HONEY
Andrew Kochan, MD
First Contact

- Humans started collecting honey from bees approximately 9000 years ago

- A rock painting found near Valencia, Spain dating from 7000 B.C. shows a man gathering honey
A rock painting dating back to the Mesolithic era, discovered in a cave near Valencia, Spain, shows an ancient woman gathering honey.
History of Apitherapy

• Drawings on Egyptian Temples built about 2400 B.C. show bee keeping and honey preparation. In the oldest medical papyri of Egypt, dating back to 1553-1550 BC, there are indications that honey was used to heal wounds.

• Ancient writings including the Talmud, the Bible, scrolls from the Orient, ancient Greece and Rome all praised honey and bee pollen as a source of youthfulness and health.
History of Honey Use

• Smith papyrus 2,600 – 2,200 BC: Grease-honey-lint compound used as wound dressing
  * Dioscorides (c.50 AD) wrote: “Honey is good for all rotten and hollow ulcers.”
  * Aristotle (350 BC) wrote of using honey to treat wounds.
A painting in the tomb of Pa-Bu-Sa (circa 620 B.C.) in Thebes, Egypt, depicts an ancient beekeeper.
In Egypt the earliest hives were cylinders made out of clay that could be stacked.
Modern Hive
History Of Honey Use

Hippocrates wrote “honey and pollen cause warmth, clean sores and ulcers, soften hard ulcers of the lips, heal carbuncles and running sores”.

Galen, the great Roman physician, considered honey an all-purpose remedy, recommending it to treat many kinds of poisoning and intestinal ailments, in particular gangrenous stomatitis.
• The Koran in a section titled “The Bee” says honey is a “medicine for men”
• In the Orient a mixture of honey and pollen was used as a poultice on wounds and as a health tonic
• In India the tonics prescribed ‘to give pleasure’ and ‘to preserve youth’ were mainly prepared from honey. A diet in which honey and milk were the main items was thought to prolong life.
HONEY

- Honey is produced in specialized glands of the honey bee by the conversion of nectar which they collect from flowers.
- A bee has to visit 1000 flowers to collect $\frac{1}{4}$th of a teaspoon (1.25 ml) of nectar.
- The moisture content of the nectar is then lowered to about 16% by the bees “blowing” on it with their wings and evaporating the water.
DIFFERENT HONEYS
The flower(s) from which the nectar is collected helps determine the taste and medicinal properties of the honey

- The free radical scavenging activity measured by DPPH method indicates that the darker honeys such as buckwheat, manuka, blueberry, and eucalyptus have higher antioxidant properties compared to lighter-colored varieties.

- Dicarbonyl Content of Commercial Honeys from Different Botanical Origins: Identification of 3,4-Dideoxyglucoson-3-ene (3,4-DGE) and Related Compounds
  
  *Agric Food Chem*, 2009 Oct 2
Honey has more than 350 Components

- 42 different sugars
  - 54-84% monosaccharides
- 23 different amino acids
  - proline is from 45-85% of the total
- Vitamins B1, B2, B3, B5, B6, A, K, C, E
  - C - 2,000 - 3,400 mcg/ 100 g
  - B2- 22 - 63 mcg / 100 g
  - B3- 20 -105 mcg /100 g
  - B5- 108 - 978 mcg / 100 g
  - B1- 3.5 -22 mcg / 100 g
  - B6- 7.6 - 299 mcg / 100
More Components

• Enzymes
• Aliphatic esters- (37)
• Phenolic compounds- (15) acids
• Flavinoids- (19)
• Nitric oxide
• Minerals- copper
  - iodine
  - magnesium
  - phosphorous
Nitric Oxide Levels in Honey

The levels of NO metabolites varied between the honey samples. The highest level was in the fresh dark honey collected from Yemen, and the lowest in 1-year-stored dark honey collected from India.

• Darker or fresh honeys contained more NO metabolites than light or stored honey.
• Heating decreased NO metabolites in all the kinds of honey.
Honey Has Many Uses

- Broad spectrum anti-microbial activity
- Anti-inflammatory effects
- Pulmonary and respiratory benefits
- Gastric ulcer and dyspepsia treatment
- Ophthalmological problems
- Wound healing
- Dermatologic lesions
- Blood sugar control
- Facilitation of sleep
- Sports Performance
Anti-bacterial Properties Related to several Factors

- High Sugar Content: Osmotic Content
- Glucose oxidase enzyme: production of hydrogen peroxide killing bacteria and providing debriding action
- Acid pH 3.2-4.5: inhibits bacterial growth
- Plant-derived factors- Present in some honeys and not yet well characterized but probably accounts for the differences in anti-microbial activity
- Mechanical sealant keeping wound moist and clean
- Simple sugars directly absorbed into the tissue stimulate tissue growth
High Sugar Content

• The high osmolarity of the honey causes water from inside any cell (bacterium or fungus) to move outside the cell thus dehydrating and killing the cell.

• Since honey is a supersaturated solution of sugar it has a tendency to crystallize if there are impurities in it. Several factors affect its tendency to do this- water content, types of sugars and their ratios, amounts of impurities blossoming season, and storage temperature.
Crystallization

• Glucose crystallizes first since it is less soluble than fructose.

• If crystallization starts the remaining solution is less concentrated. If the concentration of water is greater than 20% the honey can start to ferment due to naturally occurring yeasts in the honey.

• To reverse crystallization need to heat the honey for a short time at high enough but not too high a temperature.
Temperature effects on Honey

- If honey is heated too much it will destroy its enzyme activity, it will turn color and flavor will be off. Fructose will be converted to HMF.
- Hydroxy Methyl Furfural (HMF) is an indicator for honey damage.
- Heating honey to 63°C sharply increases HMF.
- Honey at 18°C (64°F) shows a moderate increase in HMF.
- Storing honey at 6°C (43°F) for 12 months- no increase.

- Chemical Composition of Honey, Faten Abd El-Hady and Ahmed G. Hegazi.
Glucose oxidase enzyme

• Glucose Oxidase + glucose in acid- no reaction
• Glucose Oxidase + glucose in pH >6.1 (as in blood or in contact with tissue) = H2O2 + gluconic acid

• Thus hydrogen peroxide is produced, killing bacteria and providing debriding action in the wound. Also pH is lowered which slows the reaction unless there is more exposed tissue.
Acid pH 3.2-4.5: inhibits bacterial growth

- Bacteria, fungi and viruses don’t grow or reproduce well in acid environments.
- Blood in wounds will act to buffer the acid so will allow bacterial growth if the honey is not replenished frequently enough.
Plant-derived factors- one example

• A fraction of New Zealand manuka honey has been isolated, which gives rise to the non-peroxide antibacterial activity. This fraction proved to be methylglyoxal, a highly reactive precursor in the formation of advanced glycation end products (AGEs).

• Isolation by HPLC and Characterisation of the Bioactive Fraction of New Zealand Manuka (Leptospernum Scoparium) Honey
  Carbohydrate Research,
Neutralization of the anti-bacterial potency

- Blood- acts to buffer the pH
- Heat- 85°C for 15 min. inactivates the glucose oxidase
- Photosensitivity
Broad spectrum anti-microbial activity

- Topical Manuka Honey for MRSA Contaminated Skin Ulcers

- The Intracellular Effects of Manuka Honey on Staphylococcus aureus
  *European Journal of Clinical Microbiology & Infectious Diseases*, October 08, 2009
Antibacterial Honey (Medihoney™): in-vitro Activity Against Clinical Isolates of MRSA, VRE, and Other Multiresistant Gram-negative Organisms Including Pseudomonas aeruginosa

- Narelle M. George; Keith F. Cutting, Wounds. 2007;19(9):231-236
- Medical grade honey is filtered, gamma irradiated, and produced under exacting standards of hygiene.
- The results are clear and provide additional *in-vitro* evidence that Medihoney Antibacterial Honey is an effective antibacterial agent, the implication being that Medihoney provides a valuable opportunity to manage wound infection caused by a range of multiresistant strains of bacteria.
Rediscovering the Antibiotics of the Hive

Boukraa, L Sulaiman SA
Department of Pharmacology, School of Medical Sciences, Universiti Sains Malaysia, Health Campus, 16150 Kubang Kerian, Kelantan, Malaysia.

• Even antibiotic-resistant strains such as epidemic strains of methicillin-resistant Staphylococcus aureus (MRSA) and Vancomycine resistant Enterococcus (VRE) have been found to be as sensitive to honey as the antibiotic-sensitive strains of the same species.
In Vitro Anti-Staphylococcal Activity of Honey and Two Standard Antibiotics

• 50 isolates of Staph aureus and Staph albus were exposed to dilutions of honey and Ampicillin and Cloxacillin.
• “Cloxacillin recorded higher antibacterial activity than ampicillin but both exerted less antibacterial activity than honey.”

Antimicrobial Activity of Honey from the Stingless Bee Trigona carbonaria…

Stingless bee honey has broad-spectrum antibacterial activity although activity against Candida was limited.

Journal of Applied Microbiology, Published Online: 7 Oct 2009
When Antibiotics Fail, Nurses Turn to Maggots and Manuka Honey to Beat Superbugs

- At the Royal United Hospital in Bath, England, many wounds are now being disinfected with Manuka honey because they are faced with a growing prevalence of antibiotic-resistant bacteria
Anti-Yeast Activity

• All of the 40 yeast strains (Candida albicans, C. krusei, C. glabrata and Trichosporon spp.) tested were inhibited by honeys in this study.

• Rhododendron and multiflora honeys generally are more inhibitory than eucalyptus and orange honeys.

• Antifungal Activity of Turkish Honey Against Candida spp. and Trichosporon spp: An in vitro Evaluation, Medical Mycology, Volume 47, Issue 7 November 2009, pages 707 - 12
Honey and Cough

- Honey may modestly decrease frequency and severity of cough compared with Dextromethorphan or no treatment.

- Do OTC remedies relieve cough in acute upper respiratory infections?

  *J Fam Pract*, 2009 Oct;58(10):559a-c
Pulmonary and Respiratory Benefits

- **BEE HONEY NEBULIZATION AS A NON TRADITIONAL TREATMENT OF ACUTE BRONCHIAL ASTHMA IN INFANTS AND CHILDREN** *Dr. Mamdouh Abdul Maksoud Mohammed Abdul Rahman 2003*

- Children treated for 30 minutes with Bee Honey Nebulization.
- In 35% wheezes resolved and in 31% significantly decreased.
- pO2 on room air increased and heart and respiratory rates decreased significantly.

- In a separate respiratory trial inhalation of a honey solution for 10 minutes resulted in a increase of 11-16% in peak expiratory flow rate.
Anti-inflammatory Properties

- Honey is known to have anti-inflammatory properties and case studies have demonstrated its usefulness on non-healing wounds (Dunford, 2005; 2000).
- A laboratory study on the effect of honey on cells implicated in prolonged inflammation demonstrated that the honey was able to modulate the activity of monocytes to release growth factors and anti-inflammatory agents (Tonks et al, 2003), although how this is achieved is not yet understood.
Gastric Ulcer and Dyspepsia Treatment

- A placebo-controlled trial of honey for gastric ulcer and dyspepsia resulted in a 66% cure rate.
Ulcerative Colitis

Oral administration of MHoney (5g/kg) and combination with sulfasalazine (360 mg/kg) with MH (5g/kg) significantly reduced the colonic inflammation.

- Effect of Manuka Honey and Sulfasalazine in Combination to Promote Antioxidant Defense System in Experimentally Induced Ulcerative Colitis Model in Rats

Ophthalmological problems

- Dry eye syndrome, Cataracts, Herpetic Keratitis, Corneal abrasions and ulcers
- Ancient texts and the Koran advocate honey for cataracts.
- Local honey as an ointment (i.e. concentration 100%) is very effective in treatment of keratitis even in the presence of ulceration. Honey will be effective whatever the cause of keratitis because it has antimicrobial (including viruses and fungi), anti-inflammatory and wound healing effects.
Treatment with 20% Honey Eye Drops in Patients with Dry Eye Syndrome

• After treatment with 20 % honey eye drops improvement of ocular changes was observed in most of patients with dry eye syndrome comparing with conventional treatment with artificial tears. We found a positive effect of 20 % honey eye drops on the state of the cornea.

• J.Jankauskienė—, D.Jankauskaitė— Kaunas University of Medicine Eye Clinic, Mickeviciaus 9, Kaunas, Lithuania, LT-44248
Honey and Cataracts

• A cataract is the opacification of the ocular lens
• Researchers in Venezuela have found that luteolin derivatives which are a major component of the honey from the stingless bee found in Brazil and Venezuela reduced lens opacification. Cataracts of patients in Brazil have been successfully treated by using a few drops of this honey in their eyes.
Honey and Cataracts

In Romania Dr. Popescu has treated thousands of patients with a 2% solution of honey in saline in the eyes for 10 days, followed by royal jelly in the eyes. Dr. Mansour in Egypt treated 32 patients with cataracts with one drop of honey in the eye 4 or 5 times a day and had good improvement in visual acuity.
“…there are no proven means to prevent age related cataracts. There are no medications, eye drops, or glasses that will make a cataract disappear.”

Recent Advances and Future Frontiers In Treating Age-Related Cataracts, JAMA, July 9, 2003 pp248-251
Wound Healing

• "The Evidence Supporting the Use of Honey as a Wound Dressing“, 
• The International Journal of Lower Extremity Wounds, Dr. P.C. Molan of New Zealand's University Waikato
• As of 2007 scientists had published 22 trials (17 randomized) involving 2,062 patients treated with honey, as well as an additional 16 trials that were performed on experimental animals. Honey was found to be beneficial as a wound dressing in the following ways:
Wound Healing - Continued

- Honey's antibacterial quality not only rapidly clears existing infection, it protects wounds from additional infection
- Honey debrides wounds and removes malodor
- Honey's anti-inflammatory activity reduces edema and minimizes scarring
- Honey stimulates growth of granulation and epithelial tissues to speed healing
Wound Healing Mechanisms

Keratinocytes, which are known to be involved in wound healing, are responsible for elevated production of mediators including cytokines (TNF-alpha, IL-1beta and TGF-beta) and matrix metalloproteinase-9 (MMP-9) after incubation with honey.

- This data demonstrates that honey activates keratinocytes and supports the findings that honey may accelerate wound healing process with the up-regulation of expression of certain cytokines (TNF-a, IL-1b and TGF-b) and MMP-9.

- Effect of Honey and Its Major Royal Jelly Protein 1 on Cytokine and MMP-9 mRNA Transcripts in Human Keratinocytes, *Exp Dermatology*, 2009 Oct 21
TREATMENT of WOUNDS with HONEY

Glucose Oxidase enzyme activity produces H2O2 which stimulates the growth and division of cells by activating nuclear transcription factors in fibroblasts & epithelial cells and activates insulin receptors on cells which promotes healing.
WOUND HEALING

• Topical applications under controlled conditions have shown accelerated wound healing in animals (Bergman et al., 1983, El Banby et al. 1989) and of experimental burn wounds in rats (Burlando, 1978) but also of various types of wounds, including post-operative ones in humans (Cavanagh et al., 1970; Kandil et al., 1987a, b and 1989; Effem, 1988 and Green, 1988).
WOUND HEALING

• Honey applied directly on open wounds, sores, bed sores, ulcers, varicose ulcers and burns, in its pure, unprocessed form, helps against infections, promotes tissue regeneration, and reduces scarring (Hutton, 1966; Manjo, 1975; Armon, 1980 and Dumronglert, 1983).

• If applied immediately, honey reduces blistering of burns and speeds regeneration of new tissue.
Diabetic Ulcer Treatment

• Dr. Jennifer Eddy at the University of Wisconsin salvaged a severely gangrenous diabetic foot ulcer using honey treatment.

59 patients with diabetic ulcers, burns, traumatic ulcers, gangrene, and other types of wounds for periods of between 1 month and 2 years. 51 of the 59 wounds had been infected prior to honey treatment.

All were free of infection within one week of starting honey dressing applications. In addition, inflammation and odor were markedly reduced and healing rapidly ensued.
Journal of Wound, Ostomy and Continence Nursing, 2002;29:295-300

• 900 participants with partial-thickness burns were randomly assigned to receive either honey dressings or other dressings. Honey was applied directly to the burns and covered with sterile dressings on alternate days.

• Those whose burns were treated with honey had faster healing and less scarring than those treated with other dressings.

• In the case of full-thickness burns, however, honey has been found to be inferior to other treatments.
The Evidence Supporting the use of Honey as a Wound Dressing

A review of more than 20 published studies. The author recommends that wounds—especially those which are infected with antibiotic resistant bacteria be treated with honey.

An In Vitro Evaluation of the Cell Toxicity of Honey and Silver Dressings

• Human keratinocyte and fibroblast tissue cultures were co-cultured with monofloral medicinal honey and nanocrystalline silver.

• No cell toxicity was observed after four months of continuous tissue culture with honey, but marked toxicity and poor viability was noted with the silver dressing.

Journal of Wound Care, Vol. 18, No. 9, 10 Sept 2009, pp 383-389
Dermatologic lesions

Reportedly good for

• Acne
• Epidermolysis Bullosa- 20 year duration of non-healing in 15 weeks closed after application of honey dressing (Hon, 2005)
The patients were divided into two groups.

Group I- 21 patients were treated with broad-spectrum triple antimicrobial therapy, broad debridement, exhaustive cleaning, and then they underwent split-thickness skin grafts or delayed closure as needed.

Group II- 12 patients (Group II) were treated with unprocessed honey (20-50 mL daily) and broad-spectrum triple antimicrobial therapy without debridement...

The clinical and cosmetic results were better in Group II than Group I.
Greek Honey

- Pine honey and thyme honey extracts showed weak estrogenic activity at high concentrations (20-100µg/ml). But acted as potent antiestrogens at low concentrations (2-5µg/ml), both when examined alone and in presence of estradiol.
- Fir honey exhibited also estrogenic effects at high concentration (20-100µg/ml) but anti-estrogenic effects at low concentrations (2-5 µg/ml).
- Prostate CA cells had no response to fir and pine honey but thyme honey reduced cell viability.
- Breast CA cells had no response to thyme and pine honey but fir honey stimulated significantly the viability of the cells.

A. Tsiapara, et al. Dept of Biological Chem, Med School, University of Athens
Personal Experience

- Small bowel-cutaneous fistula
- 3\textsuperscript{rd} degree road rash
- Alkali burn on knees
- Abrasion tip of finger
Cardiac

• Cardioprotective to persons in a hyper-adrenergic state. Rakha, Miran K., Zoology Department, Suez Canal University, Ismailia, Egypt
Blood Sugar Control

• In healthy individuals, the consumption of honey produced lower blood sugar readings than the consumption of the same quantity of sucrose (Shambaugh et al., 1990).

• Honey compared to dextrose and sucrose caused a lower elevation of blood sugar in diabetics and reduced blood lipids, homocysteine and CRP in normal and hyperlipidemic persons (Al-Waili, 2004)
Facilitation of Sleep

• Honey improves, facilitates and lengthens restorative sleep.
• Insures adequate liver glycogen stores for 8 hrs. of sleep thus limiting early morning release of cortisol and adrenalin
• Stabilizes blood sugar levels
• Contributes to the release of Melatonin

Products of Apiculture and Preventive Maintenance of Aging

- Examination of 193 beekeepers daily using honey in quantity of 57.2 +/- 8.6 gram with definition of their biological age was carried out.
- The research has shown that the biological age of 70% of beekeepers is lower than that of the average in population, 15% of beekeepers are of the same and 15% are of higher biological age than that of the average in population.
- The biological age of beekeepers was less than of persons who are not using products of beekeeping

- Adv Gerontol, 2008; 21(2):252-7
Other uses of Honey

- Dental - gum disease due to antimicrobial effects
- Hypoglycemia - can be used and absorbed sublingually. Low glycemic index so doesn’t stimulate insulin as much as other sweeteners
- Hayfever - Oral honey reduced symptoms in 76%
Sports Performance

• Endurance. “We found honey to be one of the most effective forms of carbohydrate gels to ingest just prior to exercise. This could translate into greater endurance during a workout or race. Honey…relatively mild in it’s effects on blood sugar”. Dr. Richard Kreider, University of Memphis Exercise and Sport Nutrition Laboratory. It has a lower glycemic index and so a lesser insulin response with subsequently less fatigue later.
HONEY AND ENDURANCE PERFORMANCE

• April 4, 2003- a new study presented at the annual Experimental Biology meeting indicates that using honey as a carbohydrate source during exercise significantly improved performance and power during endurance cycling trials.

• Honey has a milder effect on blood sugar than other forms of carbohydrate gel and when used with a protein supplement has been shown to speed muscle recovery after a workout.

• Honey contributes 350 kcal/100gr
Greek Honey

- Pine honey and thyme honey extracts showed weak estrogenic activity at high concentrations (20-100µg/ml). But acted as potent antiestrogens at low concentrations (2-5µg/ml), both when examined alone and in presence of estradiol.
- Fir honey exhibited also estrogenic effects at high concentration (20-100µg/ml) but anti-estrogenic effects at low concentrations (2-5 µg/ml).
- Prostate CA- no response to fir and pine honey but thyme honey reduced cell viability.
- Breast CA cells had no response to thyme and pine honey but fir honey stimulated significantly the viability of the cells.

A. Tsiapara, et al. Dept of Biological Chem, Med School, University of Athens
Specific Honeys for Specific Purposes

- Wild Rose- angina, arteriosclerosis, hypertension
- Heather- cystitis, prostatitis, intestinal infections
- Eucalyptus (Spain)- bronchitis, cough, UTI
- Lavender- respiratory system, burns, infected wounds
- Orange tree- anxiety, headache, nervousness
- Clover- asthenia, physical tiredness, sports
- Honey of stingless Meliponini bees tropical plant origin has in it royal jelly, and is known to produce large amounts of H2O2 and gluconic acid- good for wounds, ocular infections, cataracts, skin diseases, hemorroids, loss of teeth, and respiratory infections.
END