PHOTOCHEMICAL MODULATION OF WOUND HEALING AND INHIBITION OF TISSUE DEGRADATION

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- Wellman Center for Photomedicine, Mass General Hospital
- PDT=photodynamic therapy
  - Need a nontoxic dye
  - Light
  - Together causes an excited state that interacts with oxygen and kills cells
  - Started as a cancer therapy in 1905
  - Dye which absorbs visible light
  - Red light penetrates tissue better, so tend to use this wavelength
  - Dual selectivity for target: selective accumulation of photosensitizer (PZ dye)
  - Excited states of PS, singlet, double, triplet is longer lived can degrade as phosphorescence but is longer lasting and can interact with oxygen to cause a cytotoxic species, which can oxidize DNA, proteins, lipids
- Photosensitizers are usually natural pigments: tetrapyrroles, such as heme, chlorophyll, bacteriochlorophyll
- Why do we use PDT against microorganisms?
  - For localized infections (not systemic)
  - Photosensitizer is delivered locally to infection
  - World-wide increase in multi-antibiotic resistant bacteria
  - Systemic antibiotics cannot get into dead or damaged tissue
  - Even if antibiotics work they take several days
- Antibiotic resistance
  - 70% of bacteria that cause infections in hospitals are resistant to at least one antibiotic
  - Food producing animals
  - Given to pt more often than necessary
  - Pt c\don't complete the course
- What do we know about antimicrobial PDT?
  - Gram + specials easily killed by usual PS + light
  - Gram - species need cationic PS or special means to increase bacterial permeability
  - Choice of PS: chlorin E6 good absorption peak at 660 nM
- Bioluminescence imaging
  - Genetically engineered bacteria which emit light, “glow in the dark”
  - Can prove the efficacy of PDT treatment
• Test with Pseudomonas aeruginosa, causes systemic ds and death in 2-4 days, but PDT treatment stops the infection, and the wound infection healed better than treatment with silver nitrate
• PDT does not accelerate wound healing but contradicts later
• Silver nitrate does not accelerate or slow wounding healing
• PDT appears to destroy bacterial virulence factors that otherwise would slow wound healing
• Topical PDT with 665 nm light improves wound healing with some PS and delays wound healing with toluidine blue + 630 nm
• Low dose 630 nm light improves wound healing – not a big effect 10 J / cm2
• High dose 50J/cm2 630 nm light has no effect
• CONCLUSIONS:
  o Stimulation of wound healing is complicated
  o Light alone may have an effect
  o Ps identity
  o Ps dose
  o Ps delivery route
  o Time between PS and light
  o Wavelength
  o Fluence
  o Fluence rate
• Questions: may be better lower dose, possibly 1-2 joules
• Comment: may be given a higher dose than they think
• Some of this research has been done by Mary Dyson
• This research are excisional wounds are mice
• Wounds all heal by contraction, the amount of granulation tissue is clearly different, a lot of granulation tissue slows healing
• Why hasn’t this caught on clinically? Need a good PS, the FDA approved ones are not good for bacteria. The only clinical application is in UK, toluidine blue and then red laser to sterilize a cavity in dental work.