Exploring Honey for Wound Management

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CCAM Research Partners &
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Wound incidence

Every year in the U.S., more than 1.25 million people have burns and 6.5 million have chronic skin ulcers caused by pressure, venous stasis, or diabetes mellitus (Brigham, P.A. and McLoughlin, E. (1996) Burn incidence and medical care use in the United States: estimate, trends, and data sources. *J. Burn Care Rehabil)*. Diabetes represents a major impact on wound healing outcome. In 2004, according to the World Health Organization (WHO), more than 150 million people worldwide suffered from diabetes. Its incidence is increasing rapidly and it is estimated that by the year 2025, this number will double.

Wound Type	Worldwide Prevalence (millions)	Healing time (days)	CAGR 2005-14
Surgical wounds	102.8	14	3.1
Traumatic wounds	1.5	28	1.4
Lacerations	19.9	14	1.0
Burn wounds (out-patient)	3.3	21	1.0
Burn wounds (medically treated)	6.3	21	1.0
Burn wounds (hospitalized)	0.2	50	1.1
Pressure ulcers	7.4	-	6.2
Venous ulcers	11.0	-	6.4
Diabetic ulcers	11.3	-	9.4
Amputations	0.2	-	0.9
Carcinomas	0.6	14	3.0
Melanoma	0.1	14	3.0
Complicated skin cancer	0.1	28	3.0

CAGR = Compound annual growth rate

Wound pathophysiology

Definition

A wound is a disruption of the continuity of a tissue structure. Injury, by surgery or accident, causes destruction of tissue, disruption of blood vessels, and extravasation of blood constituents and hypoxia.

Process – Phase 1

Wound healing is a complex, continual process that has three phases: inflammation, a proliferative phase, and tissue remodeling. Basically, wound healing is the result of interactions among cytokines, growth factors, blood and cellular elements, and the extracellular matrix. The cytokines promote healing by various pathways, such as stimulating the production of components of the basement membrane, preventing dehydration, and increasing inflammation and formation of granulation tissue.

Wound pathophysiology

Process – Phase 2

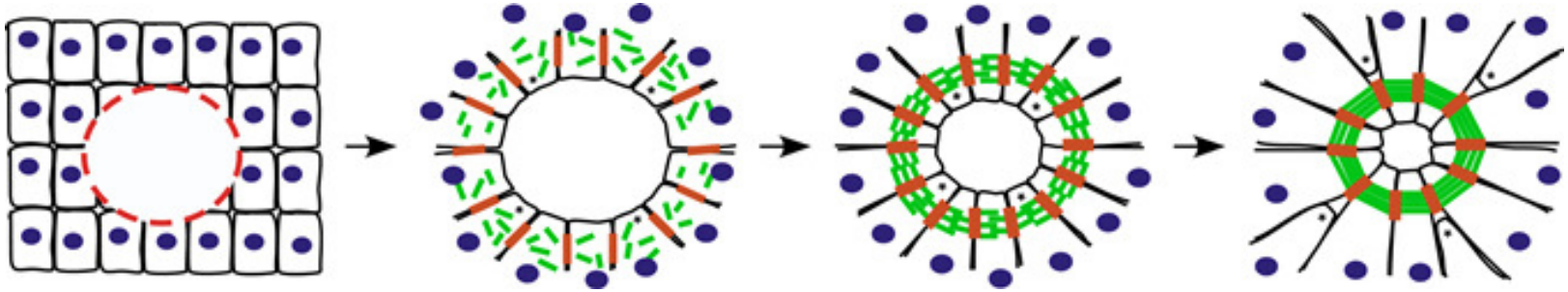
At the cellular level, monocytes infiltrate the wound site and become activated macrophages that release growth factors, such as platelet-derived growth factor (PDGF) and vascular endothelial growth factor (VEGF), which initiate the formation of granulation tissue. Macrophages have a key role in inflammation and repair. It has been found that macrophage-depleted animals have defective wound repair. Macrophage transfusion accelerates wound healing in patients with nonhealing wounds. Platelets facilitate the formation of a hemostatic plug and secrete PDGF, which attracts and activates macrophages and fibroblasts. Re-epithelialization of wounds begins shortly after injury. Epidermal cells at the wound margin begin to proliferate within 1 to 2 days after injury. On day 4 after injury, new granulation tissue begins to invade the wound gap and numerous new capillaries grow through the new stroma with its granular appearance. After migrating into wounds, fibroblasts begin the synthesis of the extracellular matrix.

Wound pathophysiology

Process - Phase 3

The induction of angiogenesis was initially attributed to acidic or basic fibroblast growth factors, which are released from macrophages after cell disruption. Angiogenesis is the process of new vessel formation from an existing vasculature network. Once the wound is filled with new granulation tissue, angiogenesis ceases and many of the new blood vessels disintegrate as a result of apoptosis. Wound contraction involves a complex interaction of cells, extracellular matrix, and cytokines.

Wound pathophysiology



Tissue Wound Repair

Tissue wound repair could be achieved by lamellipodial crawling or by contraction of an actin purse string. This diagram illustrates wound repair using an actin purse string. The individual actin filaments (green bars) anchor to adherens junctions (orange rectangles) formed between adjacent cells. Contraction of the actin cable in each cell leads to apical cell constriction and reduced wound circumference. As wound closure proceeds, some cells are squeezed out of the front row such that fewer epithelial cells remain in the front row. The remaining cells form new adherens junctions and apical actin cable contraction continues until the contralateral cells meet and fuse. Asterisks indicate cells that will be lost from the leading edge; nuclei are blue dots.

Challenges in wound care:

Endogenous and Exogenous Factors

Wound healing can be affected by endogenous (pathophysiology) and exogenous (microorganisms) factors. The risk of wound infection increases as local conditions favor bacterial invasion and growth. Therefore, microbial colonization of both acute and chronic wounds is inevitable. Many species of bacteria have been recovered from wounds, but *Staphylococcus aureus* is the most frequently isolated from wound pathogens. In addition, *Pseudomonas aeruginosa* is an important pathogen in chronic wounds and burns; its presence has been demonstrated in numerous studies and has been found in onethird of chronic leg ulcers. Infection with *S. aureus and pseudomonads* retards ulcer healing rates and, with *pseudomonads* and *B-hemolytic streptococcus*, reduces the success of skin grafts used for leg ulcers.

Challenges in wound care:

Development of antibiotic-resistant bacteria

The widespread development of antibiotic-resistant bacteria is a challenging problem. Current interest is focused on an alternative to antibiotics and conventional therapies, such as honey, antimicrobial moisture-retentive dressings, essential oils and cationic peptides, topical enzymes, biosurgical therapies, and vacuum therapies. In addition, unregulated inflammation caused by both microorganisms and underlying abnormal pathophysiological conditions is a major factor associated with the process of healing in chronic wounds

Substances that promote wound healing

Vitamins C, E, and A, glucose, amino acids, antioxidants, fatty acids, proteins, water, and zinc are important for wound healing. Administration of ascorbic acid protected mice against radiation-induced sickness and mortality, and improved healing of wounds after exposure to whole-body gamma radiation. Low levels of antioxidants accompanied by raised levels of markers of free radical damage play a significant role in the delay of wound healing. In diabetic rats, reduced glutathione levels had a role in delaying the healing process. Hydrogen peroxide is one of the mediators of healing responses. Electrolyzed, strong acid aqueous solution irrigation may promote tissue growth in burn wounds. Acidic media enhances wound contraction.

Why Honey?

The widespread existence of unhealed wounds, ulcers, and burns has a great impact on public health and economy. Many interventions, including new medications and technologies, are being used to help achieve significant wound healing and to eliminate infections. Therefore, to find an intervention that has both therapeutic effect on the healing process and the ability to kill microbes is of great value. Honey is a natural product that has been recently introduced in modern medical practice. Honey's antibacterial properties and its effects on wound healing have been thoroughly investigated. Laboratory studies and clinical trials have shown that honey is an effective broad-spectrum antibacterial agent.

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Why Honey?

The data show that the wound healing properties of honey include stimulation of tissue growth, enhanced epithelialization, and minimized scar formation. These effectsare ascribed to honey's acidity, hydrogen peroxide content, osmotic effect, nutritional and antioxidant contents, stimulation of immunity, and to unidentified compounds. Prostaglandins and nitric oxide play a major role in inflammation, microbial killing, and the healing process. Honey was found to lower prostaglandin levels and elevate nitric oxide end products. These properties might help to explain some biological and therapeutic properties of honey, particularly as an antibacterial agent or wound healer.

As a dressing on wounds, honey provides a moist healing environment, rapidly clears infection, deodorizes, and reduces inflammation, edema, and exudation. It increases the rate of healing by stimulation of angiogenesis, granulation, and epithelialization.

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TABLE 1
Effects of Honey on Wounds Healing

Origin of Honey	Type of Lesion	Effects of Honey
Iran[31]	Surgical incision on rabbits	Less edema, fewer polymorphonuclear and mononuclear cell infiltrations, less necrosis, better wound contraction, improved epithelialization, and lower glycosaminoglycan and proteoglycan concentrations
India[39]	Wounds created on buffalo calves	Promotes granulation and scar formation, complete healing of full-thickness wounds occurred faster with honey than with nitrofurazone or sterilized petrolatum
India[40]	Wounds created on buffalo calves infected with *S. aureus*	Faster rate of healing compared with ampicillin ointment and saline treatments, the least inflammation, the most rapid fibroblastic and angioblastic activity and epithelialization
India[42]	Full-thickness skin wounds made on back of rats	Increases significantly the quantity of collagen synthesized and degree of cross-linking of the collagen in the granulation tissue
Egypt[64]	Infected diabetic foot wounds	Fast healing and significant decrease of bacterial load
Turkey[65]	Split-thickness skin graft donor site	Wounds show faster epithelialization time and a low sense of pain than paraffin gauzes and saline-soaked gauzes
Turkey[44]	An adhesion model constituted in the cecum and terminal ileum of rats	Intraperitoneal honey administration reduces postoperative peritoneal adhesion
Turkey[66]	Intraurethral injury in rats	Prevents inflammation, accelerates urethral healing, and provides perfect healing

TABLE 1
Effects of Honey on Wounds Healing

United Arab Emirates[67]	Injured skin or conjunctiva in mice or rat	Accelerates wound healing and eradicates infection
Yemen[68]	Postoperative wound	Eradicates bacterial infection, accelerates wound healing, and minimizes scar formation
Thailand[69]	Postoperative wound disruption	Complete wound healing within 2 weeks
Nepal[71]	Radiation-induced oral mucositis	Strongly protective against the development of mucositis
Nigeria[72]	Wounds and ulcers	Debrides wounds rapidly, replacing sloughs with granulation tissue, promotes rapid epithelialization, and absorption of edema
Nigeria[73]	Fournier's gangrene	Accelerates wound healing
Mexico[33]	Fournier's gangrene	Accelerates wound healing
Malawi[76]	Patients with open or infected wounds	More effective than sugar in reducing bacterial contamination and promoting wound healing
Norway[80]	Chronic wound infection	Eradicates wound bacterial infections and penetrates biofilm
Ireland[81]	Nonhealing ulcers	Manuka honey decreases wound pH and causes a reduction in wound size
France[82]	Wounds	Accelerates wound healing

TABLE 1
Effects of Honey on Wounds Healing

Germany[84]	Resistant wound infection in seven patients	Complete wound healing
U.K.[85]	Toenail surgery	Partial avulsion wounds healed faster with paraffin tulle gras than with the honey dressing
U.K.[88]	Chronic wounds	Clinical benefits from using honey in wound care
U.K.[89]	Meningococcal skin lesions	Helps skin healing
Netherlands[91]	Sixty patients with chronic wounds	Honey is easy to apply, helpful in cleaning the wounds, and without side effects

For references, please see Sources slides at end of powerpoint

TABLE 2
General Effects of Honey on Wound Healing

1.	Causes greater wound contraction[31,32,33,34,35,36,37,211])
2.	Promotes the formation of granulation tissue[32,33,34,35,36,37,39,92]
3.	Promotes epithelialization of wounds[32,33,34,35,36,37,66,73,92]
4.	Stimulates tissue growth, synthesis of collagen[38,39,40,41,42,43,92]
5.	Stimulates development of new blood vessels in the bed of wounds[38,39,40,41,42,43,62,93]
6.	Reduces postoperative adhesion[44]
7.	Reduces edema[62,73,92,93]
8.	Reduces inflammation[61,62,68,92,93,119]
9.	Deodorizes wounds[62,92,93]
10.	Promotes moist wound healing[61,92]
11.	Facilitates debridement[61,72,93]
12.	Reduces pain[66,84,92]

For references, please see Sources slides at end of powerpoint

Wound Care:
Diabetic Foot Ulcers

Thirty infected diabetic foot wounds were randomly selected from patients presenting to Surgery Department, Suez Canal University Hospital, Ismailia, Egypt. Honey dressing was applied to wounds for 3 months till healing, grafting or failure of treatment. Changes in grade and stage of wounds, using University of Texas Diabetic Wound Classification, as well as surface area were recorded weekly. Bacterial load was determined before and after honey dressing.

Complete healing was significantly achieved in 43.3% of ulcers. Decrease in size and healthy granulation was significantly observed in another 43.3% of patients. Bacterial load of all ulcers was significantly reduced after the first week of honey dressing. Failure of treatment was observed in 6.7% of ulcers.

This study proves that commercial clover honey is a clinical and cost-effective dressing for diabetic wound in developing countries. It is omnipresence and concordance with cultural beliefs makes it a typical environmentally based method for treating these conditions

The clinical and cost effectiveness of bee honey dressing in the treatment of diabetic foot ulcers.
A.M. Moghazy et al., Faculty of Medicine, Suez Canal University, Ismailia, Egypt
2010, Elsevier Publications/

Wound Care:
Diabetic Foot Ulcers

Wound Dressing

The wound was meticulously debrided (sometimes under anesthesia) and thoroughly washed using normal saline (no antiseptic). Heavily infected wounds were rinsed with warm tap water after debridement. After drying the wound, honey impregnated gauze was applied. The gauze was held from the non-impregnated part (removed after application by scissors). Fluffy dressing was applied over the gauze and kept in place by bandage.

Frequency of dressing depended upon the amount of exudates; whenever the dressing is soaked, it should e changed by the same technique. Once single daily dressing was reached, provided all the other parameters were accepted, the patient was discharged and followed up in the outpatient clinic on weekly basis.

All patients received vitamin B complex for life. Health education was provided to all patients. The education program emphasized on the importance of: follow-up in the clinic, foot hygiene, nail care, proper footwear, nutritional regimen and management of newly healed foot ulcer.

Wound Care:
Diabetic Foot Ulcers

Presence of microbial agents before and after honey dressings

Table 7 – The frequency of isolated microorganisms from the studied group before and after honey dressing.

Microorganisms	Before		After	
	N = 30	100%	N = 30	100%
No	0	0	0	0
Staphylococcus aureus	12	40	0	0
Staphylococcus epidermidis	6	20	28	93.3
Echerichia coli	5	16.7	0	0
Proteous	3	10	0	0
Klebsiella spp.	2	6.7	0	0
Provedentia	1	3.3	0	0
Pseudomonas aerugenosa	1	3.3	2	6.7

Wound Care: Diabetic Foot Ulcers

Added Benefits

This study revealed **rapid diminution of the inflammatory signs** (e.g. edema, hotness and redness) within 10 days in all patients. This was partially due to its anti-edema effect and partially to its antimicrobial effect.

In our study, most of the **wounds became sterile** by the end of the first month of honey application.

No **hospital acquired infection** was detected in all our series. This might be referred to the viscosity of honey, which provided a protective barrier thus preventing cross-infection.

Honey is ideal as dressing in cases of diabetic foot wounds particularly in the developing countries. It is an **environmentally based cost and clinically effective dressing.**

More importantly, it is **very safe** as it did not result in any com-plication (local or systemic), or emergence of resistant bacterial strains.

- **Rapid Diminution of Inflammation**
- **Wounds Become Sterile**
- **No Hospital Acquired Cross-Infections**
- **Environmentally Based Cost Benefits**
- **Clinically Effective**
- **Very Safe**

Wound Care:
Burns

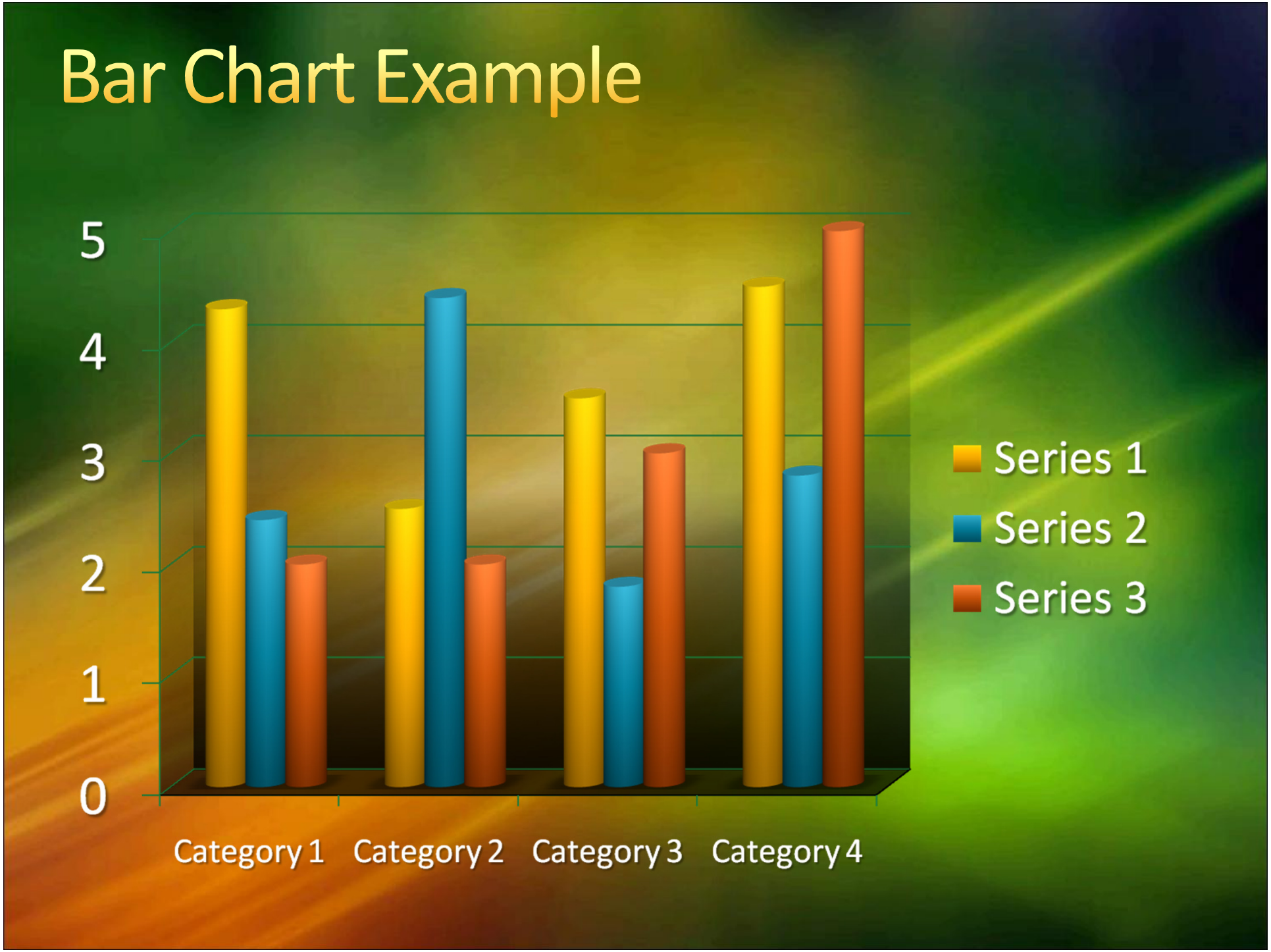
Burn injuries are associated with a high incidence of death and disability. Split-thickness skin grafting with autografts is the standard of care. Honey was used for management of burns and the use of honey for burns has been reviewed.

Various modalities have been reviewed, including honey, human amnion, xenograft, allograft, cultured epithelial autograft, and various engineered commercial products, for use in the biologic treatment of burn wounds.

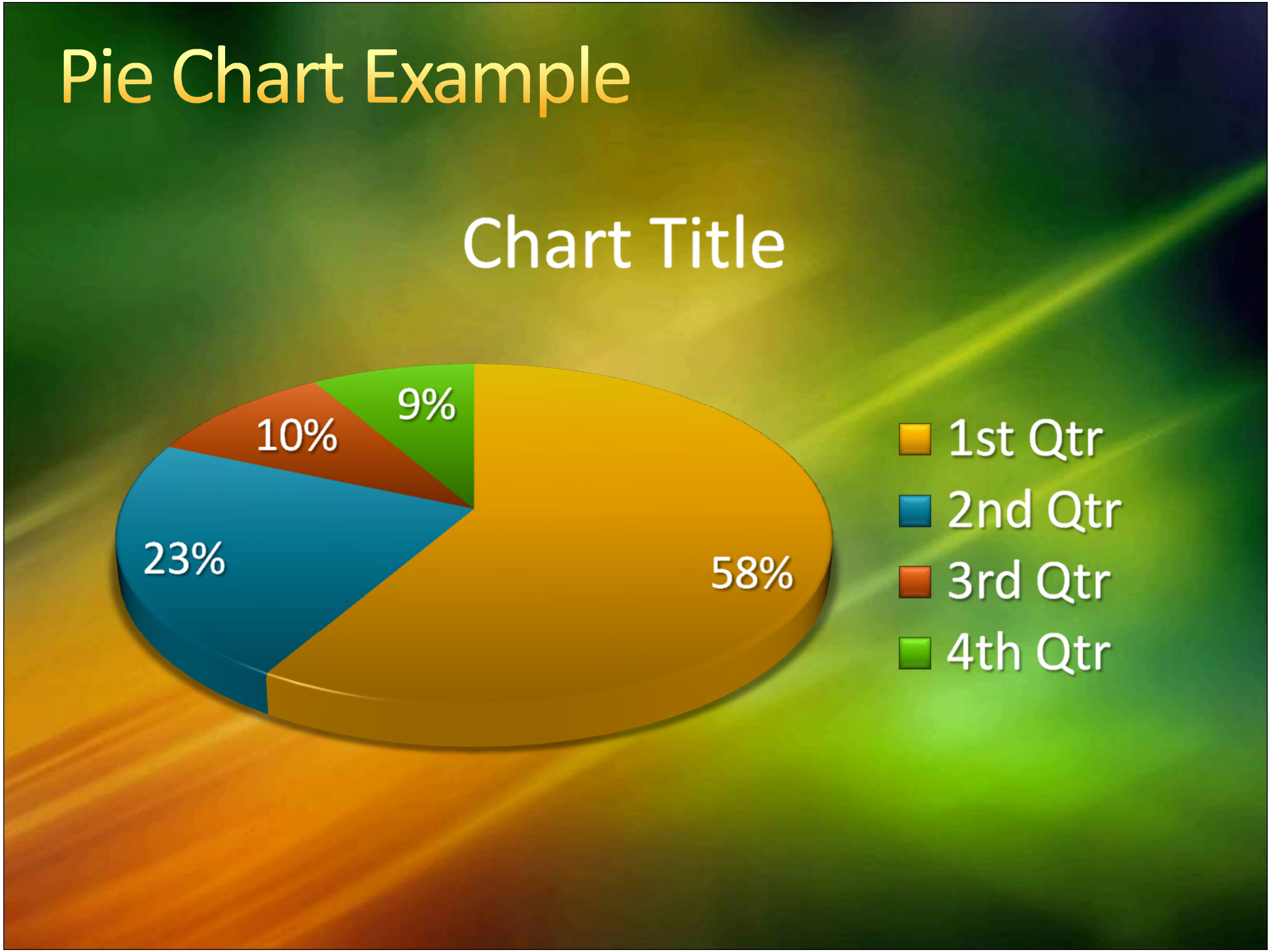
A systematic review and meta-analysis of randomized controlled trials that compared the efficacy of honey with a comparator dressing treatment in the management of burns was conducted. Eight studies with 624 subjects were included. It was found that in most studies, honey covered by sterile gauze was compared with silver sulfadiazine–impregnated gauze. **The fixed effects odds ratio for healing at 15 days was 6.1 (95% CI 3.7–9.9) in favor of honey having a superior effect.** The secondary outcome variables all showed significantly greater efficacy for honey treatment.

It was concluded that available evidence indicates markedly greater efficacy of honey compared with alternative dressing treatments for superficial or partial-thickness burns.

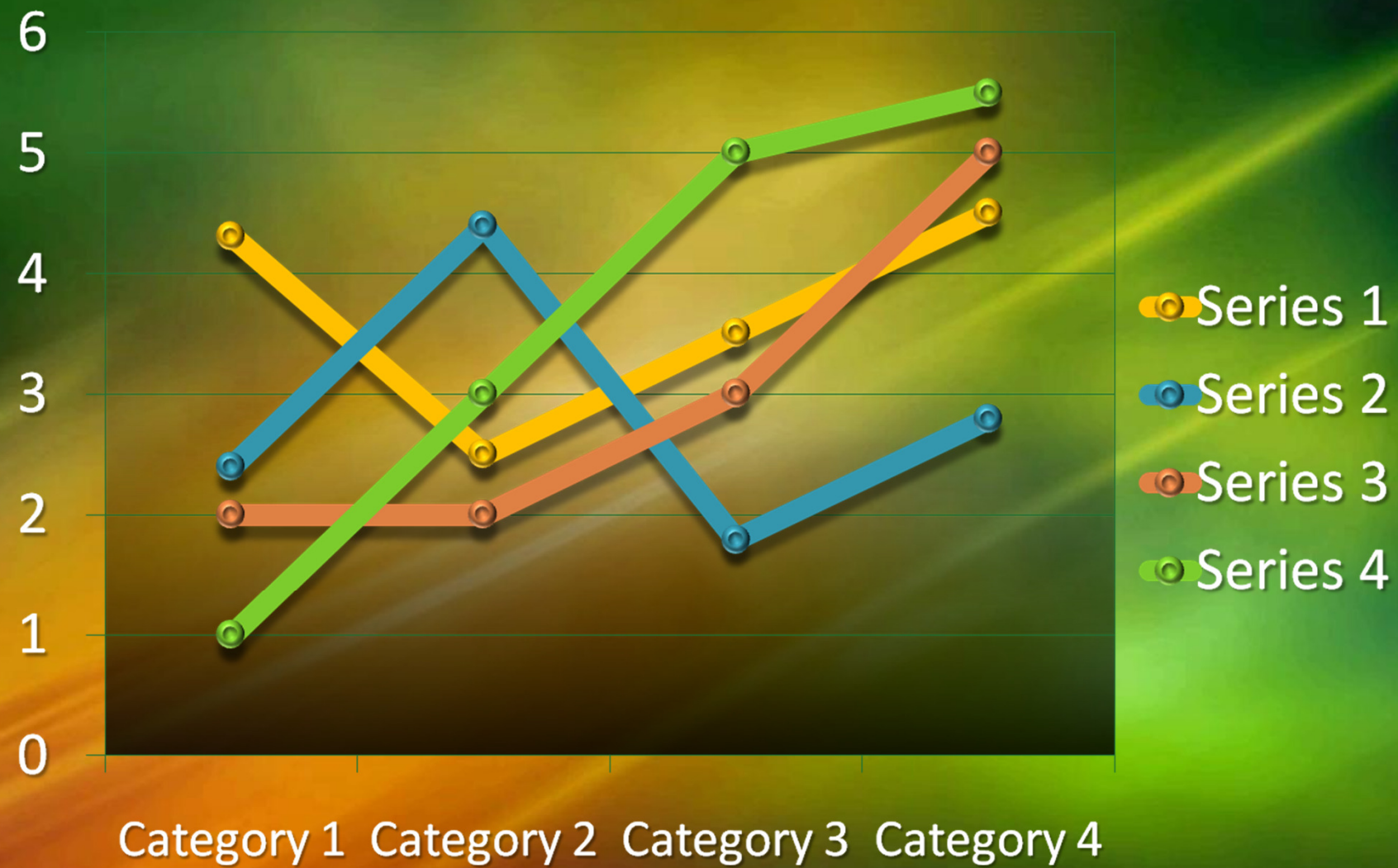
Bar Chart Example



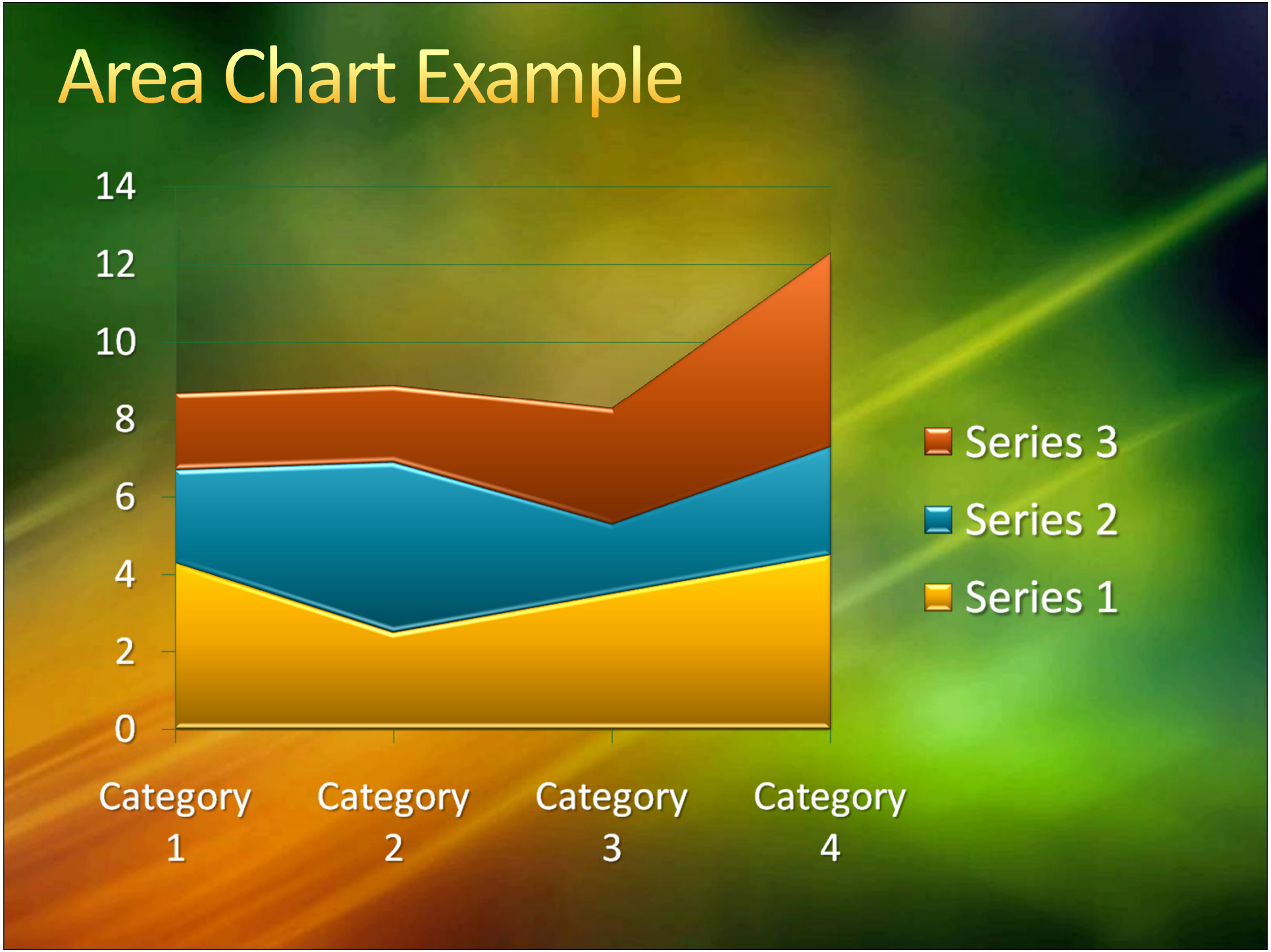
Pie Chart Example



Line Chart Example



Area Chart Example



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