

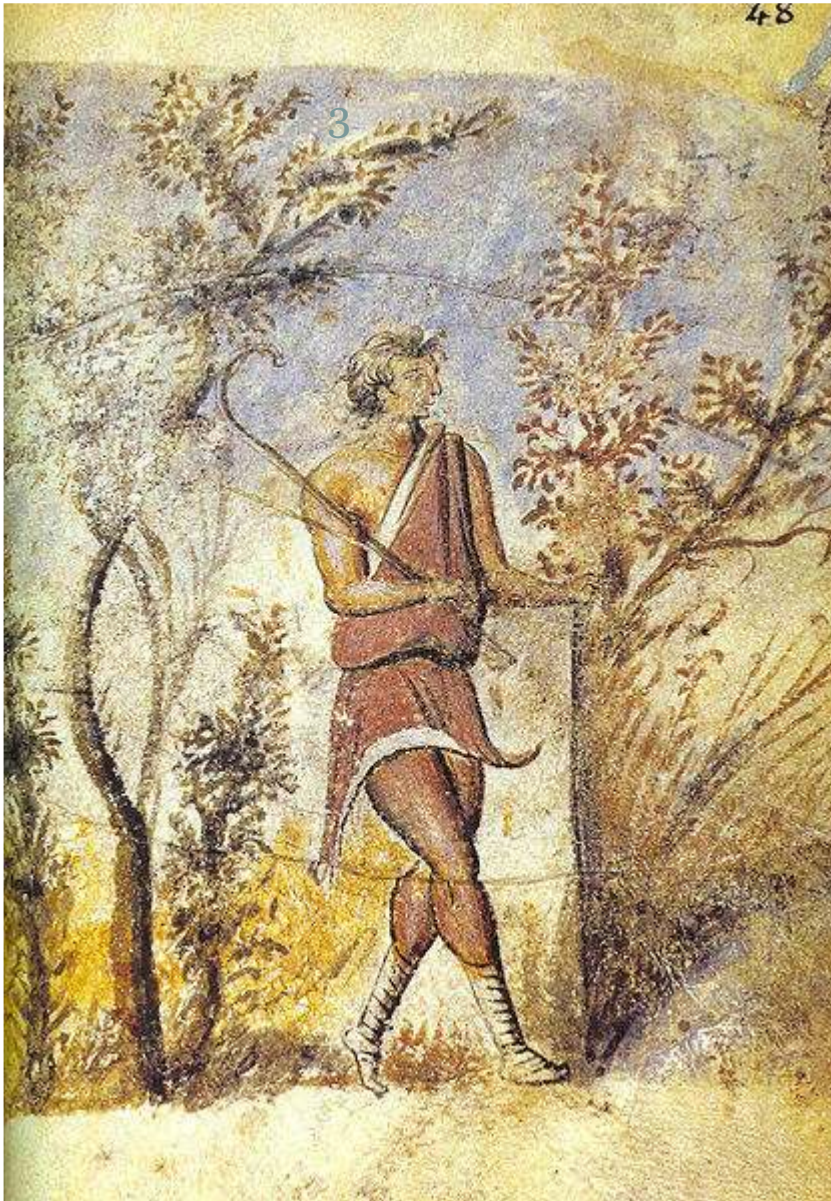
ZEHİRLENMELERDE ANTİDOT TEDAVİSİ



DR ÖZLEM GÜNEYSEL
MARMARA Ü ACİL TIP AD

Proposed list of specific antidotes in the European Community (Council of Europe, 1990)

Antidote	Indication/toxic agent
Acetylcysteine	Paracetamol; carbon tetrachloride
Amyl nitrite	Cyanide
Antivenins and antitoxins	
Atropine	Cholinergic syndrome
Benzylpenicillin	Amanitotoxins
Calcium gluconate	Hydrogen fluoride; fluorides; oxalates
Calcium disodium edetate	Lead
Dantrolene	Malignant hyperthermia; malignant neuroleptic syndrome
Deferoxamine	Iron; aluminium
Diazepam	Seizures; chloroquine
Dicobalt edetate	Cyanide
Digoxin-specific (Fab) antibody fragments	Digoxin; digitoxin; digitalis glycosides
Dimercaprol (BAL)	Arsenic; gold; inorganic mercury
4-Dimethylaminophenol	Cyanide
Diphenhydramine	Drug-induced dystonias
Ethanol	Methanol; ethylene glycol
Etybenzotropine (ethybenztropine)	Drug-induced dystonias
Flumazenil	Benzodiazepines
Folinic acid	Folic acid antagonists
Glucagon	Beta-blockers
Hydroxocobalamin	Cyanide
Methionine	Paracetamol
4-Methylpyrazole	Methanol; ethylene glycol
Methylthioninium chloride (methylene blue)	Methaemoglobinaemia
N-Acetylpenicillamine	Mercury (organic and elemental)
Naloxone	Opiates
Neostigmine	Neuromuscular block (curare type); peripheral anticholinergic poisoning
Oximes	Organophosphates
Oxygen	Carbon monoxide; cyanide; hydrogen sulfide
D-Penicillamine	Copper; gold; lead; mercury (elemental); zinc
Pentetic acid (DTPA); diethylene-triamine pentaacetic acid	Plutonium; actinides
Phentolamine	Alpha-adrenergic poisoning
Physostigmine	Central anticholinergic syndrome from atropine and derivatives
Phytomenadione	Coumarin and indanedione anticoagulants
Potassium ferric hexacyanoferrate (Prussian blue)	Thallium
Prenalterol	Beta-blockers
Protamine sulfate	Heparin
Pyridoxine (Vitamin B6)	Isoniazid; crimidine; gyromitrin; hydrazines
Silibinin	Amanitotoxins
Sodium nitrite	Cyanide
Sodium thiosulfate	Cyanide
Succimer (DMSA) Dimercaptosuccinic acid	Lead; mercury (inorganic and organic); arsenic
Tolonium chloride (toluidine blue)	Methaemoglobinaemia
Trientine (triethylene tetramine)	Copper
Unithiol (DMPS) 2,3-dimercapto-1-propanesulfonic acid	Mercury (methyl- and inorganic); lead



Nikander, "*Theriaca*", 10th century, Constantinople

Yazılı tarih öncesinden bu yana evrensel antidot aranıyor

Nicander of Colophon
(Ahmetbeyli, Izmir)



Yunanlılar evrensel antidotu aleksifarmika veya tearik olarak adlandırdılar. Aleksifarmika terimi zehirden sakınmak anlamındaki aleksifarmakos ve antifarmakon veya antidot kelimelerinden oluşmaktadır. Aleksifarmika zaman içinde giderek, kuştüyü kullanarak kusmayı indükleme gibi tedavi yöntemleri için kullanılmaya başlandı [3]. Milattan önce 5. yüzyıldan itibaren adsorban bir ajan olan terra sigillata veya kutsal mühürlü toprak evrensel antidot olarak kabul edildi. Bu ajan sadece Yunan Adalarından Lemnos'ta bulunan kırmızı bir çamurdan oluşuyordu ve tüm zehirlerin üstesinden gelinmesinde etkin olduğu düşünülüyordu. Tarih boyunca evrensel antidotlar olarak taraftar toplayan birçok diğer ajan varolmuştur: bezoar taşları (intestinal taşlar), fosil taşları ve efsanevi tek boynuzlar.

Antidot...

5

- Hayal kurmak güzeldir...
- Klinik zorunluluklarından ayrı olarak toplumsal ve duygusal beklenti

Tarihçe

6

- Tarihte zehirlenmeler kazara / bilinçli (?)
- Zehirlenmelere karşı kullanılan ilk yöntem ***“kusturma”***
- 1800'lere kadar genellikle bitkisel kaynaklı (daha az hayvansal ve mineral katkı)
- Ortodoks doktorların humoral tedaviyi keşfinden sonra çeşitlendi (hayvan kanı, zehirleri, boynuzu, vb)

Tarihçe

7

- “Unicorn’s corn”
- “Bone of a stag’s heart”
- “Limni toprağı”,
- “Ermeni kütüğü”





Sonraları ..

- “*Panzehir*” (antidot)
L. antidotum, Gr. antidoton ve modern tıp
- “*Bir zehiri etkisiz hale getirmek (kimyasal antidot) ya da fizyolojik etkileriyle savaşmak (fizyolojik antidot) için tedavide kullanılan madde.*”

Antidot



- Yetim ilaç (*Orphan drug*) statüsündedirler
- Üretim maliyetleri yüksek,
- İmalat ve ruhsatlandırılması belirli ülkelerde gerçekleştirilen,
- Normal bir ilaç olarak üretilmesi ve ruhsatlandırılması zorunluluğu olmayan,
- İhtiyaca bağlı olarak, üretimi gerçekleştiren ülkeden ithal edilen,

İLAÇLARDIR...

Antidot

Antidotlar hakkında bilgiler,
uluslararası
organizasyonlar tarafından
yayınlanır:

- IPCS INTOX Databank
- IPCS INCHEM
- IPCS Poisons Information Monographs
- IPCS Treatment Guides
- IPCS/European Commission Evaluation of Antidote Series (IPCS INCHEM, 2006)
 - Antidotes for poisoning by cyanide
 - Antidotes for poisoning by paracetamol
 - Naloxone, flumazenil and dantrolene as antidotes
 - Deferoxamine
 - Pralidoxime (in preparation)
 - Obidoxime (in preparation)
- IPCS Guidelines for the Prevention of Toxic Exposures
- IPCS International Chemical Safety Cards (ICSCs)
- IPCS Environmental Health Criteria Monographs (EHCs)
- CCOHS CHEMINFO Database
- WHO/FAO Information Documents
- UK Poison Information Documents (UK PIDs)
- International Agency for Research on Cancer monographs (IARC)



Available online at www.sciencedirect.com



Toxicology 233 (2007) 13–19

TOXICOLOGY

www.elsevier.com/locate/toxicol

The dilemma of approving antidotes

Christian Steffen*

Clinical Trials Unit, Federal Institute for Drugs and Medical Devices, Kurt-Georg-Kiesinger-Allee 3, 53175 Bonn, Germany

Received 13 November 2006; received in revised form 22 November 2006; accepted 24 November 2006

Available online 1 December 2006

Antidot Referans Bilgi Kaynakları

12

The International Programme
on Chemical Safety (IPCS)



- WHO (World Health Organisation)
- UNEP (United Nations Environment Programme)
- ILO (International Labour Organisation)

Antidot Referans Bilgi Kaynakları

13

<http://www.who.int/ipcs/poisons/centre/en/index.html>

WHO | Poisons centres - Windows Internet Explorer

WHOOMS

http://www.who.int/ipcs/poisons/centre/en/index.html

DAEMON Search

Dosya Düzen Görünüm Sık Kullanılanlar Araçlar Yardım

WHOOMS

WHO | Poisons centres

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The International Programme on Chemical Safety (IPCS)



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Methods for chemicals assessment

Chemicals in food

Poisons information, prevention and management

Chemical incidents and emergencies

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[International Programme on Chemical Safety > Poisoning Prevention and Management](#)

Poisons centres

What is a poisons centre?

A poisons centre is a specialized unit that advises on, or assists with, the prevention, diagnosis and management of poisoning. The structure and function of poisons centres varies around the world. At a minimum a poisons centre is an information service. Some poisons centres may also include a toxicology laboratory and/or a clinical treatment unit.

What does a poisons centre do?

A poisons centre provides an emergency poisons information service. It may also provide an analytical toxicology service and a clinical service. In addition the poisons centre may play an important role in developing contingency plans for, and responding to, chemical disasters, and may be involved in monitoring the adverse effects of drugs, and in handling problems of substance abuse. It may also be involved in research, education and training.

Poisons Information Service

The poisons information service is concerned with the risk assessment, diagnosis, management and prevention of exposure to any substance, by any route, in patients of any age, and arising from any circumstance, be it accidental, intentional, occupational etc. In addition the poisons centre can provide general information about substances, their properties and toxicity.

YELLOWTOX



[World directory of poisons centres](#)



Read a day in the life of a Poisons Information Centre pharmacist
[Full text](#)

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[IPCS INCHEM](#)

IFCS Forum V
Essential tools for chemical safety
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**INTERNATIONAL PROGRAMME
ON CHEMICAL SAFETY**



GUIDELINES ON THE PREVENTION OF TOXIC EXPOSURES

**Education and public
awareness activities**



**Published by the World Health Organization in collaboration with
the United Nations Environment Programme and
the International Labour Organization**

Antidot Referans Bilgi Kaynakları

16

- AB Komisyonu, 1990;
- EMEA (The European Medicines Agency)



European Medicines Agency - Windows Internet Explorer

http://www.ema.europa.eu/ema/index.jsp?curl=/pages/home/Home_Page.jsp&jsenabled=true

DAEMON Search

Dosya Düzen Görünüm Sık Kullanılanlar Araçlar Yardım

European Medicines Agency

An Agency of the European Union

 **EUROPEAN MEDICINES AGENCY**
SCIENCE MEDICINES HEALTH

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About the Agency

The European Medicines Agency is a decentralised body of the European Union, located in London.

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[2015 Roadmap](#)

Latest news

- ⚠ Patient safety**
- ⚠ Veterinary alerts**
- New Medicines**
- Public Consultations**

09/09/2010 **European Medicines Agency holds international workshop on clinical trials in the context of global medicines development**
Participants from around the world emphasise the need for cooperation to ensure a robust global framework for clinical trials ... [Read more](#)

08/09/2010 **CHMP meets to discuss Avandia and Pandemrix**
The Committee for Medicinal Products for Human Use (CHMP) met on Wednesday 8 September to discuss the ongoing benefit-risk review of the rosiglitazone-containing

Proposed list of specific antidotes in the European Community (Council of Europe, 1990)

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Trientine (triethylene tetramine)	Copper
Unithiol (DMPS) 2,3-dimercapto-1-propanesulfonic acid	Mercury (methyl- and inorganic); lead

Antidot üretimi

19

- Sürekli kullanıma gereksinim olmaması ve buna bağlı raf ömürlerinin tükenmesi nedeniyle finansman desteği gereklidir.
- Yeni antidot üretimi için finansal destek olmadığından; durumları yetim ilaç (*Orphan drug*) pozisyonundadır ve aynı yasal avantajlara sahiptirler.

Orphan Medicinal Products (OMP)

20

- Nadir görülen ciddi, hayatı tehdit edici veya kronik yetisizliğe neden olabilecek hastalıklara karşı üretilirler (Genel yaklaşım ~5/10.000 kişi).
- İlk tanımlama..
 - US Orphan Drug 1983
 - Japonya 1993
 - Avustralya 1998

Etik Boyut

21

- Akut zehirlenmelerde antidot uygulaması için aydınlatılmış onam alınmaz ! (?)
- Yasal düzenleme yoktur (!).
- Antidot olarak kullanılacak maddenin etkinliği bilimsel olarak kanıtlanmış olmalıdır.

Klinik ve antidot sorgulama

22

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UPDATES

Türkiye

24

- Antidotları üreten firmalar dünyada sınırlı sayıda,
 - Üretim kapasiteleri yıllık planlamayla sınırlı,
 - Belirlenmiş miktarın, belli merkezlerde stoklanmış olması gerekli.
-
- Sorumlu olan kurum 2001 yılından bu yana
RSHM Başkanlığı Zehir Danışma Merkezi

**Pestisit Zehirlenmeleri**

Pestisitlerle zehirlenmeler genellikle kazaen olmaktadır. Genellikle de bu tür zehirlenmeler, gerek ilaçlama yaparken koruyucu önlemlerin alınmaması gerekse pestisitlerin kolay ulaşılabilir yerlerde bırakılması sonucunda, özellikle çocuklar başta olmak üzere, insanların yanlışlıkla bu ilaçlarla temas etmeleriyle olmaktadır. (Devamı...)

114 UZEM Hakkında

Halka Yönelik Bilgiler

Sağlık Çalışanlarına Yönelik Bilgiler

Kozmetik Bildirimleri

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Şifre

Beni Hatırla ☐

Giriş Yap

[Şifrenizi mi unuttunuz?](#)

"Hiçbir Lezzet Ölecek Kadar Güzel Değildir"

**YABANI MANTARLARI
YEMEYİN**





T.C. SAĞLIK BAKANLIĞI

BİRİNCİ BASAMAĞA YÖNELİK
**ZEHİRLENMELER
TANI ve TEDAVİ
REHBERLERİ
2007**



REFİK SAYDAM HIFZISSIHHA MERKEZİ BAŞKANLIĞI - HIFZISSIHHA MENTEPE MÜDÜRLÜĞÜ

Ulusal Zehir Merkezi (UZEM)
Refik Saydam Hıfzıssıhha Merkezi Başkanlığı
(24 saat)
Tel: 114
(<http://www.rshm.saglik.gov.tr/uzem>)

Türkiye'de Zehirlenme Olgularına İlişkin
Danışmanlık Hizmeti Veren Kurumlar

Dokuz Eylül Üniversitesi Tıp Fakültesi
İlaç ve Zehir Danışma Merkezi
(24 saat)
Tel: 0-232-4123939
(<http://web.deu.edu.tr/zdm>)

Uludağ Zehir Danışma Merkezi
(24 saat)
Tel: 0-224-4428293
(<http://zehirinf.uludag.edu.tr>)

Hacettepe İlaç ve Zehir Bilgi Merkezi
(HİZBİM)
(08:30-17:30)
Tel: 0-312-3118940

(<http://www.farma.hacettepe.edu.tr/hizbim/hizbim.shtml>)



ZEHİRLENME TEDAVİSİNDE KULLANILAN İLAÇLAR ve ÖZGÜL ANTİDOTLAR - 2007

BİRİNCİ BASAMAĞA YÖNELİK TANI VE TEDAVİ REHBERİ

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Ev Kimyasallarıyla Olan Zehirlenmeler

Ev kimyasallarına bağlı zehirlenmeler, kimyasalların kazara alınması veya ürünlerin yanlış kullanılmaları sonucu meydana gelebilmektedir. Bu tür zehirlenmeler, özellikle de çocuklarda görülmektedir. Ayrıca, insanlar canlarına kastetmek maksadıyla da ev kimyasallarını kullanarak zehirlenebilmektedirler. (Devamı...)

114 UZEM Hakkında

Halka Yönelik Bilgiler

Sağlık Çalışanlarına Yönelik Bilgiler

Kozmetik Bildirimleri

Site içi hızlı arama...

Anasayfa » Sağlık Çalışanlarına Yönelik Bilgiler

Ana Menü

Anasayfa

Sıkça Sorulan Sorular

İletişim

Detaylı Arama

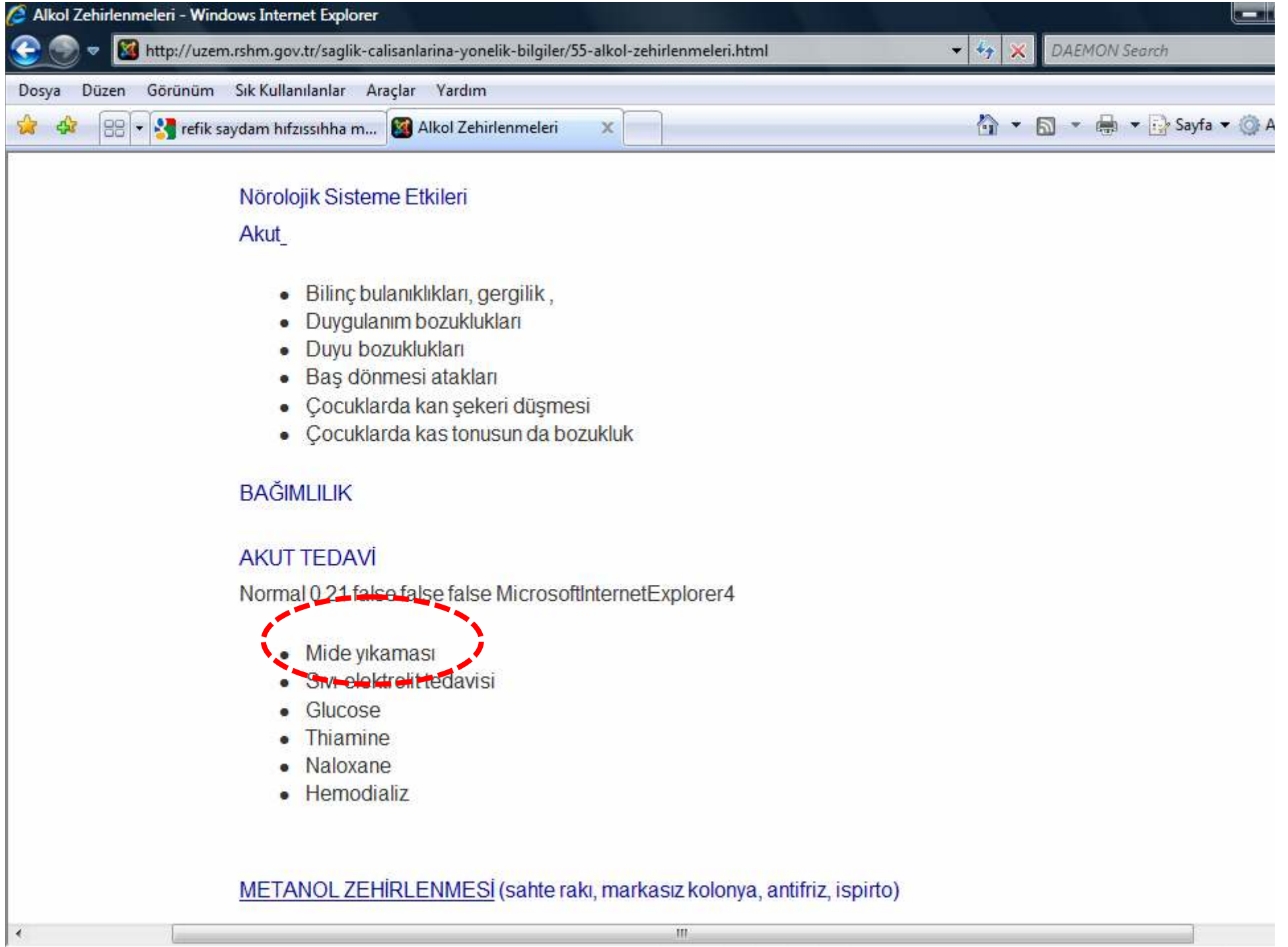
Site Haritası

Sağlık Çalışanlarına Yönelik Bilgiler

1	Zehirlenmeler Tanı ve Tedavi Rehberleri	10318
2	Akrep Sokması	5246
3	Alkol Zehirlenmeleri	4753
4	Hidrokarbon Zehirlenmeleri	4028
5	Bağımlılık Yapıcı Madde Zehirlenmeleri	2792
6	Spesifik Toksik Sendromu Olmayan Akut Zehirlenme Vakalarında Temel Yaklaşımlar	391
7	İlaç Dışı Bazı Maddelerle Oluşan Zehirlenmelerde İlk Yaklaşım Önerileri	415

Telif Hakkı © 2008 - Tüm Hakları Saklıdır

Sağlık Bakanlığı - Refik Saydam Hıfzıssıhha Merkezi Başkanlığı



RSHM’de bulunan Antidotlar

30

1. Pralidoksim

Ülkemizde yaygın olarak kullanılan tarım ilaçlarından organofosforlu insektisitler ve özel koşullarda karbamatlı insektisitlerle meydana gelen zehirlenmelerde kullanılmaktadır.

2. Botulismus Antitoksini

3. BAL (Dimercaprol)

Kurşun, antimon, bizmut, arsenik, altın, krom, bakır, nikel, çinko ve civa gibi metallerle meydana gelen zehirlenmelerde

4. Succimer

Civa, kadmiyum, kurşun zehirlenmelerinde,

5. Kelocyanor (Dikobalt EDTA)

Siyanür zehirlenmesinde;

“Ayrıca diğer antidotların bazılarının temini, bir bölümünün de ruhsatlandırılması konusu İlaç ve Eczacılık Genel Müdürlüğü’ne yazılmıştır. Konu henüz yazışma aşamasındadır.”

Teşkilat Ve Birimler
Mevzuat
Seminer-Konferans
RSHM Bilim Kurulu
Haberler / Duyurular
İletişim -Tel Rehberi
Kütüphane-Yayınlar
Halkla İlişkiler- Bilgi Edinme
Yenidoğan Tarama
E-Devlet

- Kamu Hizmet Standartları
- Misyonumuz
- Vizyonumuz
- Değerlerimiz

**TÜRK HİJYEN ve
DENEYSEL BİYOLOJİ DERGİSİ**

**Refik Saydam
Hıfzıssıhha Merkezi
Başkanlığı**



Cemal Gürsel Cad. No: 18
Tel : (0312) 458 20 00
Faks: (0312) 458 24 08

• Zehir Araştırmaları Müdürlüğü
Tel No : (312) 458 21 92
e-mail : zehir@rshm.gov.tr

RSHM Kod	UBB Kod		Satış Fiyatı TL
131.100		ANTİDOT	
131.103	15.03.01.12.02.13.01	Botulismus Polivalan Antiserumu (Tip A. B ve E)	9.770,00
131.105	15.03.01.12.02.14.01	Calcium Edtate De Sodium	450,00
131.106	15.03.01.12.02.15.01	Dicobalt EDTA (Kelocyanor) (6 Amp/kutu)	445,00
131.107	15.03.01.12.02.16.01	Digifab (Digoxin İmmune Fab) 40 mg vial	1.450,00
131.112	15.03.01.12.02.17.01	Dimercaprol (BAL) (British Anti-Lewisite) 12 amp/kutu	380,00
131.115	15.03.01.12.02.18.01	DMPS (Dimercaptopropane-1-sulfonate) (Dimaval) 5 amp/kutu	629,00
131.116	15.03.01.12.02.18.02	DMPS (Dimercaptopropane-1-sulfonate) (Dimaval) 20 cap/kutu	325,00
131.118	15.03.01.12.02.26.01	DMSA (Dimercaptosuccinic acid) Succimer 15 cap/kutu	487,00
131.121	15.03.01.12.02.19.02	D-Penicilamin (Metacaptase) 300mg/100 cap. Kutu	353,00
131.122	15.03.01.12.02.19.01	D-Penicilamin (Metacaptase) 150mg/100 cap. Kutu	60,00
131.124	15.03.01.12.02.20.01	Etil Alkol (%10) 500cc şişe	16,00
131.127	15.03.01.12.02.21.01	Fomepizol (4-methypyrazole) (5 Amp/Kutu=)	3.029,00
131.130	15.03.01.12.02.23.01	Metilen Mavisi (10 mL) %1	2,50
131.133	15.03.01.12.02.22.01	Physostigmin salicylat (5 Amp)	231,00
131.136	15.03.01.12.02.24.01	2- PAM (200 mg 10 Amp)Pralidoksime tuzları	76,33
131.139	15.03.01.12.02.12.01	Silibinin (4 Vialık kit)	2.430,00
131.142	15.03.01.12.02.25.01	Siyanür Antidot Kiti (Amil nitrit. Sodyum nitrit. Sodyum thiosülfat) (bir hastalık kit)	3.228,00

Internet | Korunmalı Mod: Kapalı

Popüler/Güncel Antidotlar-1

Antidote	Primary Indication by Substance	Dose and Administration
High dose insulin euglycemic therapy (HIE)	Severe calcium channel blocker poisoning	• Bolus of Regular Insulin 1U/kg followed by infusion at 0.5–1.0 U/kg/h. Give 25 gm (50 cc of D50W) initially and monitor glucose frequently to prevent hypoglycemia. Monitor serum potassium and replace as needed to avoid hypokalemia.

The proposed mechanism by which HIET reverses hemodynamic collapse is through direct metabolic effects on myocardial cells.^{6–8} It is hypothesized that in a state of shock, myocytes switch from the utilization of free fatty acids to glucose in order to meet metabolic demands. CCBs induce a state of hypoinsulinemia, preventing the uptake of glucose by myocytes and causing a loss of inotropy, decreased peripheral vascular resistance, and shock.^{6–8} High doses of insulin might therefore be able to reverse these metabolic derangements.

*Emerg Med Clin North Am. 2010 Feb;28(1):149-61, ix.

Popüler/Güncel Antidotlar-1

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HIGH-DOSE INSULIN EUGLYCEMIC THERAPY FOR THE TREATMENT OF CALCIUM CHANNEL BLOCKER OVERDOSE

It should not be overlooked, however, that there are many published case reports demonstrating the failure of HIET to reverse CCB-induced hemodynamic collapse. Some of these reports have in common the late initiation of HIET, after the development of severe symptoms,¹⁶⁻¹⁸ and may indicate that HIET should be considered early in severe CCB toxicity rather than as a therapy of “last resort.”

Popüler/Güncel Antidotlar-2

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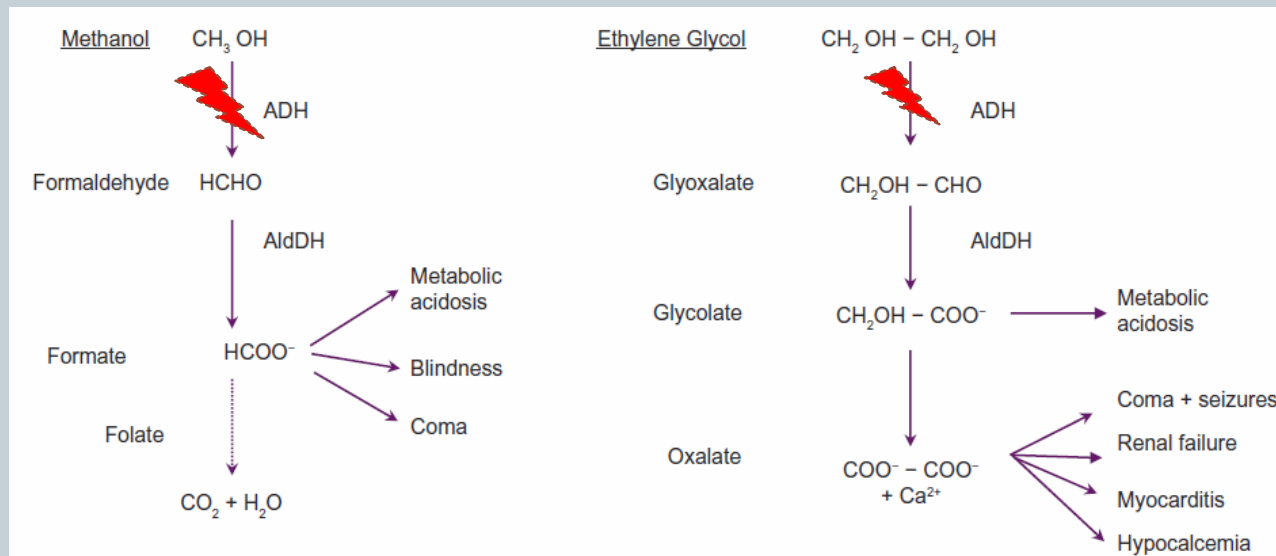
Antidote	Primary Indication by Substance	Dose and Administration
Intravenous lipid emulsion (Intralipid)	Lipophilic cardiotoxic agents	• 1.5 mL/kg of 20% intralipid as an initial bolus followed by 0.25 mL/kg/min for 30–60 min. • Depending upon response, bolus could be repeated 1-2 times and infusion rate increased.

Several mechanisms of action have been suggested. One theory is that ILE acts as a “lipid sink,” expanding the lipid compartment within the intravascular space, and sequestering lipid-soluble drugs from the tissues. The success of ILE in the treatment of poisoning by lipid-soluble drugs such as bupivacaine, propranolol, and verapamil supports this theory. Another explanation suggests that its efficacy is related to metabolic effects in the myocardium, specifically its ability to enhance fatty acid intracellular transport in myocardial cells.¹⁹

Popüler/Güncel Antidotlar-3

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Fomepizole



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New Developments in Antidotes

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Popüler/Güncel Antidotlar-3

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Fomepizole and ethanol are two effective antidotes for the treatment of ethylene glycol (EG) and methanol poisoning [9]. Both fomepizole and ethanol are inhibitors of the alcohol dehydrogenase (ADH) enzyme; fomepizole is a more potent ADH inhibitor than ethanol [10,11]. In addition, fomepizole is eliminated more slowly than ethanol, has more predictable pharmacokinetics, is easier to administer, and requires less laboratory monitoring [12,13].

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REVIEW

Treatment of patients with ethylene glycol or methanol poisoning: focus on fomepizole

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Popüler/Güncel Antidotlar-3

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Dosage and available formulations

Fomepizole is available in 1.5 mL vials containing 1 g/mL [16]. Intravenous (IV) administration is the recommended route, but fomepizole may be administered orally if IV access cannot be obtained [17]. Fomepizole is administered as an IV loading dose of 15 mg/kg, diluted in at least 100 mL of normal saline, or 5% dextrose in water, and infused over 30 minutes. The maintenance dose is 10 mg/kg IV every 12 hours for four doses. Administration beyond the initial five doses (48 hours) should be given at 15 mg/kg IV every 12 hours [16]. The recommended increase in the maintenance dose after the initial five doses is due to the autoinduction of fomepizole metabolism [18–21]. Fomepizole as monotherapy for EG or methanol intoxication should be given until the patient is asymptomatic, and the EG or methanol serum concentration is below 20 mg/dL [16].



TEŞEKKÜRLER...