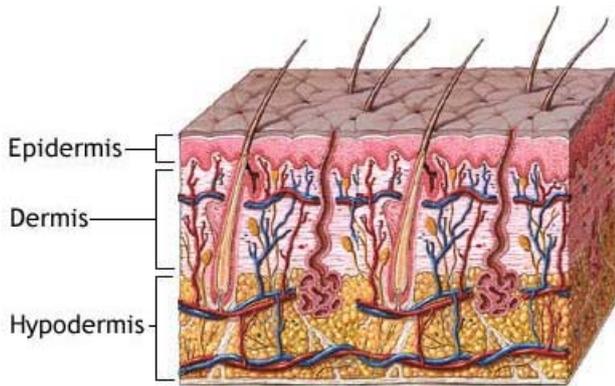
Circulation , Time

- Hemisphere to Trefoil shape
- Width \geq Depth



What is the temperature inside the cryoleison?

- Not isothermic!
- -27°C will induce cryonecrosis

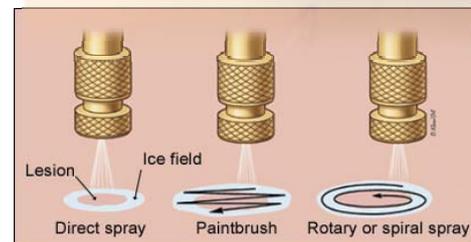


Liquid Nitrogen

- Gold standard
- Previous literature preferred method
- Consistent result
 - Direct application, therefore surface temp is consistent
- “cheap”
- Powerful
 - Vs dimethyletherpropane (histofreezer, wartner)
 - at 2mm subcut., temp is much lower than -27°C

Technique

- <2cm diameter leison
 - Spot freeze by spray
 - probe
- >2cm diameter leison
 - Overlapping spot freeze
 - Paint-brush, spiral & rotatory



Cheap?

- As boiling point is at -196°C
- Close system will explode
- Must use leaky container
- 10L cryo-container will empty by 45 days

And

- Not portable
- Bulky and terrifying
- Once leak, damage incurred will be \$\$
- Not precise (collateral damage is painful)
- Risky to go around eyes and face



Other options

- Histofreezer, Wartner
- Dimethyletherpropane
- Low surface temperature (? -57°C)
- Delivery system cannot allow continuous supply of volatile liquid
 - (so, the effective temp is around -20°C)
- Ice ball cannot progress
 - Slow freeze, ice is a poor heat conductor
- Crude applicator (sponge)
- In analogue with q-tip technique for liquid nitrogen



What does Cryopen|c offer?

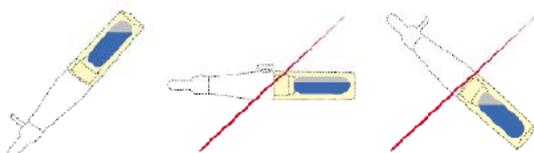
- Direct application as liquid nitrogen spray
- Accuracy, 1mm margin
 - Focused jet of cryogen (contrast to divergent liquid nitrogen spray)
 - 30um micro-applicator
 - 55 bar (725psi) N₂O
 - Decreased (almost nil) collateral damage
 - Pain free
- Consistent result
 - Penetrate 1mm every 5 seconds
- Biofeedback to determine depth
- Medical PEEK (non-sticky) outer shell



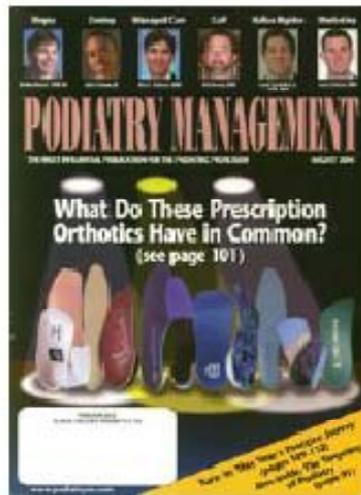
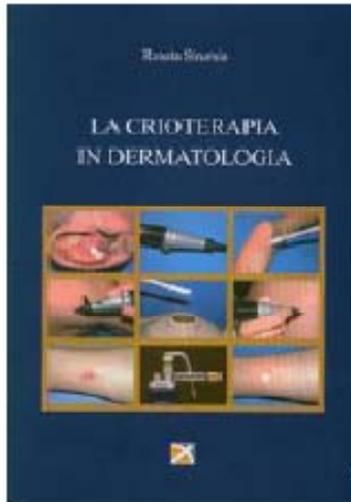
Cryopen|c



Joule Thomson Effect



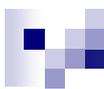
Literature support



Important note!

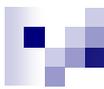
- Cryopen|c is not something new in concept
- It is just a **refined** technique
- Indication is the same as cryosurgery by liquid nitrogen
- Best result is from clinical competence





Get Start with Cryopen|c

- Hand-tighten the body, applicator and cap
- Disassemble the cartridge compartment
- Replace the filter unit and cartridge
 - in correct alignment (refer to manual)
- Screwing tight the cartridge compartment
 - Swift, in one-go.
 - You will hear a quick hissing sound
 - Continuing to screwing tight, the sound will stop



Preparation

- Position the client
 - Lesion is horizontal
 - so that the Cryopen|c can be upright
 - Avoid exhale over the lesion
 - Might need to turn client's face
 - Wear a mask and hold the breath
 - moisture will freeze
 - Disinfect with alcohol, and let it dry
- Uncap the micro-applicator



Preparation – Cryo-point



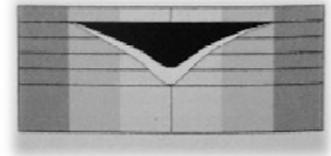
- Note the Cryo-point is around 3mm from tip
 - Cryo-point is where the jet of cryogen gasifies
 - At the tip,
 - maximal freezing power
 - Unfocused jet of cryogen; difficult to control
 - flooding the lesion when the tip is in contact with skin
 - Jet is converging to the Cryo-point
 - No significant lost in freezing power
 - Beyond Cryo-point there is no freezing power

Application

- Bringing the Cryo-point to the skin lesion
- Approaching from 1cm and closing the gap
- Slowly, till you see a minute (<1mm) ice ball
- Hold at that distance
- The ice ball (Cryolesion) will expand with continuous delivery of freezing power
- Depth is shallower than horizontal diameter

Judgement of depth

- Skin lesion usually has 1-3mm thickness
- Need clinical experience to estimate



- Remember!
 - Depth is smaller than horizontal diameter
 - So you need a 5mm span iceball for a 3mm depth lesion
 - Sometimes you need additional 0-2mm margin



A more accurate way!

- Biofeedback!
- As skin lesion has no free nerve ending
- So it will not sense pain
- But surrounding tissue has pain fiber
- Therefore if the cryolesion is within the skin lesion, the patient will not feel pain





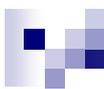
Cryopen|c allows biofeedback!

- Previously not possible for cryosurgery
- Cryopen|c offers minimal collateral damage
 - Ice ball can be controlled to 1mm size
- Therefore when you hold the cryopen
- The ice ball expands at Cryo-point
- The patient won't feel pain until its border goes beyond the skin lesion
- Ask patient to tell you when (pain, not just cold only)
- Then you add 5 more second for a 1mm margin



Then

- Cover the cap and allow thawing
- There will be a droplet of water
- Let it evaporate (might need 1 minute)
 - Wipe it dry will not allow the tissue have enough time to resume the body temperature
- Repeat the procedure
- The second freezing cycle might be quicker
 - The tissue might have a lower temperature



Follow-up

- Every lesion will need 1 freeze-thaw-freeze cycle to ensure all cells are destroyed
- Wheal will appear in 10th minute and last 24 hours
- Since the cuticle is intact, there is no need to avoid shower, but remind patient not to rub the lesion
- No special “wound” care is needed
- FU at 2 week, see if second treatment is needed (less than 15% of cases usually)



Pearls

- Avoid warm and humid operating environment
- Do not apply to moist surface
 - Raw wound / when alcohol is still present
 - Icing of liquid cause significant collateral injury
- Prime the patient about the procedure
 - Especially about the biofeedback depth
- If a 3mm margin is needed, and patient cannot tolerate 15sec of pain, consider LA
- Pigmented lesion is susceptible, but its pigment will be taken up by surrounding cells
 - Clinically appears as a blurred mole



Benign

- Viral Wart
 - Common
 - Planar
 - Plantar
 - Filiform / digitate
 - Anogenital
 - Molluscum contagiosum
- Seborrhoeic keratosis
- Acrochordon (skin tag)
- Adenoma sebaceum
- Angioma
- Chondrodermatitis nodularis helcis
- Digital myxoid cyst
- Granuloma annulare
- Dermatofibroma (Histiocytoma)
- Keloid
- Labial mucoid cyst
- All benign hyperpigmented leisons
- Prurigo nodularis
- Sebaceous hyperplasia
- Tattoos
- xantehlasma



Viral Warts

- HPV induced
- 15% in any time
- 65% disappear spontaneously in 2 yrs



Viral Wart

- mm to cm
- Face, hands, knees
- Rough surface
- Epidermal ridges do not cross
- Morphology and Sites
 - Common
 - Planar
 - Plantar
 - Filiform (digitate)
 - Anogenital
 - Molluscum contagiosum



Common Wart

- Include periungual wart
 - Overzealous treatment might damage nail matrix



Planar wart

- Might last for years
- Can be multiple
- Might undergo pigmentary change



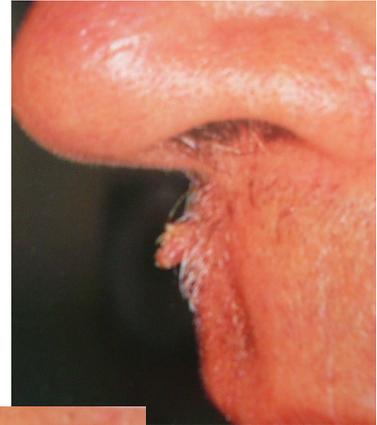
Plantar wart (verruca)

- Minimal protrusion ?due to pressure effect
- Surrounding horny collar
- Painful
- Capillary bleeding on paring down
- To differentiate from corn
 - Epidermal ridges do not cross
- **Need to trim before cryosurgery**
 - Keratin is a poor thermal conductor



Filiform / digitate wart

- Finger like
- Men
- Neck and above



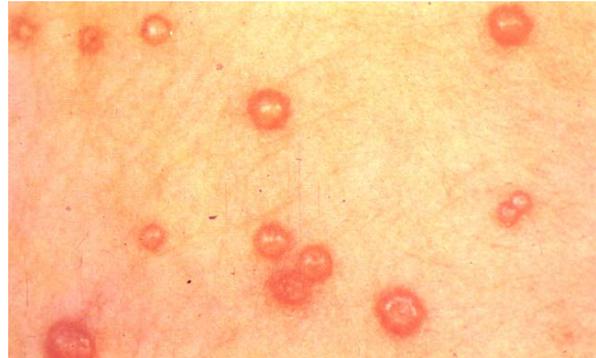
Anogenital wart

- Contact tracing
- Rule out other STD
- Need topical podophyllin for best result
- Still have a higher failure and recurrence rate



Molluscum contagiosum

- Children
- Esp with eczema
- 1 to hundreds
- May persist for years
- Central dimple +/- cheesy material



Viral wart - treatment

- Classic treatment requires salicylate acid containing ointment for 12 weeks
- Now you can consider cryosurgery with Cryopen|c
 - First pare down thick keratin (use scalpel / emery board)
 - Do not deeper than the level of “moist” dermis
 - Not to puncture molluscum contagiosum
 - A last layer of cutis is important
 - Avoid icing moist surface
 - Barrier for easier post-op care



Viral wart - cryosurgery

- 1-3mm thick skin lesion
 - Thus needs 5-15 sec (5sec for 1mm)
- 1-2mm margin beyond the wart
 - Except molluscum contagiosum, which does not need any margin
 - Can extend to 30sec for plantar wart (thick cuticle, poor conductance)
- Maintain for 5-10 sec for the 1-2mm margin
- Single freeze-thaw-freeze cycle
- FU at 4th week,
 - consider salicylate acid cream on 2nd week
 - Redo the procedure if not effective
 - Overall >75% success rate even for inexperienced (verruca 60%)

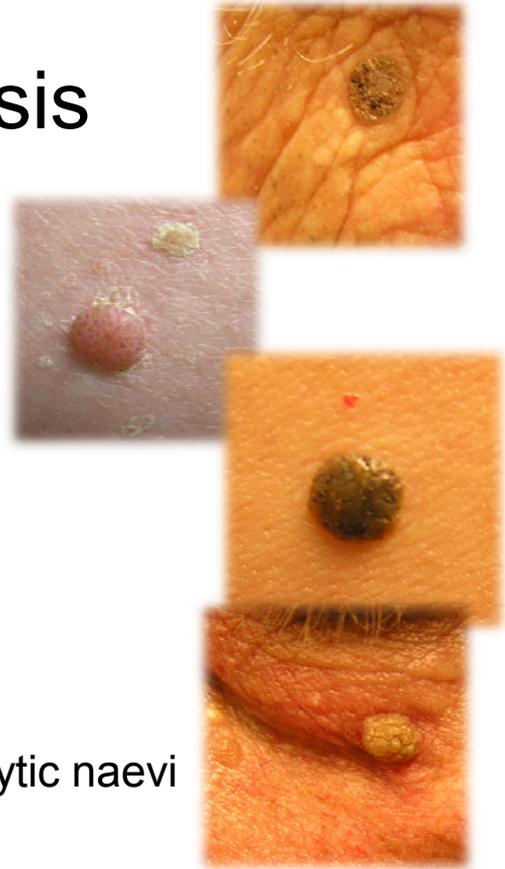


What is the expected result



Seborrhoeic keratosis

- More common in Caucasian
- >50yr-old
- Variable
- Rough surface, plaque on skin
- Grey, yellow, brown, black...
- 2mm to 3cm wide, 1-3mm deep
- Face, trunk
- NEVER “fleshy”
- Flat lesion ddx lentigo maligna
- Pedunculated lesion ddx melanocytic naevi



Seborrhoeic keratosis - treatment

- Consider Bx if in doubt
- Excellent result, re-epithelised in 1 week
- If large lesion, consider shaving under LA
- Cryosurgery
 - Usually takes 5-15sec
 - Maintain 5-10sec for the 1-2mm margin
 - Single freeze-thaw-freeze cycle
 - FU at 4th week
 - Usually very successful for thin lesion

Acrochordon (skin tag)

- Tempting for excision / cauterisation but need LA
- Cryosurgery
 - Usually takes 5sec if approach at base
 - Maintain for 5 sec for 1mm margin
 - Single freeze-thaw-freeze cycle
 - Follow-up at 4th week



Adenoma sebaceum

- Uncommon condition of tuberose sclerosis
- 1-2mm thick
- If extensive, consider laser as chance of hypopigmentation is significant
- Small lesion consider cryosurgery
 - Usually takes 5-10sec
 - Maintain for less than 5sec (0-1mm margin)
 - Single freeze-thaw-freeze cycle
 - Usually need at least twice monthly treatment



Angioma



- Spider naevi & Campbell de Morgan spot
- Laser / cryosurgery is equally applicable
- 1-2mm thick
- Cryosurgery
 - Usually takes 5-10sec
 - Compress to empty (by a ball pen), quickly apply Cryopen|c
 - Maintain for less than 5sec (0-1mm margin)
 - Single freeze-thaw-freeze cycle
 - Usually no need to repeat



Chondrodermatitis nodularis helcis

- Tender nodule at the pinna
- 2-5mm thick (mostly keratin)
- Excision if well developed
- If early, consider cryosurgery
- Cryosurgery
 - Usually takes 10sec
 - Maintain for 10sec for the 2mm margin
 - Single freeze-thaw-freeze cycle
 - Usually need three sessions with 6 weeks interval
 - Only 50% success rate for small lesion
 - Late case is usually filled with keratin (poor heat conductance)
 - Luckily cartilage is insensitive to cryosurgery,
 - little chance of auricular deformity as complication



Digital myxoid cyst

- Myxoid degenerative cyst arising from DIPJ
- Not to be confused with Herberden's node (bony)
- 1/3 recurrence with surgery even in best hand
- Surgery might need flap coverage
- **Can damage the nail matrix and germinal layer**
 - For both surgery and cryosurgery
- Cryosurgery
 - Aspirate to dry
 - Usually takes 10sec
 - Maintain for 10sec for 2mm margin
 - Single freeze-thaw-freeze cycle
 - Usually no need to repeat
 - 80% success rate



Granuloma annulare

- Not to be confused with tinea
- Inflammatory skin disease
- 1-2mm thick
- Asymptomatic
 - +/- tender
 - or itch
- Usually clear in 3 yrs, but can last for decade
- Cryosurgery
 - Usually takes 5-10sec
 - Maintain for < 5sec for 0-1mm margin
 - Single freeze-thaw-freeze cycle
 - Usually need to repeat at 2nd month
 - Success rate is around than 50%



Dermatofibroma

- Nodular, pink to brown
- Attached to deep tissue (pinch test)
- 3-4mm thick
- Cryosurgery
 - Usually takes 20sec
 - Maintain for 10sec for 2mm margin
 - Single freeze-thaw-freeze cycle
 - Usually need to repeat once at 2nd month
 - May cause hypopigmentation
 - 90% success rate



Hypertrophic scar

- Scar tissue elevated but not invade beyond its margin
- 2-4mm thick
- Early, consider pressure garment / silicon
- Cryosurgery
 - Usually takes 10-20sec
 - Maintain for 10-15sec for 2-3mm margin
 - Single freeze-thaw-freeze cycle
 - Usually no need to repeat
 - Additional “advantage”: hypopigmentation

Keloid

- Invasive scar tissue going beyond its margin
- 2-4mm thick
- Cryosurgery
 - Usually takes 10-20sec
 - Maintain for 15-20 sec for 3-4mm margin
 - Single freeze-thaw-freeze cycle
 - Usually need to repeat three times every 2-month
 - May cause hypopigmentation



Labial mucoid cyst

- Also known as
 - mucocoele
 - mucous retention cyst
- Usually at lower lip, soft,
- <1cm wide, 2-3mm thick
- Cryosurgery
 - Usually takes 10-15sec
 - Maintain for 5sec for 0-1mm margin
 - Single freeze-thaw-freeze cycle
 - Usually no need to repeat



All benign pigmented lesions

- Take advantage melanocyte is cryosensitive
- Include freckle
- 1-3mm thick
- Cryosurgery
 - Usually takes 5-15sec
 - Maintain for 5-15sec (0-1mm margin)
 - Single freeze-thaw-freeze cycle
 - Usually no need to repeat
 - Might result as a “blurred mole”
 - Melanocyte is susceptible
 - But pigment is taken by surrounding cells



Prurigo nodularis, pruritus ani

- Hundreds of pruritic nodules
- pea sized, firm and erythematous / copper-brown
- Chronic lesions may appear fissured, crusted or verrucal.
- Unbearable itch
 - ? Innervated by fine free nerve ending
- initial treatment of choice is topical steroids
- 1-2mm thick skin lesion
- Cryosurgery
 - Usually takes 10sec
 - Maintain for 5-10sec for 1mm margin (depends on keratin thickness)
 - Single freeze-thaw-freeze cycle
 - Usually no need to repeat



Sebaceous hyperplasia

- Central face
- Shiny, yellow
- 1-2mm thick lesion
- Cryosurgery
 - Usually takes 10sec
 - Maintain for 5sec (1mm margin)
 - Single freeze-thaw-freeze cycle
 - Usually no need to repeat



Tattoos

- Consider laser
- Locate at least 2mm below cutis
- Cryosurgery
 - Usually takes 10-20sec
 - Maintain for 15sec
 - Single freeze-thaw-freeze cycle
 - Usually need to repeat 3x2-month
 - Likely cause hypopigmentation
 - Only has 50% clear rate



Xanthelasma

- Fatty deposition
- Can result in significant edema with cryosurgery due to lax tissue
- 1-3mm thick lesion
- Cryosurgery
 - Usually takes 5-15sec
 - 0-2mm margin (2mm if nodular)
 - Maintain for 5-10sec
 - 1 freeze-thaw-freeze cycle
 - Might need to repeat twice at 2-month interval
 - Advise patient to have double pillow at night



Others

- Complication of Acne
 - Comedones
 - Scarring
- Acanthoma
- Cutaneous horn
 - Keratoacanthoma
 - Viral wart, seborrhoeic keratosis, solar keratosis, early SCC
- Axillary hyperhidrosis
- Ingrown toenail
- Pyogenic granuloma
- Pigmented naevi



Premalignant + Malignant

- Actinic / solar keratosis
- Actinic cheilitis
- Bowen's disease
- Leucoplakia
- Lentigo maligna
- BCC, SCC, melanoma, cutaneous metastasis
- Should seriously consider surgery which can **biopsy**
- Cryosurgery is **only** for confirmed case / palliative
- A wider margin (~3-5mm) is needed



Solar Keratosis

- Sun exposed area
- Adherent scale on a telegiectatic area
- Feel like sandpaper
- Surrounding skin can be red, atrophic or wrinkled
- Far majority never become malignant
- Significant portion regress



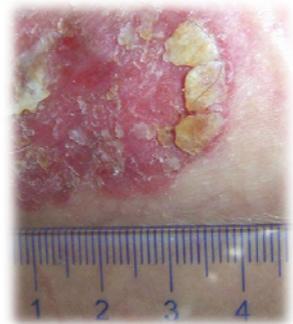
Actinic cheilitis

- Lower lip
- Dry then with a thickened grey plaque
- Not leukoplakia / lichen planus



Bowen's disease

- Pink, scaly or crusted, like psoriasis
- Slow radial growth pattern
- Can be like a horn, affect glans penis
- Also known as carcinoma insitu
- ? Related to HPV
- Malignant change in 3-5%



Lentigo maligna

- Melanoma in situ
- AKA Hutchinson's freckle
- ABCD
 - Asymmetry
 - border irregularity
 - color variation and
 - diameter greater than 5mm



Malignant

- Indurated
- Rapid growth
- Cryosurgery esp for debilitated
 - Usually takes 10-30sec
 - Maintain for 30sec (5 mm margin)
 - 3 freeze-thaw cycles
 - Need long term monitor
 - despite initial regression





Contraindication

- When tissue histopathology is needed
- Raynaud's phenomenon
- Cryoglobulinemia
- None are absolute contraindication



Complications

- Acute
 - Blister
 - Pain
 - Bleeding
 - Edema
- Subacute
 - Bleeding
 - Hypertrophic scar
 - rare if freeze time <30s
 - Infection (rare)
 - Hyperpigmentation (uncommon)
 - Altered sensation
- Chronic
 - Hypopigmentation
 - Local hair loss





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