



ANTHEM
WOUND MATRIX
FENESTRATED

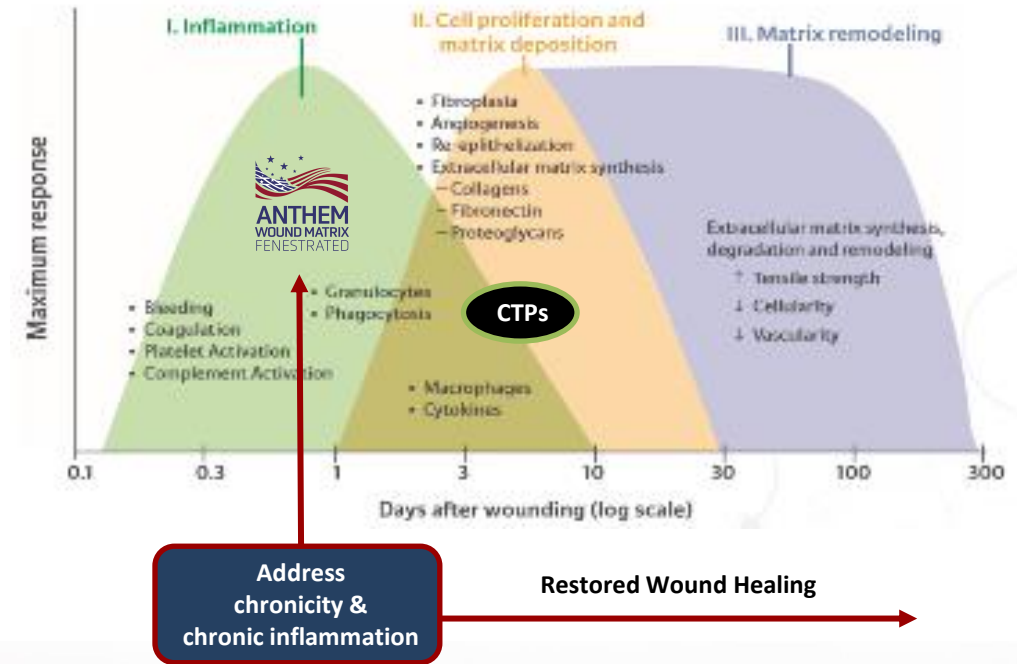
INNOVATING WOUND HEALING
OUTCOMES for OUR VETERANS!



THE VALUE OF ANTHEM WOUND MATRIX

ANTHEM Wound Matrix Fenestrated is scientifically designed to **mimic native extracellular matrix (ECM)** morphology providing a **3-dimensional microporous scaffold stimulus** to facilitate natural cellular adhesion, infiltration and proliferation for tissue regeneration and repair.

Comprised of **polymers which biodegrade to α -hydroxy and fatty acids**, ANTHEM Wound Matrix Fenestrated quickly inspires a pro-healing wound environment by **supporting low pH and releasing lactate, known to address chronicity and encourage pro-regenerative cellular function to restore wound healing** of acute and chronic wounds and burns.^{1,2,3}



Acute Wounds – mitigate the risk of chronic activity occurring to allow for natural wound healing

Chronic Wounds – disrupt chronic activity to allow for accelerated wound healing

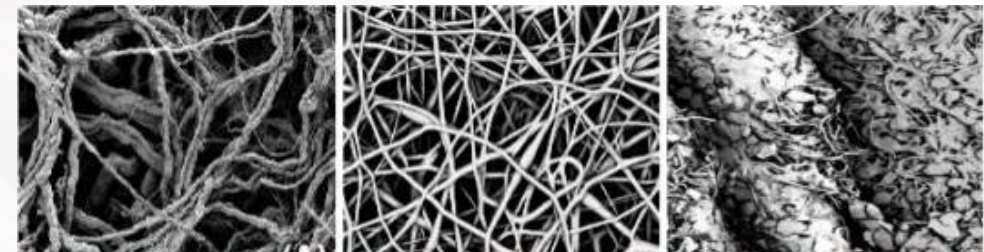
Reduce expenses and improve the quality of care for our Veterans

- Chronic activity is a fundamental issue that impedes natural wound healing
- Cellular tissue products are used to combat stalled, chronic wounds however, CTPs do not address the root issue of chronicity and chronic inflammation
 - High cost products requiring many applications to heal wound
 - **Approximately 50% of cases where CTPs are used do not heal in 12 weeks***
 - Phoenix Wound Matrix is typically less than 50% of the cost of CTP's
- **PHOENIX Wound Matrix is engineered to:**
 - Quickly establish a balanced pro-healing wound environment by helping to address the chronicity
 - Accelerate the body's natural wound healing process
 - Help decrease the over utilization of cellular tissue products
 - Consistently heal with improved wound closure outcomes
 - Potentially reduce costs and impact throughput by reducing patient return visits
 - Save limbs and save lives by healing complex and chronic wounds

Understanding the clinical value of ANTHEM™ Wound Matrix Fenestrated

ANTHEM Wound Matrix Fenestrated is :

- Engineered to mimic native ECM morphology
- Fiber diameters and porosity scientifically designed to support pro-regenerative cellular adherence, infiltration and proliferation
- Comprised of bioresorbable synthetic polymers that degrade into α -hydroxy and fatty acids, known to aid in the wound healing process
 - Lowers pH to support a pro-healing wound environment^{1,2}
 - Supports lactate-mediated effects known to promote angiogenesis, oxygenation and accelerated wound healing³
- *In vitro* testing demonstrated a significant increase of cell proliferation with ANTHEM Wound Matrix compared to TCP over 24 hours of culture⁴
- Case studies demonstrate consistent healing trajectories through to wound closure⁵
- Offers a first-line, cost-effective synthetic polymer solution to optimize your wound healing outcomes



Dermal Tissue

ANTHEM Wound Matrix

ANTHEM with Fibroblast Migration

Scientifically engineered to mimic native ECM

AWM offers a consistent ECM structure designed to encourage pro-regenerative cellular function

Pore size and structure promotes cellular adhesion, infiltration and proliferation

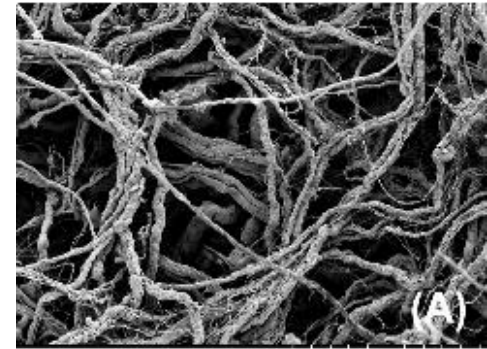
1 μm (micron) = 1 millionth meter

1 nm (nanometer) = 1 billionth meter = 1/1000 micron

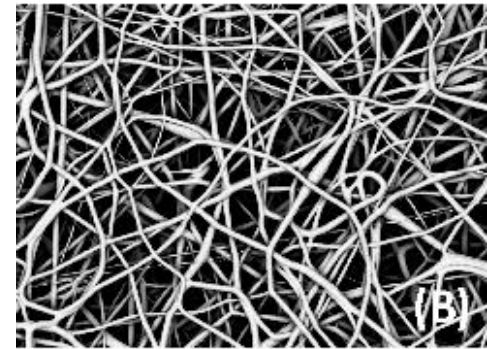
Fibroblast average dia.: 10-15 μm (10,000-15,000 nm)

ANTHEM fibers dia. range: <5 μm

Comprised of natural synthetic polymers – *In vitro* testing demonstrated a significant increase of cell proliferation with ANTHEM Wound Matrix compared to TCP over 24 hours of culture⁴



Dermal Tissue

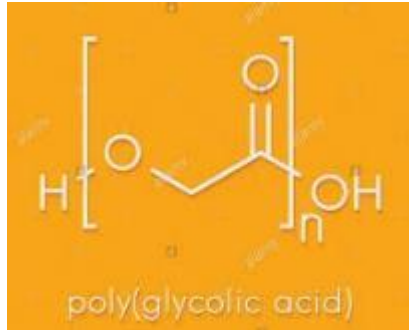


ANTHEM Wound Matrix



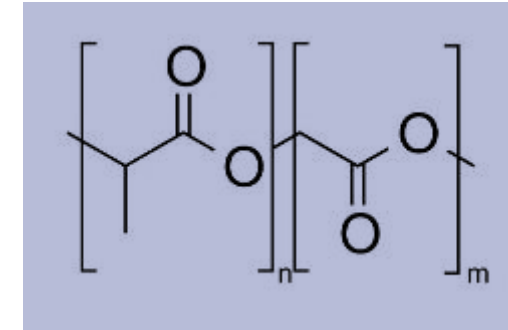
ANTHEM with Fibroblast Migration

Scientifically designed to inspire a pro-healing wound environment



Polyglycolide or poly(glycolic acid) (PGA)

- Degradants represent weakly acidic monomers that encourage a low pH within the wound environment
- Low pH is known to:^{1,2,3}
 - Decreases destructive protease enzyme activity
 - Increases macrophage and fibroblast activity**
 - Increases available oxygen
 - Decrease pro-inflammatory cytokines
- **Helps to re-establish microbiome homeostasis**



poly(L-lactide-co-caprolactone) (PLCL)

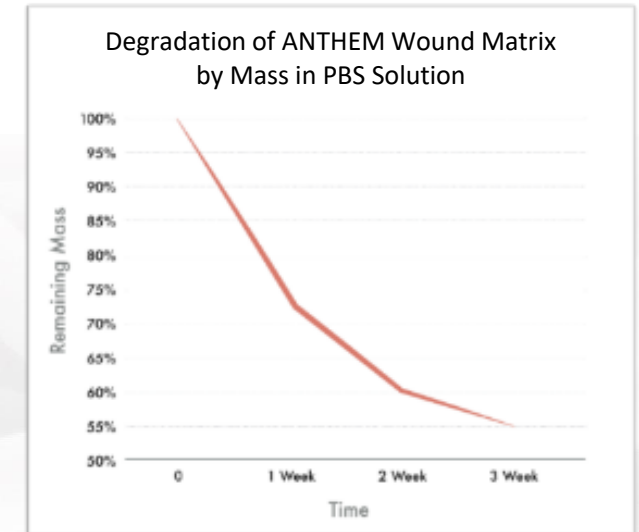
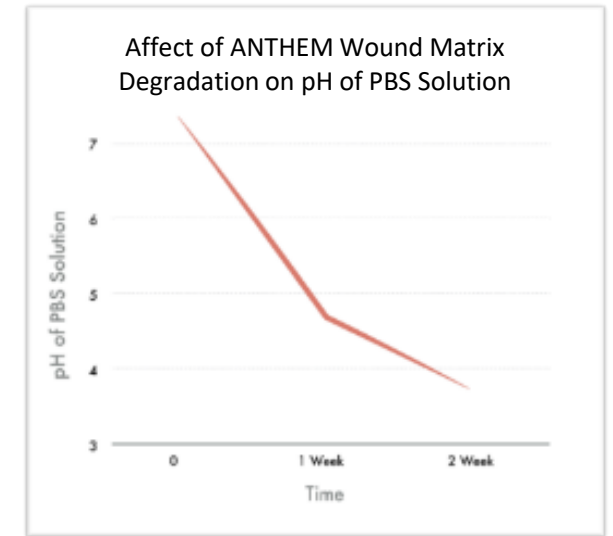
- Supports lactate mediated effects/action
- Encourages a hypoxic event which elicits pro-regenerative macrophages
- Macrophages engulf endotoxins and releases reactive oxygen species to reduce protease activity and bacterial load
- Neutralizes chronic activity and sustained inflammatory response
- Oxygen perfusion allows for the stimulation of VEGF, collagen gene expression, endothelial progenitor cells
- **Vital factor in supporting angiogenesis and re-establishing tissue homeostasis**

Supports a physiological change in the wound environment

ANTHEM Wound Matrix Fenestrated polymers

- ❑ Degrade via hydrolysis to Glycolic acid, Lactic acid, and Caproic acid monomers
- ❑ Demonstrated a drop in pH from 7.4 to 4.75 over a 1-week period during an *in vitro* degradation test in isotonic PBS solution
- ❑ Synthetic graft typically degrades within 7-14 days

Note: These weakly acidic degradants are not released from other collagen products.

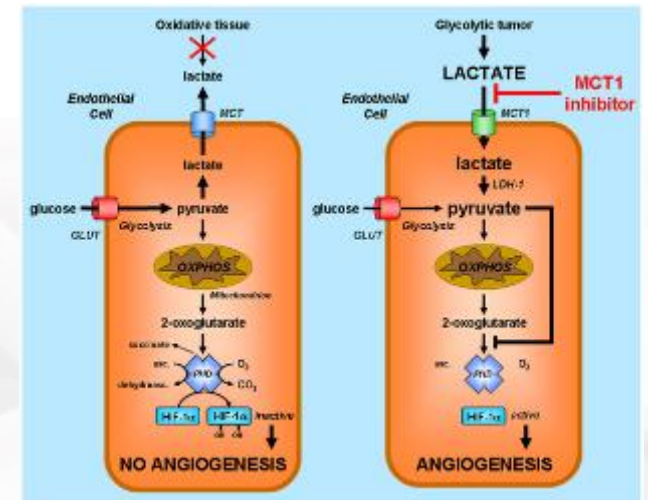
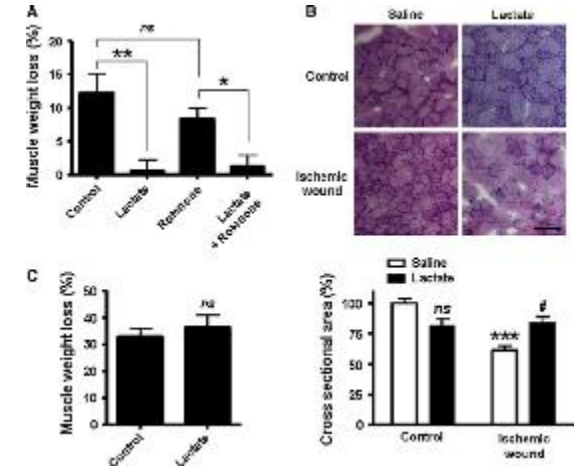
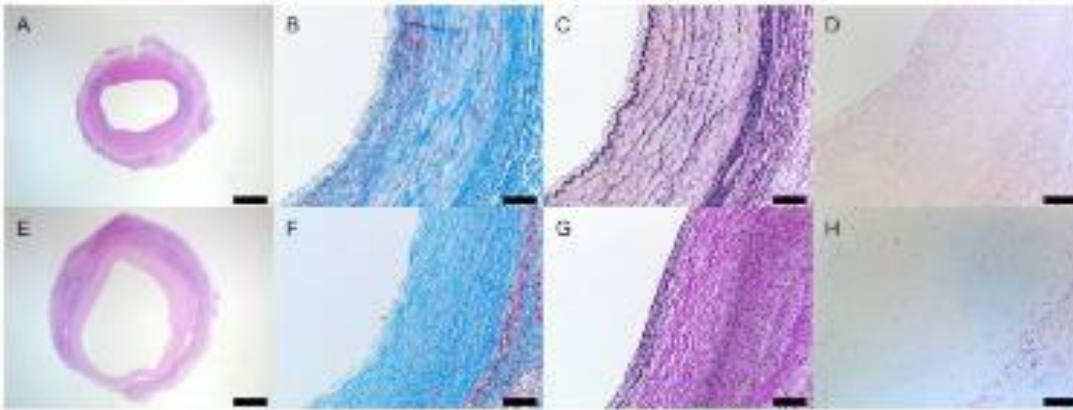


Engineered to promote physiological change in the wound environment

poly(L-lactide-co-caprolactone) (PLCL) releases lactate to support lactate mediated effects

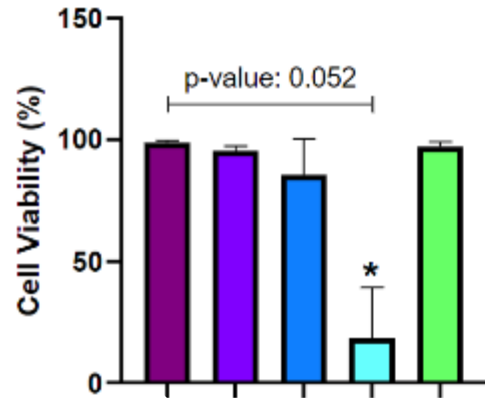
Lactate mediated effects:³

- Encourage an immunomodulatory response, endothelial cell migration and tube formation in vitro*
- Recruits vascular progenitor cells and promotes vascular morphogenesis in vivo**
- Vital factor in supporting angiogenesis and re-establishing tissue homeostasis*



In-vitro Study: Cell Adhesion and Viability‡

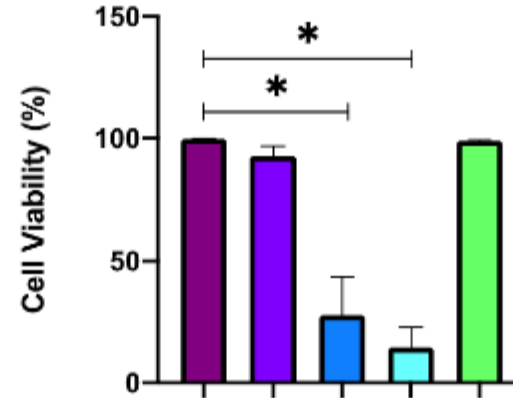
24 hours after culture



Matrix

* Indicates significant difference compared to other dressings, p-value <0.001

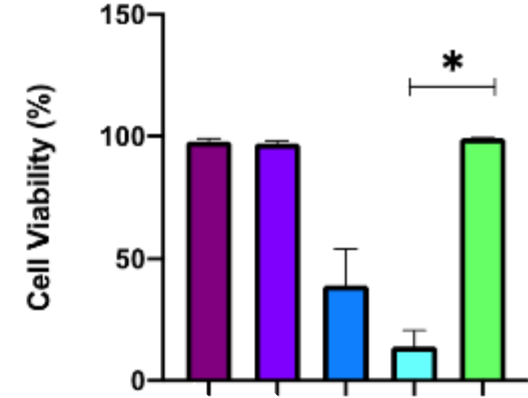
48 hours after culture



Matrix

** p-value <0.001

72 hours after culture



Matrix

* p-value=0.047

Adult primary Human Dermal Fibroblast cells (HDFa, ATCC) were cultured on ANTHEM Wound Matrix Fenestrated (both with and w/o proprietary surface treatment), PuraPly Wound Matrix (Organogenesis), and Oasis Ultra Tri-Layer Matrix (Smith&Nephew) to quantify and to contrast cell adhesion and viability. Cell Viability = % of live cells (live cells/total cells).

Indications

ANTHEM Wound Matrix Fenestrated is indicated for the management of **partial to full-thickness wounds and burns.**

Wound types include:

- Diabetic ulcers
- Venous ulcers, chronic vascular ulcers
- Pressure ulcers
- Surgical wounds (e.g., donor sites/grafts, post-Mohs' surgery, post-laser surgery, podiatric, wound dehiscence)
- Trauma wounds (e.g., abrasions, lacerations, burns, skin tears)
- Tunneled/undermined wounds
- Draining wounds



A clinical & economic solution for wound healing⁵



100%

demonstrated rapid reduction in inflammation and tissue appearance

82%

average wound area reduction in **35 days**

2 – 4*

Average number of product applications

~8.7 weeks

Average time to wound closure



ANTHEM Wound Matrix Fenestrated Post Market Surveillance Case Series Summary⁵

	All Cases	Pressure Ulcer	Diabetic/ Complex Ulcer	Vascular/ Mixed	Surgical Wound	Trauma Wound	Necrotizing Fasciitis Wound	Burn
Patients	14	3	5	2	1	1	1	1
Wounds	19	3	10	2	1	1	1	1
Wound Granulation	100%	100%	100%	100%	100%	100%	100%	100%
Area Reduction at 35 Days (%)	82%	82%	81%	100%	62%	62%	77%	100%
Closure/Area Reduction (%)	99.6%	100%	100%	100%	93%	100%	100%	100%
Side effects	0%	0%	0%	0%	0%	0%	0%	0%
Adverse events	0%	0%	0%	0%	0%	0%	0%	0%

*National average for CTP applications: 5-8

⁵50% of wounds where a CTP was used are still not healed at 12 weeks.

DFU Pressure Injury

Wound persistent for 4 months prior to utilization of PHOENIX



				
<p>Day 0 1st ANTHEM Application Planimetric area: 11.8 cm²</p>	<p>Day 7 2nd ANTHEM Application Planimetric area: 11.3 cm² Plan. area reduction: 4%</p>	<p>Day 42 Planimetric area: 3.6 cm² Plan. area reduction: 70%</p>	<p>Day 77 11 weeks Wound closed</p>	<p>Day 91 Remission Period</p>

Images courtesy of Frank Aviles, Jr., PT CWS FACCSW CLT AWCC

70%
reduction in
wound area
within
6 weeks

Case Report:

90-year old male with paraplegia presented with right heel **pressure ulcer of over 4 months duration**. Additionally, at presentation, a **2.2 cm tunnel** was observed superomedially. Despite receiving best practice standard of care plus other advanced modalities, patient developed osteomyelitis and required surgical debridement. Following surgical debridement, the 1st ANTHEM Wound Matrix was applied on Day 0. Robust granulation tissue was noted within days; second ANTHEM was applied on Day 7, and accelerated progress continued. On Day 42, 70% decrease in planimetric area was observed. **Full wound closure was achieved on Day 77.**

Summary:

90-year-old male with paraplegia and **heel pressure injury** achieved **wound closure** in **11 weeks** with **2 ANTHEM applications**, combined with wound care best practices, including NPWT and offloading.

DFU Pressure Injury Complicated by Charcot-Marie-Tooth

			
<p>Day 0 1st ANTHEM Application Area: 10.89 cm²</p>	<p>Day 10 2nd ANTHEM Application Area: 7.84 cm² Area reduction: 28%</p>	<p>Day 35 Wound closed Week 5</p>	<p>Day 50 Remission Period</p>
<p>Images courtesy of Dan Davis, DPM</p>			

Wound closure achieved in **35 days**

Case Report:





66-year-old male with **Charcot-Marie-Tooth (CMT)** disease, **peripheral neuropathy** and **neurological issues** presented on Day 0 with a plantar pressure ulcer over the left 5th metatarsal. Wound measured 3.3cm x 3.3cm x 0.2cm. Sharp debridement was performed, followed by application of becaplermin gel (recombinant PDGF) and ANTHEM Wound Matrix. Patient was not a candidate for total contact casting; bolstered padding was utilized to offload. By Day 10, a 28% reduction in total wound size was noted with wound measuring 2.8cm x 2.8cm x 0.2cm. **By Day 35, complete wound closure was achieved.** On further evaluation at Day 50, the wound remained closed and continued healthy tissue remodeling was noted.

Summary:

ANTHEM was selected as **first-line treatment option**, and wound closure of pressure ulcer in **66-year-old male** with **CMT** was achieved in **5 weeks** with **3 ANTHEM applications**, combined with wound care best practices.

Diabetic Ulcer/Trauma – Complicated by Multiple Sclerosis and Raynaud’s Disease



			
Day 0 1 st ANTHEM Application Planimetric area: 1.63 cm ²	Day 7 2 nd ANTHEM Application Planimetric area: 1.51 cm ² Plan. area reduction: 7%	Day 14 Planimetric area: 0.86 cm ² Plan. area reduction: 43%	Day 49 Wound Closed 7 weeks

43%
reduction in
wound area
within
2 weeks

40-year-old female with history of type 1 diabetes, multiple sclerosis, and Raynaud’s disease, presented to the wound care clinic status post a fall 4 weeks earlier. Following thorough debridement, ANTHEM was applied. Wound depth was visibly reduced within 1 week of treatment. **The planimetric area decreased by 43% within 2 weeks of treatment and 2 applications of ANTHEM.** The wound closed following 49 days of treatment.

Necrotizing Fasciitis

				
<p>Day 0 1st Application Planimetric area: 256.9 cm²</p>	<p>Day 11 2nd Application Planimetric area: 115.7 cm² Plan. area reduction: 55%</p>	<p>Day 32 3rd Application Planimetric area: 58.4 cm² Plan. area reduction: 77%</p>	<p>Day 67 Planimetric area: 11.4 cm² Plan. area reduction: 96%</p>	<p>Day 121 17.3 weeks Planimetric area: 0.96 cm² Plan. area reduction: >99.9%</p>

77%
Wound Area
Reduction in
32 Days

Images courtesy of Frank Aviles, Jr., PT CWS FACCS CLT AWCC

57-year-old male with type 2 diabetes and hypertension, presented 3-weeks after sustaining a fall to the sacral area. Patient was diagnosed with **necrotizing fasciitis**, requiring **extensive surgical debridement**, antibiotics, and hyperbaric oxygen therapy (HBOT). The resulting wound extended from upper right inguinal region, through perineum, to perianal area. Patient reported significant wound pain requiring pain medication for dressing changes. ANTHEM Wound Matrix was applied to anterior aspect of wound, and negative pressure wound therapy (NPWT) was also applied in combination with ANTHEM. **By Day 7, patient reported considerable decrease in pain, no longer required pain medication**, and healthy granulation tissue was observed. By Day 32, planimetric area of anterior wound decreased 77%. By Day 67, 96% reduction in planimetric area was achieved. **Wound closure was achieved on Day 125.**

Summary:
57-year-old male with diabetes and large open wound, resulting from extensive surgical debridement of necrotizing fasciitis tissue, **closed in 18 weeks with 3 ANTHEM applications**, combined with wound care best practices, including HBO and NPWT.

Arterial Leg Ulcer



			
<p>Day 0 1st Application 3.8cm x 3.7cm x 0.1cm Area: 14.06 cm²</p>	<p>Day 4 2nd Application 3.8cm x 2.8cm x 0.1cm Area: 10.64 cm² Area reduction: 24%</p>	<p>Day 11 3rd Application 0.7cm x 0.5cm x 0.1cm Area: 0.35 cm² Area reduction: 97%</p>	<p>Day 25 Wound closed</p>

Wound
closure within
25 Days

Images courtesy of Dan Davis, DMP and Denise Riera, DPM

Case Report:

84-year-old male with **peripheral artery disease**, **coronary artery disease**, and **peripheral neuropathy** presented with a left lower leg ischemic ulcer measuring 3.7 x 3.6 x 0.1 cm. Treatment with ANTHEM Wound Matrix was initiated on Day 0. On Day 4, a 24% reduction in wound area was noted. The matrix was still visible on the wound bed, therefore, no new graft was applied. On Day 11, accelerated wound healing was noted with an 97% reduction in wound area. Remarkably, wound closure was achieved on Day 25.

Summary:

84-year-old patient with an **arterial leg wound** achieved **wound closure in 4 weeks** of treatment and **2 applications of ANTHEM Wound Matrix**. Ischemic wounds are challenging to manage and often exceed 6 months in duration.

Venous Leg Ulcer



I N I T I A L U L C E R				
	Day 0 1 st Application Area: 20.46 cm ²	Day 7 2 nd Application Area: 13.75 cm ² Area reduction: 33%	Day 22 3 rd Application Area: 12.6 cm ² Area reduction: 38%	Day 28 Wound closed
	Day 0 1 st Application Area: 1.21 cm ²	Day 21 Wound closed	Images courtesy of Dan Davis, DMP and Denise Riera, DPM	

Wound closure achieved in **28 days**

Case Report:

66-year-old male with history of **recurrent leg ulcers** with multiple comorbidities including **type 2 diabetes, congestive heart failure, peripheral artery disease, peripheral neuropathy,** and **hypertension**, presented with a right, lower leg venous ulcer measuring 3.3 x 6.2 x 0.2 cm. ANTHEM Wound Matrix Fenestrated treatment was initiated as **first-line therapy** on Day 0, along with Regranex Gel for moisture. By Day 7, a 33% reduction in wound size was noted, measuring 2.5 x 5.5 x 0.1 cm. Wound closure was achieved in 28 days with 3 applications of ANTHEM. One-week post closure, patient presented with a recurrence measuring 1.1 x 1.1 x 0.1 cm. ANTHEM was applied once and wound closure was achieved in 3 weeks.

Complex Arterial Diabetic Foot Ulcers

					
<p>Day 0 1st Application</p> <p>Hallux: 0.5cm x 0.8cm x 0.2cm 2nd toe: 3.5cm x 2.0cm x 0.2cm 3rd toe: 3.6cm x 0.7cm x 0.1cm 4th toe: 3.6cm x 4.5cm x 0.1cm 5th toe: 0.3cm x 0.2cm x 0.1cm</p> <p>Combined area: 26.18cm²</p>	<p>Day 7 2nd Application</p> <p>Hallux: Epithelialized 2nd toe: 1.8cm x 1.1cm x 0.2cm 3rd toe: 2.7cm x 1.2cm x 0.1cm 4th toe: 3.5cm x 2.7cm x 0.2cm 5th toe: Epithelialized</p> <p>Combined area: 26.18cm² Area reduction: 44%</p>	<p>Day 36 6th Application</p> <p>Hallux: Epithelialized 2nd toe: 2.8cm x 2.0cm x 0.2cm 3rd toe: 0.8cm x 0.5cm x 0.1cm 4th toe: 1.8cm x 1.9cm x 0.3cm 5th toe: Epithelialized</p> <p>Combined area: 26.18cm² Area reduction: 64%</p>	<p>Day 49 8th Application</p> <p>Hallux: Epithelialized 2nd toe: 2.0cm x 2.7cm x 0.2cm 3rd toe: Epithelialized 4th toe: 1.4cm 2.0cm x 0.3cm 5th toe: Epithelialized</p> <p>Combined area: 26.18cm² Area reduction: 69%</p>	<p>Day 84</p> <p>Hallux: Epithelialized 2nd toe: 1.5cm x 1.2cm x 0.2cm 3rd toe: Epithelialized 4th toe: 1.3cm 1.7cm x 0.3cm 5th toe: Epithelialized</p> <p>Combined area: 26.18cm² Area reduction: 85%</p>	<p>Day 155 Wound Closure</p> <p>Hallux: Epithelialized 2nd toe: Epithelialized 3rd toe: Epithelialized 4th toe: Epithelialized 5th met: Epithelialized</p>

Images courtesy of Dan Davis, DMP and Denise Riera, DPM

Case Report:
74-year-old male with **type 2 diabetes**, **severe peripheral artery disease** resulting in markedly **inadequate perfusion status**, and **peripheral neuropathy** presented with **5 ischemic diabetic toe ulcers** of the left foot, after having failed SOC for 4 weeks. Prior consult recommended amputation of the gangrenous 2nd and 4th toes. Collectively, wound areas measured 26.18cm². On Day 0, sharp debridement was performed and treatment with ANTHEM Wound Matrix initiated. **By Day 7, epithelialization of Hallux and 5th toe wounds** was achieved, along with a 44% reduction in combined wound area. **By Day 36**, the Hallux and 5th toe remained epithelialized and a **combined wound area reduction of 64%** noted. Patient continued to respond well to treatment with ANTHEM achieving an 85% reduction in combined wound area in 12 weeks. **100% reduction in combined wound area was achieved in 22 weeks with closure of the 2 initially gangrenous toes.**

Summary:
5 ischemic diabetic ulcers achieved closure of all wounds in 22 weeks with 8 applications of ANTHEM, avoiding the loss of 2 gangrenous toes.

Stalled Diabetic Foot Ulcer

Nonpalpable pulse



Day 1
5.2cm x 1.1cm x
0.8cm

Day 21
3.9cm x 0.8cm x
0.6cm

**59% wound
closure**

3rd Application

Day 31
Blood flow restored.

4th Application

Day 45
0.9cm x 0.3cm x
0.2cm

**98% wound
closure**

5th Application

Day 66
Continued closure

Day 80
CLOSED

Case Brief: 68 y/o male with DMII, HO neuropathy and PVD presented to Graft Clinic 2 weeks after surgery. Wound measuring 5.2cm x 1.1cm x 0.8cm **with nonpalpable pedal pulses**. Patient had a long-standing plantar ulceration sub 2nd metatarsal that contributed to osteomyelitis of the second ray. By Day 21, after 2 applications of ANTHEM, a 59% reduction in wound size was achieved. By Day 31, restored blood flow was accomplished with continued progression of wound healing. By Day 45, 98% wound closure was achieved with complete wound closure of this nonpalpable 2nd ray resection foot wound by Day 80.

Diabetic Foot Ulcer

Wound persistent for 2 months prior to utilization of PHOENIX



83%
closure
within **14**
days

Day 1

4.9cm x 1.3cm x
2.1cm

1st Application

Day 7

5.3cm x 0.9cm x
2.0cm

**29% wound
closure**

2nd Application

Day 14

2.5cm x 1.0cm x
1.0cm

**83% wound
closure**

3rd Application

Day 21

Continued closure
**Transitioned to
amniotic**

Day 81

Closed

Case Brief: Patient is a 61y/o male with DM, lumbar radiculopathy, Hypertension, MRSA, Neuropathy, Osteomyelitis presented with a 4.9cm x 1.3cm x 2.1cm wound subsequent to an IND. Just removed from pic line, currently on Doxycycline. Positive drainage, negative probe to bone. Pulses 2/4 bilateral. **Would has been open for 2 months.** Initiation of ANTHEM Wound Matrix jump started wound healing of this stalled ulcer. After three applications of PWM, by Day 14, 83% wound closure was achieved by day 14. Transitioned to an amniotic for closure.

Neuropathic DFU, Charcot Joint

R I G H T F O O T					
	Day 0 Planimetric Area: 1.09 cm ²	Day 13 Planimetric Area: 0.33 cm ² Plan. Area reduction: 70%	Day 28 Planimetric Area: 0.10 cm ² Plan. Area reduction: 91%	Day 36 Wound closed	
	L E F T F O O T				
		Day 0 Planimetric Area: 3.78 cm ²	Day 28 Planimetric Area: 1.42 cm ² Plan. Area reduction: 62%	Day 43 Planimetric Area: 1.03 cm ² Plan. Area reduction: 73%	Day 71 Wound closed

Images courtesy of Scott Littrell, DPM

Right Foot



Left Foot



Case Report:

53-year-old male with bilateral **diabetic** foot ulcers (DFU), history of **Charcot neuropathic osteoarthropathy** (right foot), **BMI 33.4**. **Failed 8 weeks** of antibiotics, silver alginate and offloading with Crowe Walker® (right foot). Right foot wound area decreased 70% following 2 weeks of treatment; wound closure was achieved on Day 36. Left foot wound area decreased 62% following 4 weeks of treatment; wound closure was achieved on Day 71.

Summary:

53-year-old male with **diabetes** and **Charcot joint**, right foot **DFU** healed in **5 weeks** with **3 applications**. Left foot **DFU** healed in **10 weeks** with **6 applications**.

Diabetic Foot Ulcer –

Wound persistent for 7 months prior to utilization of PHOENIX



Day 1

0.3cm x 0.2cm x 0.2cm

1st Application

Day 7

0.2cm x 0.1cm x 0.1cm

83% wound closure

2nd Application

Day 14

CLOSED

83%
reduction in
7 days

Case Brief: Case Brief: 51 y/o DM male with neuropathy. Pedal pulses were 2/4 bilateral with hair growth presented with a diabetic ulcer of left toe. **Ulcer was present for 7 months without resolution.** The area has been off-loaded in cam boot for over 6 months. Previous treatments include Iodosorb, Medihoney, amniotic membrane. Treatment strategy switched to utilize ANTHEM Wound Matrix. Patient RTC after one week with 83% reduction in wound volume, ANTHEM reapplied 1X. Complete closure in two weeks.

References

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3. Porporato PE, Payen VL, Saedeleer CJD, et al. Lactate stimulates angiogenesis and accelerates the healing of superficial and ischemic wounds in mice. *Angiogenesis*. 2012;15(4):581-592. doi:10.1007/s10456-012-9282-0.
4. Bell AL, Cavorsi J. Noncontact ultrasound therapy for adjunctive treatment of nonhealing wounds: retrospective analysis. *Phys Ther*. 2008;88:1517–1524.
5. Clinical case documentation. Data on file.

*Advanced wound care device, also known as cellular and/or tissue-based product (CTP) or skin substitute.

† All claims supported by human use studies, Good Lab Practice (GLP), porcine animal study and veterinary case studies