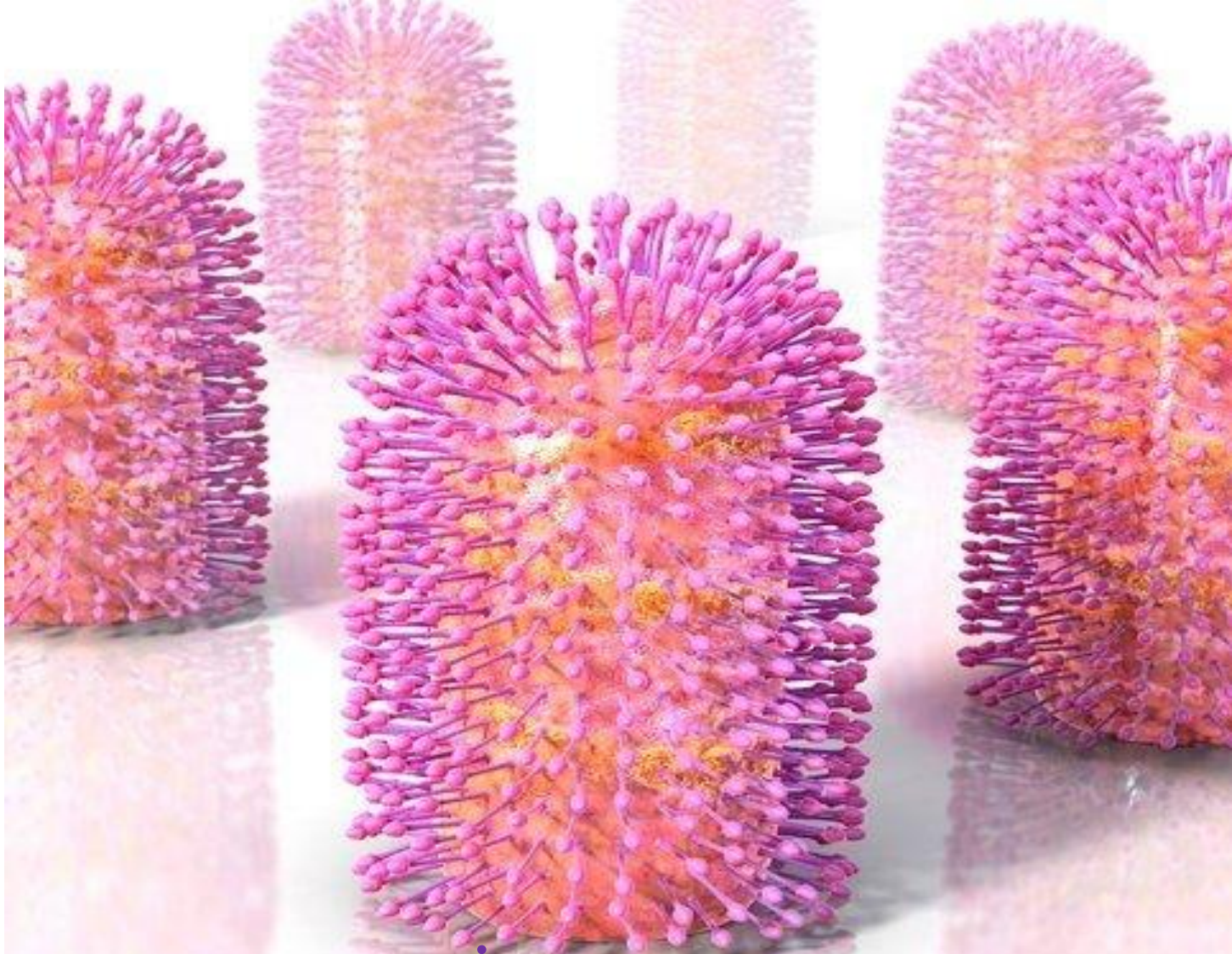




İNSAN KUDUZU

Dr. Esra KAYA KILIÇ

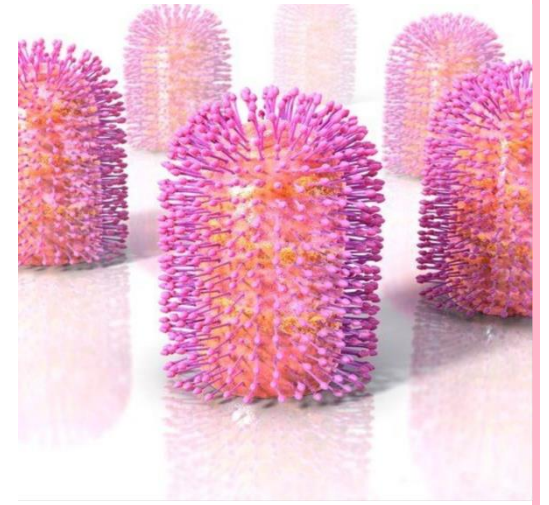
Aralık 2014

Ankara Eğitim ve Araştırma Hastanesi

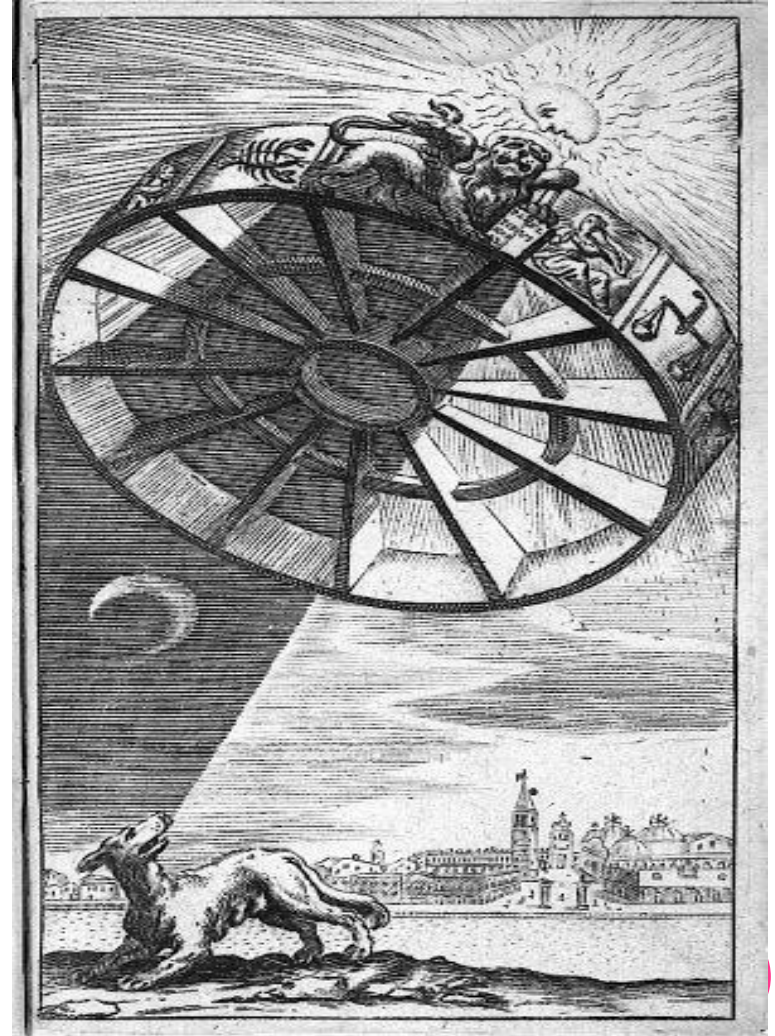


SUNUM PLANI

- Kuduz virüsü
- Epidemiyolojisi
- Bulaş yolları
- Patogenez
- Klinik
- Profilaksi
- Tedavi



- Rabies, Latince saldırgan, rabere
- Latince kelimenin de kökeninin de Sanskritçe olan rabhas
- Yunanca adı ise lyssa ya da lytta



PASTEUR'S LATEST DISCOVERY.

Five years ago the great French chemist Louis Pasteur determined to find a remedy for hydrophobia. His discovery of a method of inoculation by which rabid and chary were enabled to defy asphyxia, or epidemic fever, had led him to believe that the virus of rabies could be used in a similar way for the prevention of human beings. In June, 1884, he had solved the problem so far as the inoculation of dogs was concerned, but not until October last was able to announce that by inoculation man could be protected. That announcement was made at a meeting of the French Academy of Sciences. M. Pasteur then had two patients on hand for treatment. He now has more than seventy. The process is described as follows: A rabbit is inoculated with a fragment of spinal marrow taken from a rabid dog. In 6-10 days the rabbit becomes mad and dies. A second rabbit is inoculated with a bit of spinal marrow taken from the first, and the inoculation is repeated until thirty rabbits have been used. With each successive inoculation the virus becomes stronger, and the period of incubation is shortened, until, in the case of the thirtieth rabbit, it is only seven days. The chemist discovered some years ago, while experimenting with the virus of foot disease, that it could be weakened or attenuated only by exposure to dried air. Bits of marrow from the inoculated rabbits, graded with reference to the strength of the virus and the cause of extinction, are exposed to dried air in bottles. In this way M. Pasteur produces a supply of virus graded from a specimen that is first and that will cause hydrophobia in an animal in seven days. The person who has been bitten is then inoculated under the skin by means of a Pravaz syringe containing sterilized liquid in which a small piece of marrow has been dissolved. The narrow containing virus of the great inoculation is first used. Virus of greater power is used in successive inoculations, until at last the more powerful is introduced. By degrees the system becomes accustomed to it, and M. Pasteur holds that after safely undergoing the last inoculation of the series the patient is proof against hydrophobia.

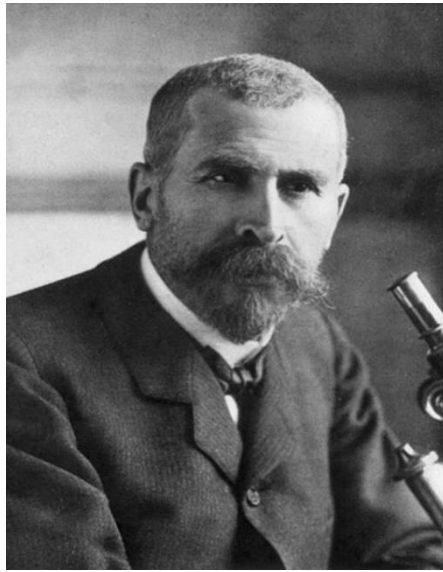
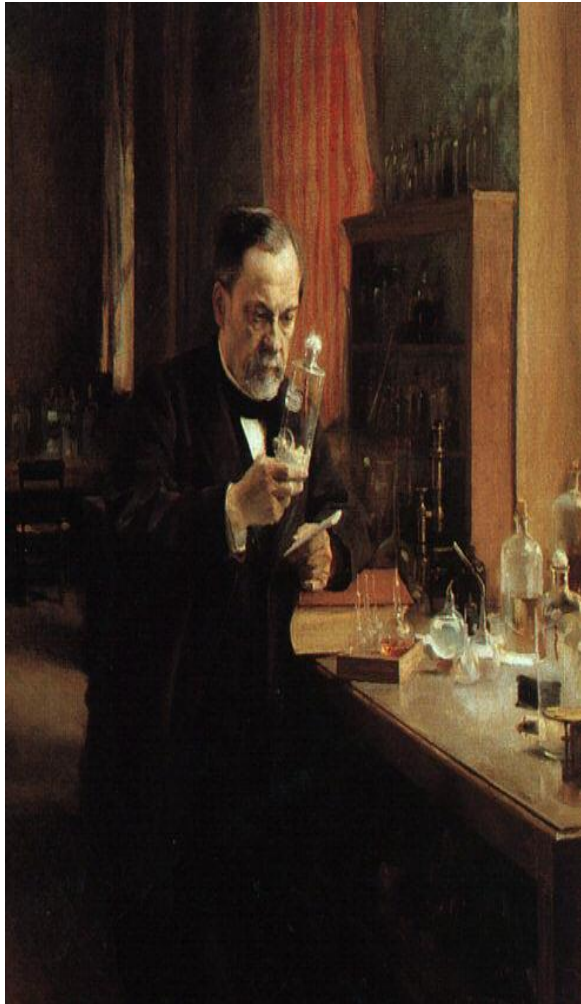
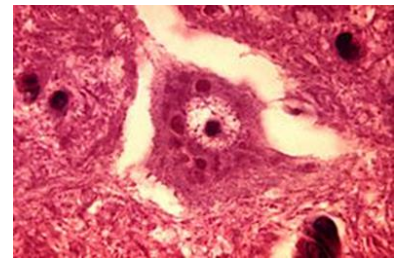
The first of the chemist's patients was Jeanne Marrea, an Alsatian. He was bitten in July last. Eminent physicians of Paris were of the opinion that he could not escape a terrible death unless he should be saved by this process. In ten days he was inoculated thirteen times, and the virus used in the thirteenth operation was of the greatest strength. It caused the death of a rabbit in seven days, but had no effect upon Marrea. When the discovery was made known to the Academy of Sciences the inoculation year was one hundred days old, but Marrea was in perfect health.

The length of the period of incubation in cases of hydrophobia varies greatly, ranging from twenty days or thirty days to one year, and cases are reported in which the disease did not appear for two or three years. In a great majority of cases, however, rabies is developed within six months. M. Pasteur is confident that his treatment will be effective if it shall be applied at any time before actual hydrophobia appears. Four children living in Alsace were bitten on August 20. That the dog was mad is proved by the fact that one of them died in October of acute hydrophobia. The three who survived reached Paris on October 25, and were inoculated. They have remained in Alsace, and are said to be in good health, living in the varying length of the period of incubation, cautious physicians are ready to admit at present that the assumed value of inoculation has been proved. They prefer to wait until time and numerous cases

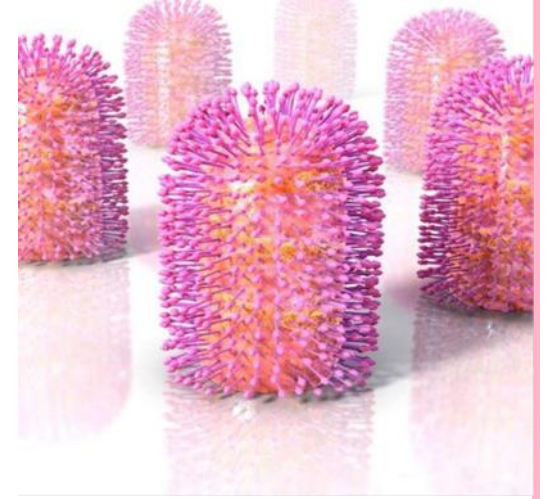


M. Pasteur.
AN INOCULATION FOR HYDROPHOBIA.—From "L'Illustration."

"An Inoculation for Hydrophobia—From L'Illustration,"
Harper's Weekly 29:1513 (December 19, 1885), p. 836.
Bert Hansen Collection, New York



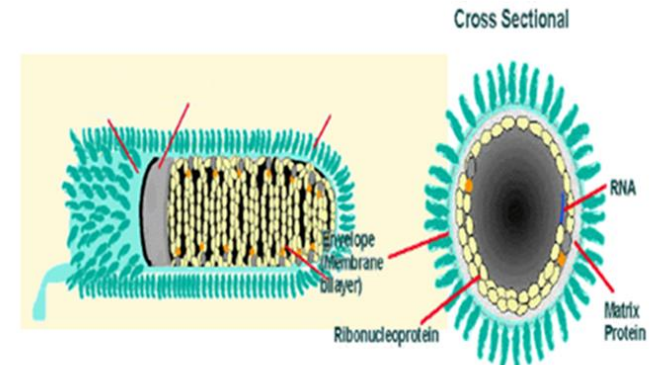
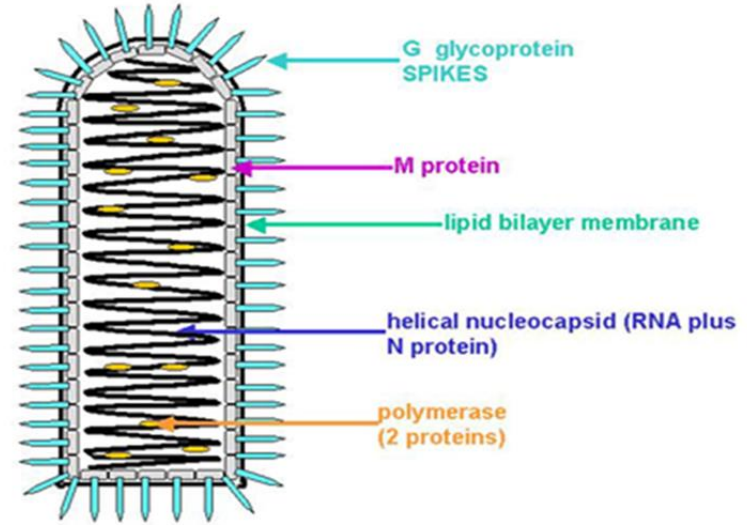
- Kuduz virüsü
- Epidemiyolojisi
- Bulaş yolları
- Patogenez
- Klinik
- Profilaksi
- Tedavi



KUDUZ VIRÜSÜ

Rhabdoviridae
ailesi Lyssavirus
genusunda yer alır

Zarflı bir RNA
virüsüdür



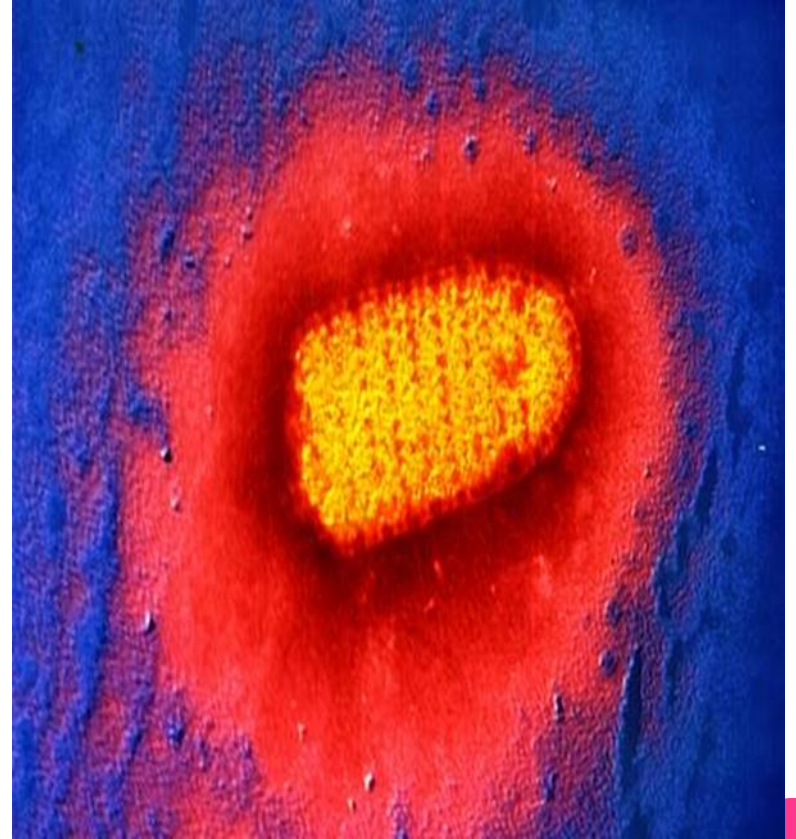
KUDUZ VIRÜSÜ

Kuruluk, ısı, UV ile inaktive olur.

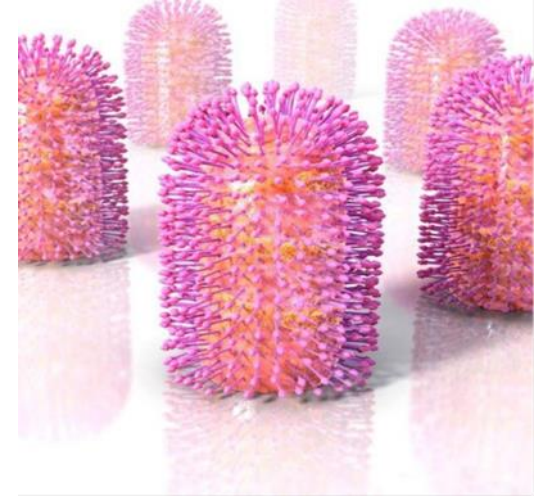
Soğuğa dayanıklıdır.

Lipit eriticilerin çoğuna duyarlıdır.

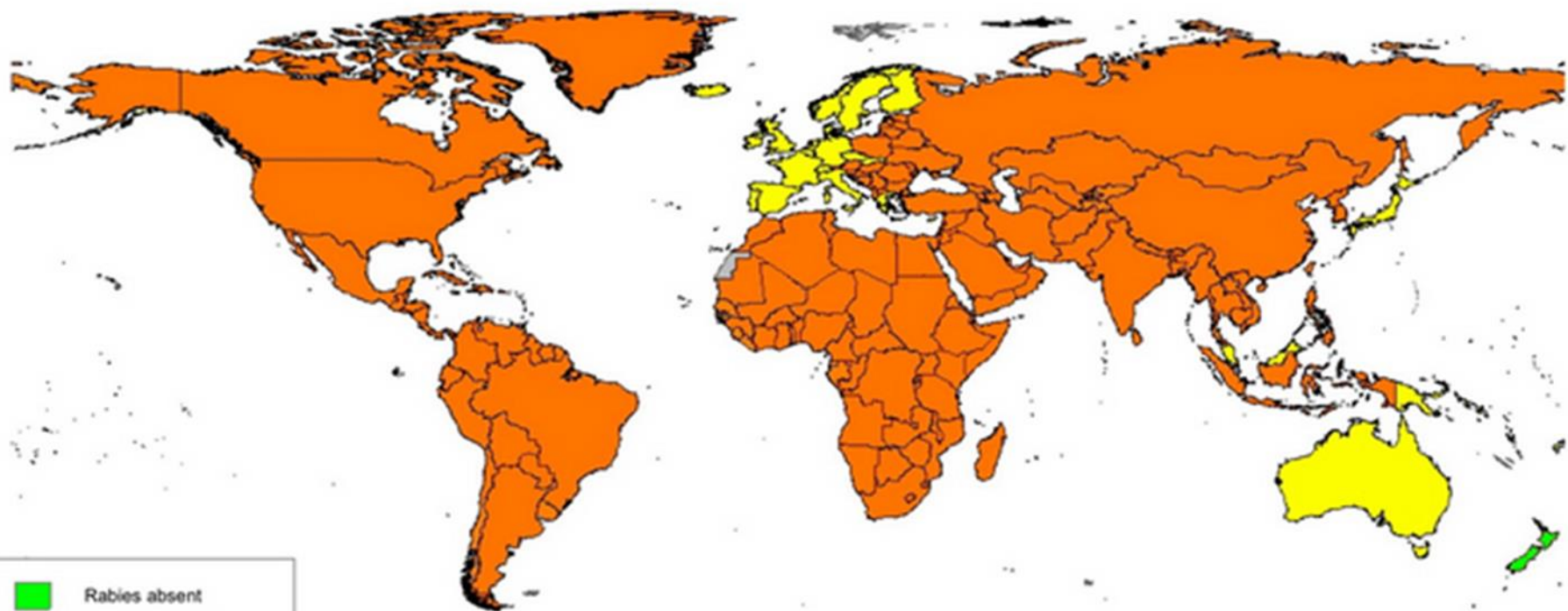
Eter, alkol, %20 sabun çözeltisinde, deterjanlarla kolay inaktive olur.



- Kuduz virüsü
- Epidemiyolojisi
- Bulaş yolları
- Patogenez
- Klinik
- Profilaksi
- Tedavi



Presence/ absence of rabies in 2007



-  Rabies absent
-  Only bat rabies present
-  Rabies present
-  No data available

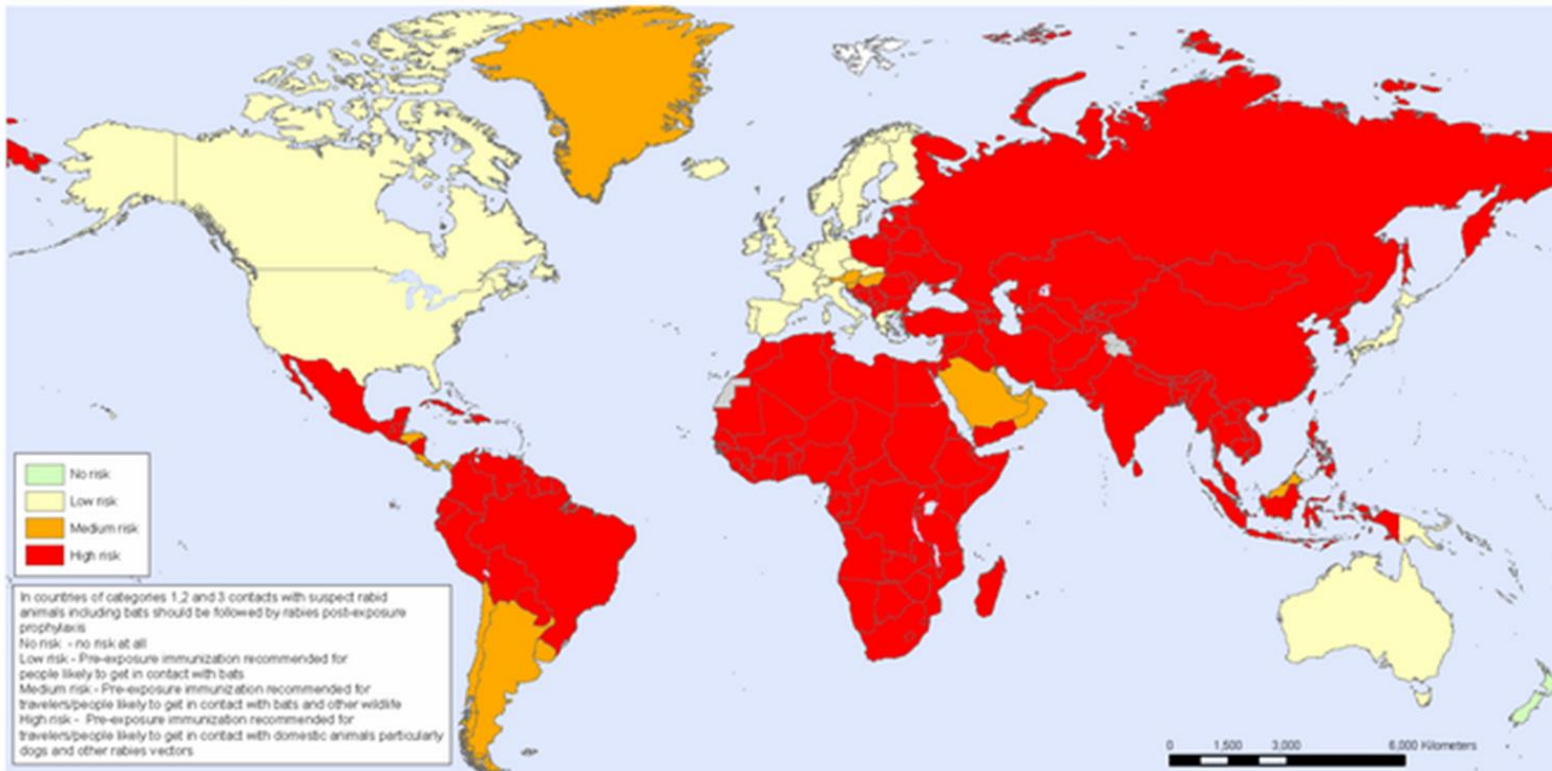
Disclaimer: © World Health Organization. The boundaries and names shown and the designations used on this map do not imply the expression of an opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.



**World Health
Organization**

DÜNYADA KUDUZ

Rabies, countries or areas at risk



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

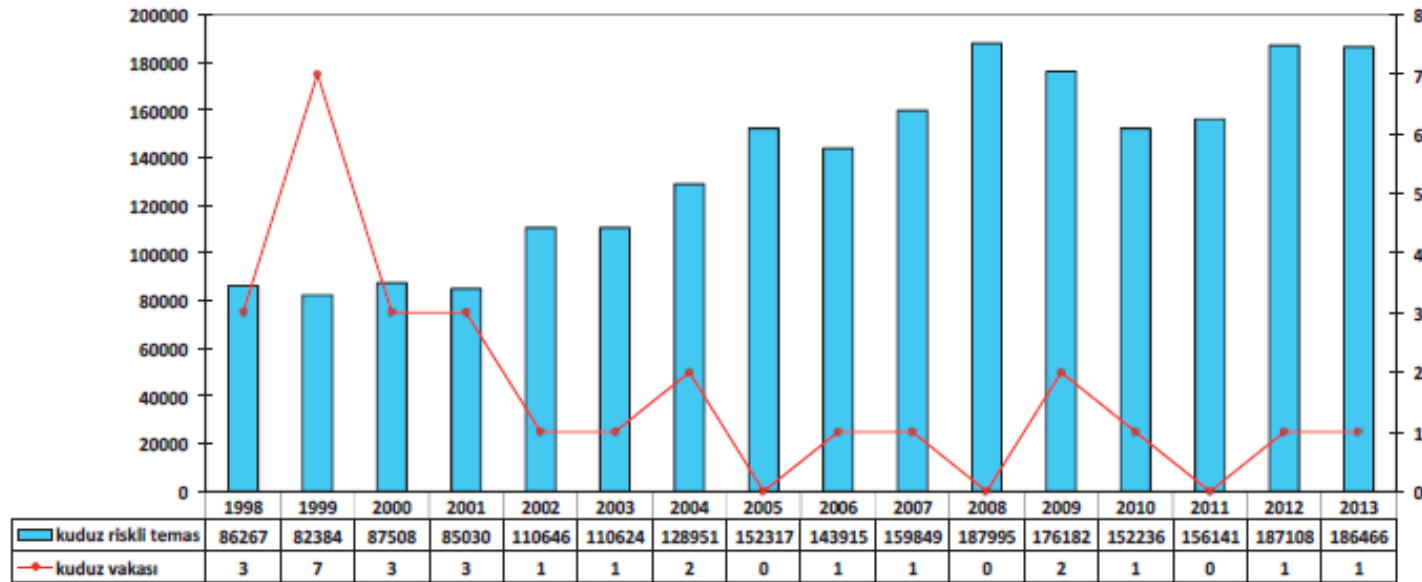
Data Source: WHO RabNet/CDC
Map Production: Public Health Information
and Geographic Information Systems (GIS)
World Health Organization



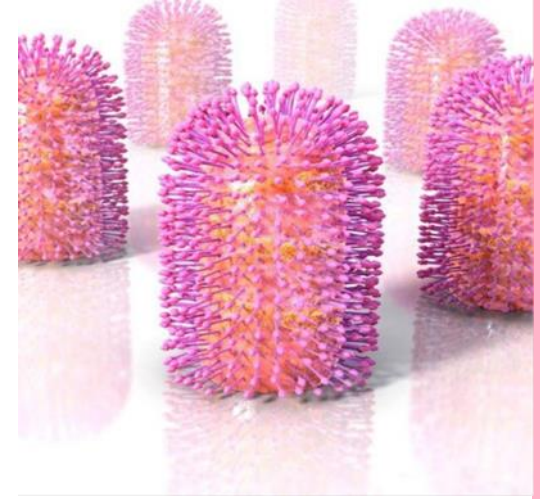
© WHO 2008. All rights reserved

ÜLKEMİZDE KUDUZ

Kuduz Riskli Temas ve Kuduz Vakalarının yıllara göre Dağılımı (1998-2013)



- Kuduz virüsü
- Epidemiyolojisi
- Bulaş yolları
- Patogenez
- Klinik
- Profilaksi
- Tedavi



BULAŞ YOLLARI

Hayvandan insana bulaş

- Isırık
- Tırmalama
- Bütünlüğü bozulmuş derinin yalanması
- Mukozanın yalanması
- Aerosol
 - İnfekte yaralarının olduğu mağara
 - İnfekte sinir dokusu ile çalışılan laboratuvar
- Oral
 - İnfekte ineğin çiğ sütünü içmek
 - İnfekte hayvanın çiğ etini yemek

İnsandan insana bulaş

- Transplantasyon
 - Kornea transplantı
 - Solid organ transplantı
- Kuduz insan tarafından ısırılma



Airborne transmission of lyssaviruses

N. Johnson,¹ R. Phillpotts² and A. R. Fooks¹

Correspondence

A. R. Fooks

t.fooks@vla.defra.gsi.gov.uk

¹Rabies and Wildlife Zoonoses Group, Veterinary Laboratories Agency (VLA, Weybridge), WHO Collaborating Centre for the Characterisation of Rabies and Rabies-related Viruses, New Haw, Addlestone KT15 3NB, UK

²Defence, Science and Technology Laboratory (DSTL), Porton Down, Salisbury, UK

Doza bağı bir olarak Lyssaviruses ve RABV, aerosol yoluyla yayılır. Bu durum laboratuvar ortamında kazara maruz kalan personel için tehlike olabilir.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transmission of Rabies Virus from an Organ Donor to Four Transplant Recipients

Hastaların dördünde de bulgular ortaya çıkış süresi ortalama 30 gün
Olguların üçünde mental değişiklikler ve tremor ilk bulgular
Hastaların birinde abdominal ağrı sonrasında mental değişiklikler
Semptomlar başladıktan ortalama 14 gün sonra ex

N Engl J Med 2005;352:1103-11.



Contents lists available at SciVerse ScienceDirect

Journal of Clinical Virology

journal homepage: www.elsevier.com/locate/jcv



Six fatal cases of classical rabies virus without biting incidents, Iran 1990–2010

Susan Simani, Ahmad Fayaz, Pooneh Rahimi*, Naser Eslami, Nader Howeizi, Peyvand Biglari

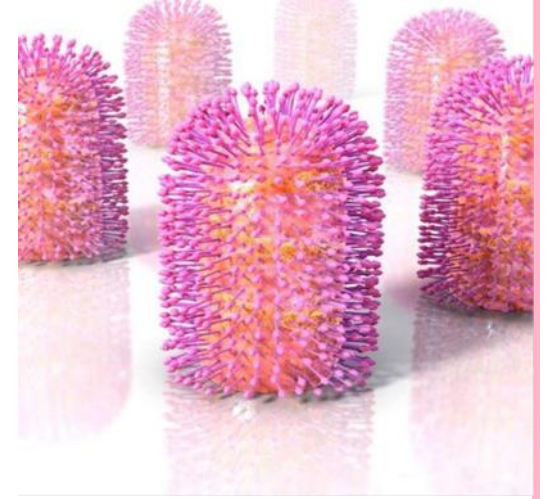
WHO Collaborating Center for Reference and Research on Rabies, Institute Pasteur, 12 Farvardin Ave., Enghelab Square, Tehran, Iran

Nosocomial Rabies: Investigation of Contacts of Human Rabies Cases Associated with a Corneal Transplant

LARRY J. ANDERSON, MD, L. PAUL WILLIAMS, JR., DVM, JOSEPH B. LAYDE, MD,
FRITZ R. DIXON, MD, AND WILLIAM G. WINKLER, DVM



- Kuduz virüsü
- Epidemiyolojisi
- Bulaş yolları
- Patogenez
- Klinik
- Profilaksi
- Tedavi



Merkez

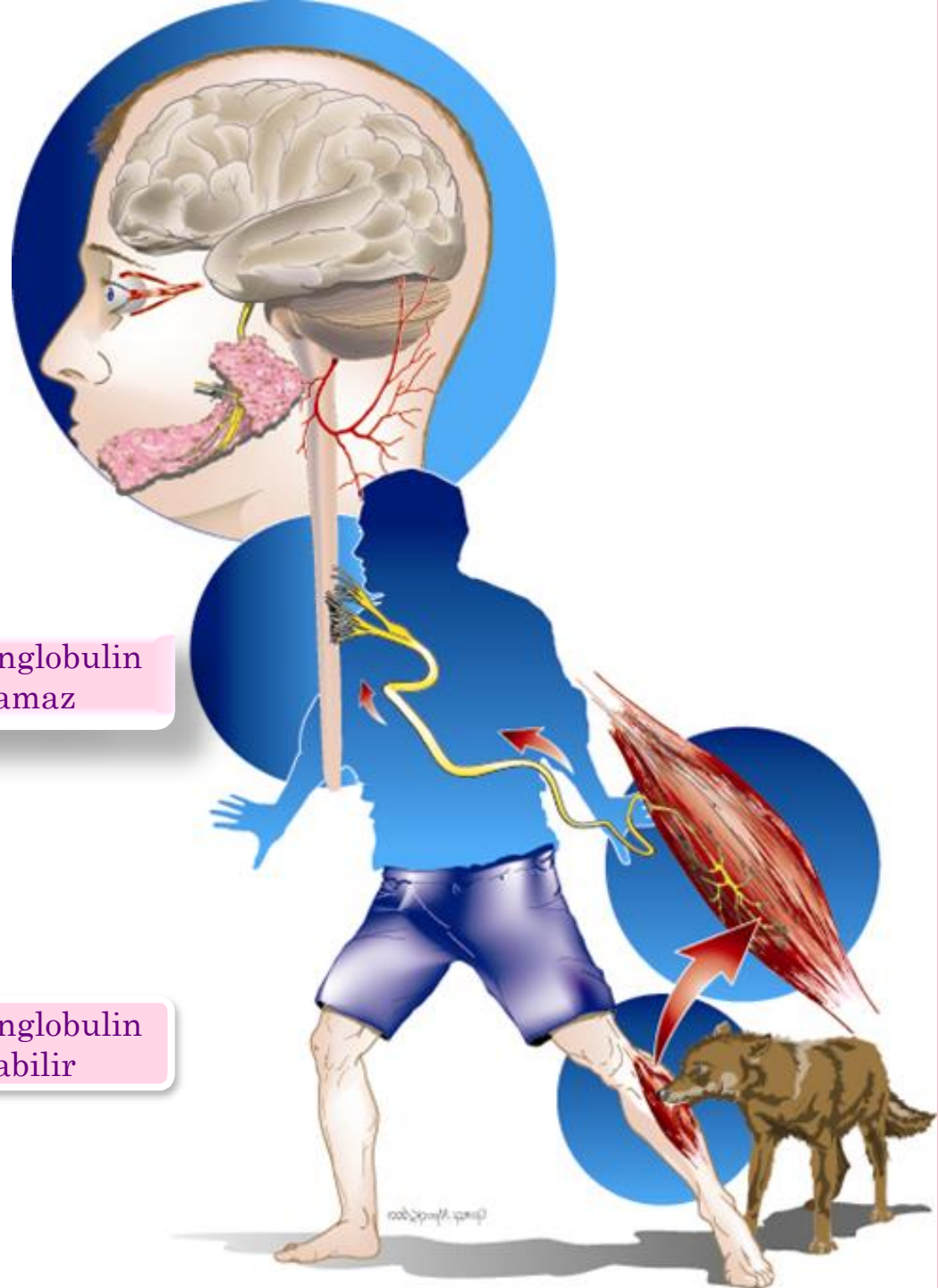
Periferik
sinirler

Nikotinik Ach
reseptörleri

Kas Hücreleri

Aşı ve İmmunglobulin
uygulanamaz

Aşı ve İmmunglobulin
uygulanabilir



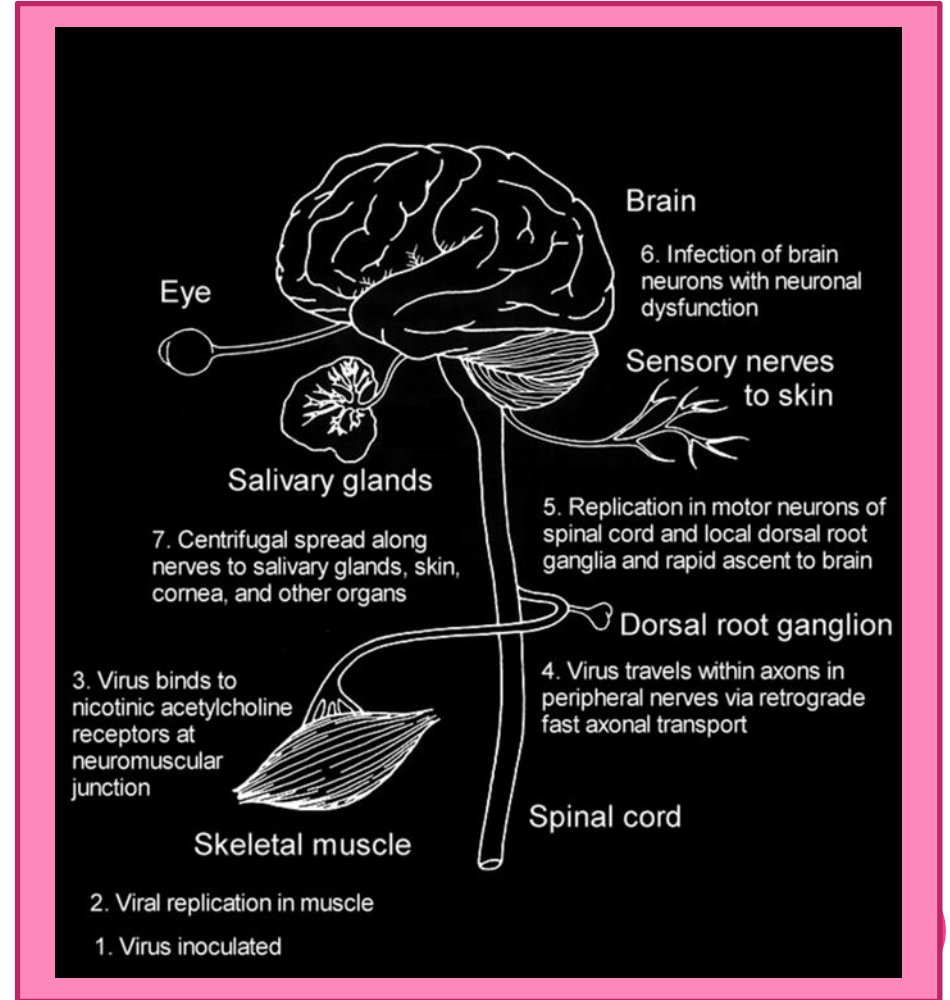
Merkez

Tükrük bezleri ve
diğer dokular

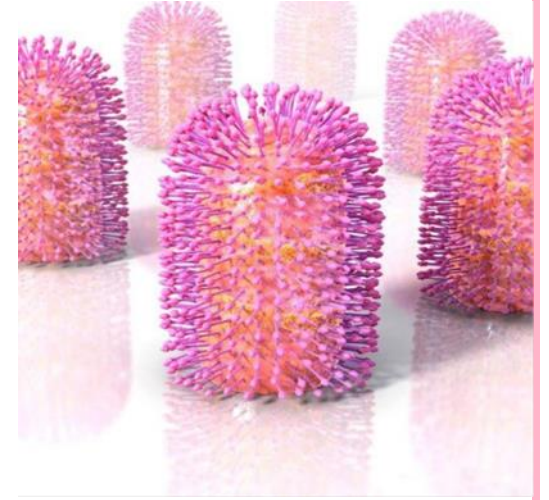
Virüsün tükrükle
atılım

Ensefalit

Ensefalit



- Kuduz virüsü
- Epidemiyolojisi
- Bulaş yolları
- Patogenez
- Klinik
- Profilaksi
- Tedavi



KLINİK

- Kuluçka dönemi
- Prodromal dönem
- Akut nörolojik dönem
- Koma ve ölüm



KULUÇKA DÖNEMİ

- Olguların % 75 i 90 gün içinde belirti vermektedir.
 - Transplant hastalarında 45 gün
 - Alınan virüsün miktarı fazla ise,
 - Virülansı yüksekse,
 - Yara merkezi sinir sistemine yakınsa,
 - Yara bölgesi sinir ağı zenginse,
 - Yara büyük ya da çok sayıda ise,
 - Temas yeri korunmasızsa
- KISADIR**

KLINİK FORMLAR

• Ensefalitik kuduz

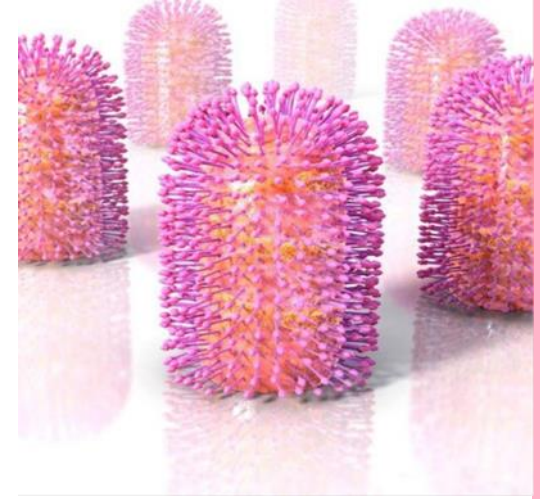
- Hallusinasyon
- Davranış değişiklikleri
- Anksiyete
- Ajitasyon
- Otonomik disfonksiyon
- Pupiller dilatasyon, anizokori
- Salya artışı, terleme, priapizm
- Diabetes insipidus
- Hidrofobi
- Aerofobi
- Hiperventilasyon

• Paralitik kuduz

- Asenden flask paralizi
- Guillain Barré sendromu gibidir
- Simetrik quadriparezi görülür
- Virüsün alındığı ekstremitelerde daha ciddidir Spinal kord ve beyin sapı tutulumu vardır
- Serebral bulgular geç dönemde ortaya çıkar
- Hidrofobi, aerofobi, nöbet görülmez
- Şuur açık olmasına rağmen meningeal bulgular

	Enefalitik Kuduz	Paralitik Kuduz
Prevelans	2/3 (%67)	1/3 (%33)
Yoğun Bakım Desteği Olmakasız Yaşam Süresi	5-7 gün (n=80)	11 gün (n=33)
Prodromal Semptomlar	Spesifik lokal nörapatik ağrı Φ	Spesifik lokal nörapatik ağrı Φ
Kuduz Karakteristiği	Mevcut ancak tüm evreler Φ	Minimal fobik inspiratuar spasm Deltoid kas ve göğüs duvarında miyödem
Duyusal Değişikler	Duyu kaybı ardından eklem pozisyon duygusu kaybı	Duyu kaybı ardından eklem pozisyon duygusu kaybı
Güçsüzlük ve Arefleksi	Sadece koma durumunda	Proksimal ve fasial kaslardan başlamak üzere motor güçsüzlük
Elektrofizyolojik özellikler	Subklinik ön boynuz hücre disfonksiyonu, nöropati	Aksonopati veya periferik demiyelizasyon, nöropati

- Kuduz virüsü
- Epidemiyolojisi
- Bulaş yolları
- Patogenez
- Klinik
- Profilaksi
- Tedavi



Same Dog Bite and Different Outcome in Two Cases – Case Report

GADEKAR RD¹, DOMPLE VK², INAMDAR IF³, ASWAR NR⁴, DOIBALE MK⁵

ABSTRACT

There is still no cure for rabies and survival from clinical rabies is extremely rare. It is a preventable disease if the post exposure prophylaxis is initiated in time and administered as per WHO guidelines including administration of rabies immunoglobulin. The role of passive rabies immunization products is to provide the immediate availability of neutralizing antibodies at the site of the exposure before it is physiologically possible for the patient to begin producing his or her own antibodies after vaccination. In this case report, the same dog has bitten to a boy and to an adult. Local wound treatment and use of human rabies immunoglobulin as well as gluteal region as a site of bite were the probable reasons for survival of the boy. On the other hand no local wound treatment, no use of rabies immunoglobulin and finger as a site of bite are the probable reasons for death of an adult due to rabies.



WHO Technical Report Series
982

WHO Expert Consultation on Rabies

Second report

This report contains the collective views of WHO experts and does not necessarily represent the decisions or the stated policy of WHO.



KUDUZ SAHA REHBERİ

TÜRKİYE-2014

MWR
and Mortality Weekly Report
www.cdc.gov/mmwr

March 19, 2010 / Vol. 59 / No. RR-2

Reduced (4-Dose) Vaccine
Postexposure Prophylaxis
for Susceptible Human Rabies
Cases: Recommendations
of the Advisory Committee
on Immunization Practices

DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION

TEMAS ÖNCESİ PROFILAKSI

- Mesleki risk
 - Veteriner hekimler
 - Kuduz laboratuvarı çalışanları
 - Hayvan bakıcıları
- Doğa sporları yapanlar
- Seyahat
 - Güneydoğu Asya
 - Hindistan
 - Kuzey Amerika
 - Genç yaş
 - Turistik gezi



TEMAS ÖNCESİ PROFILAKSI

- 0., 7. ve 21. / 28. günlerde
- Rapel
 - Kuduz laboratuvar ve aşı üretimde çalışanlarda 2 yılda antikor ölçümü
 - RIFT ve FAVN 1/5 ↓
 - Antikor ölçülemiyorsa 2 yılda bir rapel tek doz



TEMAS SONRASı YAKLAŞıM



- Yara bakımı
- Antibiyotik profilaksisi
- Tetanoz profilaksisi
- Kuduz aşısı uygulaması
- Kuduz immünglobulin uygulaması



ANTİBİYOTİK PROFİLAKSİSİ

Yüzden ısırılmalar

Elden ısırılmalar

Kemik ve eklem penetrasyonu olasılığı

İmmün yetmezlikli kişiler

Protez ekleme yakın yaralar

Genital bölge yaralanmaları



ANTİBİYOTİK PROFİLAKSİSİ



İlk sekiz saat içerisindeki
başvurularda;
ezilme ve ödem varlığında

Antibiyotik verilmeli

Profilaksi süresi üç
gün

Erişkinlerde:

Amoksisilin/klavulanat
875-125 mg, 2x1
veya
500-125 mg, 3x1

Çocuklarda:

Amoksisilin/klavulanat
45-100 mg/kg/gün, 2-3 doza
bölünerek

PROFILAKSI



Profilaksi Gerektirmeyen Temaslar

- Fare
- Sıçan
- Sincap
- Hamster
- Kobay
- Gerbil
- Tavşan
- Yabani tavşan

Yarasa

- Eve giren yarasaların ısırığı
- Evde yarasa bulunması
- Doğal ortamdaki mağaralarda olan temas
- Vaka bazlı değerlendirilir

Soğukkanlı

hayvanlar

- Yılan
- Kertenkele
- Kaplumbağa



PROFILAKSI



Profilaksi Gerektirmeyen Temaslar

Kuduz olduğu anlaşılan bir hayvan;

- Beslemiş olmak
- Temas
- Kan
- idrar
- Süt
- Feçes

- Kümes hayvanları ısırıkları
- Sağlam derinin yalanması
- Bilinen ve halen sağlam bir hayvan tarafından 10 günden daha önce ısırılmış veya temas etmiş olma



PROFILAKSI



ERIG 40 IU/kg

HRIG 20 IU/kg

İlk doz aşıdan sonraki 7
gün içinde

RIG uygulama öncesi cilt testi önerilmemekte.

PROFILAKSI

TEMAS SONRASI PROFİLAKSİ





Kategori	Temas Tipi	Hayvanın Durumu	Önerilen Yaklaşım
I	1. Hayvana dokunma ya da besleme 2. Sağlam derinin yaralanması		Herhangi bir işlem yapılmasına gerek yok



Kategori	Temas Tipi	Hayvanın Durumu		Önerilen Yaklaşım
II	1. Çıplak derinin hafifçe sıyrılması (deri altına geçmeyen yaralanmalar) 2. Kanama olmayan küçük tırmalama veya zedeleme	A. Temas eden evcil hayvanın son bir yılda kuduz aşısı yapılmışsa		- Yara bakımı - Tetanoz profilaksisi - Hayvanın 10 gün gözlemi
		B. Temas eden evcil hayvanın son bir yıl içinde kuduz aşısı yapılmamış veya bilinmiyorsa	Hayvan sağlıklı ve gözlemi yapılabildiğinde	- Yara bakımı - Tetanoz profilaksisi - Hayvanın 10 gün gözlemi
			Hayvanın gözlenemediği durumda	- Yara bakımı - Tetanoz profilaksisi - Aşılamaya hemen başlanır

Kategori	Temas Tipi	Hayvanın Durumu		Önerilen Yaklaşım
III	- Deriyi zedeleyen tek ya da çok sayıda ısırıklar - Mukozaların, açık cilt yaralarının hayvanın salyası ile temas etmesi - Lezyonun kafa, boyun, parmak uçları gibi sinir uçlarının yoğun olduğu bölgelerde olması	A. Temas eden evcil hayvanın son bir yılda kuduz aşısı yapılmışsa		- Yara bakımı - Tetanoz profilaksisi - Hayvanın 10 gün gözlemi
		B. Temas eden evcil hayvanın son bir yıl içinde kuduz aşısı yapılmamış veya bilinmiyorsa	Hayvan sağlıklı ve gözlemi yapılabildiğinde	- Yara bakımı - Tetanoz profilaksisi - Aşılamaya hemen başlanır - Hayvanın 10 gün gözlemi - İmmunglobulin
			Hayvanın gözlenemediği durumda	- Yara bakımı - Tetanoz profilaksisi - Aşılamaya hemen başlanır - İlk doz aşı ile birlikte hemen immunglobulin



Kategori	Temas Tipi	Hayvanın Durumu	Önerilen Yaklaşım
IV	1. Kuduza yakalanma ihtimali olan riskli yabani hayvan türleri ile temas		Yara bakımı Tetanoz profilaksisi Aşılamaya hemen başlanır İlk doz aşı ile birlikte hemen immunglobulin

Kurt
Tilki
Çakal
Domuz
Sansar
Kokarca
Gelinci





	Kategori	Önerilen Yaklaşım
İmmün sistemi baskılanmış hastalar	Kategori I	Herhangi bir işlem yapılmasına gerek yok
	Kategori II-III-IV	Yara bakımı Tetanoz profilaksisi Aşılamaya hemen başlanır İlk doz aşı ile birlikte hemen immunglobulin

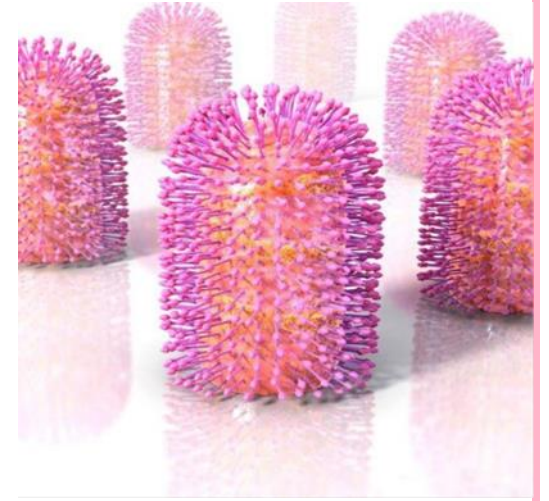




Bağışıklama Durumu	Kuduz II Temas Riski		Kuduz III-IV Temas Riski	
	Td	TIG	Td	TIG
Bilinmiyor veya < 3 doz	Evet	Hayır	Evet	Evet
≥ 3 doz	Hayır/Evet	Hayır	Hayır/Evet	Hayır



- Kuduz virüsü
- Epidemiyolojisi
- Bulaş yolları
- Patogenez
- Klinik
- Profilaksi
- Tedavi



Management and Outcomes after Multiple Corneal and Solid Organ Transplantations from a Donor Infected with Rabies Virus

T. Maier,^{1,a} A. Schwarting,^{2,a} D. Mauer,⁴ R. S. Ross,⁵ A. Martens,⁶ V. Kliem,⁷ J. Wahl,³ M. Panning,⁸ S. Baumgarte,⁹ T. Müller,¹⁰ S. Pfefferle,⁸ H. Ebel,¹ J. Schmidt,¹¹ K. Tenner-Racz,⁸ P. Racz,⁸ M. Schmid,⁴ M. Strüber,⁶ B. Wolters,⁵ D. Gotthardt,¹² F. Bitz,⁷ L. Frisch,³ N. Pfeiffer,³ H. Fickenscher,^{13,b} P. Sauer,¹² C. E. Rupprecht,¹⁴ M. Roggendorf,⁵ A. Haverich,⁶ P. Galle,² J. Hoyer,¹ and C. Drosten^{8,b}

¹Department of Internal Medicine and Nephrology, University of Marburg Medical Centre, Marburg, Departments of ²Medicine and ³Ophthalmology, University of Mainz Medical Centre, Mainz, ⁴German Organ Donor Procurement Organisation, Neu Isenburg, ⁵Institute of Virology, University of Essen Medical Centre, Essen, ⁶Clinic for Cardiac, Thoracic, Transplantation and Vascular Surgery, Hannover Medical School, Hannover, ⁷Nephrological Centre of Lower Saxony, Hannoversch-Münden, ⁸Bernhard Nocht Institute for Tropical Medicine and ⁹Institute for Hygiene and Environmental Medicine, Hamburg, ¹⁰Friedrich-Loeffler Institute—Federal Research Institute for Animal Health, Wusterhausen, and ¹¹Department of Surgery, ¹²Liver Transplantation Section, Department of Medicine, and ¹³Department of Virology, University of Heidelberg Medical Centre, Heidelberg, Germany; and ¹⁴Rabies Section, Centers for Disease Control and Prevention, Atlanta, Georgia

Background. This article describes multiple transmissions of rabies via transplanted solid organ from a single infected donor. The empirical Milwaukee treatment regimen was used in the recipients.

Methods. Symptomatic patients were treated by deep sedation (ketamine, midazolam, and phenobarbital), ribavirin, interferon, and active and passive vaccination. Viral loads and antibodies were continuously monitored.

Results. Recipients of both cornea and liver transplants developed no symptoms. The recipient of the liver transplant had been vaccinated ~20 years before transplantation. Two recipients of kidney and lung transplants developed rabies and died within days of symptomatic disease. Another kidney recipient was treated 7 weeks before he died. The cerebrospinal fluid viral load remained at constant low levels (<10,000 copies/mL) for ~5 weeks; it increased suddenly by almost 5 orders of magnitude thereafter. After death, no virus was found in peripheral compartments (nerve tissue, heart, liver, or the small intestine) in this patient, in contrast to in patients in the same cohort who died early.

Conclusions. Our report includes, to our knowledge, the longest documented treatment course of symptomatic rabies and the first time that the virus concentration was measured over time and in different body compartments. The postmortem virus concentration in the periphery was low, but there was no evidence of a reduction of virus in the brain.

TEDAVI



The NEW ENGLAND JOURNAL *of* MEDICINE

BRIEF REPORT

Survival after Treatment of Rabies
with Induction of Coma

N Engl J Med 2005;352:2508-14.



Teşekkürler...

