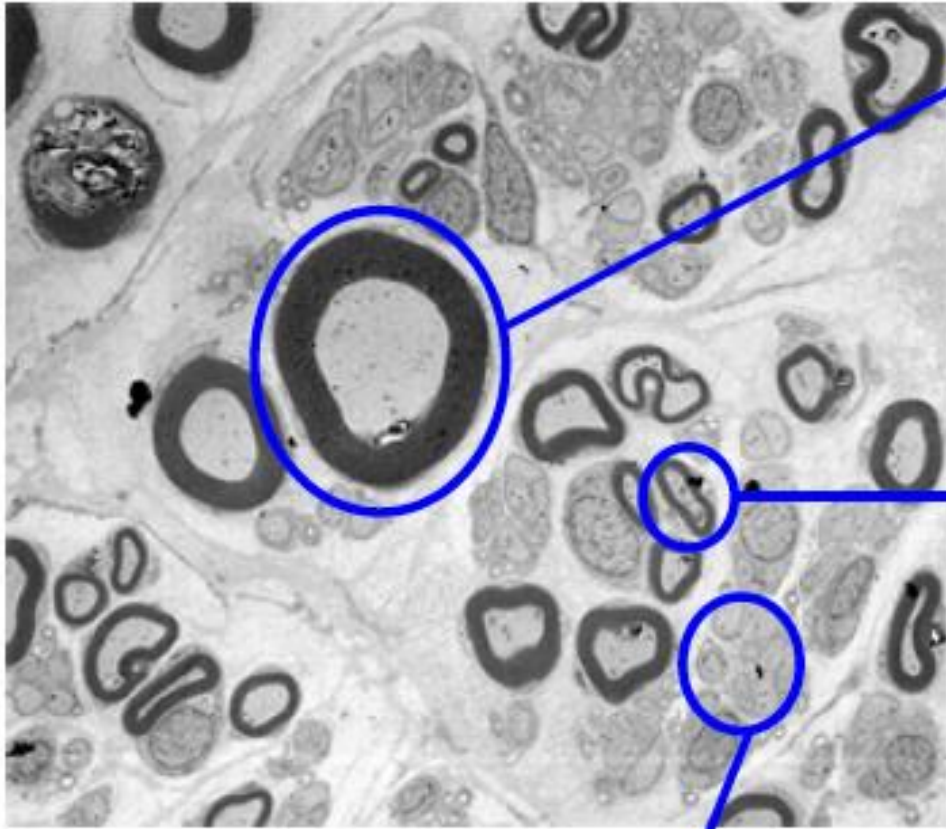


Toksik Nöropatiler

Dr. Can Ebru Kurt

Hacettepe Üniversitesi Tıp Fakültesi Nöroloji AD
Nöromusküler Hastalıklar Araştırma Laboratuvarı



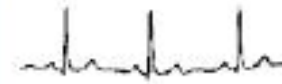
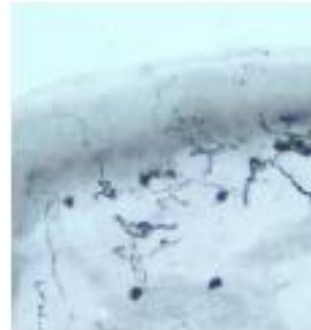
Large Myelinated Fibers

- Motor - **weakness**
- Touch sensation – **numbness (pain)**
- Proprioception/vibration- **unsteadiness**



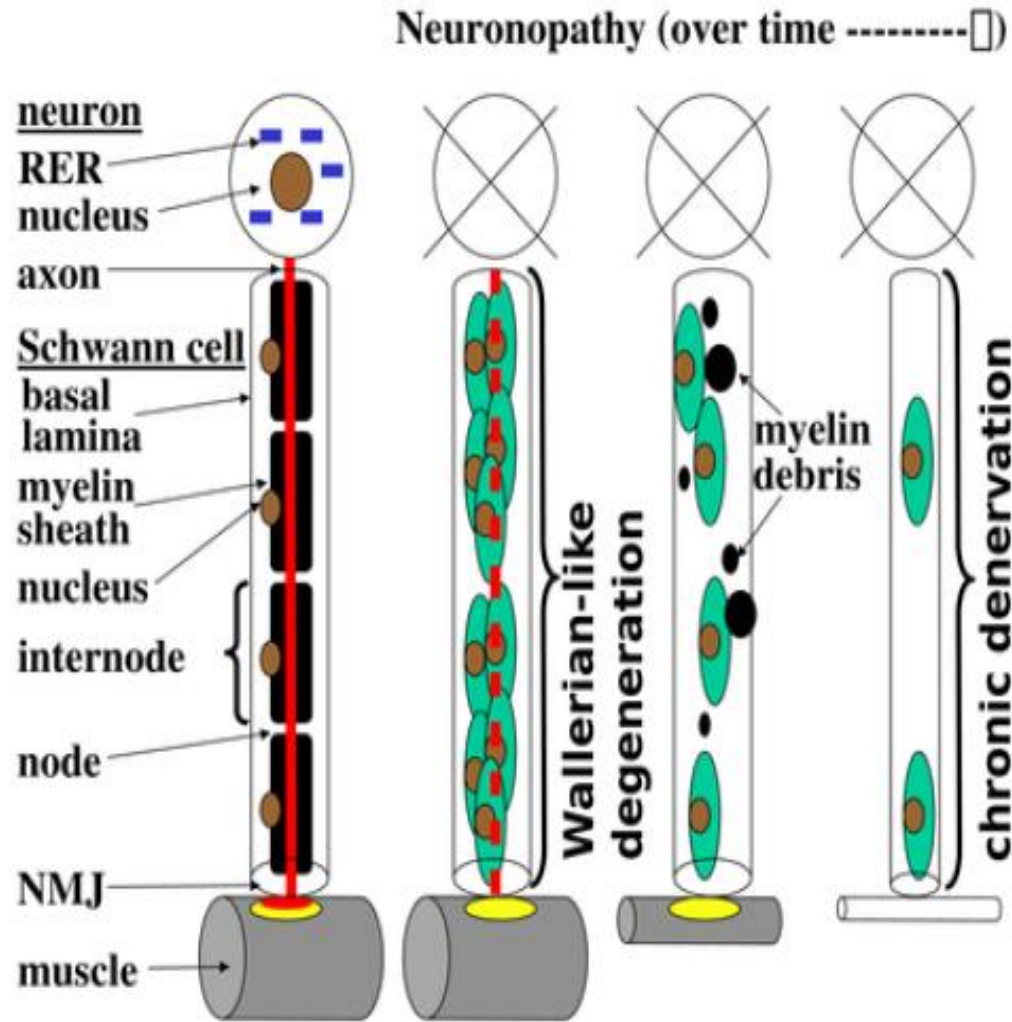
Small Myelinated Fibers

- Pain sensation– **painful paresthesias**
- Temperature – **thermal sensory loss**



Small Un-myelinated Fibers

- Pain sensation- **painful paresthesias**
- Autonomic – **dizziness, syncope, GI etc.**



Pathological classification:

- Wallerian degeneration,
- Axonal degeneration / axonopathy,
- Primary neuronal degeneration / neuronopathy,
- Segmental demyelination / myelinopathy

Tanıya yönelik testler

- ENMG

- L/P

Hastalık	Tanı testleri
Diabetes mellitus ve bozulmuş glukoz toleransı	Oral glukoz tolerans testi, açlık kan şekeri ve HbA1C
Vitamin eksiklikleri	CRP, ESR, kan biyokimyası, tam kan sayımı, TFT
Vaskülit ve bağ dokusu hastalıkları	Serum folik asit, homosistein, B12
Paraproteinemiler	RF, antinükleer antikorlar, sitoplazmik antikorlar, kompleman faktörleri ve hepatit belirteçleri
Enfeksiyon	Serum ve idrar elektroforezi
Celiac Hastalığı	HIV, sifiliz
Amiloidoz	Transglutaminaz antikorlar
	Dokuda amiloid incelemesi, genetik analiz

Nedenler

- İntihar
- Kaza (ev, işyeri, doğa)
- Başkası tarafından bilerek
- Endüstriyel (arsenik, benzen, karbonmonoksit, hidrokarbonlar,vb)
- Tarımsal
- Tıbbi
- İlaçlar
- Keyif verici maddeler (alkol, sigara vb)
- Ev kaynaklı toksik maddeler (temizlik vb)
- Doğal kaynaklı (zehirli bitkiler, hayvan sokması, doğal gaz)
- Besin (konserve, bozulmuş gıda)

Zehirlenme yolları

- Gastrointestinal
- İnhalasyon
- Deri ve mukoza
- İntravenöz

Metabolizma

- Karaciğer
- Plazma enzimleri
- Böbrekler
- Akciğerler
- Gastrointestinal sistem

Eliminasyon

- Böbrekler
- Safra
- Akciğerler

Klinik bulgular

α

- Toksik güç
- Miktar
- Enzim indüksiyonu
- Böbrek fonksiyonları
- Dokularda konsantrasyon

Toksik Nöropatiler - Klinik

- **Motor Ağırıklı:**

- Amiodarone
- Dapsone

- **Duyusal nöronopati:**

- Sisplatin
- Metronidazol
- Piridoksin
- Taksanlar
- Talidomid

- **Hızlı gelişen**

- Amiodaron
- Suramin
- Altın tuzları
- Nitrofurantoin
- Vinkristin

Tedavi

- Destekleyici tedavi
- Toksik maddenin vücuttan uzaklaştırılması
- Antidot

Civa

- Kaynak: manometre, sfigmomanometre, termometre
- İnhalasyon, intravenöz
- Santral ve periferik lezyon: **miyelin kılıf ve ganglion hücrelerinde dejenerasyon**

Miyakawa T et al. Acta Neuropathol 1970; 15: 45–55.

Miyakawa T et al. Acta Neuropathol 1976; 35: 131–138.

Miyakawa T et al. Acta Neuropathol 1974; 30: 30–41.

Nagashima K. Toxicol Pathol 1997; 25: 624–631.

Eto K et al. Toxicol Pathol 2002; 30: 723–34.

Hunter D, Russell DS. J Neurol Neurosurg Psychiatry 1954; 17: 235–241

Mercury intoxication and neuropathic pain

Pediatric Anesthesia, 18, 439–452

NALAN CELIBI
ÖZGÜR CANBAŞ
İLKER Ö. AYCAN
ALTAN SAHİN
ULKU AYPAR

*Department of Anesthesiology and Resuscitation,
Faculty of Medicine,
Hacettepe University, Ankara,
Turkey
(email: nalanmd@hotmail.com)*

- 5 hasta
- Yaş 5-16
- Nöropatik ağrı
- 3 hastaya Gabapentin (+ Tramadol + amitriptilin)
- 5-10 ay tedavi

İNCE LİF NÖROPATİSİ SEMPTOMATOLOJİ

Pozitif (%60)

- ✓ Yanma
- ✓ Karıncalanma
- ✓ Batma
- ✓ Elektriklenme
- ✓ Allodini: Çorap ve yorgan intoleransı
- ✓ Kaşıntı

- ✓ Kramp
- ✓ Huzursuz bacak sendromu

Negatif (%40)

- ✓ His kaybı
- ✓ Yorgunluk
- ✓ Egzersiz intoleransı

Otonomik

- ✓ Terlemede artma/azalma
- ✓ Kuru göz ve ağız
- ✓ Yüzde "flushing"
- ✓ Erektile disfonksiyon
- ✓ Deride renk değişiklikleri
- ✓ GIS dismotilitesi:
Diare,
konstipasyon,
irritabilite,
gastroparezi,
kramplar

Arsenik

- Hipokrat (MÖ 370)
- Dioscorides zehir olarak tanımladı
- Neron kardeşi Tiberius'u zehirledi (MS 55)
- Paracelsus sifilis tedavisi
- Thomas Fowler sıtma, ateş, baş ağrısı tedavisi
- 1. Dünya savaşı biyolojik silah (Adamcite, Lewicite)

Arsenik

- Çevre kirliliđi
- Simetrik sensorimotor nöropati
- Parestezi ve ayak tabanlarında ağrı

De Wolff FA, Edelbroek PM. Vinken & Bruyn's, ed. Handbook of clinical neurology. 1994: 283–291.

Vahidnia A, van der Voet GB, de Wolff FA. Hum Exp Toxicol 2007; 26; 823-832.

Research | Article

Arsenic Groundwater Contamination in Middle Ganga Plain, Bihar, India: A Future Danger?

Dipankar Chakraborti,¹ Subhash C. Mukherjee,² Shyamapada Pati,³ Mrinal K. Sengupta,¹ Mohammad M. Rahman,¹ Uttam K. Chowdhury,¹ Dilip Lodh,¹ Chitta R. Chanda,¹ Anil K. Chakraborti,¹ and Gautam K. Basu¹

¹School of Environmental Studies, Jadavpur University, Kolkata, India; ²Department of Neurology, Medical College, Kolkata, India;

³Department of Obstetrics and Gynaecology, Institute of Post Graduate Medical Education and Research, S.S.K.M. Hospital, Kolkata, India

Table 5. Presenting features, incidence, type, and severity of arsenic-induced peripheral neuropathy in Semria Ojha Patti village.

	No. of patients (%)
Presenting features (<i>n</i> = 40)	
Distal paresthesias	16 (40)
Limb pains	5 (12.5)
Hyperpathia/allodynia	4 (10)
Distal hypesthesias	14 (35)
Calf tenderness	4 (10)
Distal limb weakness/atrophy	3 (7.5)
Diminished or absent tendon reflexes	5 (12.5)
Tremor	3 (7.5)
Abnormal sweating	2 (5)
Overall incidence of neuropathy (<i>n</i> = 40)	21 (52.5)
Type of neuropathy (<i>n</i> = 21)	
Sensory	18 (45)
Sensorimotor	3 (7.5)
Severity of neuropathy (<i>n</i> = 21)	
Mild	17 (42.5)
Moderate	4 (10)

Kronik arsenik maruziyeti olan 451 kişide nöropatik ağrı gelişme oranı %11.1 ile %73.7

ARTICLE

Arsenic Toxicity from Homeopathic Treatment

Dipankar Chakraborti,^{1,*} Subhash Chandra Mukherjee,²
Khitish Chandra Saha,³ Uttam Kumar Chowdhury,¹
Mohammad Mahmudur Rahman,¹ and Mrinal Kumar Sengupta¹

¹School of Environmental Studies, Jadavpur University, Kolkata, India

²Department of Neurology, Medical College, Kolkata, India

³Retired Professor of Dermatology, School of Tropical Medicine, Kolkata, India

Homeopathic medicine is commonly believed to be relatively harmless. However, treatment with improperly used homeopathic preparations may be dangerous. *Case Reports.* Case 1 presented with melanosis and keratosis following short-term use of Arsenic Bromide 1-X followed by long-term use of other arsenic-containing homeopathic preparations. Case 2 developed melanotic arsenical skin lesions after taking Arsenicum Sulfuratum Flavum-1-X (Arsenic S.F. 1-X) in an effort to treat his white skin patches. Case 3 consumed Arsenic Bromide 1-X for 6 days in an effort to treat his diabetes and developed an acute gastrointestinal illness followed by leukopenia, thrombocytopenia, and diffuse dermal melanosis with patchy desquamation. Within ~2 weeks, he developed a toxic polyneuropathy resulting in quadriparesis. Arsenic concentrations in all three patients were significantly elevated in integument tissue samples. In all three cases, arsenic concentrations in drinking water were normal but arsenic concentrations in samples of the homeopathic medications were elevated. *Conclusion.* Arsenic used therapeutically in homeopathic medicines can cause clinical toxicity if the medications are improperly used.

ALKOLİK NÖROPATİ

- Direkt toksik etki? Nütrisyonel eksiklik?
- Klinik bulgular kronik alkoliklerin %10-15'inde görülür.
- EMG verileri ile 1/3'ünde
- Yavaş gelişen distal duyu kaybı,
- Bacaklarda ağrı, yanıcı disestezi
- Ağır durumlarda distal güç kaybı
- Distal hiporefleksi
- Trofik değişiklikler
- Proprioseptif duyu kaybı
- EMG: aksonal nöropati
- Patoloji: Her çapta myelinli lif kaybı, aksonal dejenerasyon, sekonder demyelinizasyon.

Nöropati tek başına ya da kronik alkolizmin diğer komplikasyonları (serebellar dejenerasyon, Wernicke Korsakoff sendromu, alkolik demans) ile birlikte görülebilir.

- Tedavi: alkol kesimi, tiamin ve çoklu vitamin desteği,

RESEARCH REPORT

Large and small fiber neuropathy in chronic alcohol-dependent subjects

Thomas Zambelis¹, Nikos Karandreas¹, Elias Tzavellas², Panagiotis Kokotis¹, and John Liappas²

¹EMG Laboratory, Department of Neurology; and ²Department of Psychiatry, University of Athens, Aeginion Hospital, Athens, Greece

Periferik sinir sisteminde küçük liflerden kaynaklanan
ağrılı periferik nöropati

Alcohol-induced stress in painful alcoholic neuropathy

Olayinka A. Dina,^{1,2} Sachia G. Khasar,^{1,2} Nicole Alessandri-Haber,^{1,2} Paul G. Green,^{1,2} Robert O. Messing^{3,4,5}
and Jon D. Levine^{1,2,4,6}

¹Department of Oral & Maxillofacial Surgery, University of California at San Francisco, CA 94143-0440, USA

²UCSF NIH Pain Center, University of California at San Francisco, CA 94143-0440, USA

³Department of Neurology, University of California at San Francisco, CA 94143-0440, USA

⁴Division of Neuroscience and Biomedical Sciences, University of California at San Francisco, CA 94143-0440, USA

⁵Ernest Gallo Clinic and Research Center, Emeryville, CA 94608, USA

⁶Department of Medicine, University of California at San Francisco, CA 94143-0440, USA

Kronik alkol alımında stres hormonlarındaki artış, periferik
nöropati gelişimi ile ilgili

Ethanol withdrawal induces hyperalgesia mediated by PKC ϵ

Olayinka A. Dina,^{1,2} Robert O. Messing^{3,4,5} and Jon D. Levine^{1,2,5}

¹Department of Oral & Maxillofacial Surgery, University of California at San Francisco, USA

²UCSF NIH Pain Centre, Box 0440, C-522, University of California at San Francisco, CA 94143, USA

³Department of Neurology, University of California at San Francisco, USA

⁴Ernest Gallo Clinic and Research Centre, Emeryville, CA, USA

⁵Division of Neuroscience and Biomedical Sciences Program, University of California at San Francisco, USA

Nöropati şiddeti alkol kesildiğinde daha da belirginleşir

#6



CLINICAL NOTES

Effects of Smoking on Neuropathic Pain in Two People With Spinal Cord Injury

J. Scott Richards, PhD; Stephen C. Kogos Jr, PhD; T. J. Ness, MD, PhD; Christina V. Oleson, MD

Department of Physical Medicine and Rehabilitation, University of Alabama at Birmingham, Birmingham, Alabama

Summary: The first subject rated his pain as 4/10 when not smoking and 7/10 when smoking. The pain subsided 30 minutes after smoking was discontinued. He noted an immediate increase in neuropathic pain when smoking. The second subject quit smoking for 1 month and immediately noted that the pain disappeared, rating it 0/10. After he resumed smoking, his radicular pain was 8.5/10 in the morning and 5/10 in afternoon.

Conclusions: No similar reports have been published, based on a MEDLINE search. Nicotinic receptors have been implicated in pain perception. It is unclear to what extent these 2 cases generalize to the SCI population. We plan to explore this via survey and experimental research. Smoking cessation may have a dual benefit of increased health and decreased neuropathic pain.

- Nikotinik reseptörler ağrının algılanması ile ilgilidir
- Sigarayı bırakmak daha sağlıklı bir yaşam sunabileceği gibi nöropatik ağrı gelişimini de azaltabilir

Canadian registry to track thousands of pot smokers

Data could answer questions about safety, efficacy, and dosage

22 MAY 2015 • VOL 348 ISSUE 6237


sciencemag.org **SCIENCE**

Disease-a-Month 62 (2016) 346–352

Contents lists available at ScienceDirect

Disease-a-Month

ELSEVIER journal homepage: www.elsevier.com/locate/disamonth



Medical marijuana and pain management

Leslie Mendoza Temple, MD



Curr Pain Headache Rep (2015) 15: 30
DOI 10.1007/s11916-015-0538-x



ANESTHETIC TECHNIQUES IN PAIN MANAGEMENT (D WANG, SECTION EDITOR)

Medical Marijuana and Chronic Pain: a Review of Basic Science and Clinical Evidence

Bjorn Jensen¹ · Jeffrey Chan¹ · Tim Humick¹ · Mark Wallace¹

- Nöropatik ağrı
- MS hastalarında spastisite
- Kemoterapi alanlarda iştah ve kilo alımı

Organofosfatlar

- Pestisit
- Kronik maruziyet  ge nropati
- *İpucu: kolinergik bulgular*

Health Symptoms and Exposure to Organophosphate Pesticides in Farmworkers

Larkin L. Strong, MPH,^{1,2†} Beti Thompson, PhD,^{1,2} Gloria D. Coronado, PhD,²
William C. Griffith, PhD,³ Eric M. Vigoren, MS,³ and Ilda Islas²

- Organofosfatlara maruz kalan çiftçilerde
 - Başağrısı (%50)
 - Ekstremitte ağrısı (%35)

Kurşun

- Endüstriyel maruziyet
- Aksonal dejenerasyon
- Motor nöropati (el bileği ve parmak ekstensörleri)
- Sensorial tutulum nadir

Peripheral neuropathy in chronic occupational inorganic lead exposure: a clinical and electrophysiological study

O Rubens, I Logina, I Kravale, M Eglite, M Donaghy

- 46 kurşun nöropatisi olan işçi
- Tümünde distal parestezi, ağrı, bozulmuş pin prick hissi, otonomik vazomotor/sudomotor değişiklikler

Lead and the Deafness of Ludwig Van Beethoven

Michael H. Stevens, MM, MD; Teemarie Jacobsen, AuD; Alicia Kay Crofts, AuD

Objectives/Hypothesis: To reexamine the cause of Beethoven's hearing loss because of significant recent articles.

Data Sources: Medical and musical literature online, in print, and personal communication.

Methods: Relevant literature review.

Results: Evidence of otosclerosis is lacking because close gross examination of Beethoven's middle ears at autopsy did not find any otosclerotic foci. His slowly progressive hearing loss over a period of years differs from reported cases of autoimmune hearing loss, which are rapidly progressive over a period of months. He also lacked bloody diarrhea that is invariably present with autoimmune inflammatory bowel disease. The absence of mercury in Beethoven's hair and bone samples leads us to conclude that his deafness was not due to syphilis because in that era syphilis was treated with mercury. High levels of lead deep in the bone suggest repeated exposure over a long period of time rather than limited exposure prior to the time of death. The finding of shrunken cochlear nerves at his autopsy is consistent with axonal degeneration due to heavy metals such as lead. Chronic low-level lead exposure causes a slowly progressive hearing loss with sensory and autonomic findings, rather than the classic wrist drop due to motor neuropathy from sub-acute poisoning. Beethoven's physicians thought that he had alcohol dependence. He particularly liked wine that happened to be tainted with lead.

Conclusions: Beethoven's chronic consumption of wine tainted with lead is a better explanation of his hearing loss than other causes.

Key Words: Otosclerosis; autoimmune; syphilis; lead; alcohol.

Laryngoscope, 123:2854–2858, 2013

X-ray Fluorescence Intensity from Pb in Hair

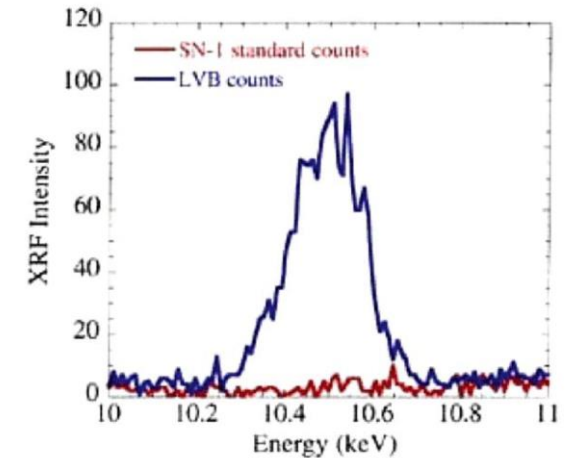




Fig. 1. Lead fluorescence intensity in Beethoven's hair (LVB) in comparison to standard counts (SN-1) of controls. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Where could the lead have come from that resulted in this devastating loss of hearing? Although lead can be acquired from a number of external sources, including dishes, lead-lined wine flasks, lead crystal, or mineral water at the spas, in our opinion the most likely source for Beethoven was wine. It is well known that at that time lead was added illegally to inexpensive wine to improve the flavor. Beethoven was particularly fond of the adulterated or fortified Hungarian wine. It has been suggested that after the death of Beethoven's mother when he was 17 years old, he began to use some wine to help deal with his loss.²⁹

Talyum

- Ağır metal
- Elektronik endüstrisi ve cam işlenmesi
- Sülfidril gruplarını bağlar  serbest radikal hasarı
- Riboflavini bağlar  akson hasarı

Davis LE, Standefer JC, Kornfeld M et al. Ann Neurol 1981; 10: 38-44.
Pau PWI. HKMJ 2000; 6:316-8

Long-term misdiagnosis and neurologic outcomes of thallium poisoning: A case report and literature review

Hailing Liu  | Geng Liao 

Brain and Behavior. 2021;11:e02032.

- Periferik sensorimotor nöropati
- Santral
 - Mental durum, konvülziyon
- Ekstrapiramidal
- Serebellar disfonksiyon
- Otonomik disfonksiyon

Karbon monoksit

- Periferik nöropati nadir (% 0.87 / %3.64)
- Yanıcı ağrı, karıncalanma, zonklayıcı ağrı, güçsüzlük

CASE REPORT

Open Access

Bilateral brachial plexus injury following acute carbon monoxide poisoning

Mounia Rahmani^{1*}, Halima Belaidi², Maria Benabdeljlil¹, Wafa Bouchhab¹, Nadia El Jazouli¹, Asmae El Brini¹, Saadia Aidi¹, Reda M Ouazzani² and Mustapha El Alaoui Faris¹

- Rabdomiyolize bağlı sinir kompresyonu
- Hipoksik sinir iskemisi
- Direkt toksisite

Kadmiyum

- Gümüş işlenmesi, pil endüstrisi

Cadmium Exposure: Health Hazards of Silver Cottage Industry in Developing Countries

PK Sethi MD,^a Dinesh Khandelwal MD,^a Nitin Sethi MD^b

^a Department of Neurology, Sir Ganga Ram Hospital, New Delhi, India

^b Department of Neurology, Saint Vincent's Hospital and Medical Center, New York, NY

JOURNAL OF MEDICAL TOXICOLOGY ■ VOLUME 2, NUMBER 1 ■ MARCH 2006

- 37 y, 12 yıllık maruziyet
- Periferik polinöropati
- Ayak bilekleri ve bilateral alt kostal künt sızı

Bromopropan

- Endüstriyel solventler
- İşyeri havalandırma koşulları önemli

CASE REPORT

Severe neurotoxicity associated with exposure to the solvent 1-bromopropane (n-propyl bromide)

JENNIFER JUHL MAJERSIK, M.D.¹, E. MARTIN CARAVATI, M.D. M.P.H.², and JOHN D. STEFFENS, M.D.³

¹*Department of Neurology, University of Michigan, Ann Arbor, Michigan, USA*

²*Utah Poison Control, Salt Lake City, Utah, USA*

³*Department of Neurology, University of Utah, Salt Lake City, Utah, USA*

- Sprey fabrikasında çalışan 6 işçi
- Alt ekstremitelerde ağrısı ve parestezisi
- Spastik paraparezi, distal duyu kaybı, hiperrefleksi

Therapeutic uses of metronidazole and its side effects: an update

A. HERNÁNDEZ CERUELOS, L.C. ROMERO-QUEZADA, J.C. RUVALCABA
LEDEZMA, L. LÓPEZ CONTRERAS

Área Académica de Medicina, Instituto de Ciencias de la Salud, Universidad Autónoma del Estado de Hidalgo, Circuito Ex Hacienda, Pachuca de Soto Hidalgo, México

- Ciddi nörotoksisite
- Optik nöropati
- Periferik nöropati
- Ensefalopati

OC (oleoresin capsicum)

Biber gazı

TRPV1 sensorial nöronun aktivasyonuna ve substans P salınımına baęlı olarak řiddetli aęrı ve yanmaya yol aęar.

REVIEW

Open Access

The “wing-heeled” traveler

Taylor Kain¹, Jordan Weinstein^{1,2}, Aaron Thompson^{3,4} and Andrea K. Boggild^{1,5*}



Abstract

Intoxication syndromes may be travel acquired, and are related to intentional or accidental inhalational or percutaneous exposures or ingestions. Due to their myriad clinical presentations, initial differential diagnosis of such intoxications in returned travelers is broad, and typically requires detailed history and laboratory investigations to disentangle. We herein use a case-based clinical problem solving approach to illumination of a mercury intoxication syndrome, which presented in a 48-year-old VFR traveler to Guyana. Common clinical presentations, differential diagnoses, laboratory investigations, and therapeutic interventions are discussed.

Keywords: Ciguatera fish poisoning, Heavy metal intoxication, Nephropathy, Neuropathy, Skin bleaching

- 48 y kadın hasta, 1 ay önce Guyana seyahati
- Ağrı, el ve ayaklarda yanma, yorgunluk, güçsüzlük, parestezi
- Siguatera toxini, cıva intoksikasyonu

Dietilen Glikol

- Antifreeze
- Akut böbrek yetmezliği
- Kronik Nörolojik sx
 - 2-7 gün içinde
 - Sensorimotor aksonal polinöropati
 - Alt ekstremitelerde hakim güzsüzlük
 - Ataksi
 - Düzeltme rapor edilmiş

Allyl chloride

- Plastik üretiminde
- Distal simetrik sensorimotor polinöropati
- Maruziyet sonlandırılması ile düzelme rapor edilmiş

Hexacarbon

- Otomotiv sektöründe
- Simetrik aksonal polinöropati

Carbon disulfide

- Pesticide, rayon (viscose) üretimi
- İnhalasyon ile
- Aksonal sensorimotor neuropati
- Santral sinir sistemi: nöropsikiyatrik semptomlar ve parkinsonizm

Etilen oksit

- Endüstri işçileri
- Uzunluk bağımlı aksonal sensorimotor polinöropati
- İyi prognoz bildirilmiş

Sonuç

- Nadir
- Öyküde akut ve kronik maruziyetin sorgulanması
- İntoksikasyon tedavisi + nöropatiye yaklaşım

- Her madde zehirdir
- Zehir olmayan bir madde yoktur
- Doğru doz ilacı zehirden ayırt eder

Paracelsus
(1493-1541)

drebru@hacettepe.edu.tr