Pudendal Neuralgia as a Component of CPP—and Treatment

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Disclosures

* Consultant for Stryker Endoscopy
* Consultant for Boston Scientific
* Research grant from Pathways Healthcare
WHAT IS PUDENDAL NEURALGIA?

It is chronic pelvic pain lasting 3 or more months due to dysfunction or compression of the pudendal nerve. Acute pain is experienced in the area surrounding the pudendal nerve, most commonly known as the “sitting area”.

The Pudendal Nerve. This somatic nerve supplies motor innervation to the skeletal muscles within the pelvic cavity, including the external sphincter of the bladder and urethralis muscle. It also supplies innervation to the skeletal muscle in the perineal region, including the external anal sphincter.
Pudendal Nerve

- Supplies skin, organs and muscles of perineum
- Distribution similar in males and females
- Pudendal nerve blockade
  - Medial to ischial tuberosity at sacrospinous ligament
  - Transvaginal
- Functions
  - Micturation
  - Defecation
  - Erection
  - Ejaculation
  - Parturition

Dr. G. Bhanu Prakash
www.gims-org.com
Pudendal Neuropathy

Coexistence of clinical findings

- Pudendal Neuropathy
- Impaired Biomechanics
- Impaired Neurodynamics
- Pelvic Floor Muscle Dysfunction
- Connective Tissue Dysfunction
- Myofascial Pain
- Visceral Pain & Dysfunction
- Central Sensitization
- History Of Trauma
Pudendal neuropathy

Mechanisms of injury

**Compression**
- prolonged sitting
- hypertonus PFM: pain, emotional stress, postural muscle imbalance
- overdeveloped PFM: gymnastics, ballet, wrestling
- fall(s) onto the buttocks
- cycling, horseback riding
- impaired biomechanics

**Tension or Traction**
- chronic constipation and straining
- extended vaginal delivery
- under-active PFM
- descending perineum syndrome
- squatting with excessive weight
- impaired biomechanics

**Chronic aberrant nerve stimulation (convergence)**
- viscero-somatic reflexes
- somato-visceral reflexes
- somatic-somatic reflexes

**Surgery related**
- post-hysterectomy
- post-radical prostatectomy
- bladder suspension surgeries
possible symptoms

* The chief symptom is pain in the area innervated by the pudendal nerves such that sitting becomes intolerable.
* The pain is often not immediate but delayed and continuous and stays long after one has discontinued the activity that caused the pain (stop sitting, cycling, sex...).
* Pain in perineum.
* Pain after orgasm
* Loss of sensation with difficulty achieving orgasm.
* Strange feeling of uncomfortable arousal without sexual desire.
* Intolerance to tight pants or elastic bands around the legs.
* Friction and feeling of inflammation along the course of the nerve when walking for too long or running.
* Constant pain even with standing or lying down.
Possible Symptoms

* Constipation
* Pain during and after intercourse is often reported.
* Buttock sciatica and everything that goes with it: numbness coldness, sizzling sensation in legs, feet, or buttock. This is more often due to a reaction of the surrounding muscles to the pain in the pelvic region. It could also be from "cross talk" of the nerves.
* Low back pain resulting from radiation of the pain.
* Some people develop conditions such as complex regional pain syndrome and even post-traumatic stress disorder after prolonged or severe pain.
Possible Symptoms

* Problem with urinary retention after urination. Need to push to empty bladder. Harder to detect the feeling of urine when passing through the urethra
* Urethral burning with or after urination
* Feeling like the bladder is never empty or feeling the need to urinate even when the bladder is empty
* Urinary frequency
* Pain after bowel movement. Sometimes sufferers also report pain prior to and during the bowel movement
* Painful muscles spasms of the pelvic floor after bowel movement
Superior gluteal nerve (L4–L5, S1)
Inferior gluteal nerve (cut) (L5, S1–S2)
Nerve to obturator internus (L5, S1–S2)
Pudendal nerve (S2–S4)
Nerve to quadratus femoris (L4–L5, S1)
Sciatic nerve:
  Common fibular division (cut) (L4–L5, S1–S2)
  Tibial division (cut) (L4–L5, S1–S3)
Pudendal Nerve Anatomy

- Piriformis Muscle
- Sacrospinous (SS) Ligament
- S2
- S3
- S4
- Obturator Internus Muscle
- Levator Ani Muscle (partially cut away)
- Deep Perineal Branch of Pudendal Nerve
- Inframesal Rectal Nerve
- Alcock's Canal
- Falciform Process of ST Ligament
- Superficial Perineal Branch of Pudendal Nerve

Between S2 and S4, the pudendal nerve emerges from the pelvis.
Pudendal Nerve Anatomy
How is PN correctly diagnosed?

A. The History and Physical

What is the history? Was exercising heavily, was there an accident, pelvic surgery, vaginal delivery, or sitting long hours? Is the pain in the distribution area innervated by the pudendal nerve? The most constant element is a replication or worsening of the pain during a rectal/vaginal touch at the ischial spine area. This touch must be done by the end of the finger on the side of the vagina for women at the ischial spine and alcock’s canal. Very often there are other painful areas in the surrounding region such as the, pelvic floor muscles, piriformis muscle or tailbone pain. Most of the time this is a reaction to the nerve pain.
Pudendal Nerve Anatomy
How is PN correctly diagnosed?

B. Pelvic floor physical therapy that includes myofascial release. Pudendal neuraglia can cause PFD and the symptoms can be similar. A course of pelvic floor physical therapy can help to determine if there is PFD. People with PNE are less likely to have good results from pelvic floor physical therapy.

C. Pudendal Block

D. Magnetic resonance imaging (MRI), CT scan, and magnetic resonance neurography.

E. Electro physiological testing including EMG’s and PNMLT — A PNMLT is an electro physiological procedure, similar to an EMG (electromyogram), which measures the speed of nerve conduction.

— The PNMLT examines only the motor function of the nerve. There is no way to test the sensory fibers of the nerve which transmit pain.
Without treatment, over time there may be a progressive worsening of symptoms starting with a small amount of perineal discomfort that develops into a chronic and constant state of pain that does not decrease even when standing or lying down.
Pudendal Nerve Palsy -

**TREATMENT**

Condition is usually transient and improves with time.

- rest
- physical therapy
- stretches and exercises
- anti-inflammatory medication
- injection/nerve block
- surgery
  (as a last resort)
Treatment Options

Avoidance and Lifestyle modification
- Stopping activity which lead to onset of pain e.g.: cycling, exercises etc.
- Limiting sitting time
- Sitting with support

Medical therapy
- Muscle relaxants: Valium, Baclofen, Belodona, Thiazodine
- Anticonvulsants: Pregabalin, Neurontin
- Pain medications

Physical therapy
- Relaxation of pelvic floor muscles

Interventional radiology
- CT guided blocks of the pudendal nerve(s)
- CT guided placement of the pain pump

Surgery
- Botox injection into pelvic floor muscles
- Transgluteal pudendal neurolysis
- Decompression of clitoral/penile branch of the nerve
Approved Exercises for People with PN

These are exercises that are generally approved by most PNE doctors but please check with your physician and physical therapist to make sure they are acceptable in your case.

Walking
Walking is considered to be a safe exercise for people with PN or PNE. Walking on an incline is not recommended as it makes the gluteus muscles work harder and therefore could put more pressure on the pudendal nerve or may cause a stretch injury. The same is true for hiking.

Swimming
Swimming is another exercise that is recommended for people with PN or PNE. The only swimming style that is not recommended is the breaststroke. The breaststroke/frog kick requires that a person flex their hips, which also works the gluteus muscles and can cause trauma to the nerve. Also, when the hip is flexed, it will stretch the pudendal nerve.

Upper Body Exercises
Upper body exercises are great for building strength and most can be used without issues. Any upper body exercise that requires use of the abdominal muscles should be avoided.

Gliding Exercises
Some PN specialists suggest gliding exercises, especially after PN decompression surgery. This exercise helps to stretch the muscles without stretching the nerve.
1. From a lying down position bend your leg at the hip and knee so that your hip is flexed. (Keep your foot on the bed as you do this.)
2. Rotate your hip so that your knee and leg go away from the center of your body.
3. Bring your leg back the other way toward the center of your body.
Exercises PNE Patients Should Avoid

* Here is a list of exercises that should be avoided by patients who might have PNE.

* Squatting, Cycling, Piriformis stretches, Gym workouts, Stair Master, Ellipse, Exercise cycle, Lifting, Bowling, Ab crunches, Leg presses, Pilates, Step aerobics, Yoga, Skiing, Sit-ups, Jogging and Spinning.

* This list was developed by Dr. Stanley Antolak, in Minnesota.
Pudendal Nerve Block and Treatment
Pudendal Nerve Blocks

A diagnostic block, or a "blockage of the nerve", is an injection with a local anesthetic such as lidocaine or one of its derivatives (also used by dentists). The block can either be done in the buttock to reach the pudendal nerve at the ischial spine where it lies between the sacrospinous and sacrotuberous ligaments, or through the vagina at Alcock’s canal. One block for each side affected is necessary. If the pain diminishes immediately or even vanishes completely as long as the effect of the local anesthetic persists, this is an indication that the pudendal nerve may be compromised in some fashion, and that possibly some damage to the nerve has occurred.

However pudendal nerve blocks can temporarily ease the pain caused by other problems in the distribution area of the pudendal nerve so the nerve block is only one of the tools used in the diagnosis of PN.

Even with image guidance it is possible for the block to miss its mark.
There are two main types of injected liquids: a local anesthetic and slow-release steroids. The local is a short term diagnostic tool. The steroids are a therapeutic attempt. In some cases they will cause the nerve, if it is irritated, to get better. This can take days or weeks, and improvement may be temporary or permanent. This delay explains why physicians prefer a delay of several weeks between nerve blocks with steroids. If the nerve is not irritated, the steroids have no effect. Some doctors use heparin, an anti-inflammatory medication, instead of steroids.
Pudendal Surgical Incision
Pudendal Nerve Surgery

4 year follow up after surgery found that 50% felt their pain had improved to various extents, although control patients were not followed up for comparison (PMID 15716208). However, Brewer et al found that pelvic pain symptoms are not reported, after five years, in over 75% of pelvic pain patients anyhow, without surgery. (AUA Meeting, 2010)
Pudendal Nerve Anatomy

- Piriformis m.
- Pudendal n.
- Obturator internus m.
- Obturator externus m.
Placental Tissues:
A Gift of Life
Regenerative Therapeutics
100 Year History of Amniotic Tissue

➢ 1910– thermal injury and ocular wound cover
   • (Davis) 550 cases
   • (Sabella similar findings)

➢ 1940 (DeRoth) - ophthalmology grafts

➢ 1970’s - fell out of favor due to HIV

➢ 1995 (Kim and Teng) - ophthalmic neurotrophic ulcers
   • Significant improvement
   • Rapid healing

➢ 2005 - Aseptic recovery, cryopreservation and sterile packaging, wound cover, tissue and bone void filler

➢ 2009 to the Present ……..
Risks

• No documented severe adverse events (SAEs)

• Noted graft-host rejections have been documented with products with chorion tissues

• **Helpful information**: If anesthetic was used during your injection it will begin to wear off in 1-2 hours. Patient may be sore the day of up to 3 days after your procedure, this is **NORMAL**.

No demonstrated amplification of existing disease related to infection, inflammation
Literature

Findings:
“The progenitor cells derived from amniotic fluid and placenta are pluripotent and have been shown to differentiate into osteogenic, adipogenic, myogenic, neurogenic, endothelial, and hepatic phenotypes in vitro and in vivo.”

Growth Factor mRNA and Protein in Preserved Human Amniotic Membrane.

Findings:
“RT-PCR revealed that human AM expresses mRNA for EGF, TGF-alpha, KGF, HGF, bFGF, TGF-beta1, -beta2, -beta3, KGF-R and HGF-R...AM without amniotic epithelium also contains all seven growth factors examined, however, in this tissue the protein levels of EGF, KGF, HGF and bFGF were found to be significantly lower than in native AM.”

Properties of the Amniotic Membrane for Potential Use in Tissue Engineering

Findings:
“AM scaffold can modulate the healing of a wound by promoting tissue reconstruction rather than promoting scar tissue formation...The AM stromal matrix markedly suppresses the expression of the potent pro-inflammatory cytokines, IL-1β and IL-6...In addition, 2 low-molecular-mass elastase inhibitors, secretory leukocyte protease inhibitor (SLPI) and elafin, are expressed in the AM (King et al., 2007; Buhimschi et al., 2004). In addition to their anti-inflammatory properties, elafin and SLPI both have antimicrobial actions and act as components of the innate immune system to protect related surfaces from infection.”

Applications of Amniotic Membrane and Fluid in Stem Cell Biology and Regenerative Medicine

Findings:
“Amniotic fluid contains electrolytes, growth factors, carbohydrates, lipids, proteins, amino acids, lactate, pyruvate, enzymes, and hormones...the presence of key growth factors such as EGF, FGF, TGF, HGF in amniotic membranes may account for their clinical effects and mechanisms of action.”

Soluble Factors of Amnion-derived Cells in Treatment of Inflammatory and Fibrotic Pathologies

Findings:
“The amnion contains various tissue inhibitors (TIMP-1, -2, -3, -4) and MMPs. They regulate many crucial processes in inflammation and fibrotic processes including chemotactic migration of inflammatory cells, mitosis of fibroblasts and synthesis and degradation of extracellular components. This can explain, at least in part, the anti-inflammatory and anti-fibrotic action of the amnion.”

The Roles of Growth Factors in Tendon and Ligament Healing

Findings:
“In vitro and in vivo studies have shown that bFGF is both a powerful stimulator of angiogenesis and a regulator of cellular migration and proliferation. Studies into the effects of the exogenous application of TGFβ, IGF-I, PDGF and bFGF into the wound site singly and in combination have shown promise, significantly decreasing a number of parameters used to define the functional deficits of a healing tendon. Application of IGF-I has been shown to increase in the Achilles Functional Index and the breaking energy of injured rat tendon. TGFβ and PDGF have both shown separately to increase the breaking energy of healing tendon. Finally, application of bFGF has been shown to promote cellular proliferation and collagen synthesis in vivo.”
Soluble Factors of Amnion-derived Cells in Treatment of Inflammatory and Fibrotic Pathologies
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Effect of Human Amniotic Fluid on Bone Healing
Findings:
"The defects from group 1, which were treated with human amniotic fluid, showed significantly higher ossification than the group 2 defects, which were instilled with saline solution. Histological examination at 6 weeks postoperatively revealed that the defects treated with human amniotic fluid (group 1) had superior ossification compared with the control group defects (group 2)."

Natural Anti-microbial Production by the Amnion
Findings:
"Natural antimicrobial proteins are ex-pressed throughout the nonpregnant female reproductive tract. In pregnancy, natural antimicrobials are found in the amniotic fluid.

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Investigating the Efficacy of Amnion-derived Compared with Bone-marrow Derived Mesenchymal Stromal Cells in Equine Tendon and Ligament Injuries
Findings:
"The possibility to inject allogeneic AMSCs in real time, before any ultrasonographic change occurs within the injured tendon and ligament, together with the higher plasticity and proliferative capacity of these cells compared with BM-MSCs, represents the main features of interest for this novel approach for the treatment of equine tendon diseases. An obvious active proliferating healing in the area injected with AMSCs makes these cells more effective than BM-MSCs."

Comparison of Cryopreserved Amnionic Membrane and Umbilical Cord Tissue with Dehydrated Amnionic Membrane/chorion Tissue
Findings:
"Cryopreservation retains the native architecture of AM/UC and AM/chorionic tissue."

Human Amnionic Allograft in Use on Talar Dome Lesions: A Prospective Report of 37 Patients
Findings:
"The addition of HAA to arthroscopic micro-fracture repair of talar dome lesions measuring less than 2 cm2 has shown to significantly improve both post-operative VAS scores, when compared to preoperative scores. This improvement in ACFAS and VAS scores speaks to the potential use of HAA in the treatment of OCD...While the use of HAA has not been delineated as far as the techniques and applications in the ankle joint, it is accepted and has shown to be an effective allograft and a naïve tissue in which its potential to differentiate can assist in healing. Possibly as an adjunct to further intervention, it is felt that this will allow hyaline cartilage development and the potential to develop into a more significant structural cartilage."
Potential Use of the Human Amniotic Membrane as a Scaffold in Human Articular Cartilage Repair


Findings:
“In vitro repair experiments showed formation on OA cartilage of new tissue containing type II collagen.”

Effects of Human Amniotic Fluid on Peritendinous Adhesion Formation and Tendon Healing after Flexor Tendon Surgery in Rabbits


Findings:
“The least adhesion and the best healing were observed in tendons treated with sheath repair and HAF application. Tendons treated with HAF had significantly higher tensile load values. Topical application of HAF immediately after tenorrhaphy was significantly effective in preventing peritendinous adhesion formation without impairment of tendon healing in this rabbit model.”

Technology Insight: Adult Mesenchymal Stem Cells for Osteoarthritis Therapy


Findings:
“Joints exposed to MSCs showed evidence of marked regeneration of the medial meniscus, and implanted cells were detected in the newly formed tissue. Articular cartilage degeneration, osteophytic remodeling, and subchondral sclerosis were also reduced in the treated joints... In the long term, we hope that MSC-based technologies will permit the...

Extracellular Matrix of Human Amnion Manufactured into Tubes as Conduits for Peripheral Nerve Regeneration


Findings:
“Reinnervation to the gastrocnemius muscle was demonstrated electrophysiologically 9 months after transplantation... Therefore, it can be said that the AMT tubes are biodegradable but persist for a long time to support the regenerating nerve fibers... It was concluded that the extracellular matrix sheet from the human amnion is an effective conduit material for peripheral nerve regeneration.”

Regeneration of Peritoneum Using Amniotic Membrane to Prevent Postoperative Adhesions


Findings:

Regenerative Medicine in Pain Management


Findings:
“Application of human amniotic membranes in the field of interventional pain management is truly a topic of great interest. Much of the current research is investigating its role in the treatment of...”

...and anamnestic membrane applications in neural and peripheral pain management is needed, but...”

“Model research studies and anecdotal reports suggest use in human subjects are promising.”
• Placental tissue
• has all of the
• Components
necessary to regenerate injured - traumatized tissue
The Cellular components:

--- MSC's aka medicinal signaling cells
aka pluripotential mesenchymal stem cells

--- fibroblasts, keratinocytes, epithelial cells

Approximately 40% of cells are MSC’s

Expansion or Culturing is NOT required for placental tissue, no potential harsh chemicals i.e. collagenase, no adverse events ever reported with placental tissue.
Messengers Role in Tissue Repair

* **Inhibit inflammation and promote transition to the proliferative stage of wound healing**
  * Secrete anti-inflammatory (IL-1RA, IDO, IL-10) and anti-microbial factors  
    (Defensins, N-GAL, LL-37)

* **Stimulate cell migration, proliferation and differentiation**
  * Epithelial cells (EGF, KGF) – faster re-epithelialization
  * Endothelial cells (VEGF, bFGF) - vascularization
  * Fibroblasts (bFGF, PDGF) - dermis regeneration
  * Host Stem Cells (SDF-1, IGF-1) - epithelial, endothelial, neural, etc.

* **Inhibit scar formation**
  * Secrete TGF beta 3 and other anti-scar factors (HGF, VEGF)
  * Regulate MMPs/TIMPs
Regenerative Therapeutic Cycle with MSC’s = Medicinal Signaling Cells

Protective

Anti-apoptotic

Anti-fibrotic

Bone

Tendon

Cartilage

Muscle

Ligament

Fat

Stroma

Tissue Protective

Anti-inflammatory

Anti-Inflammatory

• Transforming growth factor beta-1 (TGF-1)
• Insulin-like growth factor I (IGF-I)

TNF Suppression

IL-10 Production

IL-4 Production

Blocks T Cell Proliferation

Tissue Regeneration

Regenerative why – MSC’s = Medicinal Signaling Cells, mRNA, miRNA, growth factors, ECM
Clinical Applications Reported in literature:

- **Ob-Gyn:**
  - pudendal nerve, pelvic floor
- **Urology:**
  - Prostatectomy, Pelvic Floor Dysfunction, Strictures, ED
- **General Surgery:**
  - Adhesion, Fibrosis prevention
- **Extremity Surgery:**
  - Bone/Tendon/Nerve Repair
- **Cardio-Thoracic**
- **Dental restoration**
- **Dermatology:**
  - Hair restoration
  - Scar Keloid therapy
  - Cosmetic applications
- **Ophthalmic Procedures:**
  - Corneal and Conjunctival Reconstruction
  - Ocular Surface Reconstruction
  - Pterygium Repair
- **Neuro:**
  - Neurodegenerative disease
  - Nerve decompression
- **Pain Management**
  - Spine
  - Chronic Pain in upper and lower extremity joints (i.e. Shoulder or Knee)
  - Facet Joint Injections
Outcomes Post-Treatment

- As with all procedures results may vary due and no patient is the same for varies reasons
- Studies suggest the following:
  - 25-30% respond w/n 72-96 hours
  - 30% of patients respond w/n 6-8 weeks
  - 20% response occurs up to 8 weeks
  - <10% chance of failure with treatment
A Regenerative Approach to Resolution of Pudendal Neuralgia in Chronic Pelvic Pain

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Injectable allograft consists of freeze-fractured amniotic membrane contained in amniotic fluid for an injectable allograft.
How is the donor tissue handled?

- Donor tissue is recovered using the safest recovery techniques and sterile equipment to minimize any bio burden contamination. Products are aseptically processed in a Class 100 space.

- Microbial testing is performed on the amniotic fluid and the amnion solution. The final processed allografts are tested for microbiological contamination in accordance with United States Pharmacopeia (USP) guidelines to ensure compliance with regulatory requirements for sterility, mycoplasma and endotoxins.
Amniotic Tissue Regenerative Product

Preparation

1. Amnion is manually separated from chorion.

2. Amnion cut to sizes, sterilized and packaged either “wet” (hydro) or “dry.”

1. Injectable amnion – amnion subjected to freeze fracturing in liquid nitrogen. Membrane fragments range between 200 µ (0.20 mm) and 20 µ (0.02 mm).

1. A slurry of membrane fragments is prepared by adding amniotic fluid and freezing down in liquid nitrogen in various size ampules.

1. All products contain a serum-free cryopreservative.
Features of the Placental Allograft

1. Because the allograft very low expression of HLA Class II antigens, it is immunoprivileged, i.e., it does not activate an immune response or tissue rejection.

1. The allograft has been regulated by the FDA since 2006.

1. No adverse serious events have been reported. It’s worst “negative effect” so far has been no clinical response.
Amniotic tissue and fluid is regulated by the FDA under Section 361 of the Public Health Service Act as a “minimally manipulated” allograft, as outlined in 21 CFR parts 1270, 1271 and 1271.1

The term “minimally manipulated” pertains to processing that does not alter the “original characteristics” of the tissue’s utility for repair, reconstruction, and or replacement.

- Any cells therein can not be cultured and/or expanded in vitro.
- It cannot be combined with any other specific articles, e.g., antibiotics, trypsin, PRP, FBS, etc.
- It can not have a systemic effect (i.e., cannot be given i.v.)

Amniotic Tissue and Fluid is regulated as an Allograft. Hence, there are no on or off label limitations. Physicians can use this preparation as they see fit; i.e., the FDA does not regulate the practice of medicine, only the manufacture and commercialization (sales, marketing and claims) of products.
WASHINGTON — The Food and Drug Administration announced a crackdown on dangerous stem cell clinics on Monday, while at the same time pledging to ease the path to approval for companies and doctors with legitimate treatments in the growing field.

This action by the FDA is directed toward clinics using adipose-derived or bone marrow-derived live stem cells isolate using procedures that violate Section 361 of the Public Health Service Act as a “minimally manipulated” allograft, as outlined in 21 CFR parts 1270, 1271 and 1271.1.

The FDA has regulated amniotic tissue products since 2006 so they’re still comfortable with placental products so long as they do not violate Section 361 of the Public Health Service Act in 21 CFR parts 1270, 1271 and 1271.1. The amniotic placental product used in the current study are in full compliance with these regulations.
Patient selection: All patients with CPP were evaluated and those determined to have pudendal neuralgia as a component of their CPP as determined by presenting symptoms and digital pressure on the area of Alcock’s canal (n=64) were included in this study.

Treatment: all subjects were injected transvaginally with 1 cc of the amniotic tissue transplant diluted with 2 cc of sterile saline to infiltrate the area around the pudendal nerve at the level of Alcock’s canal.

Evaluation: Following the procedure, the patients were evaluated 6 weeks later by reporting to the treatment team their level of pain improvement using 3 simple metric categories:

- pain completely or near completely gone,
- pain moderately improved, or
- no improvement in pain. What symptoms? Should be more specific in the definition.
The exit of the pudendal nerve from Alcock's canal can vary.

Dorsal and perineal nerve exiting together from Alcock's canal.
After Care
patient instructions

- Local anesthetic was used during injection
- Patient may be sore the day of your procedure, this is NORMAL. The discomfort can last up to 3-4 days
- TYLENOL for pain relief is ok to take as needed.
- The following are not allowed for 8 weeks after treatment:
  - NO ASPRIN
  - NO IBUPROFEN
  - NO ADVIL
  - NO ALEVE
  - NO NAPROXEN
  - NO ICING
No significant adverse events were reported
Mechanism of Action

1. Since the cells in the Amniotic Tissue Product do not proliferate or differentiate, their effects are thus limited to the secreted materials including:
   - Growth factors (VEGF, TGFβ1, PDGF, etc.)
   - Cytokines: e.g., TLR-3, etc.
   - Hyaluronic Acid, IL-10,
   - Microparticles (exosomes) containing microRNAs
   - Scaffold: Type I, II, III, V and VI Collagen

2. Regenerative stem cells are not in the product! However, the allograft appears to stimulate the migration and differentiation of resident stem cells by the microRNAs which in turn may contribute to regenerative healing.

3. A significant benefit of MSCs is their ability to stimulate neovessels, and provide potent antibacterial and anti-inflammatory activity
Summary

1. Pudendal neuralgia underlying chronic pelvic pain is more common than believed.
2. Up to now, treatment of pudendal neuralgia has been difficult.
3. It appears that it can be effectively resolved in most patients by infiltrating the area around Alcock’s canal with an amniotic tissue allograft.
4. The allograft is immunoprivileged and thus it does not activate an immune response or tissue rejection.
5. The allograft is regulated by the FDA.
6. While we do not yet have a clear understanding of its mechanism of action, it appears to be largely due to its ability to activate resident stem cells to replace cells lost to disease, coupled to its immunomodulatory actions which may include long term suppression of chronic inflammatory genes and thus pain pathways associated with the pudendal nerve.
Questions?