Charcot Neuroarthropathy

ETIOLOGY

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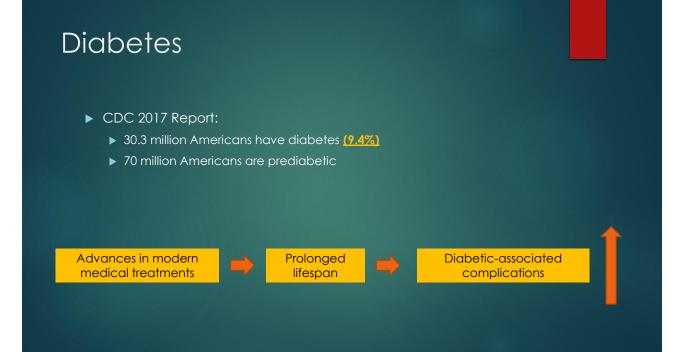
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Objectives

 Summarize and understand basic pathophysiology behind Charcot Neuroarthropathy (CN)

Definition

- Progressive, noninfectious, destructive inflammatory process of the foot and ankle (1)
- Jean-Martin Charcot
 - French Neurologist
 - > Dr. Elliott has uncovered literature to dispute the original description
- Tabes Dorsalis (Tertiary syphilis)
- Long-standing diabetes (1)



Negative Impacts of CN

- Physical disability/limitations
- Financial burden
 - Individual
 - ► Health Care System
- Social stigma



Etiology

- Peripheral Neuropathy (PN)
 - Absence of protective sensation

Causes of PN

- Diabetes
- ► <u>Alcoholism</u>
- Dietary (Vitamin deficiencies)
 - Especially B1, B6, B12, E
- Infectious
 - Viral or Bacterial
 - Lyme disease, shingles, Epstein-Barr virus, hepatitis C, leprosy, syphilis, diphtheria, HIV
- Autoimmune
 - Sjogren's syndrome, lupus, rheumatoid arthritis, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy, necrotizing vasculitis

- Hereditary
 - Charcot-Marie-Tooth disease
- Trauma
 - Motor vehicle accidents, falls or sports injuries
 - latrogenic (casts, OR positioning)
- Tumors
 - Benign or malignant
 - Can directly involve nerves or place pressure on nerves
- Other
 - Kidney disease, liver disease, connective tissue disorders and an underactive thyroid (hypothyroidism)
- Idiopathic

How does Diabetes cause PN?

- Selectively damages cells whose glucose transport rate does not rapidly decline in response to hyperglycemia, leading to high glucose levels inside the cell (2)
 - Activates four major pathways
 - Polyol, Hexosamine, Protein Kinase C, Advanced Glycation End products (AGE)
 - Inhibits a key glycolytic enzyme
 - Glyceraldehyde-3 phosphate dehydrogenase (GAPDH)

Two Explanations for CN

Neurotraumatic

- Trauma in context of PN
 - Acute, subacute, cumulative/repetitive
 - Traumatic event activates a cascade of proinflammatory cytokines, TNF-a, interleukin-1β, interleukin-6 (3-5)
 - TNF-a upregulates the receptor activator of nuclear factor-kB (RANK) ligand, i.e. RANKL system
 - Intense osteoclast activity = excessive bone turnover
 - Decreased anti-inflammatory cytokines and antagonist to RANKL system osteoprotegerin (3-5)
 - Bone breakdown ensues without regulation, leading to a collapse of the foot structure

Two Explanations for CN

Neurovascular

- Originally described by Jean-Martin Charcot (French Neurologist) in 1883
 - ▶ Hyperemia develops from overactive vaso-autonomic neuropathy (6)
 - ► Increased blood flow raises venous pressure and enhances fluid filtration through capillary leakage → Increased compartmental pressure and deep tissue ischemia → compromises tendons and ligaments in the foot & ankle → joint instability → collapse (7)
 - Additionally, increased blood flow causes increased delivery of osteoclasts and monocytes resulting in greater bone resorption (8)
- Patients with Charcot Foot demonstrate increased blood flow (macro) to the foot/ankle; patients with peripheral arterial disease (PAD) rarely develop Charcot neuroarthropathy (9-10)

Combination Theory

- CN is likely caused by a combination of both theories
- Continued weight-bearing without sufficient protection (guarding, offloading, activity restriction) leads to repetitive microtrauma and perpetuates increased proinflammatory cytokines, magnifying the intensity of a Charcot event, preventing proper bone remodeling and eventual loss of structural integrity of the bones & joints of the foot (i.e. fracture, subluxation/dislocation)



Charcot Foot



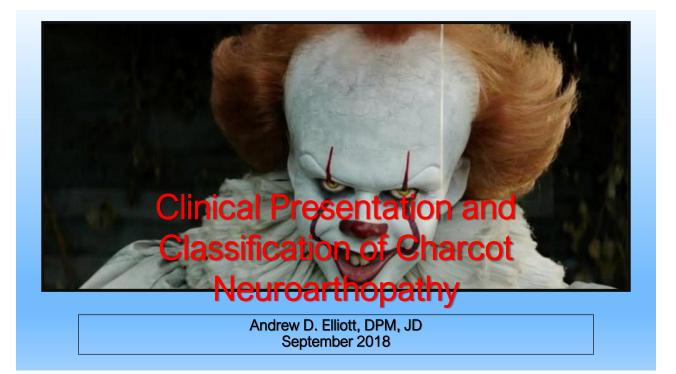
Ultimately...



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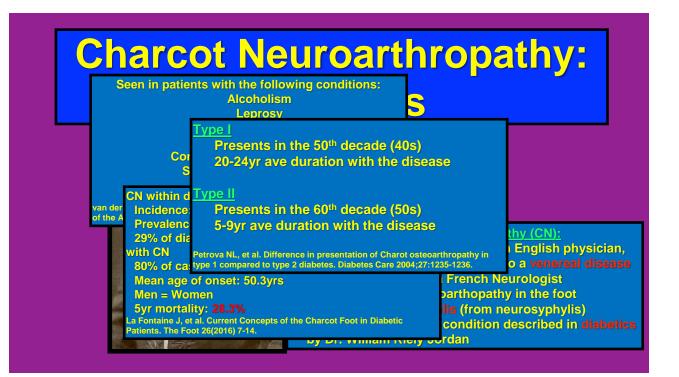
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Yes, but what does CN look like?

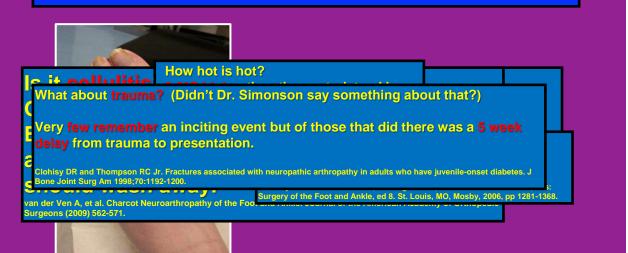


• Acute CN can look like lots of things...

• Gout

- Cellulitis/osteomyelitis
- Trauma
- Stress Fractures
- Deep Vein Thrombosis

Clinical Picture of Acute CN



Clinical Disturp of Chronic CN

le or Unstable deformities uxation or dislocation at iple joints of foot/ankle cker Bottom" foot



How to Classify CN?

Brodsky's anatomic classification system can be useful to discuss treatment option; however, it doesn't include any staging.

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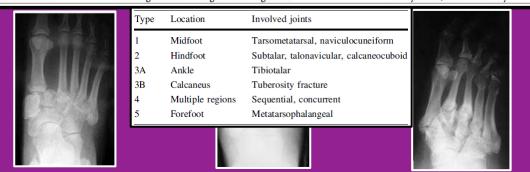
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Irodsky JW. The diabetic foot. In: Coughlin MJ, Mann RA, Saltzman CL, eds. Surgery of the Foot and Ankle. 8th ed. St. Louis. MO, JSA: Mosby; 2006;1281–1368.



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However...

Stage

Radiographic findings

Clinical findings

Treatment

Because it ignores the most clinically relevant stage, in 1990, Shibata et al. proposed a **stage 0** based primarily on clinical and scintigraphic signs without obvious radiographic findings.

fragments

III (reconstruction)

Consolidation of deformity, joint arthrosis, fibrous ankyloses, rounding and smoothing of bone fragments

Absence of warmth, absence of swelling, absence of erythema, stable joint \pm fixed deformity

orthotic walker, or clamshell ankle-foot orthosis

Plantigrade foot: custom inlay shoes with rigid shank and rocker bottom sole. Nonplantigrade foot or ulceration: débridement, exostectomy, deformity correction, or fusion with internal fixation.

Lets try MRI...

	Gra			
telau Stage	0 (low severity)	1 (high severity)		tiation
durati (acute)	Mild edema, erythema, and warmth Possible pain No deformity	Severe edema, erythema, and warmth Possible pain Gross deformity	Clinical	
ediate mmati n arth	No oseous abnormality MRI – bone marrow edema, microfractures, no cortical disruption Lamellar bone with active surface Trabeculae remodeling associated with microfracture Marrow space replaced by loose spindle cells	Active services and a subcharge of the service of t	Radiographs MRI Histopathology	es the full
Inactive (chroni	No inflammation c) No deformity No osseous abnormality MRI – no significant bone marrow edema Sclerosis of bone, broad lamellar trabeculae with collagenous replacement; low vascularity of the marrow space	No inflammation Gross deformity Osseous abnormality MRI – no significant bone marrow edema Woven bone, immature and structurally disorganized, fibrosis	Clinical Radiographs MRI Histopathology	

Schon Midfoot Classification



Medial Column Classification

Sella and Barrette's system is based on xrays, clinical findings and bone scans: Stage 0 Localized heat and swelling; xray normal Stage 1 Stage early bone involvement on radiographs Stage 2 Joint subluxation Stage 3 Joint dislocation and collapse Stage 4 healing and sclerosis Selle EJ, Barrette C, Staging of Charcot neuroarthropathy along the medial column of the foot in the diabetic patient. J Foot Ankle Surg. Jan-Feb 1999;38(1):34-40.

		Stage	Diagnosis		
0			Localized heat and midfoot swelling		
1			Localized osteoporosis, subchondral cysts, erosions, and diastasis		
2			Joint subluxations		
3			Joint dislocations		
4			Sclerosis and ultimate fusion of involved joint		
Stage	No. of	Radiographs	Scans-	Scan-	Clinical Findings
	Feet		Tc99	In/Ga	
0	10	Negative	+	-	Increased heat
1	6	Cysts, erosions, diastasis	+	-	Increased heat and swelling
2	16	Joint subluxation	+	-/1ess +	Mild pronation
3	12	Joint dislocation	+	-/less +	Bony prominences, pronation, rocker
					bottom
4	7	Joint Fusions and	-	-	Rocker bottom, bony prominences,
		Sclerosis			pronation

Predicative of outcomes?					
Pogore and Rovilacque considered	Classifying Charcot Arthropathy				
Likely accurate as it was shown in showing the risk of amputation was association with location and cor	s significantly higher in nplexity/stage of CN.				
GUESS. Rogers L, Bevilacqua N. The Diagnosis of Charcol Fool. Clin Podiatr Med Surg. 2008;25:43–51	C. Charcot with deformity and ulceration D. Charcot with Extremity osteomyelitis Amputation				

In Conclusion

-If you have a red, hot swollen foot in a long standing diabetic no obvious explination, get an MRI

-Eichenholtz is still a fairly common staging system

-Other newer staging systems are also in use that provide better, more predictive information

THANK YOU



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Charcot Neuroarthropathy

IMAGING

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Objectives

 Summarize and understand imaging considerations for Charcot Neuroarthropathy (CN)

Diagnosis

- Diagnosis of CN is primarily clinical (1-3)
- A clinical suspicion for acute CN should be followed by ordering appropriate diagnostic imaging
- Provides details to establish a definitive diagnosis and guide treatment

Venous Duplex Ultrasonography

- Performed when deep vein thrombosis (DVT) is suspected
- Results should be normal in acute CN (4)
- DVT
 - ▶ Unilateral edema, erythema, calor and pain



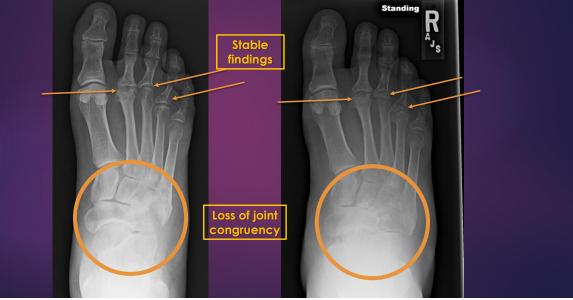
Plain Radiographs (X-rays)

- Initial imaging of choice
- Weightbearing (WB)
 - Unless patient is not able to stand
 - Better assess for subtle joint abnormalities
- Bilateral feet
 - Unless patient only has one foot
 - Allows comparison with unaffected side
- Accuracy of differentiating osteomyelitis from Charcot is only about 50-60% (1)
- Findings may be absent/negative within first 2-3 weeks of acute event (1,2) or even longer (4)

Plain Radiographs (X-rays)



Plain Radiographs (X-rays)



Plain Radiographs (X-rays)



Plain Radiographs (X-rays)



Plain Radiographs (X-rays)

- Findings most accurate:
 - Demineralization
 - Periosteal reaction
 - Cortical destruction
- Useful in ruling out other pathology (fractures, arthritis, etc.)
- Serve as a baseline for future studies, especially in at risk patients

Computed tomography (CT)

- More sensitive than plain film radiographs
- With contrast, can aid in detecting abscess formation
- Cannot determine early bone morrow edema or microfractures
 - Found in the acute phase of CN
 - Therefore is not recommended for diagnosis (2,3)

Flow

Plantar

Delaved

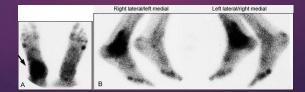
Tissue phase

Nuclear Imaging

- Well established for detecting bone infections
- Can seem complicated if you don't order these scans with regularity
- 3-phase bone scintigraphy (1)
 - ▶ Highly sensitive for osteomyelitis (80-100%)
 - Not specific
 - Trauma, arthritis, recent surgery or CN will result in high uptake
 - Negative bone scan excludes only infection



- Labeled leukocyte scans have better specificity than 3-phase alone (1-3)
 - ⁹⁹Technetium methylene diphosphonate (⁹⁹Tc MDP) labels hydroxyapatite, which is used to measure bone turnover
 - Bone turnover is high in Charcot, trauma and infection, so this scan alone cannot differentiate between Charcot and infection



Nuclear Imaging

- Labeled leukocyte scans have better specificity than 3-phase alone (1-3)
 - ¹¹¹Indium labeled leukocytes localize in neutrophil-mediated inflammatory processes, such as bacterial infections in bone – <u>should</u> <u>not appear in the absence of infection</u> (1-3)
 - ⁹⁹TC MDP & ¹¹¹Indium in combination for the diagnosis of osteomyelitis (1)
 - ▶ 50% sensitive
 - ▶ 100% specific
 - ▶ 81% accurate

Nuclear Imaging

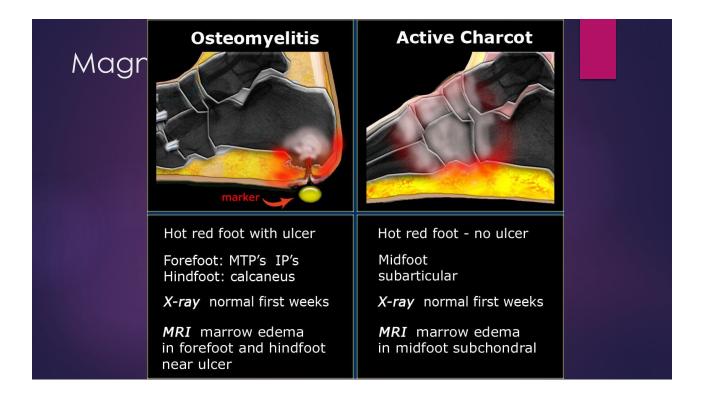
- Labeled leukocyte scans have better specificity than 3-phase alone (1-3)
 - ⁹⁹Tc sulfa colloid scans image areas of reticuloendothelial cells, found in the liver, spleen and <u>bone marrow</u>
 - Known as "bone marrow imaging"
 - No uptake in areas of bone infection
 - Using ⁹⁹Tc sulfa colloid & ¹¹¹Indium together can improve the accuracy in differentiating between infection and inflammation seen in acute Charcot (1-3)

Magnetic resonance imaging (MRI)

- Generally supported as superior to nuclear imaging tests in aiding diagnosis (1)
- Can effectively detect soft tissue edema, joint effusion and bone marrow changes in the early/acute phase
 - > Detects abnormalities earlier than plain film radiographs

Magnetic resonance imaging (MRI)

- Helpful in ruling out abscess, sinus tracts and osteomyelitis
 - Osteomyelitis focal involvement of a single bone or joint
 - Charcot arthropathy involves several joints/bones (1,5)
- More sensitive, but less specific than combined ⁹⁹Tc SC & ¹¹¹Indium bone scan (2)
- Limitations
 - Recent surgery
 - Retained hardware
 - Pacemaker, aneurysm clips or renal insufficiency preventing IV contrast



PET Scans

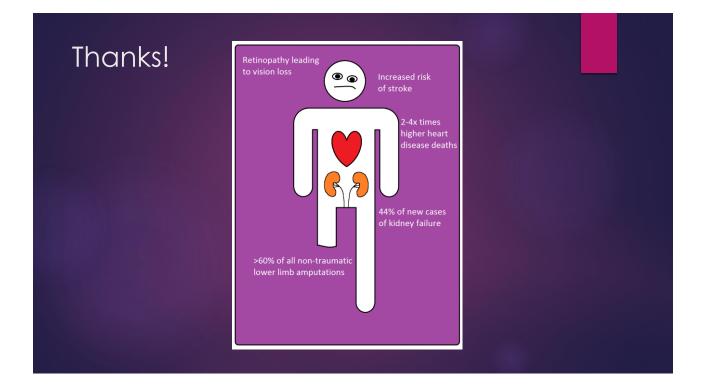
 Shows promise in differentiating CN from infection, but these techniques are not widely available, and clinical usefulness is yet to be determined (1,3)

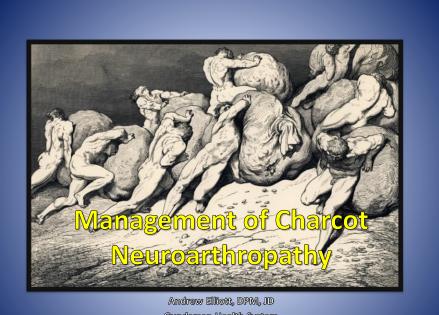
Take Home Points

- X-rays are a MUST, but may not be enough
- Don't use CT imaging
- If using bone scan/nuclear imaging, use combination of ⁹⁹Tc sulfa colloid & ¹¹¹Indium
- MRI with contrast is your best bet, unless CN & infection both present
- PET Scans?

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Gundersen Health System September 2018

DISCLAIMER

- No relevant financial relationships
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Treatment Options

- Conservative Treatment
- Pharmacological Treatment
- Surgical Treatment

Conservative Treatment

✓ Acute tx focus:

- ✓ Stabilizing the unstable externally
- ✓ Allow the inflammation to subside
- ✓ Allow the Fractures to heal
- ✓ Plantigrade foot that can be protected in a custom/rocker bottom shoe

Better to start CN treatment **earlier** rather than later: 24 patients with Eichenholtz Stage 0

11 tx'd within 1mo of onset of s/s with 3mo TCC 13 tx'd ave 3mo after onset of s/s 5mo TCC

All 13 of the delayed treatment group advanced to flatfoot/rockerbottom rigid deformities

But in the early group only 1 did

Chantelau E. The perils of procrastination: effects of early vs. delayed detection and treatment of incipient Charcot fracture.Diabet Med 2005; 22: 1707 -12.

2008;904:794-9. Christensen TM, Gade-Rasmussen B, Pedersen LW. Duration of off-loading and recurrence rate in Charcot osteoarthropathy treated with less restrictive regimen with removable walker. J Diabetes Complications 2012;26:430–4.

How important is NWB?

Although the expert consensus remains NWB immobilization in a TCC, literature exists that suggests that continued WB while immobilized does not hinder the



In a study by du Souza et al Patients were initially instructed to be NWB. However, the authors found that patients often did **not comply** with this instruction.

- 1) a lack of proprioception and inability to determine how much weight was being placed on the foot due to peripheral neuropathy,
- 2) poor eyesight secondary to diabetic retinopathy, and
- 3) <u>poor strength and coordination</u> which made the use of ambulation assistive devices difficult.

The authors found that despite the patients being WB more often than not, only one progressed to deformity of the foot during the treatment period. Thus, they allowed all subsequent natients to be WB as tolerated

de Souza LJ. Charcot arthropathy and immobilization in a weight-bearing total contact cast. J Bone Joint Surg Am 2008 90: 7549.



Put doos it work?

Small study of patients with Eichenholtz Stage 1 midfoot Charcot. The authors found that TCC immobilization provided effective resolution with maintenance of a stable, plantigrade foot in 75% of cases at 32mo, concluding that TCC immobilization remains the mainstay of treatment for midfoot Charcot.

This has been replicated in several other studies.

Myerson MS, Henderson MR, Saxby T, Short KW. Management of midfoot diabetic neuroarthropathy. Foot Ankle Int 1994: 15: 233-41.

Armstrong DG, Todd WF, Lavery LA, Harkless LB, Bushman TR. The natural history of acute Charcot's arthropathy in a diabetic foot specialty clinic. Diabet Med 1997; 14: 357-63.

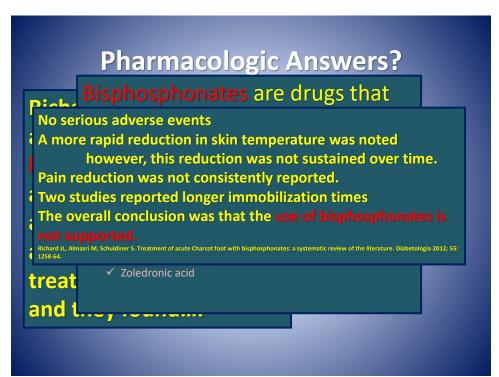
Sella EJ, Barrette C. Staging of Charcot neuroarthropathy along the medial column of the foot in the diabetic patient. J Foot Ankle Surg 1999; 38: 34-40.

Recurrence? Yes...

Some studies have shown as high as 23% within 27mo

Noncompliance and obesity (>30kg/m²) were the two main predisposing factors Osterholf G, Boni T, Berli M. Recurrence of acute Charcot neuropathic osteoarthropathy after conservative treatment. Foot Ankle Int 2013;34:35-9.





Pharmacologic Answers?

A randomized controlled trial for intranasal calcitonin as adjunct to conservative tx of CN looked at 32 pts over 6mo.

- \checkmark Markers for bone turnover were measured at 3 and 6mo.
- ✓ Significantly greater reduction in ICTP and BALP was noted at 3mo.
- ✓ Reduction in BALP was not seen at 6mo.
- Daily nasal calcitonin may be an effective adjunctive treatment modality.

Bem R, Jirkovska' A, Fejfarova' V, Skibova' J, Jude EB. Intranasal calcitonin in the treatment of acute Charcot neuroosteoarthropathy: a randomized controlled trial. Diabetes Care 2006; 29: 1392-4.

Bone stimulator?

Hanft et al. study on 31 pts with Stage 1 CN who were followed for an average of 23.3 weeks:

- Tx'd with a TCC or TCC and application of a combined magnetic field bone growth stimulator for 30 min daily.
- Bone stimulator statistically significant reduction with a mean time to osseous consolidation occurring in the study Group 12 wks before the control Group.
- Use of a combined magnetic field bone growth stimulator may be an effective adjunctive modality in the treatment of acute CN.

Hanft JR, Goggin JP, Landsman A, Surprenant M. The role of combined magnetic field bone growth stimulation as an adjunct in the treatment of neuroarthropathy/Charcot joint: an expanded pilot study. J Foot Ankle Surg 1998; 37: 510-15. discussion 550-1.



Surgical Treatment

We got options:

Exostectomy and soft tissue coverage Screw/Staple Compression Stabilization Multiple Plate & Screw Stabilization Locking Plate and Screw Stabiliz Multiple Screw Stabilization External Fixation Alone Percutaneous Stabilization Mini-Open Joint Preparation Ring External Fixation

Grim Statistics

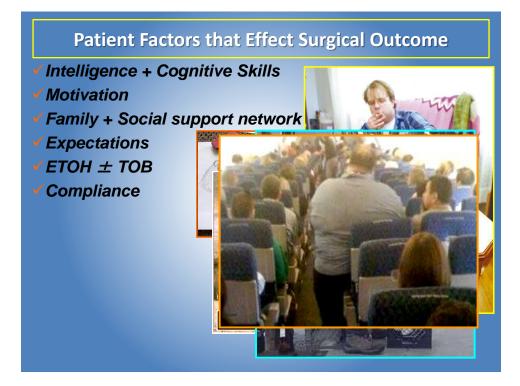
Systematic Literature Review (2011)

<u>Results</u>: 111 manuscripts reviewed in entirety

- <u>67:</u> Case Report or Retrospective Case Ser
- 29: Other [Brace Therapy; TCC; Gait Analysis; Etc.]
- <u>15:</u> QOL/Demographic Studies
- <u>Surgical Tx:</u> 389 Feet; <u>2.4 year F/U;</u> NWB 3.3 Months
 - <u>Recurrent Ulceration:</u> 15/267 (5.7%)
 - <u>Deep Infection</u>: 32/264 (12.1%)
 - Hardware Failure/Non-unions: 64/264 (24.2%)
 - <u>Re-operation</u>: 67/310 (21.6%)
 - <u>Trans-tibial Amputation</u>: 29/298 (9.8%)
 - <u>Mortality:</u> 330/1138 patients (29%) @ ∆ 5yr. F/U
- **<u>QOL:</u>** UPhysical Functioning & General Health;
 - Similar effect to TTA







THANK YOU



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