amniox®
A TissueTech Company

HARNESSING THE UNIQUE POWER OF HUMAN BIRTH TISSUE

To support regenerative healing and functional recovery as the adjunct for surgical and chronic wound applications

- Help Facilitate Wound Healing
- Help Manage Adhesions
- Help Manage Discomfort
- Help Expedite Functional Recovery

REGENERATE. RESTORE. RECOVER.

The Amniox family of cryopreserved umbilical cord and amniotic membrane allografts helps deliver the natural healing properties of human birth tissue to wound environments[1]

First to Recognize the Natural Healing Potential of the HC-HA/PTX3 Complex

For over 30 years, our pioneering scientists have focused on understanding the regenerative features of human birth tissue — ultimately identifying HC-HA/PTX3 as a key orchestrator in human birth tissue regenerative healing.[1-5]

This unique complex acts by directing the activity of other biological components in the birth tissue, including growth factors, cytokines and stem cells. As demonstrated on the ocular space, the unique power of HC-HA/PTX3 creates a more structured healing environment to help manage inflammation and scarring.[1-3,5-9]

Our Novel Preservation Process Makes all the Difference

Our proprietary CRYOTEK® cryopreservation process has been shown to preserve the structural and functional integrity of the native tissue and the HC-HA/PTX3 complex. In a clinical study, dehydrated tissues can be structurally compromised and almost completely lacked these crucial components.[1,10,11]

Having retained the supportive natural properties with CRYOTEK, the Amniox family of allografts can help assist in managing discomfort, reducing adhesions, promoting a healing environment and helping to expedite functional recovery across a wide variety of surgical, acute and chronic wound applications.[1,12-24]

35 CONSECUTIVE YEARS OF NIH-FUNDED RESEARCH

MORE THAN 600,000 TRANSPLANTATIONS PERFORMED

OVER 380 PEER-REVIEWED PUBLICATIONS

MORE THAN 40 ISSUED PATENTS

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Regenerate. Restore. Recover.

MEETING THE CLINICAL NEEDS OF COMPLEX WOUND HEALING

With innovative, cost-effective, restorative solutions[12,14,15]

The Challenge

- **6.5 MILLION PEOPLE** in the U.S. suffer from deficient chronic wound healing[22]
- The incidence rate continues to rise due to an aging population and increased risk factors, leading to complications including severe discomfort, infection and amputations[22]
- **70 MILLION SURGERIES** are performed each year — all resulting in wounds — many on patients with comorbidities that may lead to challenged healing[25]

The Impact

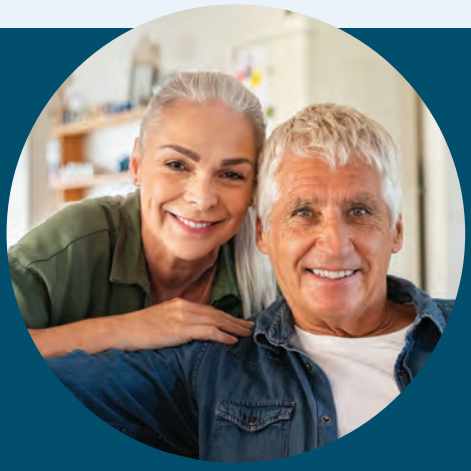
- **OVER $25 BILLION SPENT ANNUALLY** on the treatment of chronic wounds[22]
- Growing burden due to an aging population, diabetes and obesity[22]
- **$13.1 BILLION IN MEDICARE COSTS** for non-healing and infected surgical wounds (even greater than the cost of treating diabetic foot ulcers)[26]:
  - 9.4 days of additional hospitalization[26]
  - $40,323 in hospital charges
  - 61% higher odds of readmissions within 30 days
  - 9.6% mortality rate

The Solution

- Comprehensive family of umbilical cord and amniotic membrane allografts
- **NOVEL TECHNOLOGY** maintains the unique natural properties of HC-HA/PTX3[1,2,10,11]
- **DELIVERS THE NATURAL POWER** of human birth tissue to wound environments[1]
- **ACROSS A WIDE RANGE OF SPECIALTIES** and surgical, acute and chronic wound applications
- **HELPS EXPEDITE REGENERATIVE HEALING**[1,12-24]
- Helps manage discomfort, reduce adhesions and promote a healing environment[1-3,12-24]
- Promotes higher healing rates when compared to the Standard of Care[12-16,19,20]
- Cost-efficient[12,14-16]

The Outcomes

- Faster functional recovery[16,19]
- High closure rates[12-16]
- Fewer applications[12,14,15]
- Reduced cost of care[12,14-16,27]
- Enhanced patient satisfaction



HC-HA/PTX3: KEY ORCHESTRATOR BEHIND OUR TECHNOLOGY

HC-HA/PTX3, identified and characterized first by our researchers as a critical matrix component of human birth tissue, is a unique glycoprotein complex responsible for its cellular signaling.[1-10] It is responsible for several of the tissue's anti-inflammatory and anti-scarring properties in the fetal environment.[1-9]

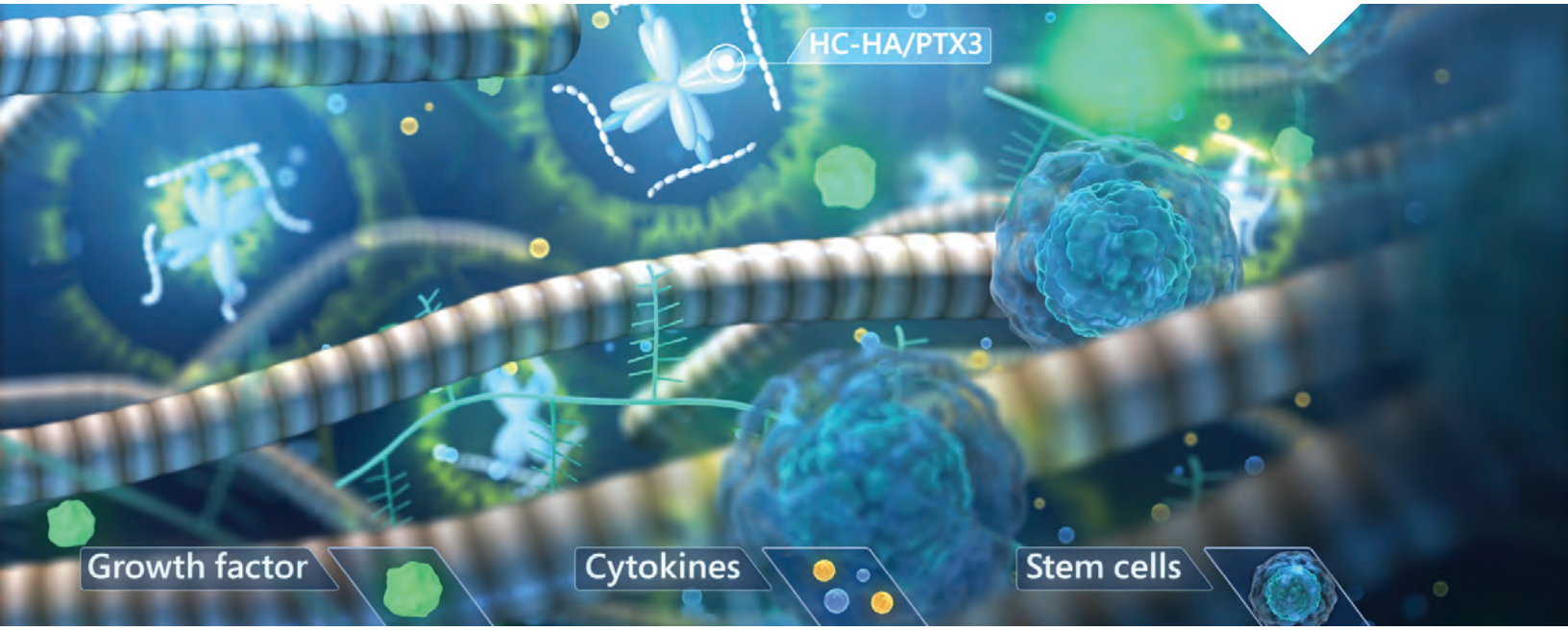
Present throughout the amniotic membrane, and highest in the umbilical cord, this complex acts by directing the activity of other biologic components — from cytokines and growth factors to stem cells — to support healing and regeneration.

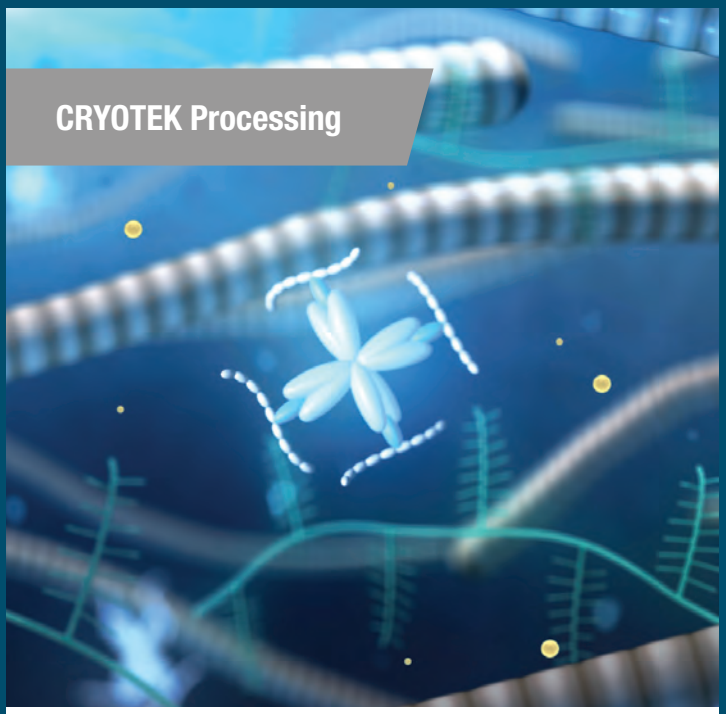
The way we process human birth tissue makes all the difference

If human birth tissue is processed appropriately, the unique properties of HC-HA/PTX3 can be preserved and transplanted into mature tissue of unrelated hosts to support regenerative wound healing and functional recovery as demonstrated on the ocular surface.[10,11,28-30]

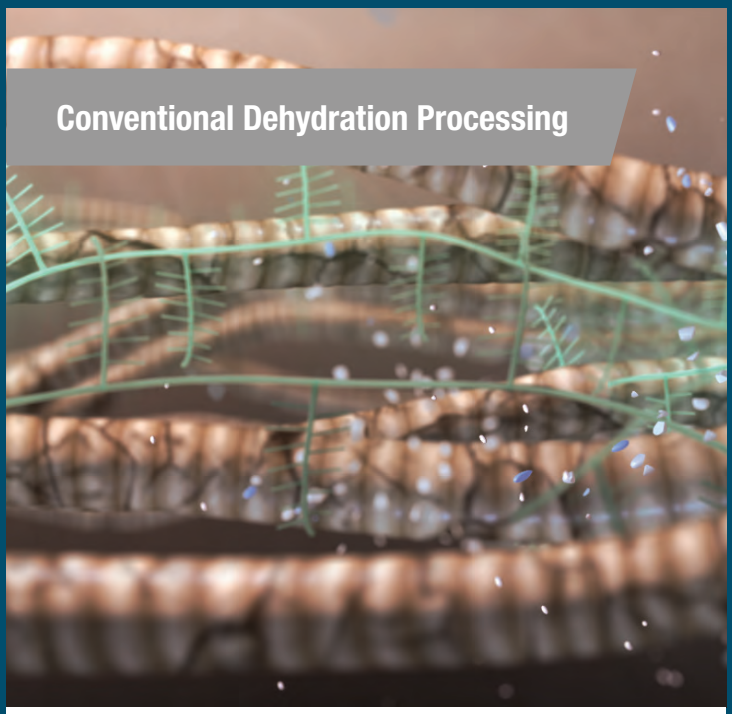
- **Modulates inflammation** by reducing the amount of pro-inflammatory cytokines and increasing that of anti-inflammatory cytokines as demonstrated on the ocular surface
- **Promotes the de-differentiation** of myofibroblasts to help prevent scar formation as demonstrated on the ocular surface
- **Supports stem cell growth** and recruitment of additional stem cells as demonstrated on the ocular surface

It has also been shown to dampen the sensitization of pain stimuli at the neurons in the fetal environment.[2-9,31]





Preserves the integrity of HC-HA/PTX3[10,11]



Critical biological components, including HC-HA/PTX3, are degraded[10]

CRYOTEK TECHNOLOGY

Preserving as Much of Nature as Possible

Our CRYOTEK cryopreservation process is the only tissue processing method shown to produce a matrix comparable to the native tissue, delivering the benefits of the natural tissue to the wound.[10,11]

In conventional dehydration processing, critical biological components — including the majority of HC-HA/PTX3 — are degraded, which may limit the processed tissue's healing capabilities.[10]

The Amniox proprietary CRYOTEK cryopreservation technology utilizes controlled deep freezing to effectively preserve the functional and structural integrity of the HC-HA/PTX3 found in birth tissue within a naturally hydrated state that can either be stored in a refrigerator or freezer.[2,10,11]

By devitalizing the living cells, while delivering the innate properties of human birth tissue, CRYOTEK minimizes the risk of an immune reaction and preserves the functional components of the extracellular matrix.

THE AMNIOX FAMILY OF UMBILICAL CORD AND AMNIOTIC MEMBRANE ALLOGRAFTS

A wide range of adjunct therapies for the management of regenerative healing of surgical, acute and chronic wounds which may help expedite functional recovery

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clarix®

CLARIX® CORD 1K

helps facilitate healing across a wide range of surgical specialties

- Market-first cryopreserved umbilical cord allograft as an adjunct for surgical applications

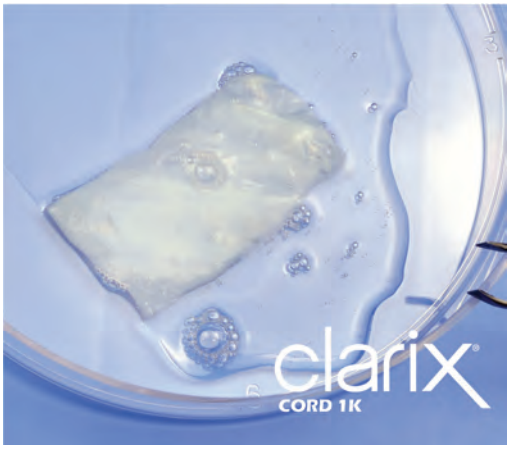
- Supports decreased wound dehiscence and scar tissue formation to help facilitate expedited wound healing and functional recovery[16-24]

- **SUPPORTED 11.5 DAY REDUCTION IN OVERALL TIME TO SKIN HEALING** (28.5 days vs. 40 days) after Total Ankle Arthroplasty (TAA)[16]
    - This benefit was most pronounced for patients with risk factors such as diabetes, tobacco use and obesity[16]

- Helps expedite healing, aids in reducing adhesion formation, and facilitates restoration of range of motion after tendon repair surgery and other soft tissue procedures[17,23]

- **UP TO 10X THICKER** than amniotic membrane,[10,11] which may increase longevity in the surgical site

- Cool storage in a standard freezer or refrigerators provides versatility, easier handling and less prep time



CLARIX 100

- Cryopreserved amniotic membrane (only) allograft for surgical applications — a thinner alternative to CLARIX CORD 1K

neox®

NEOX® CORD 1K

the "go to" adjunct therapy for treating complex wounds

- Umbilical cord allograft to address the unmet clinical needs of diabetic foot ulcers, chronic ulcers and chronic wounds
  - High closure rates[12-15]
  - Fewer applications[12,14,15]
  - Reduced cost of care[14]
- Umbilical cord allograft to help promote healing in complex diabetic foot ulcers complicated with osteomyelitis, comparing favorably to Standard of Care[12,14,15]

% Patients Achieving Complex Wound Closure With:	
NEOX CORD 1K	Standard of Care
79% at 16 weeks[12]	**31%** at 20 weeks[32]
79% at 1 year[12]	**45%** regardless of time[33]

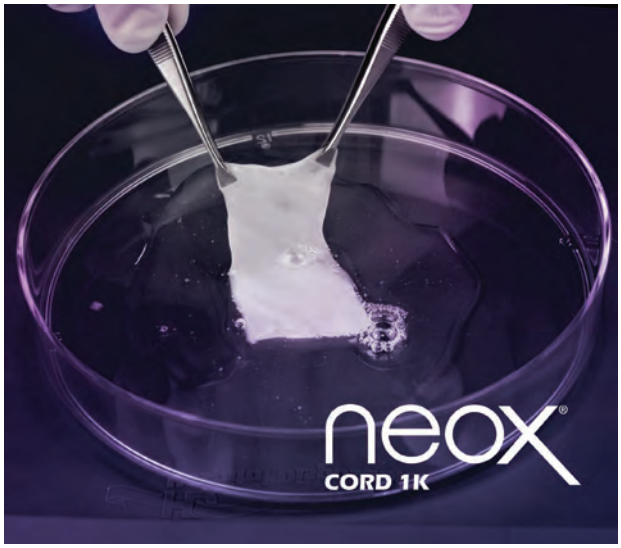
- **UP TO 10X THICKER** than amniotic membrane,[10,11] which may increase longevity in the wound bed for fewer applications and lower cost of care

NEOX CORD RT

- Hydrated umbilical cord allograft with the convenience of room-temperature storage offering similar benefits of NEOX CORD 1K

NEOX 100

- Cryopreserved amniotic membrane (only) allograft, ideal for shallow wounds or for larger wound areas



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THE AMNIOX FAMILY OF UMBILICAL CORD AND AMNIOTIC MEMBRANE ALLOGRAFTS

Supports Faster Functional Recovery Across a Wide Variety of Specialties and Applications

Specialties

- Chronic Wound Management
- Foot and Ankle
- Plastics
- Trauma
- Orthopaedics
- Sports Medicine
- Urology
- General Surgery

Applications – especially in patients with comorbidities

- Diabetic foot ulcers with and without osteomyelitis
- Venous leg ulcers
- Bone and joint reconstruction
- Soft tissue repair and reconstruction
- Nerve repair
- Cartilage debridement and repair
- Tendon/ligament repair
- Pressure ulcers
- Chronic and traumatic wounds
- Chronic tendinitis/fasciitis
- Rotator cuff/labral repair
- Meniscal and cartilage repair
- Fractures and non-unions
- Complex orthopaedic reconstruction
- Radical prostatectomy

DEMONSTRATED ECONOMIC OUTCOMES

Helps reduce the time to wound healing, reduce the cost of care[12,14,15]

NEOX Chronic and Complex Wound Allografts

- The overall cost burden associated with Diabetic Foot Ulcers (DFUs) and chronic wounds in the U.S. is conservatively estimated **>$50 BILLION ANNUALLY**[13]
- By helping to reduce time to healing, use of NEOX wound allografts has significant potential to help reduce this cost

87.5% COMPLETE CLOSURE RATE was achieved at an average 13.8 weeks with 1.68 applications in a study of patients with DFUs Wagner grade 1-3[14,15]

In a retrospective study of patients with DFUs Wagner grade 3-4 with confirmed osteomyelitis, **78.8% OF PATIENTS** demonstrated complete wound healing with 1.24 applications[12]

- Improved time to healing of DFUs may be achieved with fewer applications of NEOX compared to other tissue products[12,14,15]
- Fewer applications may translate directly to a decrease in overall treatment cost per patient[14,15]
- Similar improvements in time to healing were seen for chronic foot and ankle wounds treated with NEOX umbilical cord allograft
  - **79.7% OVERALL WOUND-HEALING RATE** was achieved in 5.5 weeks with 3.43 applications in a study of chronic foot and ankle wounds[13]
- In comparison, wound closure required 6 applications of a competitive product using amniotic membrane alone. The use of fewer applications with umbilical cord allograft may translate to decreased overall treatment cost per patient[13]
- Faster wound healing of DFUs and chronic wounds may also allow for earlier and shorter patient rehabilitation, leading to the potential for reduced cost of care

CLARIX Surgical Wound Allografts

- Delayed wound healing has a significant impact on the risk of infections and complications associated with many surgical procedures including Total Ankle Arthroplasty (TAA): Increased time to wound healing of >14 days postoperatively dramatically increased the risk of operative site infection[16]

- **USE OF CLARIX SURGICAL WOUND ALLOGRAFT AS AN ADJUNCT IN TAA HELPS REDUCE THE TIME TO WOUND HEALING** which may reduce the cost of care especially for patients with known risk factors*[16]

- A direct reduction in complications may reduce overall cost of care by decreasing the time to healing, risk of readmission, and rates of minor and major complications[16]

- The impact of reduced complications following TAA on the cost of care may be strongly suggested by reviewing information for other foot and ankle surgeries involving patients with similar comorbidities

- For example, in patients treated for ankle fractures with open reduction and internal fixation, total charges were significantly higher in patients with postoperative infection ($128,122 vs. $49,983)[16]

- Further studies needed to quantify potential reductions in cost of care for TAA and other orthopaedic procedures

*Risk factors include a history of diabetes, peripheral vascular disease, tobacco use, obesity, wound compromising medications, previous surgeries close to the TAA surgical site and post-operative non-compliance

CASE STUDIES

COMPLEX OSTEOMYELITIC FOOT ULCER[12]

Wagner 4 DFU

- 63-year old male patient with T1D and PVD presented with an open wound in the mid foot following first ray amputation (A)
- Osteomyelitis and gangrene were present
- After debridement, bone resection, biopsy and open cortex procedure, NEOX CORD 1K was used to cover the wound (B)
- At 7 weeks, the wound reduced in size (C)
- The wound remained healed with no recurrence at 28 weeks (D)

IN 28 WEEKS

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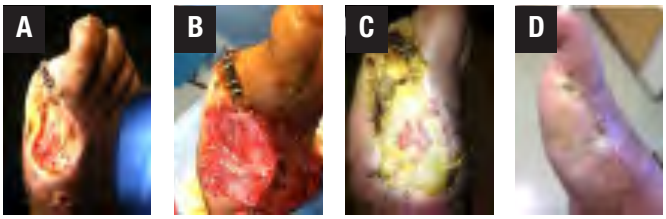

Case and photos from Caputo et al. Wound Repair Regen (2016)[12]

Why this study is relevant: Complex foot ulcers with exposed bone, tendon, muscle, and/or joint capsule, are particularly difficult to heal, especially when complicated with osteomyelitis. In a retrospective study of 33 similar complex wound cases, treated with Amniox cryopreserved allografts, 26 out of the 33 wounds achieved complete closure with an average time to healing of 16 weeks and an average of 1.24 applications.

COMPLEX FOOT RECONSTRUCTION

Medial Column Arthrodesis and Gastroc Resection

- 69-year old male patient presented with:
  - bilateral foot pain and deformities
  - pain with ambulation
  - unable to walk for exercise
- To correct the deformity, the medial column was fused (A) and the gastroc resected, leaving a large medial incision (B)
- CLARIX CORD 1K was placed subcutaneously to help with incision healing
- At 1-week post-op, the incision was calm and painless (C)
- Incision was completely healed 6 weeks post-op (D)

IN 6 WEEKS

FROM HERE...

Case and photos courtesy of Thomas Fusco, DPM, Orthopedic Associates, Fort Walton Beach, FL

...TO HERE

Why this case is relevant: Patients with complex foot deformity often require extensive hardware and soft tissue reconstruction, which can lead to challenging and prolonged recovery along with a higher risk of complications and infections. The inclusion of CLARIX CORD 1K as an adjunct to these surgical reconstructions have been shown to safely promote a healing environment that can lead to expedited recovery and restored range of motion.[16-18,23]

CHEMICAL EYE BURN

Regenerative Healing in an Avascular Space

For over 20 years, our cryopreserved umbilical cord and amniotic membrane allografts have been used in ophthalmology for the management of a wide range of ocular surface diseases and disorders by our market-leading sister company Bio-Tissue.

- Patient presents 8 days after chemical burn (A)
- PROKERA® is placed on first day of treatment (B)
- Limbal stem cell expansion evident at Day 5 (C)
- Patient achieved complete scarless healing by day 20 (D)

IN 18 DAYS

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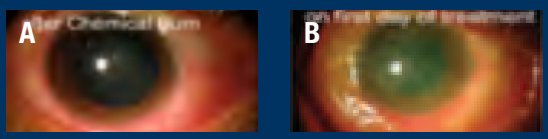

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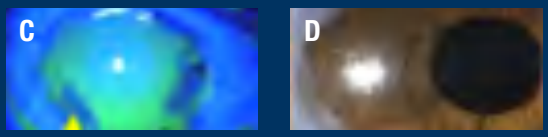

Why this case is relevant: We were the first to introduce the use of cryopreserved amniotic membrane to the ophthalmic market. The eye represents a unique and accessible model to observe the activation and development of limbal stem cells in their regenerative ability to heal corneal epithelial damage. This case demonstrates the ability of cryopreserved amniotic membrane to quickly achieve scarless healing in an avascular environment despite an extensive chemical burn.

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TRAUMA: CALCANEAL FRACTURE[21]

A Retrospective Study

- A retrospective review of 39 consecutive patients treated for calcaneal fracture by ORIF was performed to assess the ability of CLARIX CORD 1K to mitigate the high rate of complications. 19 patients were treated with CLARIX CORD 1K and were compared to a control group of 20 patients
- The group receiving CLARIX had a lower overall complication rate of only 10% versus 35% in the control group, with a notable lower rate of wound care issues (10% versus 35%) and infection (10% versus 25%)
- The readmission and reoperation rate was also lower in the CLARIX group versus the control (10% versus 30%)

IN 16 WEEKS

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Calcaneus fracture hardware fixation

Application of CLARIX over hardware and under lateral skin flap

Complete wound closure by 16 weeks

Case and photos courtesy of Christopher M. Stewart, MD, Orthopaedic Trauma Surgeon, Baptist Medical Center, Little Rock, AK.

Why this study is relevant: The complication rate after ORIF of calcaneal fractures operated on by a lateral extensile approach has been reported to be up to 25%, with the worst perioperative complications related to infection and/or wound complications. The use of CLARIX directly on the bone and hardware at the time of ORIF can be used as an adjunct to help decrease wound complications, re-operations, and infection rates.

CHRONIC ACHILLES RUPTURE

Soft Tissue Repair

- Patient presented with chronic ruptures of Achilles tendon, which required extensive turndown reconstruction and FHL transfer (A & B)
- A 6 x 3 cm CLARIX CORD 1K was placed directly over the repair (C) and the incision was closed
- 10 weeks later, the wound had healed and the patient had good ROM (D) and little pain, which improved further by the 3-month follow-up (E)
- By 6 months, the surgical scar was minimally evident, with full restoration of pigment and nominal scarring (F), and patient was back to normal activity

IN 6 MONTHS

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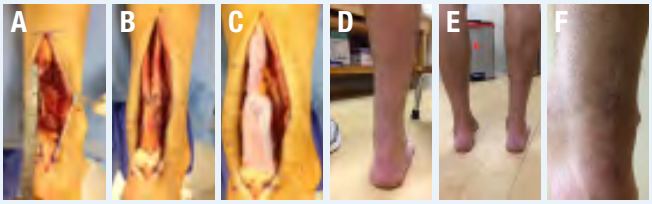

10 wks. post op. | 3 mos. post op. | 6 mos. post op.

Case and photos courtesy of Ryan Putman, MD, Carilion Clinic, Roanoke, VA.

Why this case is relevant: Extensive repairs and reconstructive procedures to soft tissues, especially in and around the ankle, present a considerable healing challenge and may lead to scarring, adhesions, and inflammation of both the soft tissue and surgical incision, along with a higher risk of complications. Combined, these factors can lead to pain and disablement during the prolonged recovery period. The adjunctive addition of CLARIX CORD 1K can help reduce discomfort, regulate adhesion development and promote healing to expedite restored range of motion and functional recovery.

IN-UTERO SPINA BIFIDA[24]

- A 21-year-old patient was referred for in-utero spina bifida repair with myeloschisis of a large 1.6 x 2.7 cm defect extending from L3 to S4
- At 24 weeks of gestation, the surgical repair was conducted in utero. Due to the large size of the defect (A), a CLARIX allograft was placed as a patch to cover the dura closure (B)
- At 37 weeks of gestation, the patient underwent scheduled cesarean delivery, at which point the lesion site appeared completely covered with no evidence of leakage (C)
- By day 28, the skin over the lesion had completely healed (D)
- At 6 months of age, the infant had full lower extremity sensory and motor function and bladder control were within normal limits

IN 4 WEEKS

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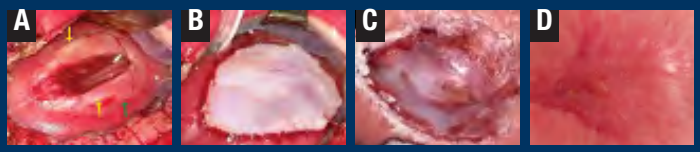

Representation of the defect from before repair to a postnatal period of 4 weeks.

Case and Photos from Papanna et al. Obstet Gynecol (2016)

Why this case is relevant: In-utero spina bifida repair poses significant challenges for the primary closure of the skin, leading to a greater risk of wound dehiscence, failure of repair, and long-term post-natal disability.

Patching the defect with CLARIX CORD 1K has been demonstrated to successfully create a barrier in-utero between the maturing spinal cord and the surrounding noxious amniotic fluid, supporting rapid ingrowth of vascularization, epithelization, and keratinization after delivery and near return to function for the baby.

Currently, there are few closure alternatives to achieve satisfactory closure, leading Amniox to secure Orphan Drug Designation by the FDA in pursuit of a biologic license application approval for this indication.

THE FUTURE IMAGINED

New Horizons. New Discoveries.
New Solutions to Complex Problems.

WE ARE PIONEERS

From our earliest research more than 30 years ago, we have been pioneers at the forefront of regenerative medicine, including:

- **FIRST TO IDENTIFY AND CHARACTERIZE THE HC-HA/PTX3 COMPLEX**[1]
- **FIRST TO COMMERCIALIZE AMNIOTIC TISSUE FOR THE OCULAR SURFACE**[34]
- **FIRST TO MARKET UMBILICAL CORD ALLOGRAFTS FOR SURGICAL, ACUTE AND CHRONIC WOUNDS**

We will continue our tradition of groundbreaking scientific research and development of innovative human birth tissue-based products to treat an ever-broadening array of clinical conditions.

Dedicated to improving healing and reducing patient suffering

We have always been dedicated to knowing more about a disease process and trying to understand if there is a better way to treat difficult diseases.

Our goal has been and always will be solving patients' unmet clinical needs through the relentless pursuit of new solutions to complex problems. Everything we do to discover, develop, and bring to market products and applications is centered on improving the lives of patients.

Where do we go from here?

As a leader in regenerative medicine, our products have always been in accordance with the FDA as a Human Cell, Tissues, and Cellular & Tissue-Based product (HCT/P). With the recent change in regulatory guidance, Amniox has elected to lead the market transition to biologic approval by pursuing multiple clinical trials for a variety of indications.*

**During this time, we will continue to offer our HCT/Ps for uses consistent with those described in this brochure*

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LEADING THE FUTURE AS A BIOLOGICS PROVIDER

The FDA has granted Amniox three Investigational New Drug approvals (INDs) to predicate to a Biologic License Application (BLA) that:

1 Helps Heal Complex Wounds

We are in the first of two Phase 3 clinical trials to determine efficacy of our products in healing very severe diabetic foot ulcers, where the bone is exposed and infected. We believe that our products may be able to promote wound healing to the point where limb amputation may be prevented or reduced. **THE FDA HAS GRANTED OUR CHRONIC AND COMPLEX WOUND PROGRAM A FAST TRACK STATUS.**

2 Helps End Pain and Restores Functionality for Patients with Osteoarthritis

We believe our products can have a significant impact on pain management. Presently, we are working on musculoskeletal pain, in the joint areas including ligament, muscle, and tendon — with osteoarthritis or degenerative processes that cause chronic pain.

3 Helps Heal Spinal Conditions Including Spina Bifida

The **FDA** has granted our cryopreserved human umbilical cord investigational biologic product TTAX02 **REGENERATIVE MEDICINE ADVANCED THERAPY (RMAT)** designation for the treatment of spina bifida in-utero. This designation aims to streamline development of regenerative medical products used in the FDA's Investigational New Drug program for the treatment of serious or life-threatening diseases such as spina bifida.

We are in a Phase 3 clinical trial to determine efficacy of our products for use in spina bifida where the wound is too large to be addressed by primary closure surgery — and typically may require a graft. Early data supports the premise that if we can use our allograft in this serious unmet need, it can play a significant role in helping to reduce complications and improve mobility.[24]

WE BELIEVE WE CAN MAKE A DIFFERENCE

For patients. For clinicians. For the healthcare system.

WITH THE SUCCESS OF OUR PLATFORM TECHNOLOGY using the natural properties of human birth tissue, we believe that we can challenge the status quo. Change lives. Change debilitating disease. Change outcomes. Challenge the paradigm of how we think about healing. And how we help solve degenerative diseases.

"WE WILL CONTINUE TO MOVE FORWARD WITH AN OPEN MIND. KNOWING THAT EVERYTHING IS POSSIBLE. NOTHING IS IMPOSSIBLE."

Scheffer Tseng, MD, PhD
Co-Founder and Chief Technology Officer

THE AMNIOX FAMILY OF CRYOPRESERVED UMBILICAL CORD AND AMNIOTIC MEMBRANE ALLOGRAFTS

Supporting regenerative healing and functional recovery as the adjunct to a wide array of surgical, acute and chronic wound treatments

- Helps improve patient outcomes and patient satisfaction
- Helps minimize complications and readmissions
- Helps reduce cost of care

WHY AMNIOX?

MANUFACTURER

Over-35-year commitment to understanding the science behind fetal regenerative healing
The leader in the transformation to becoming a biologics provider

PROCESSING

Proprietary CRYOTEK Cryopreservation Process shown to preserve more of the key biological components and structural integrity of fetal tissue

TISSUE SOURCE

Focused on delivering quality umbilical cord and amniotic membrane-based allografts, we are the only company with FDA-designation for its unique anti-inflammatory, anti-scarring and anti-angiogenic properties on the ocular surface

STORAGE

Versatile solution enables cool storage with minimal thawing and the ability to return the product to storage unopened

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