



EBOLA

Yard. Doç. Dr. Kaya Süer

Yakın Doğu Üniversitesi Tıp Fakültesi

İnfeksiyon Hastalıkları ve Klinik Mikrobiyoloji AD

Sunum Planı



- Mikroorganizma
- Tarihçe
- Epidemiyoloji
- Bulaş yolları
- Klinik
- Tedavi
- Kontrol ve önlemler

-
- 26 Ağustos 1976:
 - 44y Erkek öğretmen → → Ormanda yürüyüşten sonra yüksek ateş
 - Kinin veriliyor
 - 1 hafta sonra bulantı, kusma, diyare, nazal oral ve rektal kanama, solunum güçlüğü
 - 14. gün ex
 - Hemen sonrasında salgın → → 318 hasta → → 280 ex. (%88)





ebola

INSIDE THE DEADLY OUTBREAK

Viral Hemorajik Ateşler

- Multisistemik etkili viral infeksiyonlar
 - Damar endotelinde hasar
 - Sıklıkla hemorajilerle seyreden semptomlar
 - Yaşamı tehdit eden hastalıklar

Arenaviridae	Bunyaviridae	Filoviridae	Flaviviridae
Junin	Crimean- Congo H.F.	EBOLA	Kyasanur Forest Disease
Machupo	HANTAVIRÜS	MARBURG	Omsk H.F.
Sabia	Rift Valley fever		YELLOW FEVER
Guanarito			DENGUE
LASSA			

Ebola Virüsü



- En gizemli virüs grubu
- Patogenezi tam olarak anlaşılmamış
- Afrika'da endemik
- RNA virüsü

Virology 2013 Nov 9;10:331 doi: 10.1186/1743-422X-10-331.

Recombinant lentogenic Newcastle disease virus expressing Ebola virus GP infects cells Independently of exogenous trypsin and uses macropinocytosis as the major pathway for cell entry.

Abstract

BACKGROUND: Using reverse genetics, we generated a recombinant low-pathogenic LaSota strain Newcastle disease virus (NDV) expressing the glycoprotein (GP) of Ebola virus (EBOV), designated rLa-EBOVGP, and evaluated its biological characteristic in vivo and in vitro.

RESULTS: The introduction and expression of the EBOV GP gene did not increase the virulence of the NDV vector in poultry or mice. EBOV GP was incorporated into the particle of the vector virus and the recombinant virus rLa-EBOVGP infected cells and spread within them independently of exogenous trypsin. rLa-EBOVGP is more resistant to NDV antiserum than the vector NDV and is moderately sensitive to EBOV GP antiserum. More importantly, infection with rLa-EBOVGP was markedly inhibited by IPA3, indicating that rLa-EBOVGP uses macropinocytosis as the major internalization pathway for cell entry.

CONCLUSIONS: The results demonstrate that EBOV GP in recombinant NDV particles functions independently to mediate the viral infection of the host cells and alters the cell-entry pathway.

PLOS Pathog. 2013;9(10):e1003677.doi:10.1371/journal.ppat.1003677.Epub 2013 Oct 17.

Ebola virus RNA editing depends on the primary editing site sequence and an upstream secondary structure.

Mehedi M, Hoenen T, Robertson S, Dolan MA, Taylor T, Falzarano D, Ebihara H, Porcella SF, Feldmann H.

This is achieved RNA editing, during which non-template adenosine residues are incorporated into the EBOV mRNA at an editing site encoding for 7 adenosine residues. However, the mechanism of EBOV RNA editing is currently not understood.

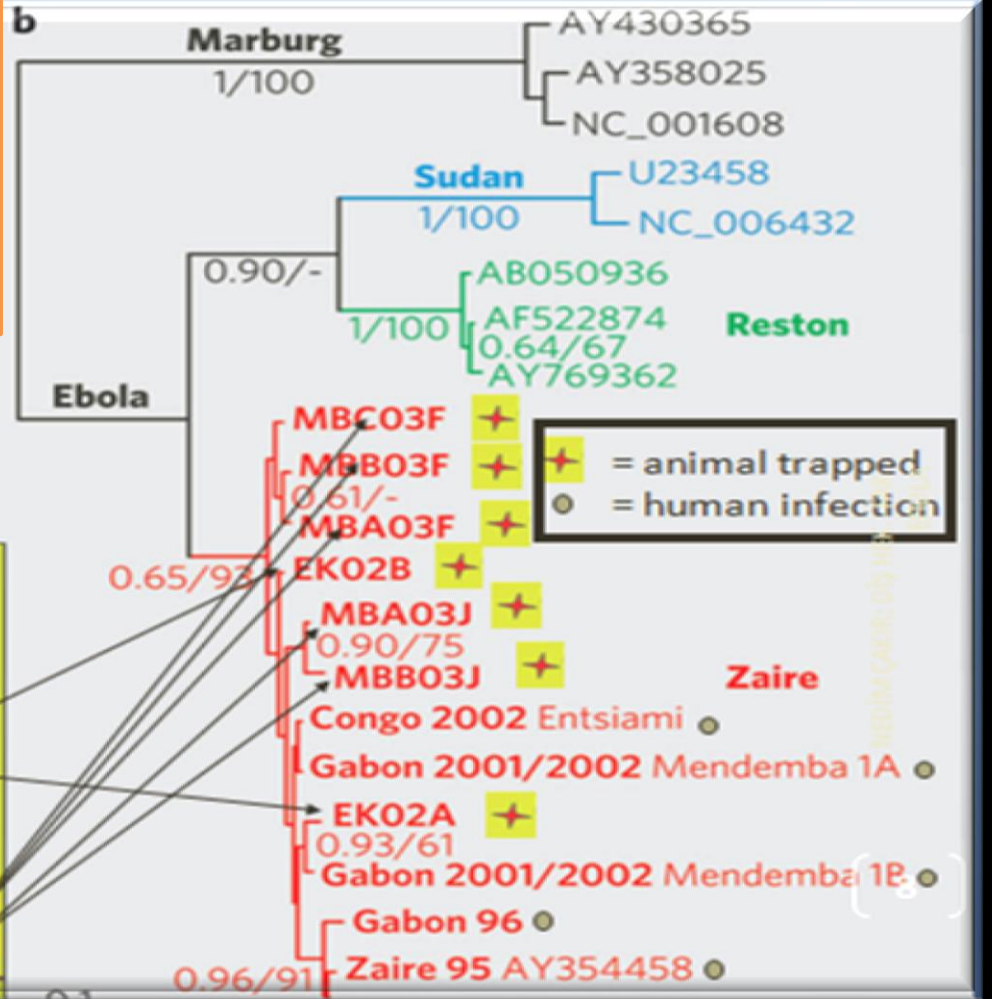
Ebola virüsü

- 5 ayrı tür

- Bundibugyo (BDBV)
 - Zaire ebolavirus (EBOV)
 - Sudan ebolavirus (SUDV)
 - Reston ebolavirus (RESTV)
 - Tai Forest ebolavirus (TAFV)
- Afrika'da endemik
- Filipinler ve Çin'de sporadik

Ebola virüsü

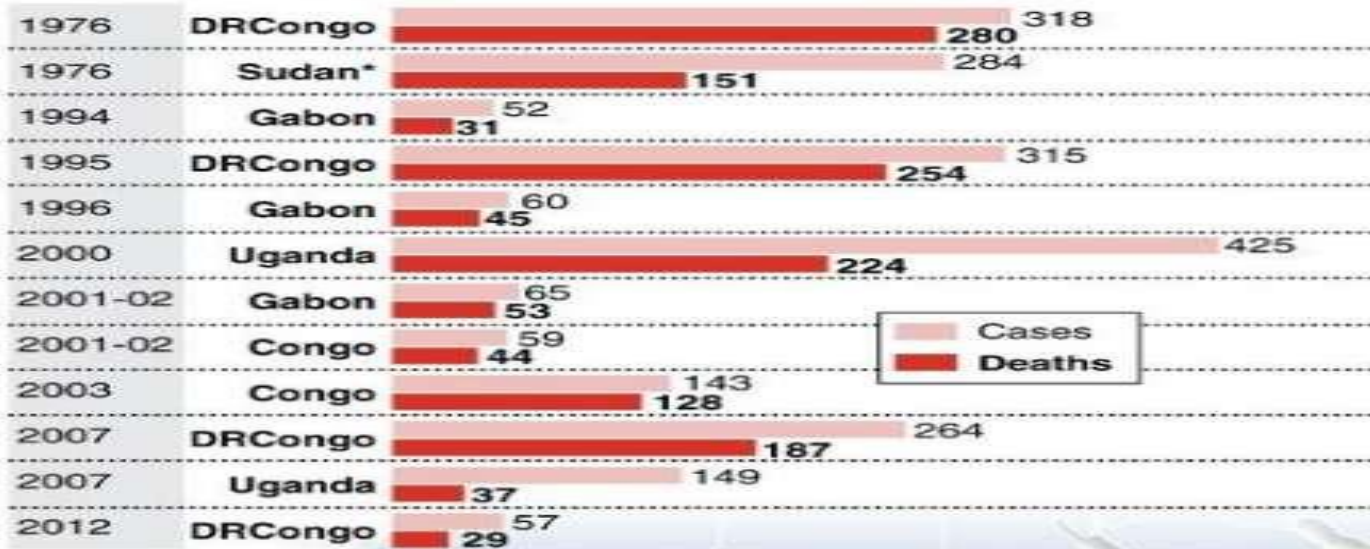
DNA akrabalık ilişkisi eski salgınla genetik ilişkisi olduğunu gösteriyor



Tarihçe

Previous major Ebola outbreaks

The latest cases are the first in West Africa

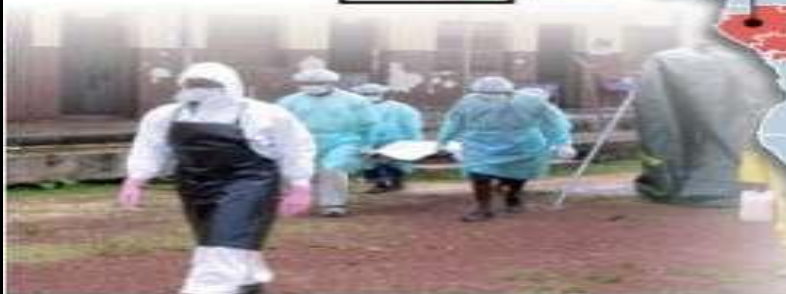


*Outbreak in South Sudan



Source: WHO

AFP



Tarihçe

Tarih	Ülke	Tür	Vaka Sayısı	Ölüm Sayısı	Ölüm Oranı
1976	Zaire	ZEBOV	318	280	88%
1976	Sudan	SEBOV	284	151	53%
1979	Sudan	SEBOV	34	22	65%
1994	Gabon	ZEBOV	52	31	60%
1994	Fil Dişi Sahili	TAFV	1	0	0%
1995	Zaire	ZEBOV	315	250	79%
1996	Gabon	ZEBOV	37	21	57%
1996–1997	Gabon	ZEBOV	60	45	75%
2000–2001	Uganda	SEBOV	425	224	53%
2001–2002	Gabon Kongo	ZEBOV	122	96	79%
2002–2003	Kongo	ZEBOV	143	128	90%

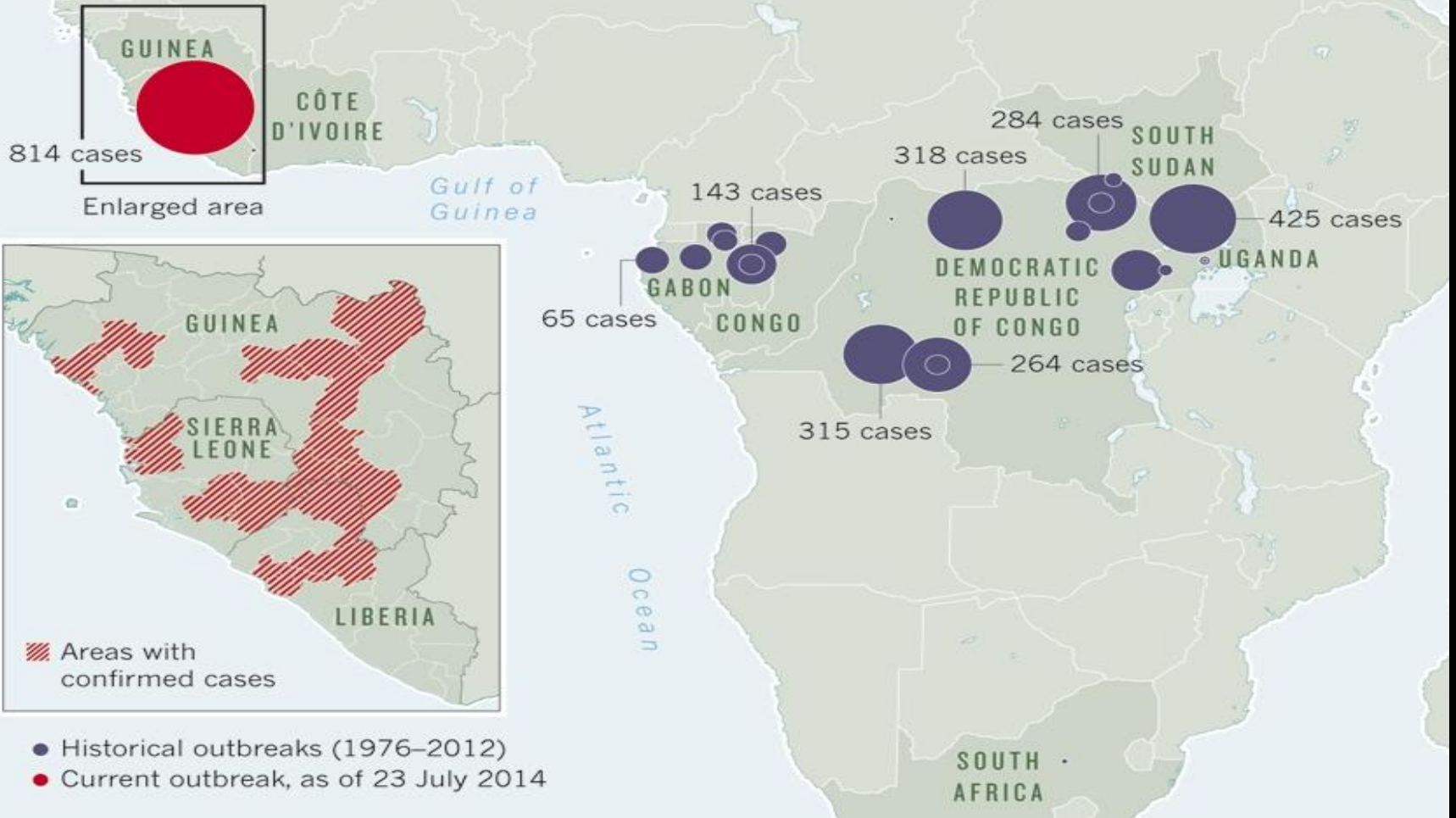
Tarihçe

Tarih	Ülke	Tür	Vaka Sayısı	Ölüm Sayısı	Ölüm Oranı
2004	Sudan	SEBOV	17	7	41%
2007	Demokratik Kongo Cumhuriyeti	ZEBOV	264	187	71%
2007–2008	Uganda	BDBV	149	37	25%
2012 Haziran–Ağu	Uganda	SEBOV	24	17	71%
2013–2014 Aralık–Ağu	Gine, Liberya Sierra Leone, Nijerya	ZEBOV	1848	1013	64%

Tarihçe

MAJOR OUTBREAKS

With more than 800 confirmed cases so far, the current Ebola virus outbreak is the largest in recorded history. After the first cases were reported in Guinea in March, the virus spread to neighbouring Liberia and Sierra Leone. Previous outbreaks were largely in central Africa.



Güncel Ebola

- Salgın Gine'de 2014 başında başladı
- Sierra Leone ve Liberia'ya sıçradı
- Bir hasta Nijerya'ya hastalığı taşıdı.



WHO: Ebola Response Roadmap Situation Report 18 September 2014

Table 1: Probable, confirmed, and suspected cases in Guinea, Liberia, and Sierra Leone as at end 14 September 2014

Country	Case definition	Cases			Deaths
		Total	Last 21 days	Last 21 days/Total (%)	
Guinea	Confirmed	750	266	36%	435
	Probable	162	21	13%	161
	Suspected	30	25	83%	5
	All	942	312	33%	601
Liberia	Confirmed	812	462	57%	631
	Probable	1233	596	46%	518
	Suspected	675	398	59%	310
	All	2710	1429	52%	1459
Sierra Leone	Confirmed	1513	584	39%	517
	Probable	37	0	0%	34
	Suspected	123	69	56%	11
	All	1673	653	39%	562
Total		5335	2394	45%	2622

Data are based on official information reported by Ministries of Health. These numbers are subject to change due to ongoing reclassification, retrospective investigation and availability of laboratory results.

Epidemiyoloji



Epidemiyoloji



Epidemiyoloji

- İnkübasyon süresi: 2-21 gün
- İnkübasyon süresinde BULAŞTIRICILIĞI YOK !!!
- Meyve yarasaları doğal konak
- Primatlar enfekte olan hayvanlar

BRIEF COMMUNICATIONS

Fruit bats as reservoirs of Ebola virus

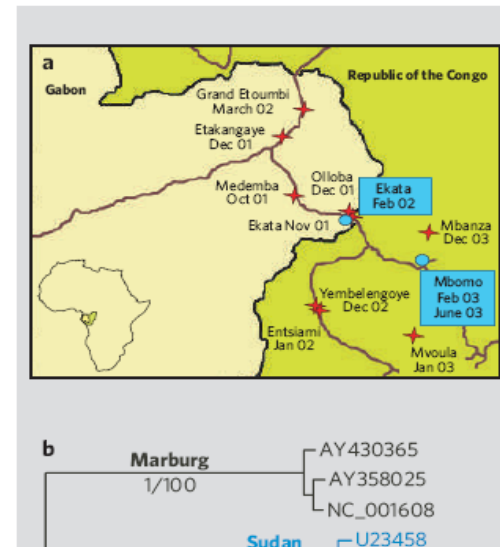
Bat species eaten by people in central Africa show evidence of symptomless Ebola infection.

The first recorded human outbreak of Ebola virus was in 1976, but the wild reservoir of this virus is still unknown¹. Here we test for Ebola in more than a thousand small vertebrates that were collected during Ebola outbreaks in humans and great apes between 2001 and 2003 in Gabon and the Republic of the Congo. We find evidence of asymptomatic infection by Ebola virus in three species of fruit bat, indicating that these animals may be acting as a reservoir for this deadly virus.

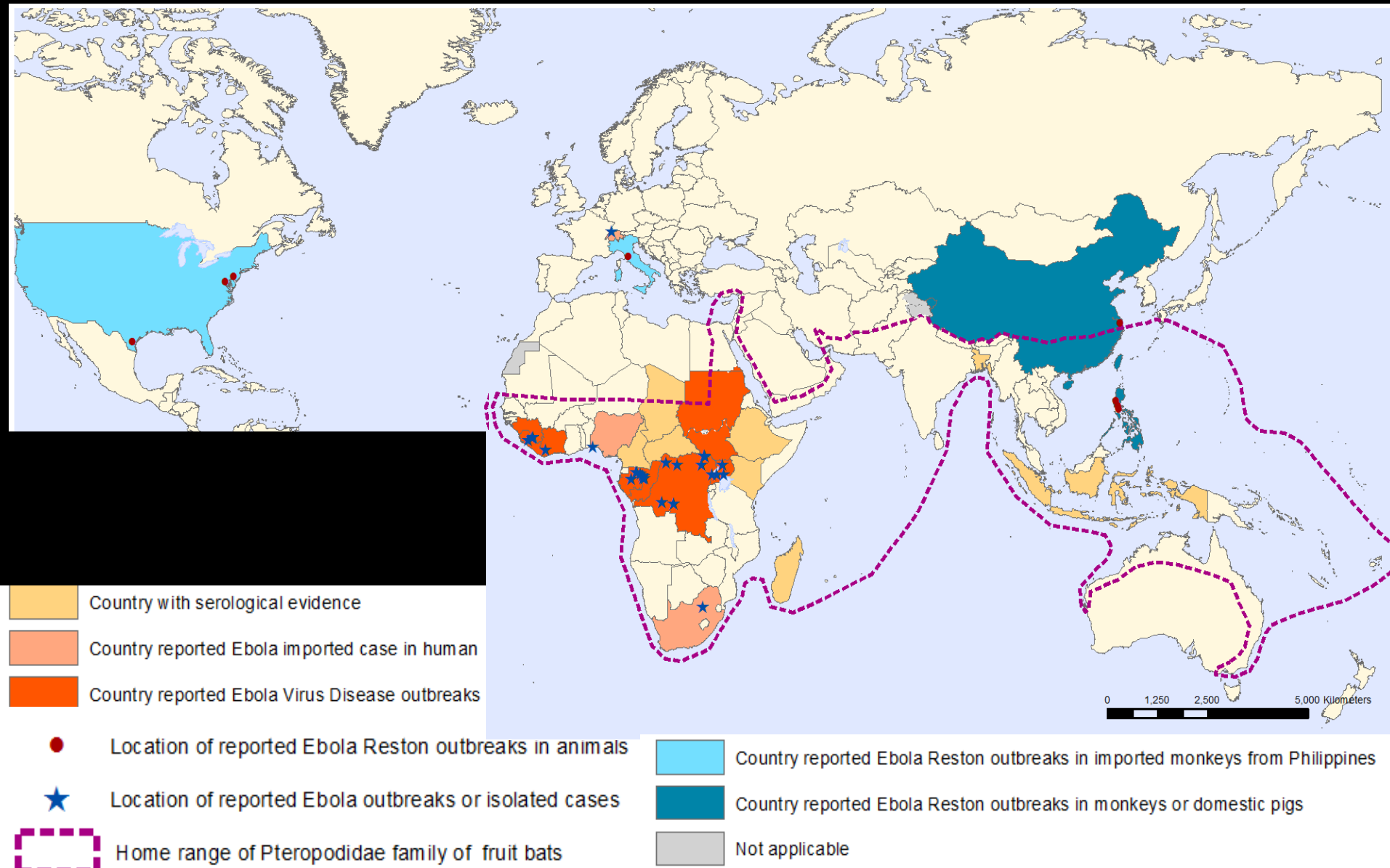
Human Ebola outbreaks that occurred between 2001 and 2005 in Gabon and the Republic of the Congo were linked to concurrent outbreaks that devastated local gorilla and chimpanzee populations^{2,3}. To identify the viral reservoir, we undertook three trapping expeditions in areas close to infected gorilla

be because PCR-positive bats were recently infected and were tested before they developed a detectable immune response. Alternatively, it could be that differences in the virulence of Ebola virus strains led to different immunological responsiveness and viral replication patterns. Of the bat species collected at Mbomo in February 2003, 7 of 31 (22.6%) and 0 of 10 (0%) were PCR-positive and IgG-positive, respectively, but five months later the corresponding results were 4 of 184 (2.2%) and 12 of 160 (7.5%). These opposite trends in the PCR and serological results are consistent with the first hypothesis.

Each of the three bat species has a broad geographical range that includes regions of Africa where human Ebola outbreaks occur⁵ (Fig. 1c). Our findings support results of



Geographic distribution of Ebola virus disease outbreaks in humans and animals



Epidemiyoloji

- Dünyada şempanze ve goril popülasyonunun % 80'nin yaşadığı yerlerde salgınlar görülüyor
- Primat leşlerinde ve insanlardaki virüs genetiği aynı

BREVIA

Ebola Outbreak Killed 5000 Gorillas

Magdalena Bermejo,^{1,2*} José Domingo Rodríguez Teijeiro,² Germán Illera,¹ Alex Barroso,² Carlos Villá,³ Peter D. Walsh⁴

Over the past decade, the Zaire strain of Ebola virus (ZEBOV) has emerged repeatedly in Gabon and Congo. During each human outbreak, carcasses of western gorillas (*Gorilla gorilla*) and chimpanzees (*Pan troglodytes*) have been found in neighboring forests (1). Opinions have differed as to the conservation implications. Were these isolated mortality events of limited impact (2)? Was ZEBOV even the cause (3)? Or, were they part of a massive die-off that threatened the very survival of these species (4)? Here, we report observations made at the L'Essi Sanctuary in northwest Republic of Congo, where ZEBOV was the confirmed cause of ape die-offs in 2002 and 2003 (5). Our results strongly support the massive die-off scenario, with gorilla mortality rates of 90 to 95% indicated both by observations on 238 gorillas in

each group was predicted by the number of home ranges separating it from the first group to experience deaths (Fig. 1A). In particular, the estimated time lag between deaths in successive

(Fig. 1C). This encounter rate difference is not explained well by hunting, because the western zone experienced substantially lower hunting pressure than that in the eastern zone (table S1). If we conservatively assume that the western zone held pre-Ebola ape densities only half as high as the 4.4 gorillas/km² typical of the sanctuary, then the east-west difference in nest encounter rate implies that ZEBOV killed about 5000 (minimum 3900 (Materials and Methods)). We lack the density data necessary to make a similar estimate for chimpanzees, but east-west differences in nest encounter rate (Fig. 1D) imply a ZEBOV-induced decline of about 83% (table S1).

We hope this study dispels any lingering doubts that ZEBOV has caused massive gorilla die-offs. The L'Essi outbreaks killed about as many gorillas as survive in the entire eastern gorilla species (*Gorilla beringei*). Yet L'Essi represents only a small fraction of the western gorillas killed by ZEBOV in the past decade or indeed of the number at high risk in the next 5 years. Add commercial hunting to the mix, and we have a recipe for rapid ecological extinction. Ape species that were abundant and widely distributed a decade ago are rapidly being reduced to tiny remnant populations.

References and Notes

Epidemiyoloji

ÜLKE 2014	NÜFUS MİL.	VAKA	EX	100.000 VAKA	100.000 EX	EX ORANI	GSMH USD
Gine	11.4	*506	*373	*4	*3	*% 73.7	491
		*942	*601	*8.3	*5.2	*% 63.8	
		*1008	*632	*8.8	*5.5	*% 62.7	
Liberya	4.19	*599	*323	*14	*7	*% 53.9	413
		*2710	*1459	*64.7	*34.8	*% 53.8	
		*3022	*1578	*72.1	*37.6	*% 52.2	
S.Leone	5.9	*730	*315	*12	*5	*% 43.1	634
		*1673	*562	*28.4	*9.5	*% 33.5	
		*1813	*593	*30.7	*10	*% 32.7	
Nijerya	168.8	*13	*2	*0.0077	*0.0012	*%15.3	775
		*21	*8	*0.012	*0.0047	*% 38	
		*21	*8	*0.012	*0.0047	*% 38	

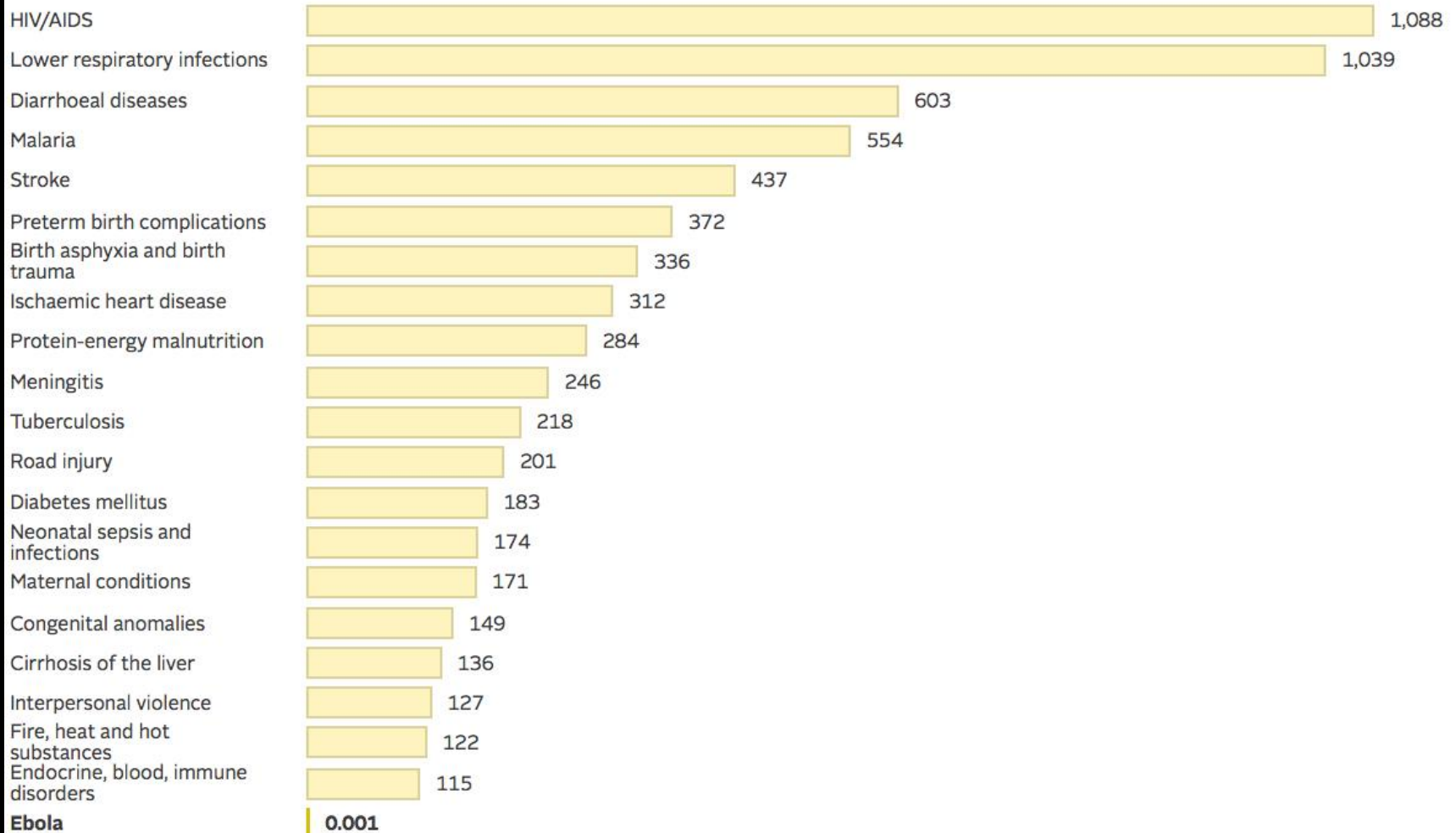
* 08 Ağustos2014 * 18 Eylül 2014 * 19 Eylül 2014


$$E=mc^2$$

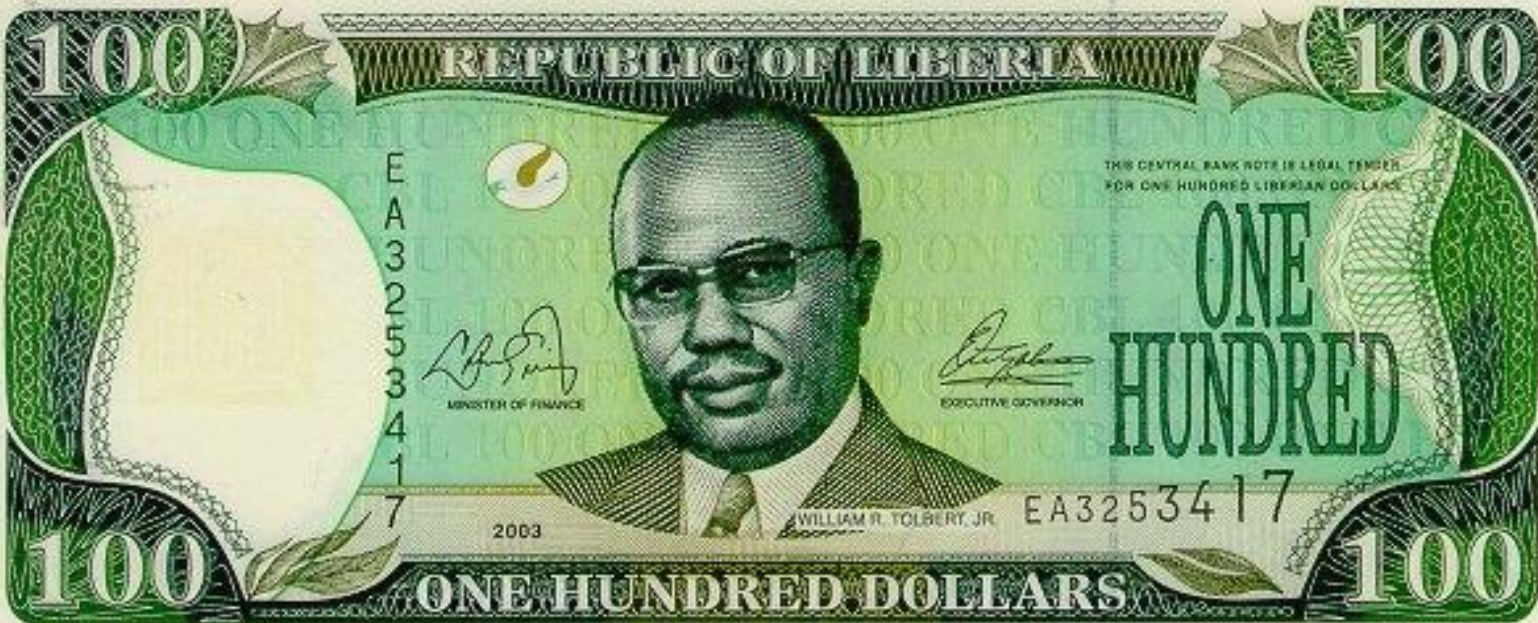
Albert Einstein

Leading causes of death in Africa

Deaths (000s)



Source: WHO 2012



100

REPUBLIC OF LIBERIA

100

EA3253417

2003

[Signature]
MINISTER OF FINANCE



[Signature]
EXECUTIVE GOVERNOR

WILLIAM R. TOLBERT, JR.

EA3253417

THIS CENTRAL BANK NOTE IS LEGAL TENDER FOR ONE HUNDRED LIBERIAN DOLLARS

ONE HUNDRED

100

ONE HUNDRED DOLLARS

100

Ebola virüsü nasıl bulaşıyor?

- Direkt temas ile :
 - ① Hasta veya ex olan kişinin vücut sıvıları ile (kan, kusmuk, mide içeriği, idrar, feçes, sperm ve diğer sıvılar)
 - ② Virüs ile kontamine olmuş objelerle (enjektör, tıbbi malzemeler)
 - ③ Enfekte hayvanlar ile (kan, vücut sıvıları ve enfekte etin tüketilmesi)

Vaka Tanımları

- **Epidemiyolojik Kriterler:** Semptomlar ortaya çıkmadan önceki 21 gün içinde;
 - Doğrulanmış veya şüpheli Ebola vakasının kan veya diğer vücut sıvıları ile temas
 - Ebola vakasının aktif olarak yayılımının olduğu bölgede yaşıyor olmak
 - Bulaşın aktif olduğu bölgeye seyahat etmek
 - Endemik bölgede yarasa, kemirgen, maymun veya şempanzeler ile doğrudan temas

Vaka Tanımları

- **Klinik Kriterler:** $\geq 38.5^{\circ}\text{C}$ ateş ile birlikte, aşağıdaki klinik bulgulardan en az birisinin varlığı
 - Ciddi baş ağrısı,
 - Kas ağrısı,
 - Aşırı halsizlik,
 - Bulantı, Kusma, İshal,
 - Karın ağrısı,
 - Açıklanamayan kanamaların varlığı,
 - **SEBEBİ AÇIKLANAMAYAN ÖLÜM**

Vaka Tanımları

ŞÜPHELİ VAKA

- Yukarıda belirtilen “Epidemiyolojik Kriterler”den
 - en az birisinin varlığında klinik kriterlerden
 - $\geq 38.5^{\circ}\text{C}$ ateş ile birlikte diğer klinik bulgulardan en az birisinin bulunduğu veya
 - sebebi açıklanamayan ölüm olan vakadır.

Vaka Tanımları

KESİN VAKA

- Şüpheli vaka tanımına uyan ve Ebola Virus Hastalığı laboratuvar tanı testleri ile doğrulanan vakadır
- **Sıtma ayırıcı tanısı özellikle yapılmalıdır**

Ayırıcı Tanı

- Sıtma
- Şigelloz
- Kolera
- Tifo
- Leptospiroz
- Riketsiyoz
- Akut Hepatitler
- Diğer viral hemorajik ateşler

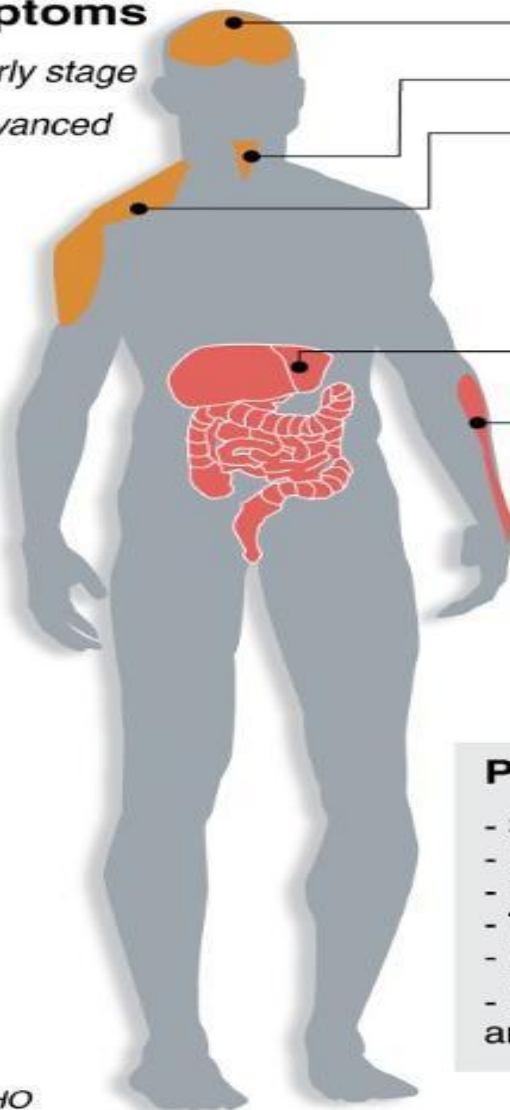
Ebola: fighting a killer virus

There is no vaccine and no cure for the disease

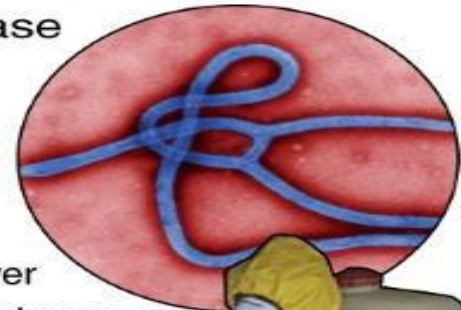
Symptoms

■ *Early stage*

■ *Advanced*



- Headache
- Sore throat
- Muscle pain
- Sudden fever
- Intense weakness
- Impaired kidney and liver
- Rash
- Vomiting
- Internal and external bleeding
- Diarrhoea



Preventive measures

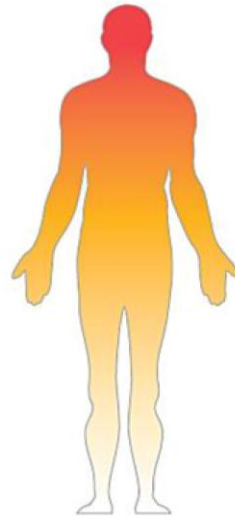
- **Stop the consumption** of animal meat
- **Isolate** the sick
- **Prompt disposal** of victims' bodies
- **Trace** those who had contact with infected
- **Disinfect** homes of the dead and the sick
- **Protective clothing** for health care workers, anyone handling infected animals

Virus's typical path through a human



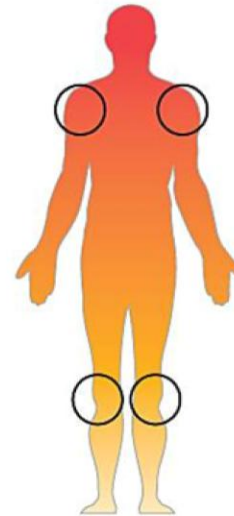
Day 7-9

Headache, fatigue, fever, muscle soreness



Day 10

Sudden high fever, vomiting blood, passive behavior



Day 11

Bruising, brain damage, bleeding from nose, mouth, eyes, anus



Day 12

Loss of consciousness, seizures, massive internal bleeding, death

NOTE: Symptoms can start as early as two days after infection.

SOURCES: World Health Organization; BBC

Melina Yingling/McClatchy-Tribune

Tanı

İnfeksiyonun Zamanı	Kullanılabilir Tanı Yöntemleri
Semptomların olduğu ilk günlerde	Elisa , PCR, Virüs izolasyonu
Hastalığın geç evresi ve iyileşenlerde	IgM ve IgG Antikorları
Retrospektif	İmmunohistokimya, PCR, Virüs izolasyonu

Tedavi

- Hayvanlar üzerinde etkili olduđu ispatlanmış tedavi seçeneđi var
- Ancak insanlar üzerinde henüz kullanılmamış



Contents lists available at ScienceDirect

Antiviral Research

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

Meeting Report

Meeting report: 27th International conference on antiviral research

R. Anthony Vere Hodge *

Vere Hodge Antivirals Ltd, Old Denshott, Leigh, Reigate, Surrey, UK

- Ebola ve Marburg virüslerine karşı etkili **BCX4430** ilaç geliřimi, büyük ilgi çekti
- Kemirgen ve primatlarda
 - Deęişik dozlarda 30, 20, 3.3 ve 1.1 mg
 - Hayatta kalım %100, %100, %95 ve %83

Tedavi

- Destek tedavisi
 - Sıvı replasmanı
 - Oral ve/veya i.v beslenme
 - Analjezik
 - GIS / Anksiyete / Ajitasyon

Ebola Vaccination: If Not Now, When? FREE ONLINE FIRST

Alison P. Galvani, PhD; Martial L. Ndeffo-Mbah, PhD; Natasha Wenzel, MPH; and James E. Childs, PhD

[\[+\] Article and Author Information](#)

Ann Intern Med. Published online 21 August 2014 doi:10.7326/M14-1904

Text Size: [A](#) [A](#) [A](#)

- Although no Ebola vaccines are currently licensed, many candidates have been developed in the past decade. A DNA vaccine has been shown to be safe and immunogenic in a phase 1 clinical trial .
- In addition, a therapeutic vaccine based on recombinant vesicular stomatitis viruses (rVSVs) expressing Ebola virus surface glycoprotein was found to confer prophylactic and post exposure protection in nonhuman primates .
- Despite the promise of these and other Ebola vaccine candidates, none have advanced to late-stage human trials and licensure.

Table. Viable Ebola Vaccine Candidates

Mechanism	Properties	Vaccination Scenario	Reference
rVSV + ZEBOV-GP	Trials in NHPs elicited immunogenic response against lethal and aerosol challenge. Conveyed protection in Ebola-exposed and immunocompromised NHPs. Potential for oral administration.	Suited for outbreak response, including postexposure prophylaxis. Also appropriate for use in immunocompromised populations, such as those with a high prevalence of HIV.	3, 7
rRABV + ZEBOV-GP	Trials in NHPs elicited immunogenic response against lethal challenge.	Suited for human and wildlife vaccination. Dual RABV/EBOV vaccine may be more acceptable in endemic areas.	8
DNA + rAd5 + ZEBOV-GP, rAd5 + ZEBOV-GP	Safe and immunogenic in phase 1 clinical trials. Multiple vaccinations may be required. Possible interference with preexisting immunity to Ad5.	Preparedness strategies for health care workers and high-risk populations.	2
Virus-like particles + ZEBOV-GP + ZEBOV-NP + ZEBOV-VP40	Trials in NHPs elicited immunogenic response against lethal challenge. Virus-like particles can be produced in insect cells, making them suitable for large-scale production.	Preparedness strategies for health care workers and high-risk populations.	9
rHPIV3 + ZEBOV-GP	Trials in guinea pigs and NHPs elicited immunogenic response against lethal challenge. Potential for needle-free administration.	Preparedness strategies for health care workers and high-risk populations.	10
rCMV + ZEBOV-NP	Trials in mice elicited immunogenic response against lethal challenge. Highly species-specific.	Suited for great ape vaccination in endemic areas.	6
rEBOV subunit vaccine + TLR agonist	Trials in mice elicited immunogenic response against lethal challenge. Subunit vaccines stable for storage and delivery at ambient temperatures.	Suited for stockpiling and vaccine delivery.	5

GP = glycoprotein; NHP = nonhuman primate; NP = nucleoprotein; rAd5 = recombinant adenovirus serotype 5; rCMV = recombinant cytomegalovirus; rEBOV = recombinant Ebola virus; rHPIV3 = recombinant human parainfluenza virus type 3; rRABV = recombinant rabies virus; rVSV = recombinant vesicular stomatitis virus; TLR = Toll-like receptor; ZEBOV = Zaire ebolavirus.

Korunma

- Aşının ve etkin tedavisi olmaması nedeni ile risk faktörlerini bilerek korunma hastalığın yayılmasını ve ölümleri en aza indirecek tek yoldur

Korunma

- Yaban hayatı ve insanlar arasında riski en aza indirmenin yolları
 - Yaban hayatından insana bulaş
 - Avcılar
 - Temasin azaltılması
 - Tüketim

Korunma

- İnsanlar arasında riski en aza indirmenin yolları
 - Yakın temastan kaçınma
 - Hastanın sekresyonları ile temas etmeme
 - Koruyucu ekipman kullanımı
 - El yıkama

Korunma

- Salgın tespit edilen ülkede halkın bilgilendirilmesi
 - Bulaş yolları
 - Defin işlemleri

Korunma



Korunma

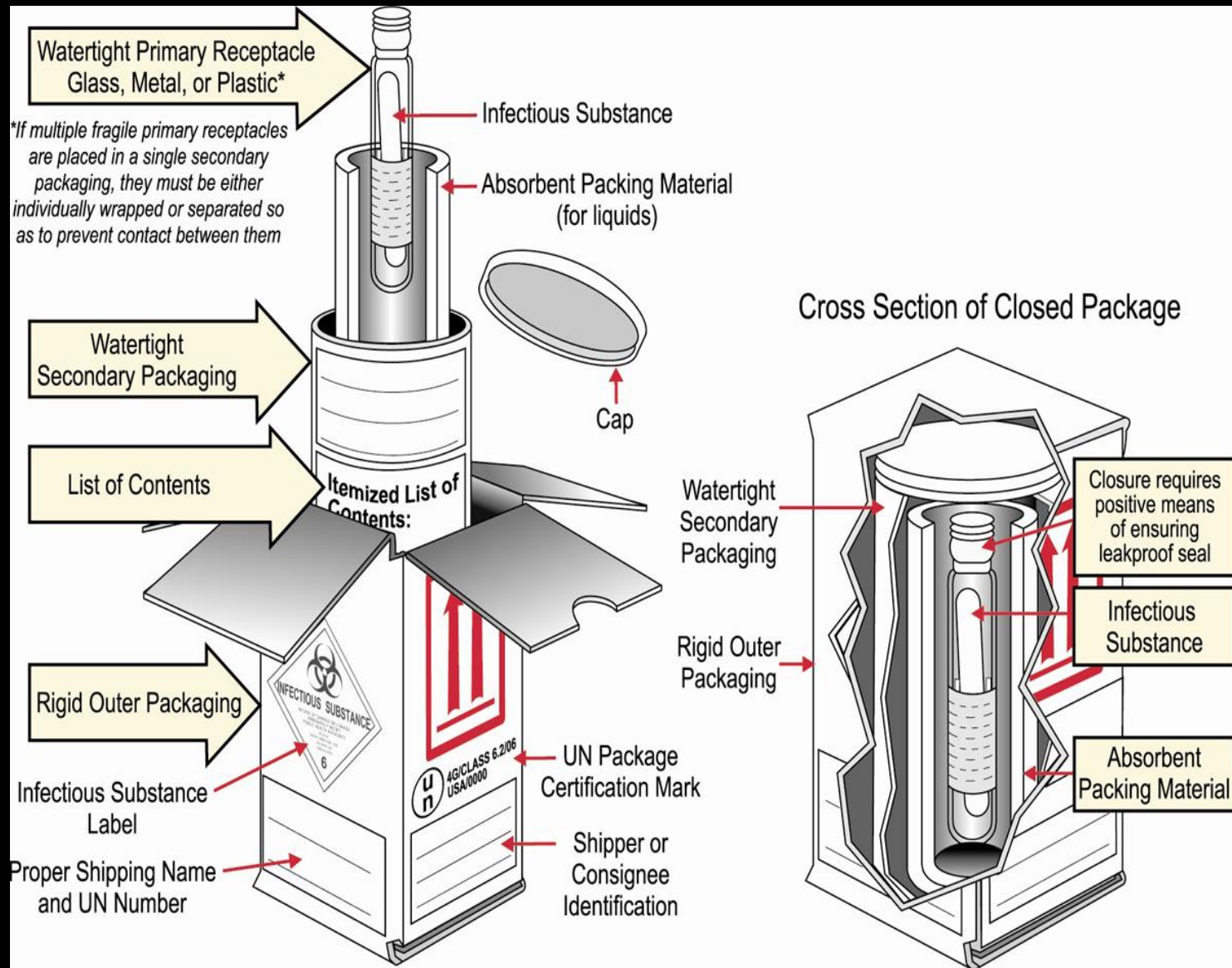
- Sağlık çalışanına bulaş bildirilen vakalarda infeksiyon kontrol önlemlerinin uygulanmadığı gösterilmiş
- Başlangıç semptomları nonspesifik olduğundan her hastaya yaklaşırken standart önlemlere kesinlikle uyulmalı
 - El yıkama
 - Damlacık önlemleri
 - Kişisel koruyucu ekipman

Korunma

Table 2: Ebola infections in healthcare workers as at end 14 September 2014

Country	Case definition	Cases			Deaths
		Total	Last 21 days	Last 21 days/total cases (%)	
Guinea	Confirmed	52	9	17%	22
	Probable	8	0	0%	8
	Suspected	1	1	100%	0
	All	61	10	16%	30
Liberia	Confirmed	66	3	4%	56
	Probable	85	18	21%	26
	Suspected	21	0	0%	3
	All	172	21	12%	85
Nigeria	Confirmed	11	2	18%	5
	Probable	0	0	0%	0
	Suspected	0	0	0%	0
	All	11	2	18%	5
Sierra Leone	Confirmed	71	1	1%	30
	Probable	1	0	0%	1
	Suspected	2	0	0%	0
	All	74	1	1%	31
Total		318	34	11%	151

Data reported are based on official information reported by Ministries of Health. These numbers are subject to change due to ongoing reclassification, retrospective investigation and availability of laboratory results.





**Sağlık Personeli
hastadan kaptığı
KKKA'dan öldü!**



Teşekkürler
