Verruca? Verrucae? Verrucee??...Plantar wart!

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Intro

- Systematic reviews show scant high quality evidence of effectiveness for warts:
  - 52% Effectiveness Salicylic Acid
  - 54% Effectiveness Cryotherapy

  (Kwok, Holland & Gibbs 2011)

- “lack robust evidence of a therapy, does not mean that it’s not worth knowing about nor worthy of use in practice, particularly when specific tx been reported with a reasonably high clinical success rate” (Lipke 2006)

- Verrucae Needling - First described by Falknor in 1969.
- SWIFT - The New Kid on the block.
Post infection, incubates up to 8 months at basal layer (no deeper).

Replication occurs as cells differentiate & migrate to surface, resulting in proliferation of prickle cell & altered epidermis/visible warty appearance of verrucae.

Virus is shed during exfoliation of epidermis.
- DNA double stranded virus > 200 subtypes of HPV, determining anatomical distribution & morphology of lesion.

- HPV’s initially benign but some types can undergo malignant change (HPV-16 & HPV-18)... NOT PLANTAR WARTS!

- The most common warts on hands & feet are subtypes 1, 2, 4, 27 & 57
HPV1, 27 & 57-
Single lesions

- Large, Painful on W/B
- Cell disturbance through entire epidermis
- Acanthosis, proliferation engorged prickle cells (rubbery)
HPV2 - Mosaic/filliform

- Less painful than HPV-1
- Large area, overlapping (scale like)
- Superficial acanthosis in Stratum Spinosum & Stratum granulosum layers
HPV4 - Multiple

- Less painful
- Numerous circular lesions
- Superficial, compact Stratum Corneum
- Vacuolisation in Stratum Granulosum
Breaking News: Black dots are NOT thrombosed capillaries! The Podiatric Dermatology Blog

- Forthcoming paper from the Journal of the American Academy of Dermatology (Fried et al, 2018)
- Evidence these are intracorneal haemorrhages, rather than “microthrombi within the blood vessels” (Neale’s Common Foot Disorders) - Trapped blood within the stratum corneum following localised trauma/tissue damage.
- The papillary dermis can leak blood into the epidermis, when a hard lesion creates secondary trauma to the tissues. “while in the stratum corneum, this blood is essentially trapped and walled off from the phagocytic cells that would normally degrade it, resulting in delayed transit through the epidermis” (Bristow, 2018)
How does HPV evade the immune system?

HPV INFECTION IS NOT INDICATIVE OF A `WEAKENED IMMUNE SYSTEM`!

▶ Epidermis is avascular
▶ Latent virus particles in adjacent cells not destroyed in keratolytic tx - Bristow & Stiles, 2011
▶ Activates anti-inflammatory T suppressor cells & alters Langerhan cell function - Frazer, 2009
▶ Down-regulates surface markers & prevents cell damage = no antigen presentation - Bergot et al, 2011

...thus the virus maintains IMMUNE-IGNORANCE
Cell-mediated immunity

Foreign microbe with antigens

Langerhans cell produces clones

Killer T-cell: Directly destroys antigens

Helper T-cell: Stimulates T- and B-cells

Suppressor T-cell: Inhibits T- and B-cells

Memory T-cell: Remembers antigen for future encounters

Macrophage ingests antigens...

Processes them...

and presents them to the T-cell
Humoral/Anti-body immunity (free-floating)

<table>
<thead>
<tr>
<th>Humoral/Anti-body immunity (free-floating)</th>
<th>Cell-mediated immunity</th>
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<tbody>
<tr>
<td>Works on viruses &amp; bacteria that are outside of cells</td>
<td>Works on viruses &amp; bacteria that have penetrated inside cells</td>
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<tr>
<td>simpler system</td>
<td>more sophisticated system</td>
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<tr>
<td>Activates B-lymphocytes</td>
<td>Activates T-lymphocytes...</td>
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Both humoral & cell-mediated responses provide an exquisite memory for the adaptive immune system to recognise & eliminate subsequent attacks from the presented antigen.
Figure 1. The T cell.
mounts an immune response against non-self antigens.

Figure 2. Mr T cell.
pitties the fool who expresses a non-self antigen.
Natural history & morbidity of Verrucae

Generally harmless (asymptomatic) and many spontaneously resolve within months to years, particularly in children. (Chapman & Visaya 1998, Sterling 2001)

But! Can be associated with impaired QOL - significant morbidity are unsightly & often painful. (Ciconte 2003)

In a study of 77 children, 31 had active warts. However, swabs taken from clinically normal skin revealed a prevalence of carriage as 80%! Sub-clinical HPV? (De Koning et al 2015)

Control of viral load rather than eradication? (Long Fu Xi et al 2011)
Topical treatments for cutaneous warts

Kwok CS, et al

85 RCT`s evaluated - Many high risk of bias in design

- Salicylic acid (SA) - Definite but modest beneficial effect compared to placebo but it may take several weeks of daily use to work.

- Cryotherapy (liquid nitrogen) - Painful with risk of scarring. One study suggested cryo is better than SA for warts on the hands, but not evident when combined with other results.

- Duct tape - demonstrated no advantage over placebo (193 participants).

- Intrallesional bleomycin - inconsistent evidence.

Conclusion; Studies were poor quality and best evidence suggests caustics, otherwise leave to allow natural resolution.

“Major trials still needed into most therapies to test effectiveness.”
The highest quality of clinical evidence for monotherapies (Lipke’s review) are:

- Cryotherapy (A, I)
- Photodynamic therapy (B, I)
- Salicylic acid, bleomycin & retinoids (B, II)
- Formaldehyde (C, II)
- Thermocautery (C, III)
- Chemical cautery, CO2 laser, pulsed dye laser & topical sensitization (C, IV)
- Cimetidine (D, I)

High quality RCT not available for most treatments, thus not considered in official treatment guidelines.... However, review of the literature suggests much higher success rates with less widely tested approaches (Lipke, 2006).
So, what`s new?

- Better understanding of cell-mediated immunologic response to HPV
- Immune response modifiers; e.g. Imiquimod (Aldara)
- Sub-type specific antiviral therapy for HPV (Gardasil for types 6, 11, 16, 18, 31, 33, 45, 52, and 58)
Swift microwave - The new kid on the block...

“..capable of supplying enough energy to agitate water molecules and cause friction and deliver less energy into the skin than most laser and electrocautery treatments...”
Case studies report 76% success rate, with multiple applications.... plus a keratolytic?

"I like the idea of exciting moisture..."

Longhurst (2016)
Needling hypothesis -

• Tissue damage alone may not produce enough cytokines to destroy latent virus particles, thus recurrence is high (Bristow & Stiles, 2011)

• The absence, or reduction, of a cellular immune response actively caused by the virus may explain why treatments are not uniformly successful, even in immune-competent individuals (Frazer, 2009).

Needling **MAY** offer;
1. Destruction of HPV infected keratinocytes
2. induces an assumed **enhanced** cell-mediated immune response.
`Mosaic verrucae-help with treatment`

Courtesy of Professor Kevin Kirby DPM
“...physical trauma without the use of chemicals... thrusting in a needle in dart fashion, so as to penetrate the full depth of the verruca & exiting through the base of the capsule into the fat...” - Falknor, 1969

“...the entire lesion was perforated enough to produce a beefy red wound.“ - Kirby, 2011
Standardised procedure:
• Informed consent
• Pre op disinfectant
• Anaesthesia (tibial, digital block or local infiltration)
• Largest/painful lesion selected if multiple
• Lesion punctured using empty needle to subcutaneous tissue, until no resistance
• Dressed and reviewed at one & eight weeks
Further evidence…..

- **Parton & Sommerville (1994)** 94% resolution rate in 4-14 year olds, by producing debriding to pinpoint bleeding, abraded with fine glass paper.
- **Chapman & Visaya (1998)** 43% resolution rate in 6-13 year olds, by producing pinpoint bleeding, observed spontaneous regression in children.
- **Skilton & Mehar (2011)** 50% resolution rate at 8 week review by needling 14 adults.
- **Longhurst & Bristow (2013)** 69% resolution rate by needling 46 adults.
- **Hashmi & Bristow (2014)** discussed autoinoculation & needling agreed around the 70% mark
- **Cunningham & et al (2014)** 64.7% resolution rate needling 18 adults.

All the above suggest that a cell-mediated response through needling, or pinpoint bleeding, can induce verrucae resolution

A recent RCT by Hashmi *et al* (comparing a single needling to sharp debridement) Interesting findings regarding efficacy, pain outcomes & participant satisfaction, leading to more research…
The Treatment of Verrucae Pedis Using Falknor’s Needling Method: A Review of 46 Cases

Belinda Longhurst 1,† and Ivan Bristow 2,†,*

Largest case series published to date

- Adult population with broad age range
- 69% [31] complete resolution (max x 2 tx)
- 3 of unresolved a reduction in size & discomfort
- 11 showed no improvement
- All patients reported post-op pain either “mild” [64%] or “none” [36%].
- No adverse events noted or reported
- No scarring or post-op bacterial infections occurred during this study.
- Authors suggest provocation of cell mediated immunity through implantation of virus deeper into tissues
Needling Versus Liquid Nitrogen Cryotherapy for the Treatment of Pedal Warts. A Randomized Controlled Pilot Study

Cunningham, DJ et al

Results: Of 37 patients enrolled in the study, 18 were allocated to receive needling and 19 to receive liquid nitrogen cryotherapy. Regression of the primary pedal wart occurred in 64.7% of the needling group (11 of 17) and in 6.2% of the liquid nitrogen cryotherapy group (1 of 16). There was no significant difference in pain, satisfaction, or cosmesis between the two groups.

Conclusions: The regression rate of the primary pedal wart was significantly higher in the needling group compared with the liquid nitrogen cryotherapy group. (J Am Podiatry Med Assoc 104(4): 394-401, 2014)
Treating plantar warts: utilising natural immunity to induce wart regression

Hashmi, Farina; Bristow, Ivan
Dermatological Nursing, 2014 13(1); 42-45

“The evidence supporting autoinoculation (autoimplantation) techniques is strong... Auto-inoculation by removing a section of a wart and implanting the tissue into a surgically made cavity.”
The EVerT2 (Effective Verruca Treatments) Trial: a randomised controlled trial of needling versus nonsurgical debridement for the treatment of plantar verrucae.

Hashmi F¹, Fairhurst C², Cockayne S², Cullen M¹, Bell K², Coleman E², Harrison-Blount M¹, Torgerson D².

Abstract

BACKGROUND: Verrucae are a common foot skin pathology which can in some cases persist for many years. Plantar verrucae can be unsightly and painful. There are a range of treatment options including needling.

OBJECTIVES: The EVerT2 trial aimed to evaluate the clinical and cost effectiveness of the needling procedure for the treatment of plantar verrucae, relative to callus debridement.

METHODS: This single centre randomised controlled trial recruited 60 participants (aged 18 years and over with a plantar verruca). Participants were randomised 1:1 to the intervention group (needling) or the control group (debridement of the overlying callus). The primary outcome was clearance of the index verruca at 12 weeks after randomisation. Secondary outcomes include recurrence of the verruca; clearance of all verrucae; number of verrucae; size of the index verruca; pain; and participant satisfaction at 12 and 24 weeks. A cost-effectiveness analysis was carried out from the NHS perspective over 12 weeks.

RESULTS: Sixty eligible patients were randomised (needling group n=29, 48.3%; debridement group n=31, 51.7%) and 53 were included in the primary analysis (needling n=28, 96.6%; debridement n=25, 80.7%). Clearance of the index verruca occurred in 8 (15.1%) participants (needling n=4, 14.3%; debridement n=4, 16.0%, p=0.86). The needling intervention costs were on average £14.33 (95% CI 5.32 to 23.35) more per patient than debridement.

CONCLUSIONS: There is no evidence that the needling technique is more clinically or cost effective than callus debridement. The results show a significant improvement in pain outcomes after needling compared to the debridement treatment alone. This article is protected by copyright. All rights reserved.
Risks to consider in VP treatment;

Despite documented adverse events, caustics are still deemed to be significantly efficacious and relatively safe IF USED APPROPRIATELY AND WITH CAUTION....much like needling.

Needling successfully utilised internationally for over 48 years & currently subject to randomised controlled trials. Meanwhile, retrospective studies continue to suggest this is a safe and efficacious treatment.

▶ Aetiology of HPV
▶ Suitability of patient
▶ Correct diagnosis!...
Diagnosis of neoplasms based on appearance – raised lesions

Benign - common

- Seborrhoeic keratosis (stuck-on appearance)
- Benign melanocytic naevus (common mole / soft or wobbly)
- Dermatofibroma (fawn with darker rim / firm / dimples when pinched)
- Blue naevus (an even blue-grey colour)
- Pyogenic granuloma (vascular lesion following trauma)

Soft ‘n’ wobbly – usually OK
Firm ‘n’ fast growing – not so!
Sun Damaged, Pre-malignant & Slow growing tumours

Actinic (Solar) Keratosis,

Cutaneous Horn - SCC can be found at the base
Squamous Cell Carcinoma – 2 week rule!

- Over 55’s.
- Sunlight exposure, industrial carcinogens, long standing ulcer, Bowens disease or SK.
- Frequently misdiagnosed for VP, ulcer & TP.
- Elevated “heaped up” rapid manifestation with central depression, wart-like growths, nodules and open sores. With crusted surface or bleeding.
- Palpate lesion – if tender & does not blanche = suspicious!
- Immuno-compromised inc risk of SCC than to BCC – opposite to immune competent population.
- Treatment- Surgical excision by CD.
Superficial spreading melanoma & Nodular melanoma

Recognition of a malignancy is more important than identifying type of melanoma!

- 11,000 cases per year in UK, 2000 deaths per year in UK
- Incident rates of melanoma have more than doubled since 1995, with 14,000 cases and over 2,200 deaths registered last year.
- Commonest cancer in 15 to 34 Y/O
- Increases faster than any other cancer
- After tx of primary mole, recurrence in 1/3 of pts & metastasize IN ANY ORGAN OF THE BODY. Eg Kidneys
- Prognosis for advanced MM; 38% less than 5 years.
- Early stage dx can dramatically increase a patient's chances of survival.
Australia - highest incidence of melanoma in the world, banned tanning salons

Previous & familial MM, immune-compromised, previous sun-burn.

Presents different in nail & plantar aspect of the foot to other parts of the body = misdiagnosis & poor prognosis.

Superficial spreading starts slightly elevated, irregular brown or black patch - `smudged look`.

$1/3$ acral melanomas are amelanotic, including subungual! (often resemble infection)

Diff dx – TP, OM, HPV, Haematoma, OC, DFO.
“Furrows are fine – ridges are risky”
- Ronald P. Rapini

Lesions with parallel pigment in the furrows are benign while those with pigment over the ridges should be considered suspicious for melanoma.
Dermoscopy For Beginners

“This day course is designed to provide GPs and AHPs with the knowledge of types of instruments, what you can rapidly learn to improve your diagnostic accuracy and to warn you when expert opinion is needed. The aim of the training is to safely differentiate the obviously benign lesions such as seborrhoeic keratosis, from possible cases of melanoma and thereby reduce the large numbers of skin lesions that are referred to Secondary Care under the 2 Week Rule.”
Know your ABC.....

...EFG rule
Nodular melanoma may lack the signs referred to above and should be considered in any skin lesion demonstrating EFG:

E = Evolving and/or Elevation
F = Firmness to touch
G = Growth Persistent growth for over one month
H = ?
Know your ABCDEFG....H
Conclusion

➢ Placebo action not determined in needling

➢ Introducing HPV infected keratinocytes into subcutaneous layer facilitates cell-mediated immune response in some patients, to reduce or eradicate the virus.

➢ No one tx can claim 100% success. However, the greater, or lengthier, the localised (innate) response - evident with inflammation - greater chance of achieving acquired (adaptive) response.

REMEMBER YOUR ABCDEFG & H!
References


- Bristow IR, Stiles CJ: The treatment of stubborn plantar warts using topical 5% imiquimod cream *Podiatry Now* 2011, 14(10):14-16


References (cont`d)


Started in 2013 at Magg’s homeless centre, Worcester by Debi Monk - Chair of FF.

Vision: to create a network of free clinics, across the UK for the homeless population.

Nov 2017 there were 6 clinics. Now approximately 45!

Formally a small constituted charity, aiming for registration with the charity commission - we need 5K in the bank!

Ways you can help:

- Fundraising events and donations.
- Charity collection boxes.
- Donations of instruments, consumables or equipment.
- Running or volunteering at a clinic in or near your area.

www.forgottenfeet.uk