Sandfly Fever Turkey virus (SFTV)

“ülkemizde saptanan yeni bir etken”

Uz. Dr. Yavuz UYAR

Refik Saydam Hıfzıssıhha Merkezi
Salgın Hastalıklar Araştırma Md.
Viroloji Referans ve Araştırma Laboratuvarı
Ankara

Sandfly fever virusları

- **Sandfly fever (tatarcık humması) virusları**

  ilk olarak tatarcık sineği türlerinden olan *Phlebotomus papatasi*' den izole edilmiştir.

SFV viruslarının yaptığı hastalık

- sandfly fever
- papatacci fever
- mosquito fever
- febris pappataci
- üç gün ateşi
- phlebotomus fever

Hastalık yaz aylarında phlebotom'ların aktif olduğu dönemde görülür.

Tatarcık Humması klinik bulguları

- İnkübasyon süresi 3–6 gün
- Ateş 39–40°C'ye kadar yükselir yükselir ve6-72 saat içinde bol terleme ile düşer (3 gün ateşi)
- En sık görülen semptomlar;
  - Baş ağrısı
  - İştahsızlık
  - Kırgınlık, miyalji
  - Fotofobi
  - Bel ağrısı, ekstremitelerde katılık
  - Supraorbital veya göz hareketleri ile artan retrobulber ağrı
  - Bulantı, kusma, ishal veya kabızlık, karın ağrısı
  - Konvelesan dönemde depresif semptomlar olabilir

SFV Sicilian/Naples Enfeksiyonu

- Bu viruslar hafif seyirli grip benzeri hastalık oluştururlar
- *Phlebotomus papatasii* isimli vektörün bulunduğu
  - Akdeniz havzası, Orta Doğu, Arap Yarımadası, Kafkasya, Pakistan ve Hindistan'da görülmektedir.
- Sandfly fever Naples ve Sicilian viruslar coğrafik olarak en yaygın görülenlerdir.

Toscana Virus Enfeksiyonu

- TOSV, hafif seyirli grip benzeri bir hastalık tablosu yapar.
  - Menenjit veya meningoensefalit gibi nörolojik hastalıklara da neden olabilir
- İtalya'da çocuklarda
  - bir numaralı ensefalit etkeni olduğu bildirilmiştir
- *Phlebotomus perniciosus* ve *P.perfiliewi* türü vektörün görüldüğü
  - İtalya, İspanya, Portekiz, Kıbrıs adası, Fransa ve Yunanistan'da insan vakalarının görüldüğü rapor edilmiştir.

Emergence of Toscana Virus in Europe

Rémi N. Charrel,* Pierre Gallian,*† José-Maria Navarro-Mari,‡ Loredana Nicoletti,§ Anna Papa,¶
Mária Paz Sánchez-Seco,# Antonio Tenorio,# and Xavier de Lamballerie*

Toscana Virus in Europe

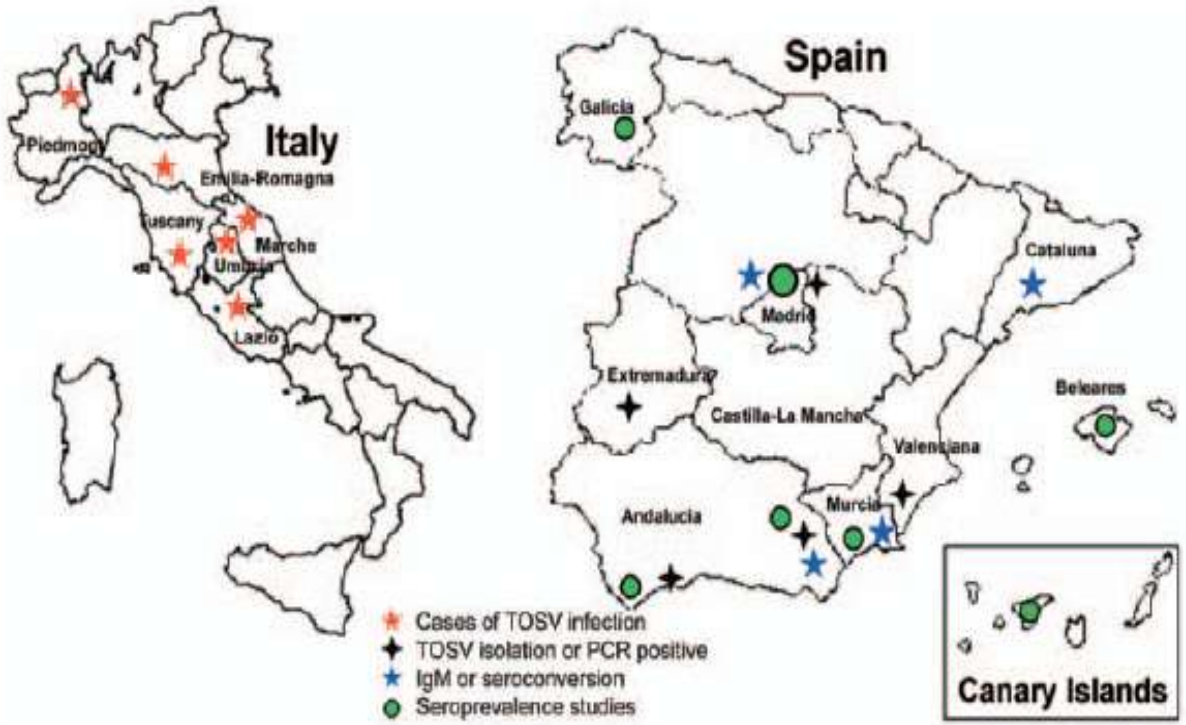


Figure 1. Provinces of Italy and Spain in which clinical cases of Toscana virus (TOSV) infection have been documented, and seroprevalence studies were conducted. PCR, polymerase chain reaction; IgM, immunoglobulin M.

Toscana Enfeksiyonu

- İtalya’da Sandfly vektörlerinin yoğun olarak görüldüğü özellikle ağustos ayında TOSV aseptik menenjit ve meningoensefalit etkeni olarak karşımıza çıkmaktadır.
- İtalya’da yaz aylarında görülen aseptik menenjit olgularınının %80‘inden sorumludur.

Neden önemli?

- Akdeniz ülkelerini her yıl milyonlarca turist ziyaret etmektedir.
- Bu nedenle importe viral hastalıklar içinde en çok görülenlerden biridir.
- İş gücü kaybı
- Panik

Sandfly Fever Virus

Sandfly Fever Virus

- **Phlebovirus genusundan**
- **Phleboviruslar, Bunyaviridea ailesinin 5 genusundan birisidir.**
- Bu virusler “class V” üyesi olup segmentli **negatif zincirli RNA** genomuna sahiptirler.

Group V:
Negative (-)sense RNA Viruses

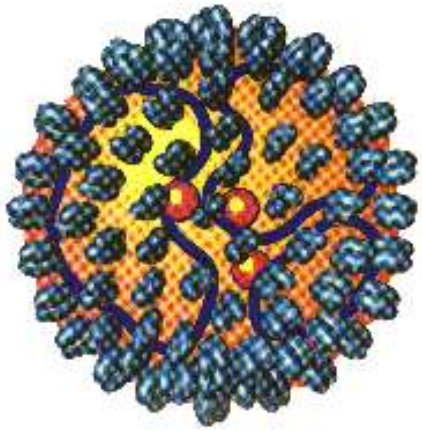
Order Mononegavirales

Family (Subfamily)	Genus	Type Species	Hosts
Bunyaviridae	*Bunyavirus*	*Bunyamwera virus*	Vertebrates
	Hantavirus	*Hantaan virus*	Vertebrates
	Nairovirus	*Nairobi sheep disease virus*	Vertebrates
	Phlebovirus	***Sandfly fever virus***	Vertebrates
	Tospovirus	*Tomato spotted wilt virus*	Plants

Virus Taxonomy: Seventh Report of the International Committee on Taxonomy of Viruses
H.V. Van Regenmortel, D.H.L. Bishop, M. H. Van Regenmortel, Claude M. Fauquet (Eds)

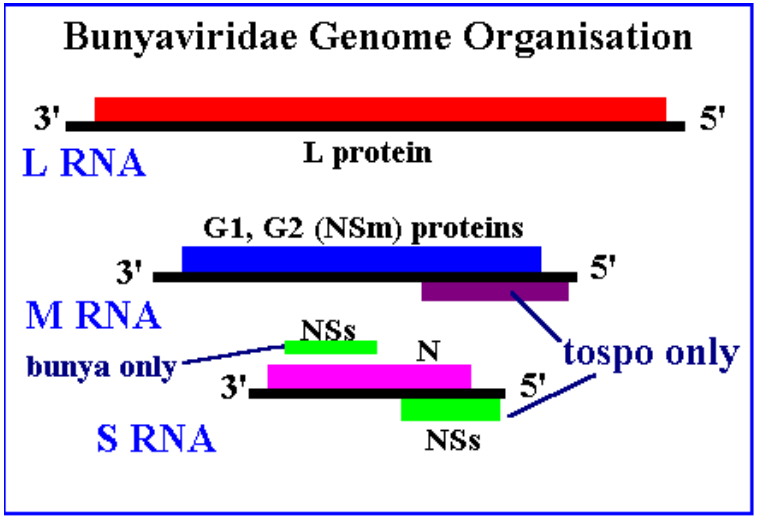
Phlebovirus Morfolojisi

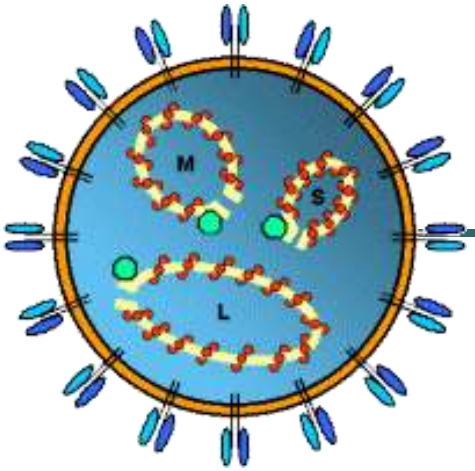
- Yuvarlak
- 80-100 nm çapında, glikoprotein çıkıntılı lipid bir zarfla sarılıdır
- 3 nukleokapsid içerir
- Mol. Ağırlığı 300-400x10^6
- Sitoplazmada çoğalır



Phlebovirus yapısı

- Nükleik Asit
  - %1-2 nukleik asit içerir
  - (-) ssRNA'nın 3 sirkular segmentini içerir
    - L (large, 6.5 - 14.4 kb)
    - M (medium, 3.2 - 6.3 kb)
    - S (small, 0.8 - 2.0 kb)
- Proteinler
  - %50'nin üzerinde protein içerir
  - 2 dış membranla ilişkili glycoprotein (G1, G2)
  - nucleocapsid protein (N)
  - large (L) protein (tahminen bir transkriptaz)
- Lipidler
  - %20-30 lipid içerir

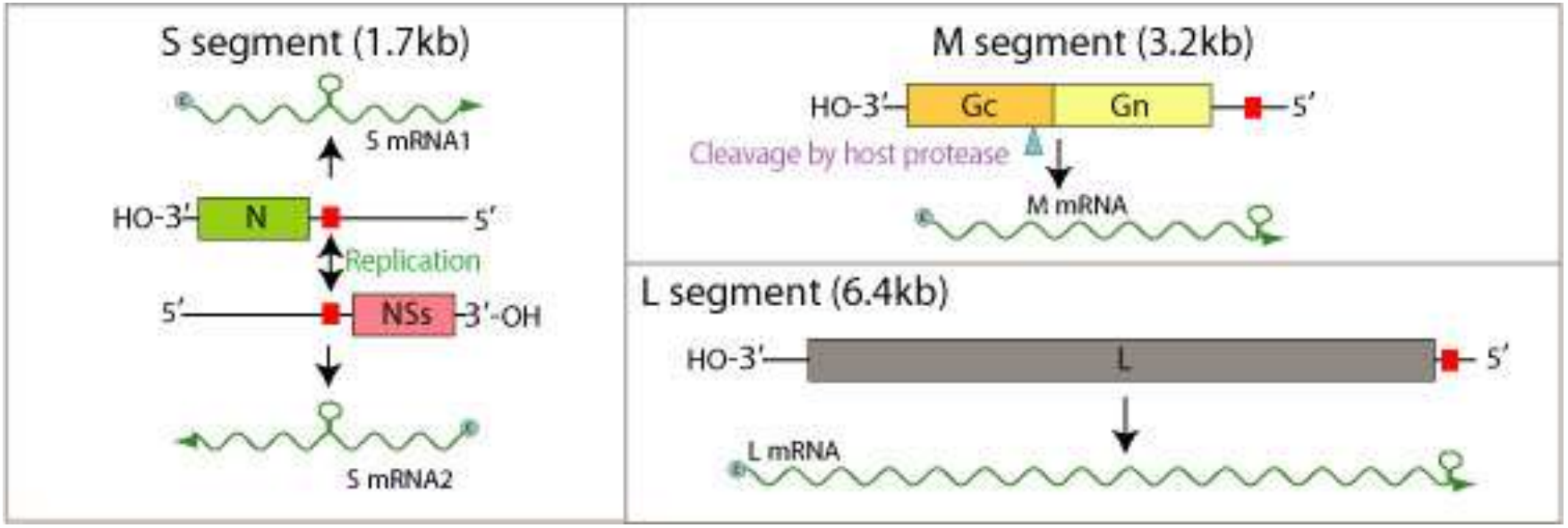




Phlebovirus yapısı

∅ 80–120 nm

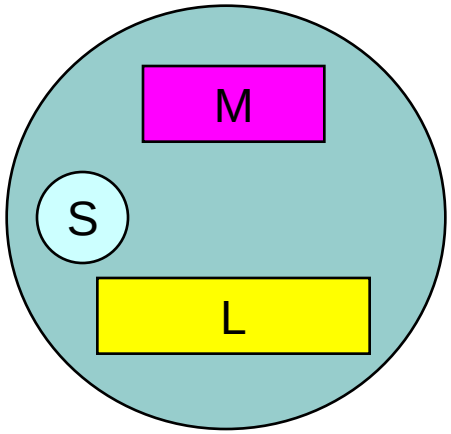
tripartite genome (S-, M-, L-segment)



Sandfly Fever Virus (SFV) Genomik Yapısı

Genom 3 segment içerir:

- small segment (**S**)
  1.7-1.9 kb
- medium sized segment (**M**)
  3.2-4.2 kb
- largest segment (**L**)
  6.4 kb



Small segment (**S**)

- 2 ORF (open reading frame) bölgesi içermektedir.
  - Nükleoprotein (N) 27 kDa
  - Non-structural (NSs) protein 30 kDa
- Beş farklı phlebovirus'un S segmentinin NSs geninden yapılan dizi analizinde;
  - aminoasit benzerlik sadece %17-30 bulunmuştur.
- S (1.7–1.9 kb)

Medium segment (**M**)

- M segment iki glikoprotein olan
  - G1 (56 kDa) ve
  - G2 (59 kDa) nin protein prekürsörlerini kodlamaktadır.
- M (3.2–4.2 kb)

Largest segment (**L**)

- L segmenti 240 kDa'luk RNA polymerase'ı kodlayan tek bir proteini kodlar.
- L (6.4 kb)

Phlebovirus'ler

- Phlebovirus genusu güncel olarak **68 adet antijenik olarak farklı serotipten** oluşmaktadır.
- Bu 68 serotipten sadece **8 tanesi insanlarla ilişkilidir**.
- **Bunlar:**
  - **Sandfly fever Naples**
  - **Sandfly fever Sicilian**
  - **Sandfly fever Toscana**
  - **Sandfly fever Punta Toro**
  - **Alenguer**
  - **Candiru**
  - **Chagres**
  - **Rift Valley Fever**

Phlebovirus'ler

- Bilinen 68 serotip iki gruba ayrılmıştır.

Phlebovirus

Phlebotomus fever virus
(Sandfly grup)
Tatarcık ile geçer
55 üyesi vardır

Uukuniemi grup
Keneler ile geçer
13 üyesi vardır

SFV

En yaygın serotipler:

- **Sandfly Fever Sicilian Virus** (SFSV),
- **Sandfly Fever Naples Virus** (SFNV),
- **Sandfly Fever Toscana Virus** (TOSV)
- **Sandfly Fever Cyprus Virus** (CYPV) serotipleridir

  - CYPV serotipi morfolojik yapısı ve semptomlarıyla SFSV serotipiyle oldukça benzer özelliktedir.

  - **SFSV ve SFNV serotipleri** en yaygın dağılım gösteren tipleridir.

Sandfly Fever Sicilian Virus (SFSV) ve
Sandfly Fever Naples Virus (SFNV) en sık görülen serotiplerdir.

- **SFNV** - Naples:

  1924 yılında İtalya'da Napoli'de görülen salgında Sabin ve Paul tarafından saptanmıştır.

- **SFSV -** Sicilian **:**

  1943 yılında II. Dünya Savaşı Sırasında Palerma, Sicilya'da İtalyan askerlerinden izole edilmiştir.

Sandfly Fever Toscana Virus (TOSV) ve **Sandfly Fever Cyprus Virus** (CYPV)

- **TOSV -** Toscana**:**

  1971 yılında İtalya'nın Tuscany bölgesinde *Phlebotomus perfiliewi*' den izole edilmiştir.

- **CYPV -** Cyprus:

  1985 yılında Kıbrıs adasında İsveçli Birleşmiş Milletler askerlerinde görülmüştür.

Phlebotom'ların (Tatarcık sineğinin) Epidemiyolojisi ve Vektör Özelliği

Serological studies on the epidemiology of sandfly fever in the Old World

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BULL. WORLD HEALTH ORGAN., Vol. 54, 1976

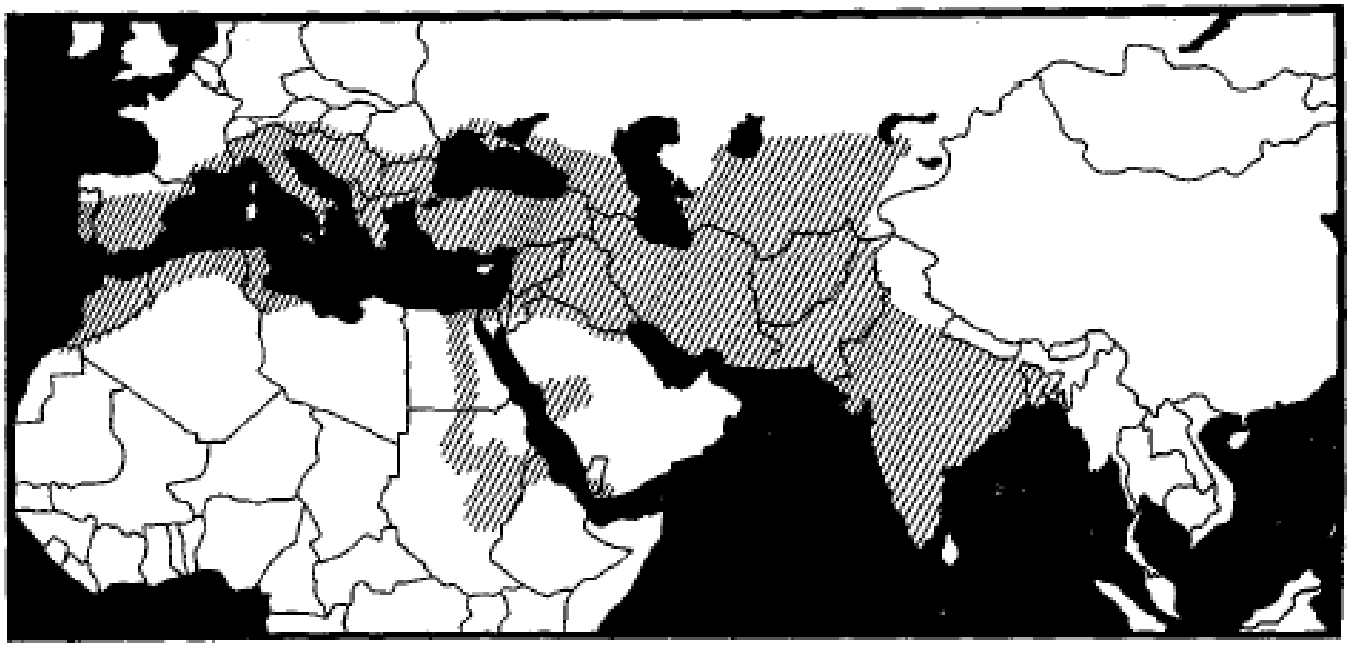

Fig. 2. A partial map of the Old World. The hatched areas represent the known distribution of *Phlebotomus papatasi*. (This map was prepared by Dr D. J. Lewis, Natural History Section, British Museum, London.)

Distribution and altitudinal structuring of phlebotomine sand flies (Diptera: Psychodidae) in southern Anatolia, Turkey: their relation to human cutaneous leishmaniasis

Fatih M. Simsek[1], Bulent Alten[2], Selim S. Caglar[2], Yusuf Ozbel[3], A. Murat Aytekin[2], Sinan Kaynas[2], Asli Belen[2], Ozge Erisoz Kasap[2], Mehmet Yaman[4], and Samiye Rastgeldi[3]

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ABSTRACT: The two Old World genera, *Phlebotomus* and *Sergentomyia*, were both recorded in southern Anatolia in Turkey. *Phlebotomus* species predominated and comprised about 93% of the entire collection (3,172 specimens). Out of the sixteen species identified, two belonged to the genus *Sergentomyia*: *S. dentata* and *S. theodori*. The remaining fourteen species in the genus *Phlebotomus* were grouped under four subgenera including some species that are elsewhere known to act as vectors of human cutaneous leishmaniasis. Most of the *Phlebotomus* were *P. tobbi* (32.5%), but *P. papatasi*, *P. transcaucasicus*, *P. halepensis*, *P. galilaeus*, *P. sergenti*, *P. syriacus*, *P. neglectus*, *P. simici*, *P. alexandri*, *P. similis*, *P. jacusieli*, *P. perfiliewi*, and *P. brevis* were also identified. There were two associations of sand fly fauna with altitudinal gradient; the first one at relatively higher altitudes and the second one at lower altitudes. The transition between these two assemblages was within the range of 800-1,000 m. It is likely that Adana and Hatay provinces are transitional areas between western and eastern Anatolia. Mountains do not appear to be important geographical barriers for sand fly distribution. We also found that the proven vector *P. sergenti* is a widely distributed species throughout southern Anatolia and this species, together with its closely related species *P. similis*, shows sympatry in Konya Province. ***Journal of Vector Ecology* 32 (2): 269-279. 2007.**

Phenotypic variation among local populations of phlebotomine sand flies (Diptera: Psychodidae) in southern Turkey

A. Murat Aytekin[1], Bulent Alten[1], Selim S. Caglar[1], Yusuf Ozbel[2], Sinan Kaynas[1], Fatih M. Simsek[3], Ozge Erisoz Kasap[1], and Asli Belen[1]

[1]*Hacettepe University, Department of Biology, Faculty of Science, ESRL, 06800 Beytepe, Ankara, Turkey*
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Received 26 March 2007; Accepted 8 May 2007

ABSTRACT: The wing-shape morphology of local populations of the medically important phlebotomine sand flies, *Phlebotomus sergenti*, *P. papatasi*, *P. tobbi*, and *P. similis*, were examined in both sexes by using geometric morphometrics. There are three major mountain ranges that may serve as geographical barriers for species distribution in the study area and four main gaps were recognized among these barriers. **We found no statistically important differences in wing morphology** in all examined species in both sexes for all local populations. These results show that the barriers are not sufficient to stop gene flow among local populations of sand flies. The graphical depiction of PCA, CVA, and F-test confirmed our morphometric study suggesting that the difference in wing morphology between *P. similis* and *P. sergenti* indicates that these are clearly different species. These two show sympatric distribution in the Konya Plain of Anatolia. ***Journal of Vector Ecology* 32 (2): 226-234. 2007.**

Keyword Index: Sand flies, *Phlebotomus*, geometric morphometrics, thin plate spline, geographical distribution, south Anatolia.

Türkiye'deki Tatarcık Türleri

Phlebotomus
- *Ph. papatasi*

Paraphlebotomus
- *Ph. sergenti*
- *Ph. similis*
- *Ph. jacusieli*
- *Ph. alexandri*
- *Ph. caucasicus*

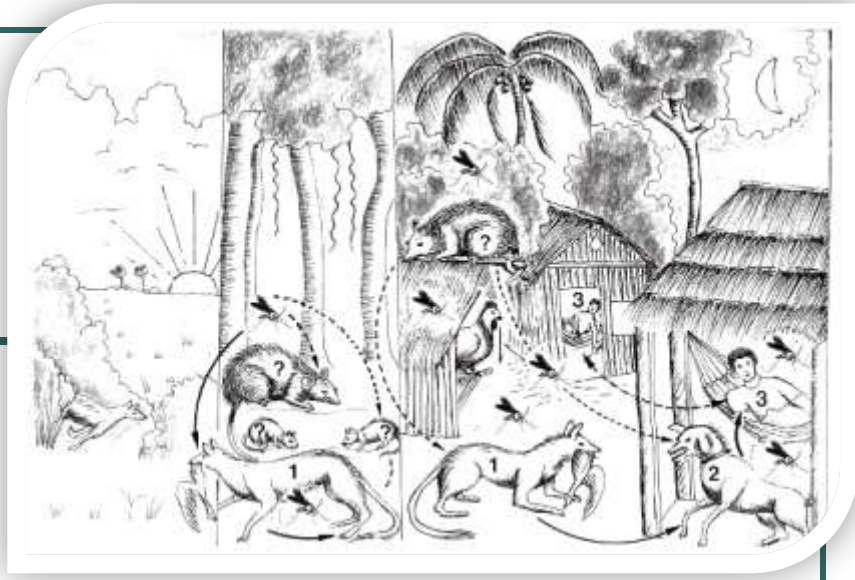
Adlerius
- *Ph. halepensis*
- *Ph. simici*
- *Ph. balcanicus*
- *Ph. kyreniae*
- *Ph. brevis*

Larroussius
- *Ph. syriacus*
- *Ph. neglectus*
- *Ph. perfiliewi*
- *Ph. tobbi*
- *Ph. kandelakii*
- *Ph. mascittii*
- *Ph. transcaucasicus*
- *Ph. galilaeus*

Sergentomyia
- *S. minuta*
- *S. dentata*
- *S. adleri*
- *S. fallax*
- *S. theodori*

Kaynak: Dr. Bülent Alten

Konak ve Habitat Tercihi



- Geceleri aktif duruma geçerler

  Gündüz
  - Ahırlar, bodrumlar
  - ağaç kovukları, duvar çatlakları
  - kemirgen yuvalarında saklanırlar
- İnsanlardan gün batımından gün doğumuna kadar kan emerler
- Gündüz ev-ahır içinde dinlenme yerinde rahatsız edilirlerse sokabilirler
- Birçoğu insanların bulunmadığı dış alanlarda, bir kısmı da evlerde yaşar
- Bazı türler kan emme sonrası yumurta gelişimi tamamlana kadar evde kalır, yumurtlamak için ayrılır

Erişkin Phlebotomus'ların Aktivitelerine Etki Eden Meteorolojik Koşullar

- En aktif oldukları sıcaklık 25 – 28 ^{o}C
- Erişkinler soğuğa çok hassas, 4. evre larvaları ise dayanıklıdır
- Erişkin için ideal nem oranı %50'nin üzeridir
- Açık havada rüzgara çok duyarlı, hızlı rüzgardan kaçmak için yere yakın uçarlar (3 m/s)
- Hafif bir esintide bile sayıları azaldığı için bina içindeki aktiviteleri dışarıdakine göre çok daha fazladır

Phlebotom'lar

- Hastalığın ana vektörü olan, *Phlebotomus papatasi*,
  - tropikal ve Asya,
  - Afrika ve
  - Amerika'nın subtropikal bölgelerinde yaygın olarak bulunmaktadır.
- Avrupa'da ise özellikle Akdeniz havzası ülkelerinde görülmektedir.

Sandfly Fever

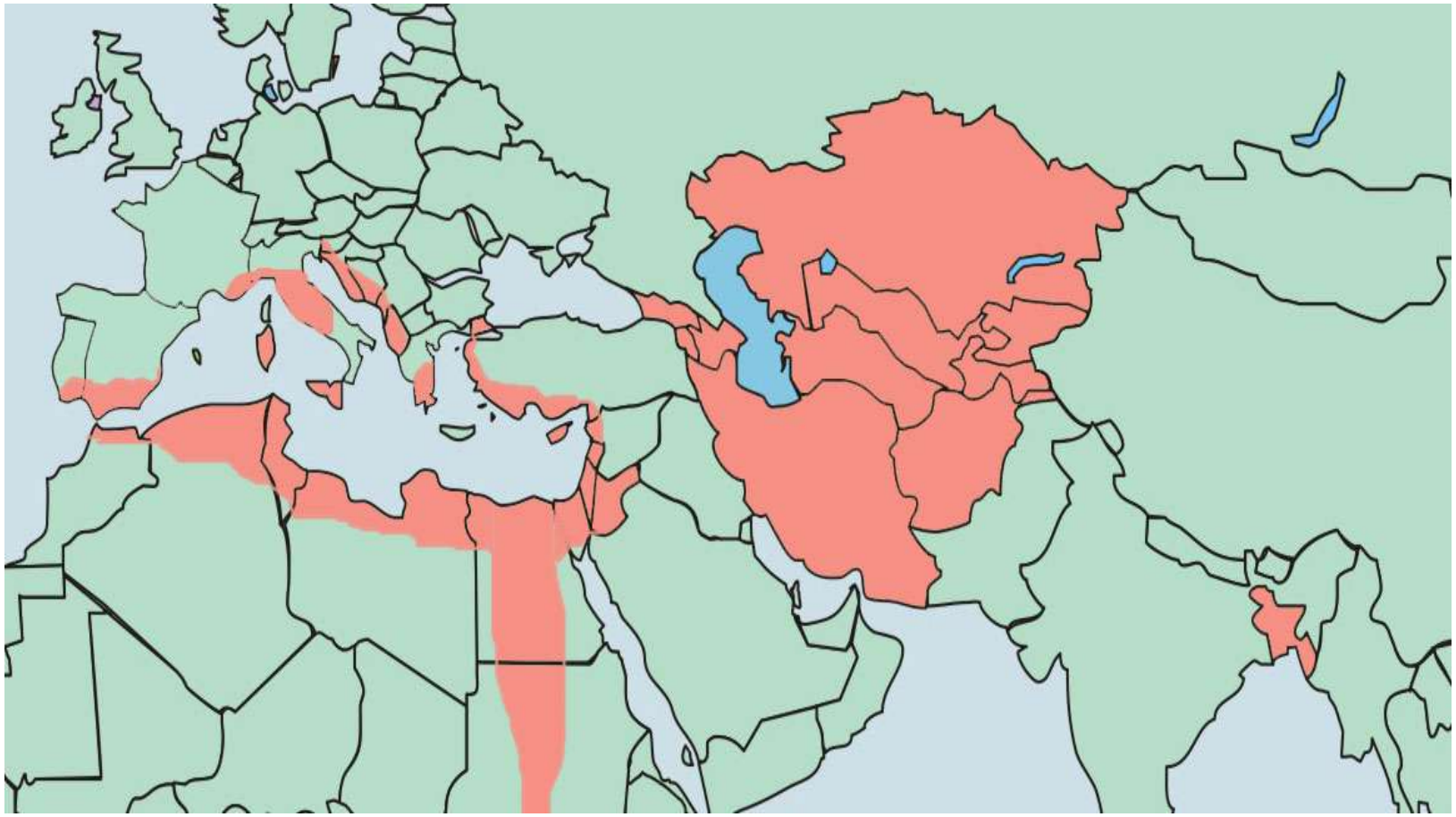
(Tatarcık humması) Epidemiyojisi

SFV

- Endemik bölgelerde
  - Hırvatistan,
  - İtalya,
  - Güney Kıbrıs Rum Kesimi,
  - Mısır
  - virusun yayılımı yüksektir ve **%60**' lara ulaşabilmektedir.
- Akdeniz'e kıyısı olan ülkelerde yaygın olarak görülebilmektedir.

The General Distribution of Sandfly Virus

(www.ENIVD.org 2010)

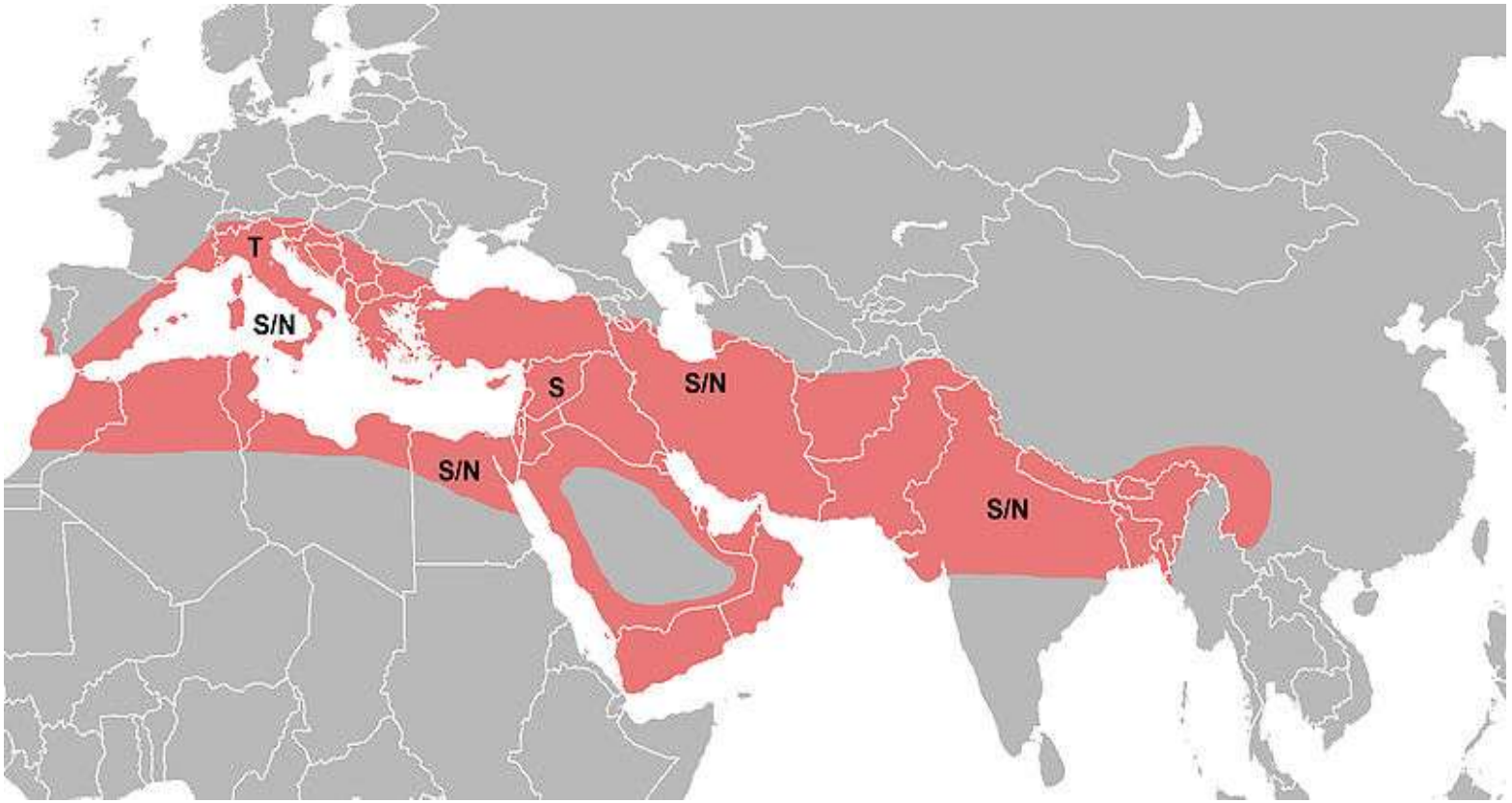


SFV

- **Kıbrıs Rum Kesimi'nde** spesifik IgG seroprevalansı
  - Naples serotipi için **%57**,
  - Sicilian için **%32** ve
  - Toscana için **%20** oranlarında bulunmuştur.
- **İsrail ordusu askerlerinde**
  - SFSV için **%48.2** oranında seropozitiflik saptanmıştır.
- **İtalya'da orman işçilerinde**
  - **%77**'nin üzerinde
- **İspanya'da** yapılan çalışmada seroprevalans
  - **%25** olarak bulunmuştur.
- **Almanya'da**
  - ise bu oran **%0.8'**ler düzeyindedir.

Distribution of sandfly fever (map) by serotype:

T, Tuscany, S, Sicily; N, Naples.



http://upload.wikimedia.org/**wikipedia**/commons/thumb/9/9d/SandFlyFeverMap.jpg/120px-**SandFlyFeverMap**.jpg

Sandfly Fever Naples (SFN) Virus
Sandfly Fever Sicilian (SFS) Virus

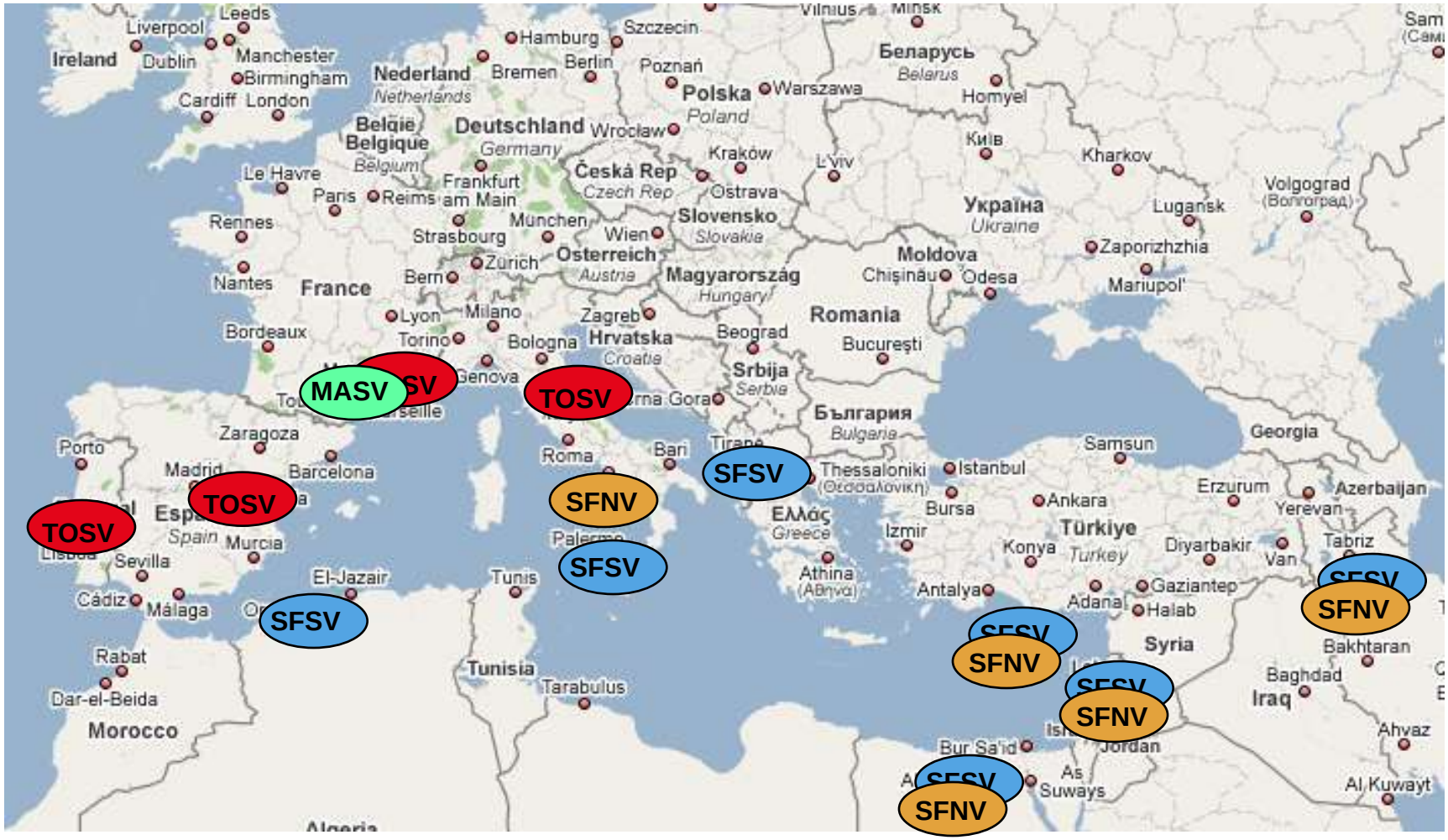
SFN ve SVS

Phlebotomus papatasi

ile bulaşır

Ülke	SFN %	SFS %
İran	17.2	25.4
Yunanistan	24.5	8.5
Mısır	6.7- 59.4	8.9 - 64
Ürdün	30.0	40.0
İspanya	11.9	2.2
İsrail	30.8	23.7

Occurrence of Phleboviruses in the Mediterranean



SFSV — Sandfly Sicilian virus

TOSV — Toscana virus

SFNV — Sandfly Naples virus

Weidmann M. 2009

Yakın Bölgemizde
Son Yıllardaki Durum

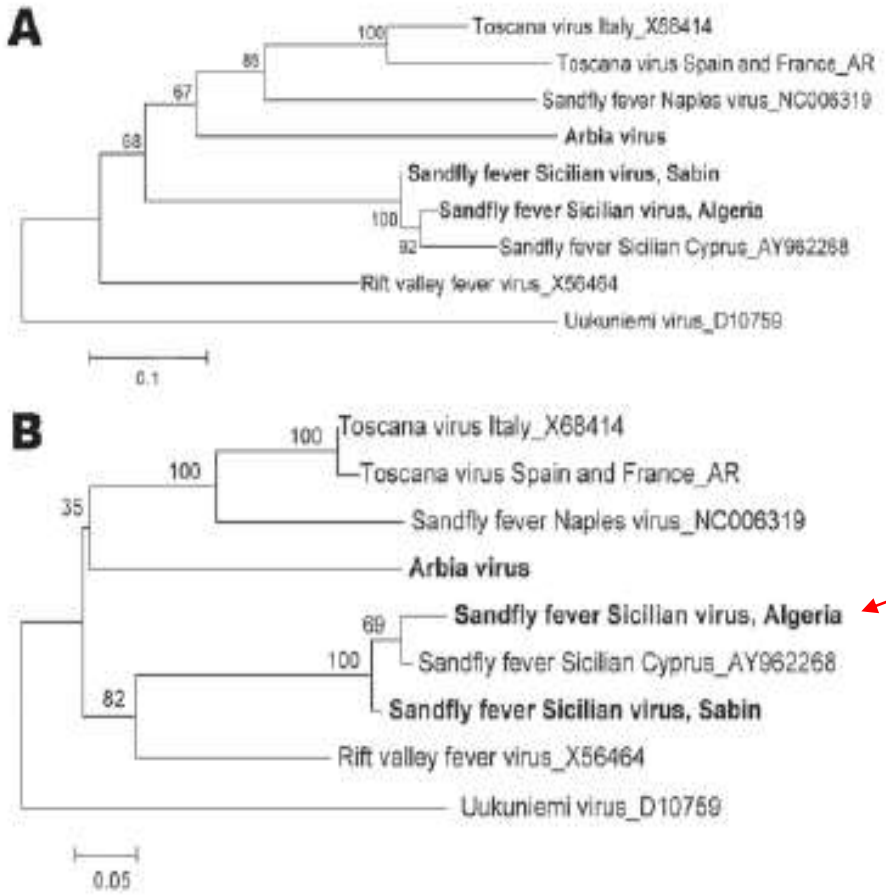


Figure 1. Map of Algeria showing where sandflies were trapped (■).

Sandfly Fever Sicilian Virus, Algeria

Arezki Izri,* Sarah Temmam,† Grégory Moureau,† Boussad Hamrioui,‡ Xavier de Lamballerie,† and Rémi N. Charrel†

MILITARY MEDICINE, 173, 10:949, 2008

Outbreak of SandFly Fever in Central Iraq, September 2007

MAJ Shannon B. Ellis, MC USA; LTC George Appenzeller, MC USA†;*
LTC Heechoon Lee, MC USA‡; CPT Keri Mullen, MC USA§; CPT Ricardo Swenness, SP USA¶;
*LCDR Guillermo Pimentel, MSC USN‖; Emad Mohareb, PhD#; MAJ Christopher Warner, MC USA***

ABSTRACT An outbreak of nonspecific febrile illnesses occurred among U.S. Army troops in September 2007 at a remote, newly established, rural-situated patrol base, south of Baghdad, Iraq. Soldiers displayed an acute flu-like syndrome with symptoms of fever, headache, malaise, and myalgia. A total of 14 cases was identified and treated presumptively as query fever. Subsequent convalescent serum specimens confirmed 13 (92.9%) positive for sandfly Sicilian virus and 3 (21.4%) positive for *Coxiella burnetii*, with two positive for both. One sandfly Sicilian virus case tested positive for *Brucella* spp. This outbreak emphasizes the potential for multiple simultaneous disease exposures to endemic diseases in nonindigenous military personnel at remote military locations in Iraq. Recommendations include increased theater disease surveillance, medical training, and vector control.

Sandfly fever virus outbreak in Cyprus

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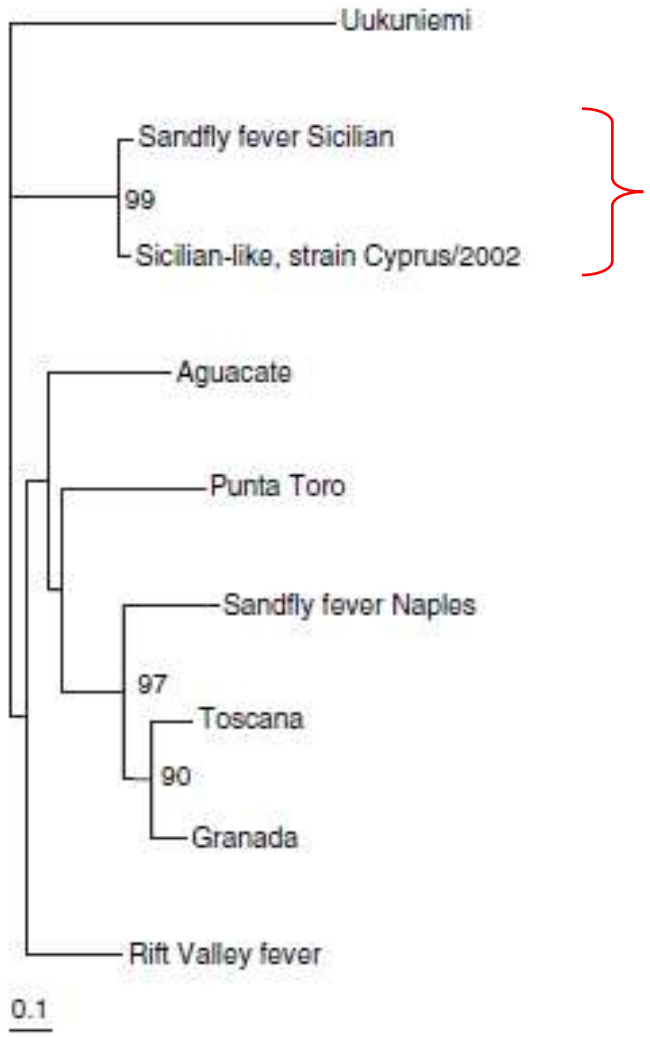
ABSTRACT

A major outbreak of febrile syndrome occurred during 2002 among the Greek Army forces in Cyprus. Serological and molecular investigations revealed that the causative agent was a Sicilian-like phlebovirus. A virus strain was isolated from a blood sample taken on the first day of the disease. Phylogenetic analysis of partial L RNA segment sequences revealed that the strain from Cyprus differed from sandfly Sicilian virus by 6.7% at the nucleotide level.

Keywords Cyprus, genetic detection, phlebovirus, sandfly fever virus, virus isolation

Original Submission: 3 May 2005; **Revised Submission:** 6 June 2005; **Accepted:** 17 August 2005

Clin Microbiol Infect 2006; 12: 192–194
10.1111/j.1469-0691.2005.01330.x



High prevalence rates of antibody to three sandfly fever viruses (Sicilian, Naples, and Toscana) among Cypriots.

Epidemiol Infect. 1991 Dec;107(3):685-91

- **Eitrem R, Stylianou M, Niklasson B. Department of Virology, National Bacteriological Laboratory, Stockholm, Sweden.**

Neutralizing antibodies to **sandfly fever Naples, sandfly fever Sicilian and Toscana viruses** were investigated among 479 sera collected from a normal human population in Cyprus. Antibody prevalence rates of **57%, 32% and 20%** were found to **Naples, Sicilian and Toscana viruses**, respectively. The observed frequency of dual and triple infections was higher than would be expected with a random chance of infection. Antibody prevalence rates were similar for men and women for all three viruses tested, but one of two study sites had significantly higher antibody prevalence to Naples and Sicilian viruses than the other. Individuals with antibodies to both Naples and Toscana viruses had higher antibody levels to Naples virus than those with antibodies to Naples virus only. If the antibody prevalence rates found in this study reflect a history of clinical disease as described in the literature, sandfly fever poses a significant public health problem in Cyprus.

Türk Mikrobiyol Cem Derg 32: 97-101

Kuzey Kıbrıs – Girne'de Tatarcık Humması Öntanılı Hastaların Bölgeye ve Mevsime Bağlı Dağılımları(*)

Çağrı ERGİN(**), Sebahattin YILMAZ (***)

ÖZET

Tatarcık humması Phlebotomus genusu tatarcıklar ile bulaştırılan ve subtropikal iklim kuşaklarında endemik olarak görülen arboviral bir infeksiyondur. Kıbrıs'ta yerleşik tatarcık humması Dünya Sağlık Örgütü tarafından takip edilmekle birlikte Kuzey Kıbrıs bölgesine ait epidemiyolojik veriler bulunmamaktadır.Bu çalışmada 1997-1999 yıllarında Girne Askeri Hastanesi'ne başvuran kişiler arasında semptomatik olarak tatarcık humması öntanısı alan hastaların bölgesel ve yıllık dağılımları incelenmiştir.

1997-1999 yıllarında hastaneye başvuran 47716 kişiden 3383'üne (%7.09) semptomatik olarak tatarcık humması öntanısı konmuştur. Bu hastalık nedeniyle hastaneye mayıs-kasım aylarında başvurulduğu, en sık hastanın haziran ayında (%21.4) görüldüğü saptanmıştır. Hastalar en çok Beylerbeyi (%27.6), Yeşiltepe (%18.3) ve Karaoğlanoğlu (%14.9) bölgelerinden gelmiştir.

SUMMARY

The Regional And Seasonal Distribution of Patients Prediagnosed as Sandfly Fever in Kyrenia, Northern Cyprus

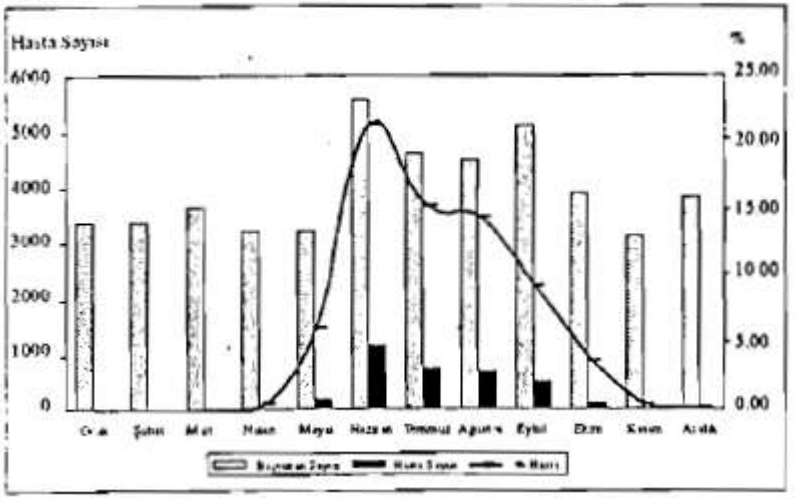
Sandfly fever is an arboviral infection that spreads by genus Phlebotomus in geographical subtropical region of the World. Although World Health Organisation has a surveillance programme of currently sandfly fever status in Cyprus, there is no epidemiological data for Northern Cyprus location. In this study, regional and seasonal period data were investigated in patients with sandfly fever who admitted and were semptomatically prediagnosed in Kyrenia Military Hospital between 1997 and 1999.

Sandfly fever has been semptomatically prediagnosed in 3383 of 47716 (7.09%) admitted patients between 1997 and 1999. Patients have admitted owing to sandfly fever in May and November period and the peek prevalence of patients was in June (21.4%). It was found that the patients

Tablo 1. Tatarcık öntanısı alan olguların yıllara ve aylara göre dağılımı

Aylar	Yıllar			Aylık Ortalama
	1997	1998	1999	
Ocak	0.00	0.00	0.00	0.00
Şubat	0.00	0.00	0.00	0.00
Mart	0.00	0.00	0.00	0.00
Nisan	0.00	0.00	0.00	0.00
Mayıs	5.11	3.76	8.10	5.66
Haziran	25.03	15.86	23.52	21.47
Temmuz	17.74	1.24	15.99	14.99
Ağustos	17.57	10.69	14.24	14.17
Eylül	10.78	6.89	10.32	9.33
Ekim	2.58	4.78	4.04	3.80
Kasım	0.22	0.51	0.10	0.23
Aralık	0.00	0.00	0.00	0.00
Yıllık Ortalama	8.95	5.40	6.91	7.09

Şekil 1. Üç yıllık verilerin ortalamasına göre hastaneye başvuran hastaların ve tatarcık humması ön tanılı olguların yıl içinde değişimi



Hastalığın üç yıllık dağılım eğrisi göz önüne alındığında farklı virus serotiplerinin ve vektör olarak farklı tatarcıkların etken olarak bulunabileceği düşünülmüştür. Hastalığın sık görüldüğü bölgelerde hijyenik alt yapı eksikliğinin en önemli etken olduğu tesbit edilmiştir.

Ülkemizdeki Durum

Türkiye'den bildirilen ilk çalışma

- 1955 yılında Amerikalı bir araştırıcının Antalya'dan topladığı 50 adet serum ile saptanan seroprevalanslar:
  - Sicilian %22
  - Naples %62

Serological studies on the epidemiology of sandfly fever in the Old World

R. B. TESH,[1] S. SAIDI,[2] S. Ja. GAJDAMOVIČ,[3] F. RODHAIN,[4] & J. VESENJAK-HIRJAN [5]

BULL. WORLD HEALTH ORGAN., Vol. 54, 1976

Serological studies on the epidemiology of sandfly fever in the Old World

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	Locality [a]	Population sampled and date	Total no. sera tested	Percentage positive [b]					
				Sicilian	Naples	Arumowot	SudAn 754-61	Karimabad	Salehabad
1	Senegal	Children — 1966	50	0.0	0.0	0.0	0.0	—	—
2	Zigida, Liberia	Mixed — 1972	99	0.0	0.0	0.0	0.0	0.0	—
3	Ghana	Adults — 1963	34	0.0	0.0	0.0	0.0	0.0	—
4	Nigeria	Mixed — 1970–74	94	0.0	0.0	0.0	0.0	—	—
5	Northern Nigeria	Adults — 1966	115	0.0	0.0	0.0	2.6	0.0	0.0
6	Northern Kenya	Mixed — 1972	24	0.0	0.0	0.0	0.0	0.0	—
7 A	Giohar District, Somalia	Adults — 1966	50	12.0	0.0	0.0	0.0	—	—
7 B	Giohar District, Somalia	Mixed — 1960–63	48	2.1	0.0	2.1	0.0	0.0	0.0
8	Territory of the Afars and Issas [c]	Mixed — 1974	127	0.0	3.1	0.0	0.0	0.0	—
9 A	Omo Valley, Ethiopia [c]	Mixed — 1972	60	0.0	3.3	0.0	0.0	0.0	—
9 B	Omo Valley, Ethiopia [c]	Mixed — 1974	89	0.0	0.0	0.0	0.0	—	—
10	Khartoum Province, Sudan	Adults — 1975	207	13.0	14.0	1.4	27.5	4.3	—
11	El Gezira Province, Sudan	Adults — 1975	80	13.8	16.3	0.0	26.3	1.3	—
12	Equatoria Province, Sudan	Adults — 1975	5	20.0	0.0	80.0	60.0	0.0	—
13	Northern Province, Sudan	Adults — 1975	6	16.7	33.3	16.7	16.7	0.0	—
14	White Nile Province, Sudan	Adults — 1975	7	14.3	14.3	0.0	0.0	0.0	—
15	Upper Nile Province, Sudan	Mixed — 1960–63	91	6.6	0.0	72.5	34.1	11.0	0.0
16	Qalyub, Egypt	Mixed — 1952–54	252	22.6	31.0	0.0	0.0	0.0	0.0
17	Cairo, Egypt	Children — 1975	181	5.0	6.1	0.0	0.0	0.0	—
18	Giza, Egypt	Adults — 1960–63	16	43.8	43.8	0.0	0.0	0.0	0.0
19	Alexandria, Egypt	Adults — 1960–63	37	27.0	21.6	0.0	0.0	0.0	0.0
20	Baltim-Boeg Burullus, Egypt	Mixed — 1960–63	45	8.9	6.7	0.0	0.0	0.0	0.0
21	Luxor, Egypt	Adults — 1960–63	64	59.4	56.3	1.6	3.1	0.0	0.0
22	Siwa, Egypt	Mixed — 1960–63	51	2.0	3.9	0.0	0.0	0.0	0.0
23	Sidi Barrâni, Egypt	Mixed — 1960–63	21	4.8	9.5	0.0	9.5	0.0	0.0
24	Behig, Egypt	Mixed — 1960–63	64	6.3	25.0	1.6	0.0	0.0	0.0
25	El Daba, Egypt	Adults — 1960–63	36	8.3	13.9	8.3	0.0	0.0	0.0
26	Aswan, Egypt	Adults — 1960–63	55	43.6	47.3	0.0	7.3	1.8	0.0
27	Tunisia	Mixed — 1975	165	1.3	0.0	0.0	0.0	0.0	—
28	Tamanrasset, Algeria	Mixed — 1975	45	0.0	0.0	0.0	0.0	0.0	—
29	Djanet, Algeria	Mixed — 1975	37	0.0	0.0	0.0	0.0	0.0	—
30	Marrakech Province, Morocco	Mixed — 1976	20	0.0	0.0	0.0	0.0	—	—
31	Beni-Mellal Province, Morocco	Mixed — 1976	30	0.0	0.0	0.0	0.0	—	—
32	d'Oujada Province, Morocco	Mixed — 1976	27	0.0	0.0	0.0	0.0	—	—
33	Midelt-Itzer, Morocco	Mixed — 1976	35	5.7	2.9	0.0	8.6	—	—
34	Crete, Greece	Adults — 1976	38	0.0	13.1	—	—	—	—
35	Athens, Greece	Mixed — 1973–75	832	8.5	24.7	—	—	—	—
36	Agrahova, Greece	Children — 1973	96	0.0	0.0	0.0	0.0	0.0	—
37	Brač, Dalmatia Province, Yugoslavia	Adults — 1975	212	15.6	57.6	—	—	—	—
38	Kosovo Province, Yugoslavia	Mixed — 1975	104	9.6	27.9	—	—	—	—
39	Antalya, Turkey	Adults — 1955	50	22.0	62.0	—	—	0.0	—
40	Massayeb-Al-Kabir, Iraq [c]	Mixed — 1972–73	40	2.5	7.5	—	—	0.0	—
41	Saudi Arabia	Adults — 1967	34	20.6	5.9	0.0	0.0	0.0	—
42	Tabriz, East Azerbaijan Province, Iran	Adults — 1971	100	12.0	26.0	—	—	1.0	0.0
43	Rasht, Gilan Province, Iran	Adults — 1971	93	12.9	21.5	—	—	0.0	0.0
44	Khorasan Province, Iran [c]	Mixed — 1971–75	336	9.5	17.9	—	—	11.0	0.0
45	Tehran Province, Iran [c]	Mixed — 1971–75	257	21.4	30.4	—	—	8.2	0.0
46	Kermanshah Province, Iran	Adults — 1975	32	9.4	28.1	—	—	0.0	0.0
47	Isfahan Province, Iran [c]	Mixed — 1974–75	620	21.8	13.5	—	—	62.1	0.0
48	Khuzestan Province, Iran [c]	Mixed — 1973–75	486	20.4	13.2	—	—	0.2	0.0
49	Moldavian SSR, USSR	Adults — 1976	163	3.7	2.6	—	—	0.0	—
50	Azerbajdžan SSR, USSR	Adults — 1976	98	3.1	3.1	—	—	1.0	—
51	Uzbek SSR, USSR	Adults — 1976	197	7.6	4.1	—	—	1.0	—
52	Tadžik SSR, USSR	Adults — 1976	158	6.3	2.5	—	—	10.1	—
53	Turkmen SSR, USSR	Adults — 1976	100	2.0	6.0	—	—	53.0	—
54	Karachi, Pakistan	Mixed — 1965	75	2.7	9.3	—	—	0.0	0.0
55	Dacca, Bangladesh	Mixed — 1965	75	2.7	12.0	—	—	0.0	0.0
56	Rangoon, Burma	Mixed —	51	0.0	0.0	—	—	—	—
57	Southern Viet Nam	Mixed — 1972	95	0.0	0.0	—	—	0.0	—
58	Northern Peninsular Malaysia	Adults — 1973	103	0.0	0.0	—	—	0.0	0.0
59	Northern China	Adults — 1974–76	379	0.0	0.0	—	—	0.0	0.0

[a] Number refers to locality identification shown in Fig. 1.
[b] No. positive sera/total no. sera tested. Sera producing ≥80 % plaque inhibition were recorded as positive. Dash = not tested.
[c] Sera tested at 1 : 20 dilution; the remainder were tested at 1 : 10 serum dilution.

Türkiye'de SFNV ve SFSV

- 1975'de Ege bölgesinde yapılan bir çalışmada (Serter D.)

  Sicilian %5.02 ve

  Naples %28.3 oranında bulunmuştur

Wolters Kluwer Health | Lippincott Williams & Wilkins

Current Opinion in Infectious Diseases

Epidemiological, clinical and laboratory aspects of sandfly fever

Dionisio, Daniele; Esperti, Francesco; Vivarelli, Angela; Valassina, Marcello
2003; 383-388.

Sicilian and Naples viruses:

Of the viruses belonging to the Phlebovirus group, only TOSV has demonstrated neurotropic activity, while SFSV and SFNV cause a febrile illness that lasts several days; nevertheless, one report of aseptic menigitis associated with SFSV in a **German tourist returning from Turkey** has been published [36].

36] Becker M, Zielen S, Schwartz TF, et al. Pappataci fever. Klin Padiatr 1997; 209:377-379.

1: Klin Padiatr. 1997 Nov-Dec; 209(6):377-9.

[Pappataci fever]

[Article in German]

Becker M, Zielen S, Schwarz TF, Linde R, Hofmann D.

Zentrum der Kinderheilkunde der Johann-Wolfgang-Goethe-Universität, Frankfurt.

Sandfly fever virus is known to cause pappataci fever. The sandfly fever virus belongs to the Genus Phlebovirus (family: Bunyaviridae) and is endemically found in areas of South Europe, Asia and Africa. In Germany, pappataci fever is only described in connection with travelling to endemic areas. **We report on a 15 year-old girl suffering from sandfly fever virus infection after vacation in Turkey.** The initial symptoms started with fever for about three days, frontal headache, nausea and arthralgia. After a short time of clinical improvement symptoms recurred and our patient entered hospital with signs of severe meningitis. Liquor analysis showed a lymphocytic meningitis. Due to multiple insect bites on her legs sandfly fever was suspected. Blood analysis confirmed an acute infection with **sandfly virus Sicilian** from which she completely recovered. ELISA and immunoblot analysis revealed an infection with sandfly virus serotype Sicilian, which was not encountered with meningitis so far. Our case report illustrates that due to increased tourism sandfly fever virus infection has to be considered as a cause of aseptic meningitis in travellers.

Laboratuvar Tanı

VAKA TANIMI

Şüpheli vaka

Kendini sınırlayan ateşli bir hastalık,

SSS bulguları içeren vakalar (özellikle Toscana)

VE "Mayıs-Ekim ayları arası" olması

VE "Akdeniz Havzası ülkelerinde" bulunmak

KONFİRME VAKA

- **<u>Aşağıdaki Laboratuvar Tanı Yöntemlerinden biri ile doğrulanmış olması:</u>**

  - Serum veya BOS'ta **IgM pozitifliği**
  - İki serum örneğinde **IgG'de 4 katlık titre artışı**
  - Serum veya BOS'tan **virus izolasyonu**
  - Serum veya BOS'ta **viral RNA**'nın saptanması

(www.ENIVD.org)

Laboratuvar Tanısı

Seroloji

Akut fazda serum ve/veya BOS'ta IgM
(IgM-capture EIA ve IFA)

Akut ve konvelesan serumda IgG titre artışı
(IFA, Nötralizasyon Testi)

- Antikor testleri kullanılışlı
- Genus ve serotipler arası çapraz reaktivite var
- Değerlendirme yapmak zor olabilir

Laboratuvar Tanısı

Virus izolasyonu

Serum veya BOS örneğinin hücre kültürüne inokulasyonu

(Vero, LLC-MK2,BHK-21)

- zaman alıcı
- duyarlılığı oldukça düşük
- Yüksek biyogüvenlik önlemleri gerekmekte

Laboratuvar Tanısı

PCR

- Serum veya BOS örneğinde PCR ile Viral nukleik asid saptanması
- Referans suşlarla kullanıldığında duyarlılığı oldukça yüksek

Laboratuvar Tanısı

Toscana virus ve Naples Sandfly fever virus grubu antijenik ve filogenetik olarak

SFV Sicilian virustan farklıdır.

Türkiye'de
Tatarcık Humması Salgını
2008-2010

Tatarcık Humması Olguları -2008-

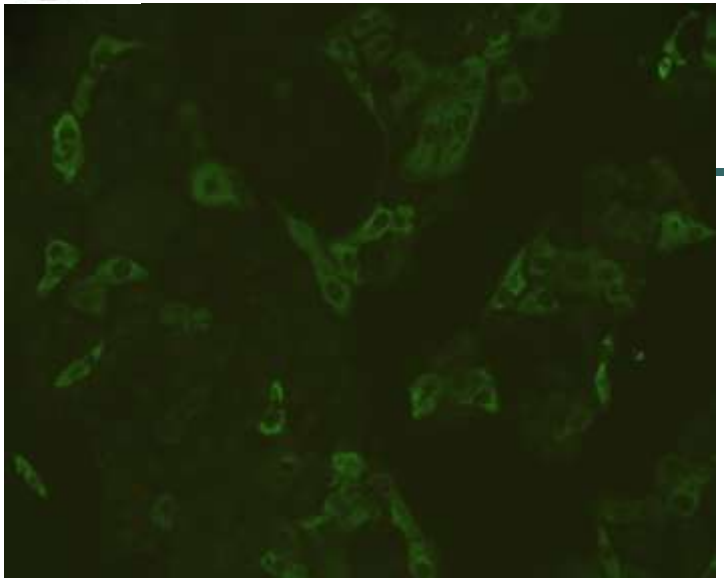
IFA Sonuçlarının Değerlendirilmesi

IgG Reaksiyonu	Sonuç
1:100'de reaksiyon yok	Negatif
1:100'de reaksiyon var	Pozitif (önceki yada akut enfeksiyon)

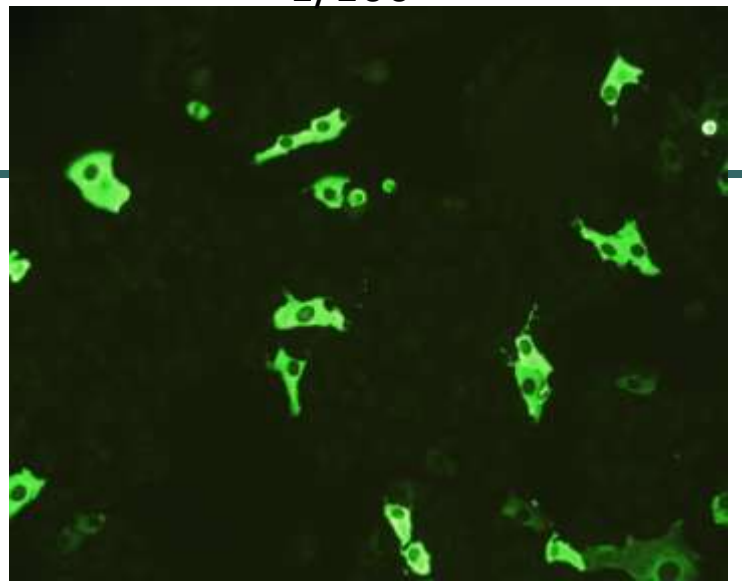
IgM Reaksiyonu	Sonuç
1:100'de reaksiyon yok	Negatif
1:100'de reaksiyon var	Pozitif (akut infeksiyon)

IIFA-IgG- SFSV pozitif (İzmir)

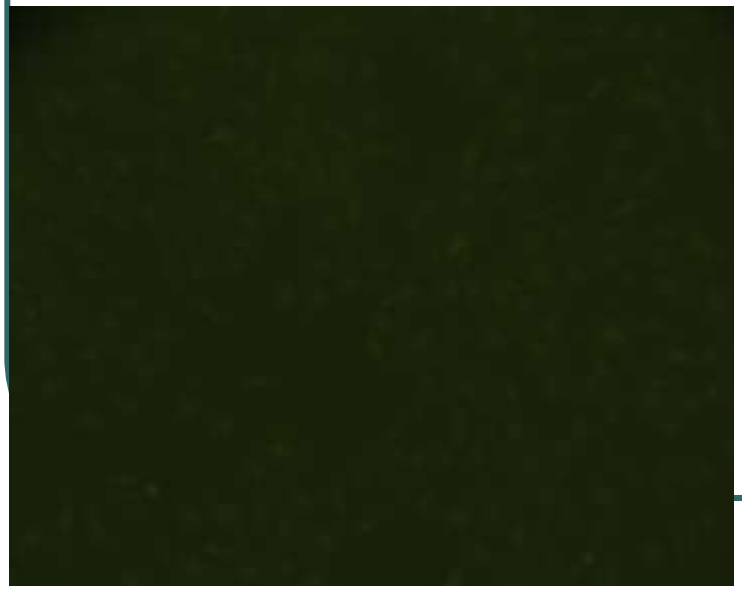
PK



1/100



NK



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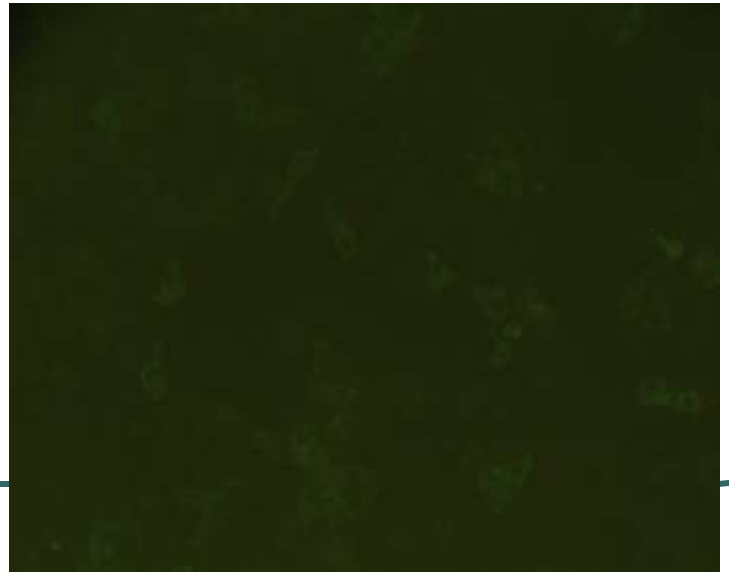
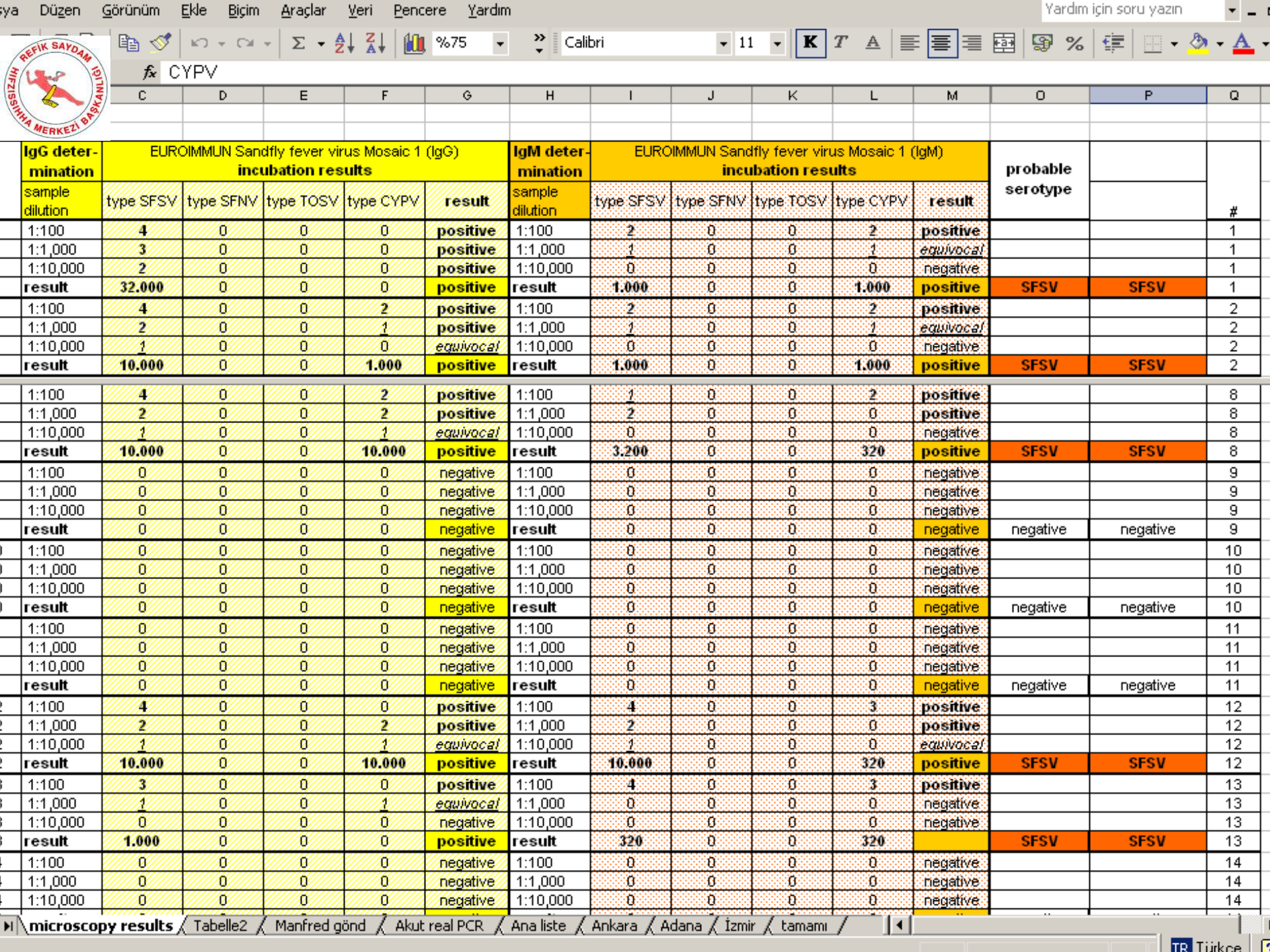
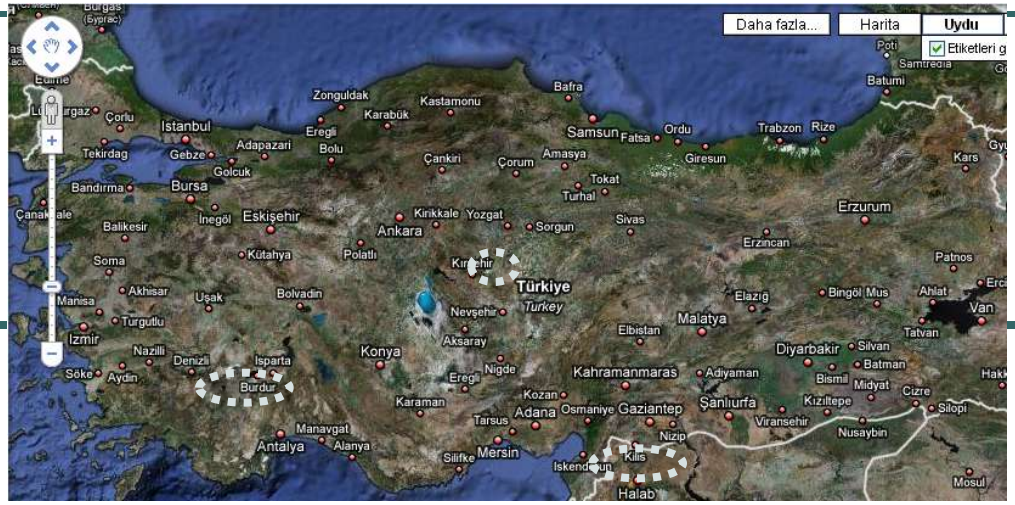




IgG determination	EUROIMMUN Sandfly fever virus Mosaic 1 (IgG) incubation results					IgM determination	EUROIMMUN Sandfly fever virus Mosaic 1 (IgM) incubation results					probable serotype		
sample dilution	type SFSV	type SFNV	type TOSV	type CYPV	result	sample dilution	type SFSV	type SFNV	type TOSV	type CYPV	result			#
1:100	4	0	0	0	positive	1:100	2	0	0	2	positive			1
1:1,000	3	0	0	0	positive	1:1,000	1	0	0	1	equivocal			1
1:10,000	2	0	0	0	positive	1:10,000	0	0	0	0	negative			1
result	32.000	0	0	0	positive	result	1.000	0	0	1.000	positive	SFSV	SFSV	1
1:100	4	0	0	2	positive	1:100	2	0	0	2	positive			2
1:1,000	2	0	0	1	positive	1:1,000	1	0	0	1	equivocal			2
1:10,000	1	0	0	0	equivocal	1:10,000	0	0	0	0	negative			2
result	10.000	0	0	1.000	positive	result	1.000	0	0	1.000	positive	SFSV	SFSV	2
1:100	4	0	0	2	positive	1:100	1	0	0	2	positive			8
1:1,000	2	0	0	2	positive	1:1,000	2	0	0	0	positive			8
1:10,000	1	0	0	1	equivocal	1:10,000	0	0	0	0	negative			8
result	10.000	0	0	10.000	positive	result	3.200	0	0	320	positive	SFSV	SFSV	8
1:100	0	0	0	0	negative	1:100	0	0	0	0	negative			9
1:1,000	0	0	0	0	negative	1:1,000	0	0	0	0	negative			9
1:10,000	0	0	0	0	negative	1:10,000	0	0	0	0	negative			9
result	0	0	0	0	negative	result	0	0	0	0	negative	negative	negative	9
1:100	0	0	0	0	negative	1:100	0	0	0	0	negative			10
1:1,000	0	0	0	0	negative	1:1,000	0	0	0	0	negative			10
1:10,000	0	0	0	0	negative	1:10,000	0	0	0	0	negative			10
result	0	0	0	0	negative	result	0	0	0	0	negative	negative	negative	10
1:100	0	0	0	0	negative	1:100	0	0	0	0	negative			11
1:1,000	0	0	0	0	negative	1:1,000	0	0	0	0	negative			11
1:10,000	0	0	0	0	negative	1:10,000	0	0	0	0	negative			11
result	0	0	0	0	negative	result	0	0	0	0	negative	negative	negative	11
1:100	4	0	0	0	positive	1:100	4	0	0	3	positive			12
1:1,000	2	0	0	2	positive	1:1,000	2	0	0	0	positive			12
1:10,000	1	0	0	1	equivocal	1:10,000	1	0	0	0	equivocal			12
result	10.000	0	0	10.000	positive	result	10.000	0	0	320	positive	SFSV	SFSV	12
1:100	3	0	0	0	positive	1:100	4	0	0	3	positive			13
1:1,000	1	0	0	1	equivocal	1:1,000	0	0	0	0	negative			13
1:10,000	0	0	0	0	negative	1:10,000	0	0	0	0	negative			13
result	1.000	0	0	0	positive	result	320	0	0	320		SFSV	SFSV	13
1:100	0	0	0	0	negative	1:100	0	0	0	0	negative			14
1:1,000	0	0	0	0	negative	1:1,000	0	0	0	0	negative			14
1:10,000	0	0	0	0	negative	1:10,000	0	0	0	0	negative			14


Daha fazla...
Harita
Uydu
Etiketleri g
Zonguldak
Kastamonu
Bafra
Karabük
Samsun
Fatsa
Ordu
Trabzon
Rize
Batumi
Istanbul
Çorlu
Eregli
Adapazari
Bolu
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Çorum
Amasya
Giresun
Tekirdag
Gebze
Golcuk
Bandirma
Bursa
Tokat
Turhal
Kars
Erzurum
Balikesir
Inegöl
Eskişehir
Kirikkale
Yozgat
Sorgun
Sivas
Ankara
Erzincan
Soma
Kütahya
Polatli
Kirşehir
Patnos
Türkiye
Turkey
Akhisar
Uşak
Bolvadin
Elazig
Bingöl
Mus
Ahlat
Van
Manisa
Turgutlu
Nevşehir
Malatya
Izmir
Aksaray
Elbistan
Tatvan
Nazilli
Denizli
Isparta
Konya
Diyarbakir
Silvan
Batman
Söke
Aydin
Burdur
Nigde
Kahramanmaras
Adiyaman
Bismil
Midyat
Cizre
Karaman
Kozan
Adana
Osmaniye
Gaziantep
Şanliurfa
Kiziltepe
Silopi
Tarsus
Viransehir
Nusaybin
Manavgat
Antalya
Alanya
Nizip
Silifke
Mersin
Kilis
Iskenderun
Halab
Mosul

- İZMİR


Daha fazla...
Harita
Uydu
Arazi
Etiketleri göster
İzmir
Burhanköy
Horzumalayaka
Kurudere
Alhan
Şahyar
D585
Baklacı
Artıcak
Horzumkeserler
Horzumsazdere
Çeşneli
Erenköy
Horzumembelli
Soğukyurt
Alasehir
Karadağ
Bozdağ
Elmabağı
Osmaniye
Bahçedere
Azıtepe
Kozluca
Evrenli
Ovacık
Dokuzlar
Çatak
Sarısu
Kestanederesi
Bayırlı
Oğuzlar
Emenler
Uzunköy
Yeşildere
Pınarbaşı
Başaran
Veliler
Cevizalanı
Saçlı
Çömlekçi
Birgi
Beyazıtlar
Aydoğdu
Kiraz
Karaburç
Çayağzı
Denizli Ödemiş Yolu
D310
Ödemis
Cumhuriyet
Akpınar
Örenköy
Bahçearası
Altınoluk
İğdeli
Kibar
Daghaciyunus
Sarıkaya
Doğancılar
Gereli
Kişlaköy
Yeniköy
Yağlar
Solaklar
Taşlıyatak
Dağarlar
Eselli
Kaymakçı
Orhangazi
Karaman
Çaylı
Alaşarlı
Sırımlı
Olgunlar
Tombullar
Sarıpınar
Mavidere
Kızılcaavlu
Mesçili
2 mi
5 km
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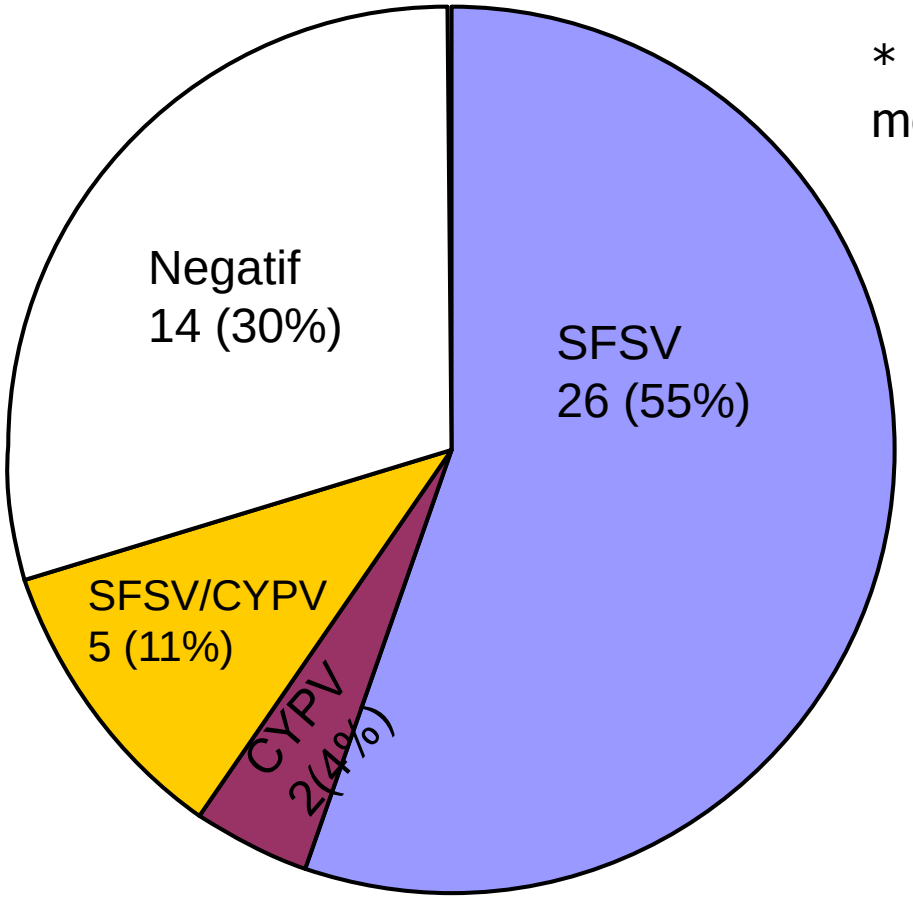
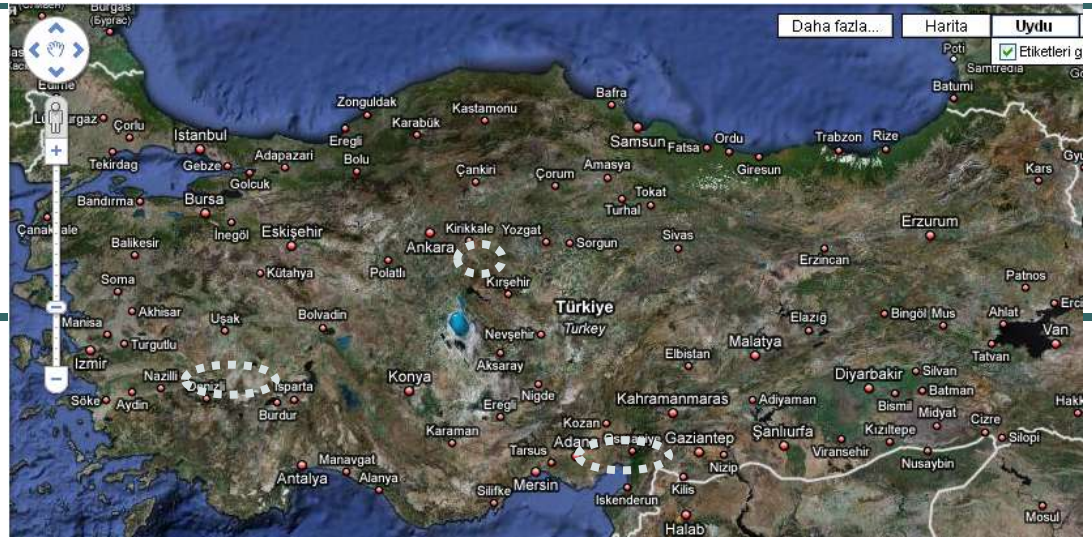
İzmir Olgularının Sonuçları

Toplam Örnek: 47



* 1 örnek İzmir merkezden (negatif)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Poti
Istanbul
Çorlu
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Bolu
Adapazari
Gebze
Tekirdag
Çankiri
Çorum
Amasya
Giresun
Kars
Golcuk
Bursa
Bandirma
Tokat
Turhal
Erzurum
Inegöl
Eskişehir
Kirikkale
Yozgat
Sorgun
Sivas
Balikesir
Ankara
Erzincan
Kütahya
Polatli
Kirşehir
Soma
Patnos
Akhisar
Uşak
Bolvadin
Türkiye
Turkey
Elazig
Bingöl
Mus
Ahlat
Manisa
Nevşehir
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- ADANA


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Çumra
Kozan
Pazarcik
Imamoglu
Kadirli
Bahçe
E90
Gaziantep
Karaman
Ceyhan
Tarsus
Osmaniye
Islahiye
Adana
Dörtyol
Kilis
Ermenek
Mut
Mersin
Iskenderun
Kirikhan
Silifke
Reyhanli
Halab
Anamur
M5
Al Lathqiyah
5
Hama
Nicosia
Famagusta
Cyprus
Larnaca
Hims
Tripoli
50 mi
100 km
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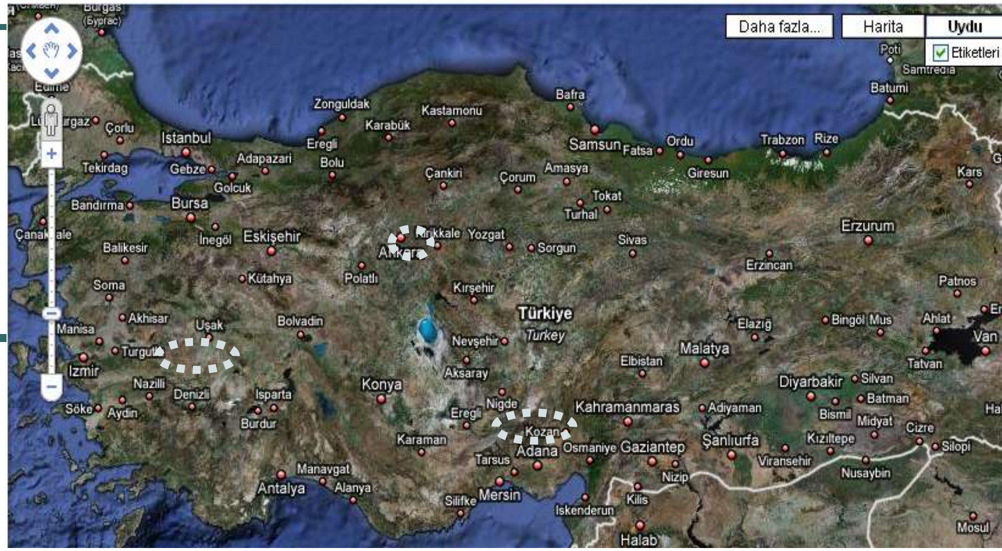
Bağözü
Andil
Eskimantaş
Köseli
Gedikli
Kizilar
Turgutlu
Durmuşlu
Kemer
Oruçlu
D815
Ferhatli
Duraluşağı
Yeniköy
Hacimirzali
Ilicaköy
Acarmantaş
Çandik
Güneri
Kozan
Bucakköy
D817
Çobanpinari
Yazıboyu
Turunçlu
Eskikabasakal
Köseli
Tufanli
Adana Sivas Yolu

Adana Olgularının Sonuçları

Toplam Örnek: 4

CYPV : 2
SFSV : 0
SFSV / CYPV: 1
Negatif : 1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Bandirma
Inegöl
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Yozgat
Ankara
Sorgun
Sivas
Erzurum
Erzincan
Balikesir
Kütahya
Polatli
Kirşehir
Soma
Türkiye
Turkey
Manisa
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Izmir
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Aksaray
Niğde
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Malatya
Elbistan
Elazig
Bingöl
Muş
Ahlat
Van
Tatvan
Patnos
Diyarbakir
Silvan
Batman
Bismil
Midyat
Cizre
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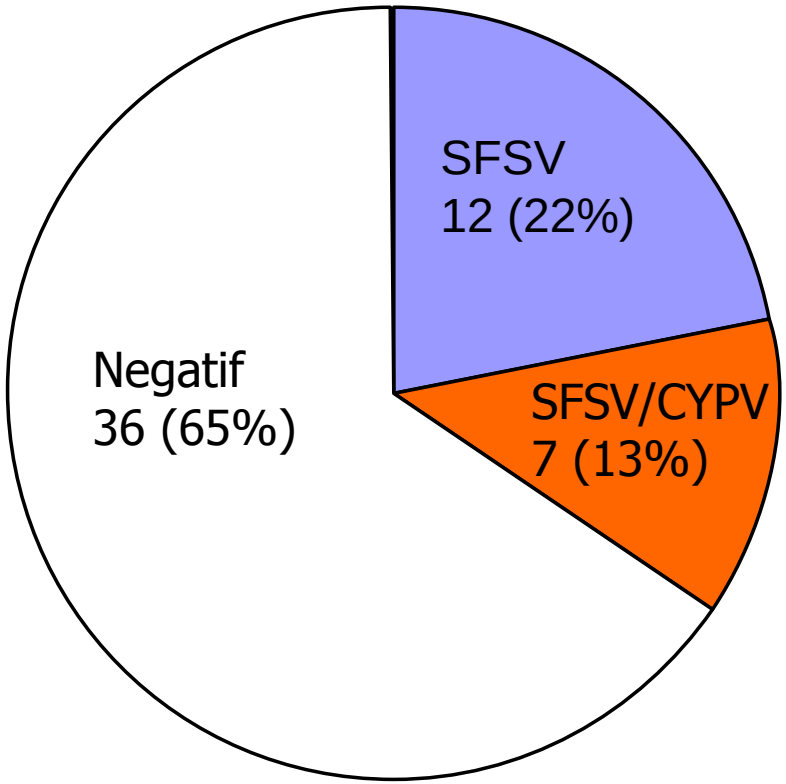
Etiketle
Esenboğa
Akyurt
Karayatak
Kozayağı
Dumlupinar
D180
D140
Ahmetadil
Arkbork
Kalecik
Karacalar
Anbardere
D765
Kazmaca
Bağlum
Karacaören
Yalımköy
Hasanoğlan
Yeşildere
Keçili
Aydınsey
Karakum
Zülfazıl
O-20
Başpınar
Lalahan
D200
D757
Kızıldere
Ankara
Çiğiltepe
Ptt Evleri
E88
Mahmutlar
Gündoğdu
Erzurum
Elmadağ
E88
D200
Hacıbalı
Boğaziçi
Barbaros
Üreğil
Bayındır
Karacaali
Bağcılar
Naci Çakır
Ediğe
Yeşilkent
Kaletepe
Etiler
Kimeski
Karacahasan
Kirikkale
Fatih
O-20
Kızılırmak
Yuva
Ahili
Yaylabağ
Segmenler
Taburlar
Kuşcuali
E90
D765
D750
Deliler
Hasandede
Aşağıkamışlı

Ankara Olgularının Sonuçları

Toplam Örnek: 55

(Retrospektif)

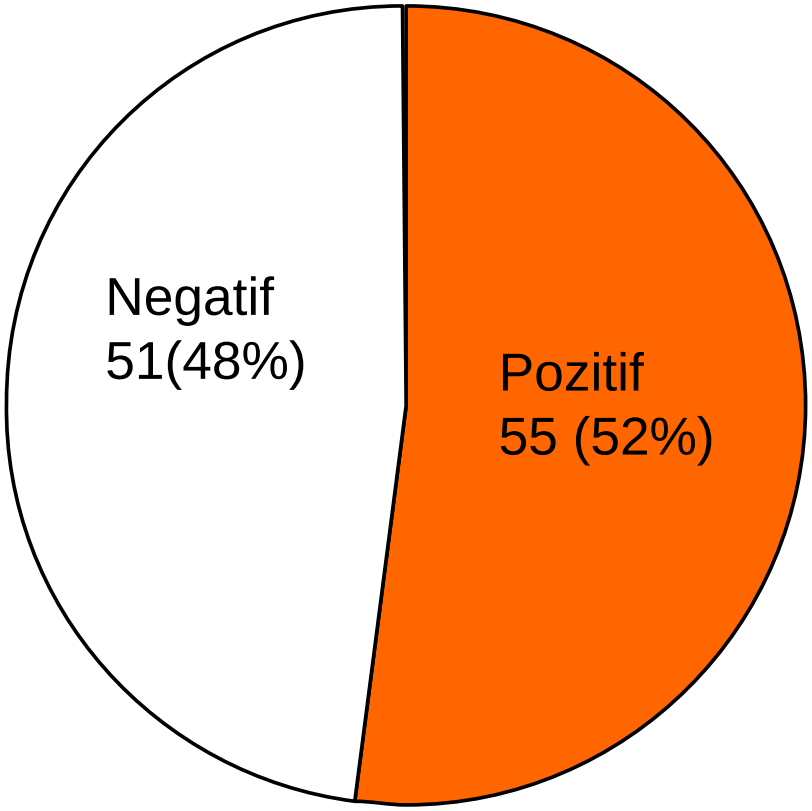


* Bütün örnekler Kuzey Ankara (Mamak bölgesinden)

* Kesin şekilde CYPV diyebileceğimiz bir örnek yok

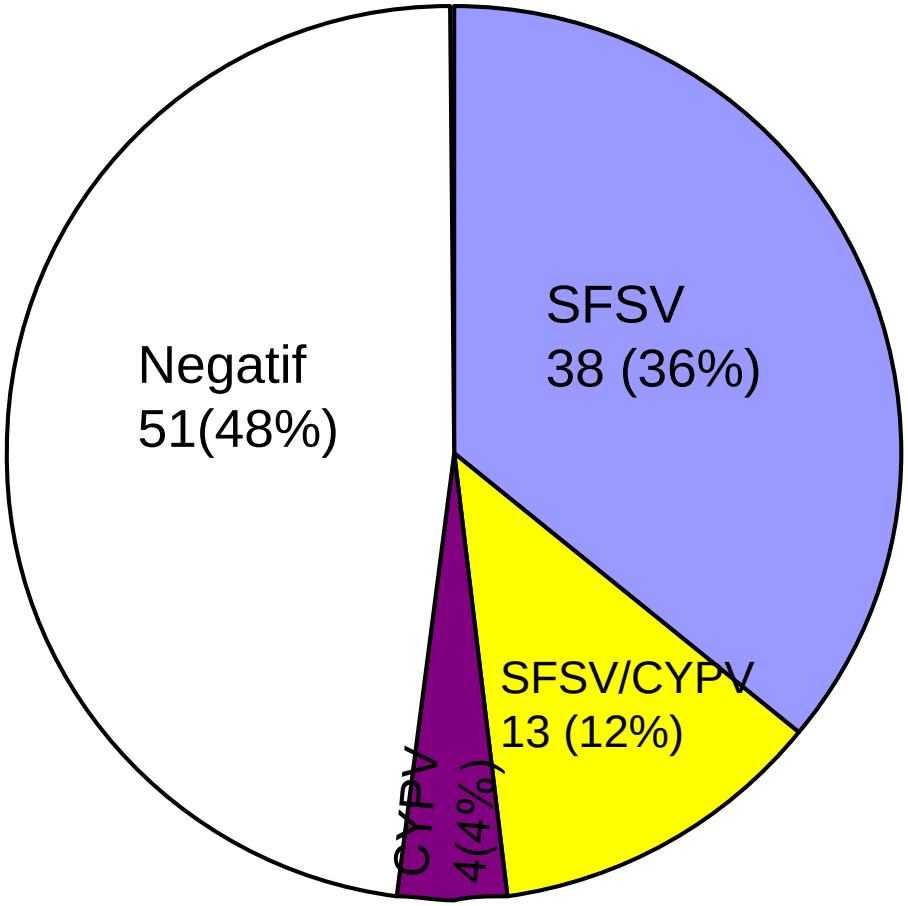
İzmir Adana Ankara - Sonuçları

Toplam Örnek: 106



İzmir Adana Ankara - Sonuçları
Sandfly virus alt tiplerine göre

Toplam Örnek: 106



Results by IFT for initial 23 patient samples

PATIENT NO	Interval	SFCyprus-IgM	SF-Cyprus-IgG	SFSicilian-IgM	SFSicilian-IgG	SFNaples-IgM	SFNaples-IgG	SFToscana-IgM	SFToscana-IgG	Virus isolation attempted	STATUS	
1	11	+++	+++	+	-	-	-	(+)	-			
2	12	+++	+++	+	-	-	-	-	-			
3		++	++	++	+	-	-	-	-			
4		-	-	-	-	-	-	-	-			
5	5	-	-	-	-	-	-	-	-			
6	4	+++	+++	+	-	-	-	(+)	-			
7	3	-	-	-	-	-	-	-	-			
8	14	-	-	-	-	-	-	-	-			
9	10	-	-	-	-	-	-	-	-			
10	3	-	-	-	-	-	-	+	-			
11	5	-	+	++	+	-	+	(+)	+			
12	8	+++	+++	-	+++	-	-	-	-			
13	10	+++	+++	-	+++	-	++	-	++			
14	11	+++	+++	-	+++	-	+	-	+			
15	5	++	-	-	-	-	-	(+)	-		ACUTE ILLNESS	
16	9	++	+++	-	+++	-	-	-	-		ACUTE ILLNESS	
17	6	-	(+)	-	(+)	-	(+)	-	-	X	ACUTE ILLNESS	
18	7	+	+++	-	+	-	-	-	-		ACUTE ILLNESS	
19	6	-	-	-	-	-	-	-	-	X	ACUTE ILLNESS	
20	2	-	-	-	-	-	-	-	-	X	ACUTE ILLNESS	FAMILY
21	2	(+)	-	-	-	-	-	-	-	X	ACUTE ILLNESS	FAMILY
22	2	-	-	-	-	-	-	-	-	X	ACUTE ILLNESS	FAMILY
23	4	-	-	-	-	-	-	-	-	X		

Moleküler Tanı-I

- Real-PCR tanısı Weidman ve ark. tarafından geliştirilen metod üzerine gerçekleştirildi

- Öncelikle pozitif kontrol plasmidi (DNA) Ambion kiti kullanılarak SP6 ve T7 RNA polimeraz enzimi kullanılarak in vitro transkribe edildi

- Takiben ortamda kalan DNA'yı uzaklaştırmak için DNaz I ile muamele edildi

Moleküler Tanı-II

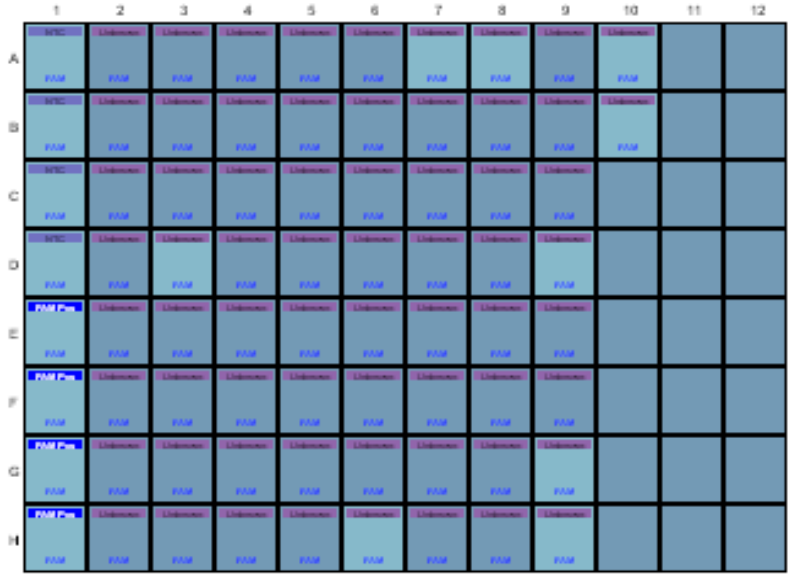
• Akut hastalardan ve IgM pozitif serum örneklerini içeren 66 adet örnek ve

• 4 pozitif ve 4 NTK örnek

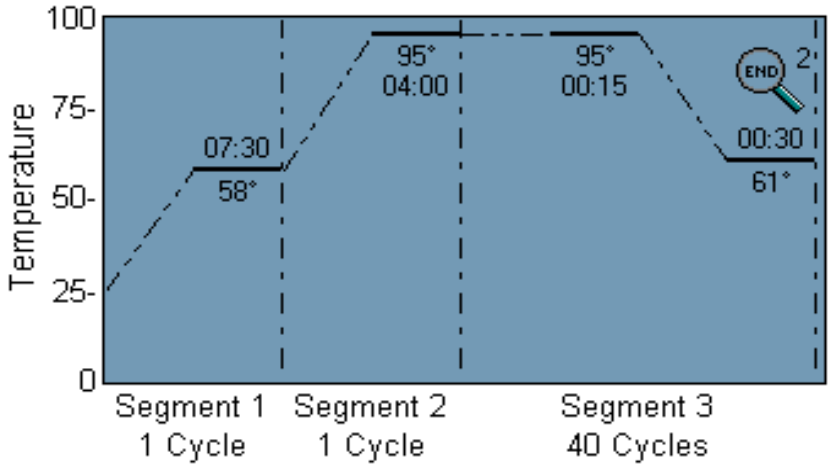
real time PCR işlemine alındı ve şu sonuç elde edildi

Tüm Rapor

Plate Setup

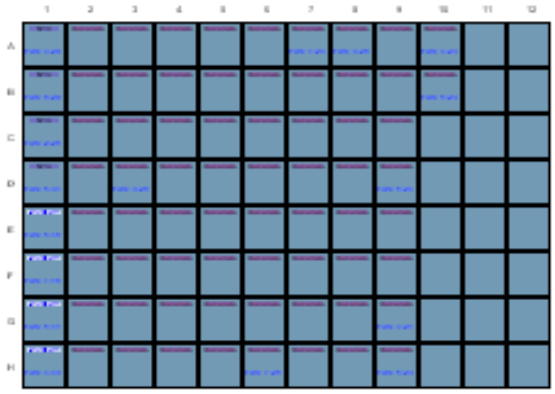


Thermal Profile

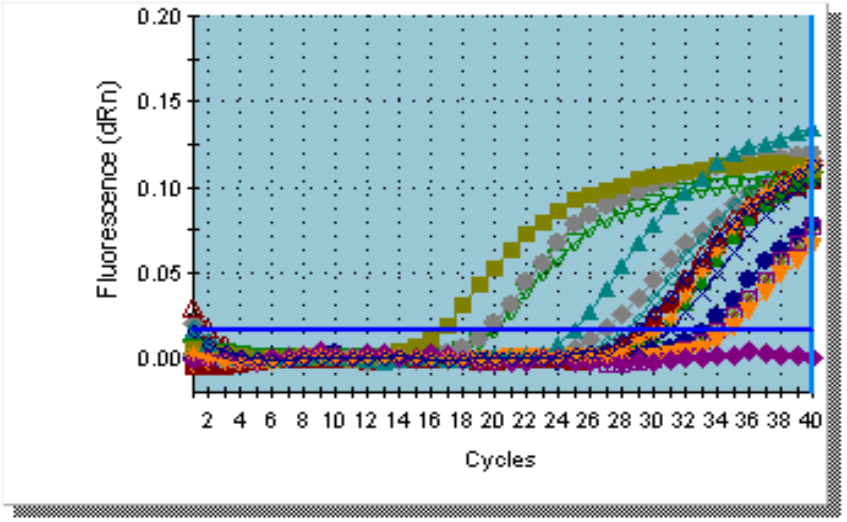


Analysis Sel./Setup-Term Settings View

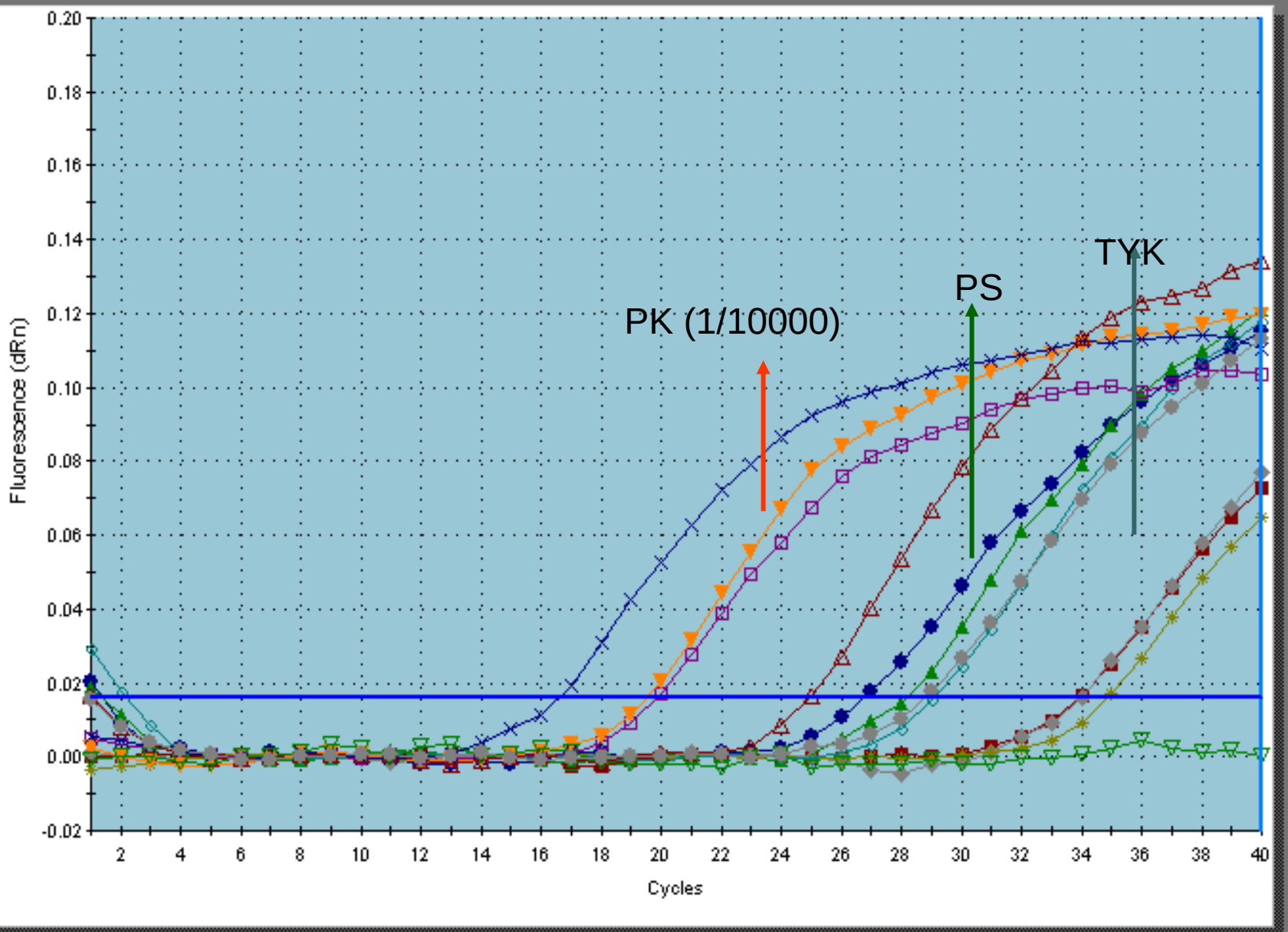
Amplification-based threshold using search range of 5 to 60 percent.
Moving average points for amplification = 3, dissociation = 3.
Dissociation graphical temperature separation = 0.50.
Baseline Settings Plate: * indicates manual baseline cycle range settings.



Amplification Plots



Amplification Plots

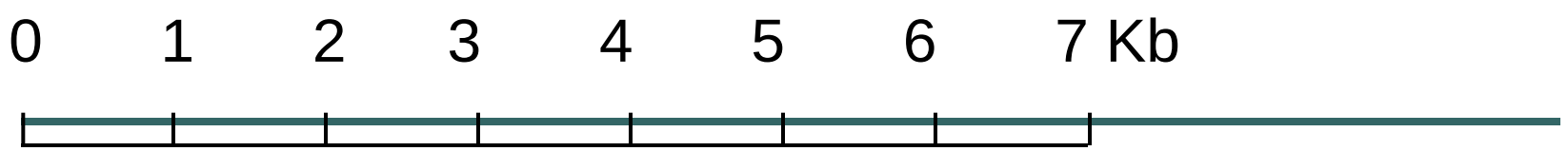


Real-time PCR sonuçları

Moleküler Tanı-III

Hasta Adı	İL	Bölgesi	Semptom başl.-örnek alınışı (gün)	IIFA sonucu	Real time PCR döngü sayısı
N.A	İzmir	Çayağzı	5	Negatif	29
F.B	İzmir	Karaburç	5	Negatif	25
İ.A	İzmir	Karaburç	1	Negatif	29
G.A	İzmir	Karaburç	1	Negatif	27
D.A	İzmir	Karaburç	1	Negatif	28

Sequence results for Turkish Isolate



S-Segment

1730 bp

Reference 15-1814 SFNV-S

Reference 1-1822 TOSV-S

M-Segment

4022bp

Reference SFSV-M (4402 bp)

TOSV-M (4215 bp)

L-Segment

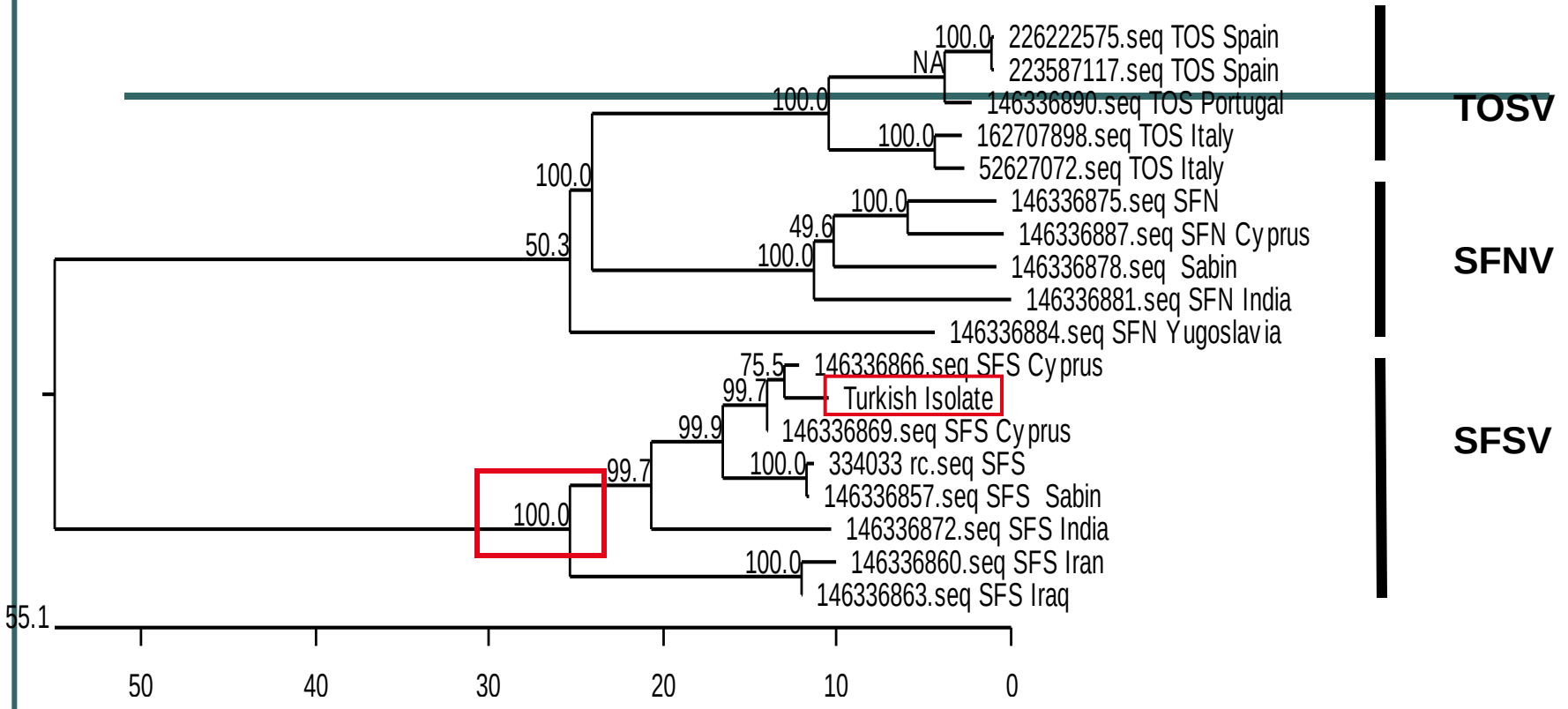
4342 bp

Reference 568-4908 TOSV-L

+ 920 bp ?

Weidmann M., Göttingen Unv., Germany

Phylogenetic analysis of S-Segment sequence results



SFT / SFS (Sabin) 91.6 %

SFT / TOS (Italy) 45.6 %

SFT / TOS (Spain) 66.3%

SFT / SFN (Sabin) 46.0 %

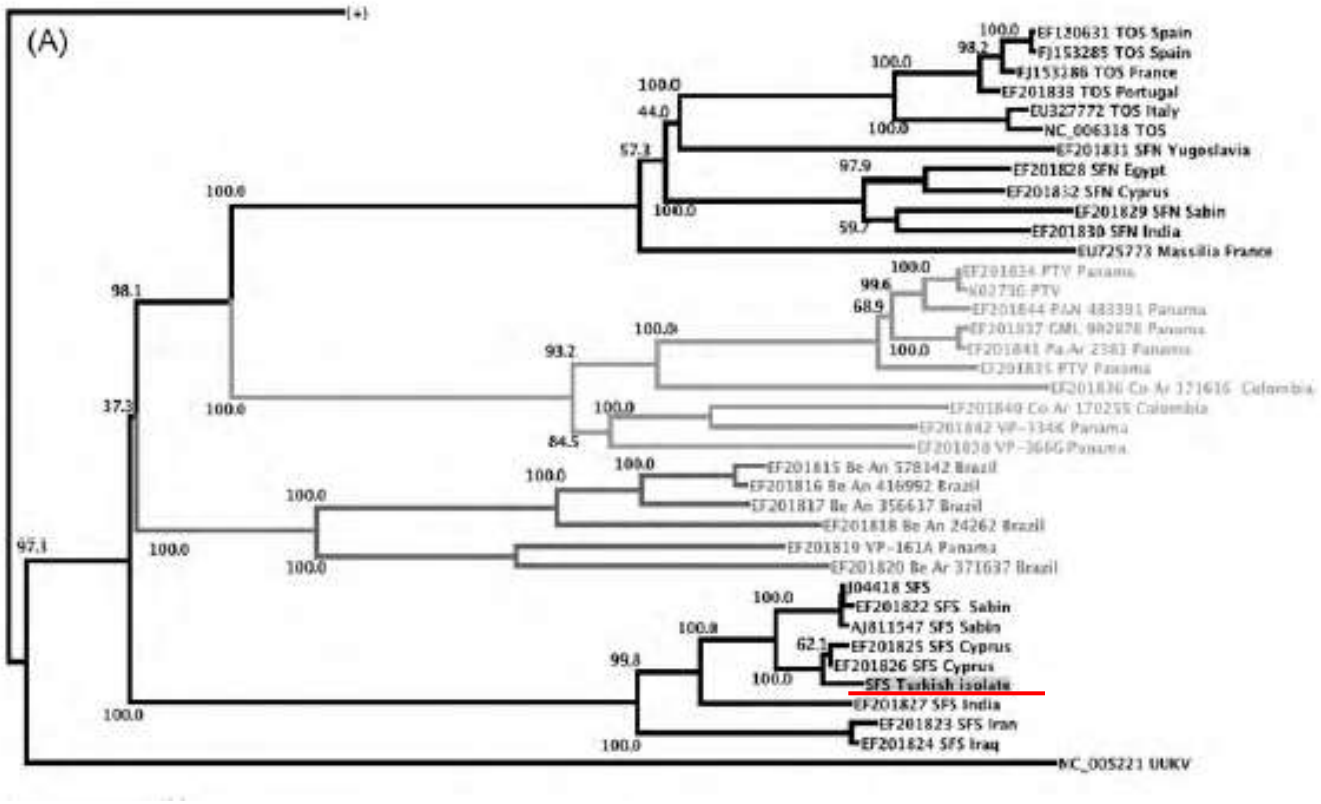


Fig. 2. Bootstraped dendrogram of Phlebovirus nucleotide sequence alignments (Clustal W, 1000 bootstraps) (A) S-segment sequences, (B) M-segment sequences, (C) L-segment sequences, (D) partial 201 nt L-segment sequence alignment. Dendrogramms (A, B, and C) respectively include 71 RVF S-, M- and L-segment sequences ((+) subtree collapsed). All dendrograms are respectively rooted to the S-, M-, L-segment sequence of the tick transmitted Phlebovirus Uukuniemi (UUK). Bootstrap values are given in percent. Sequences are given with their respective accession numbers and country association where available. The Turkish isolate sequence SFT is highlighted in grey. TOS = Toscana virus, SFS = sandfly fever Sicilian virus, SFN = sandfly fever Naples virus, PTV = Punta Toro virus, MAS = Massila virus.

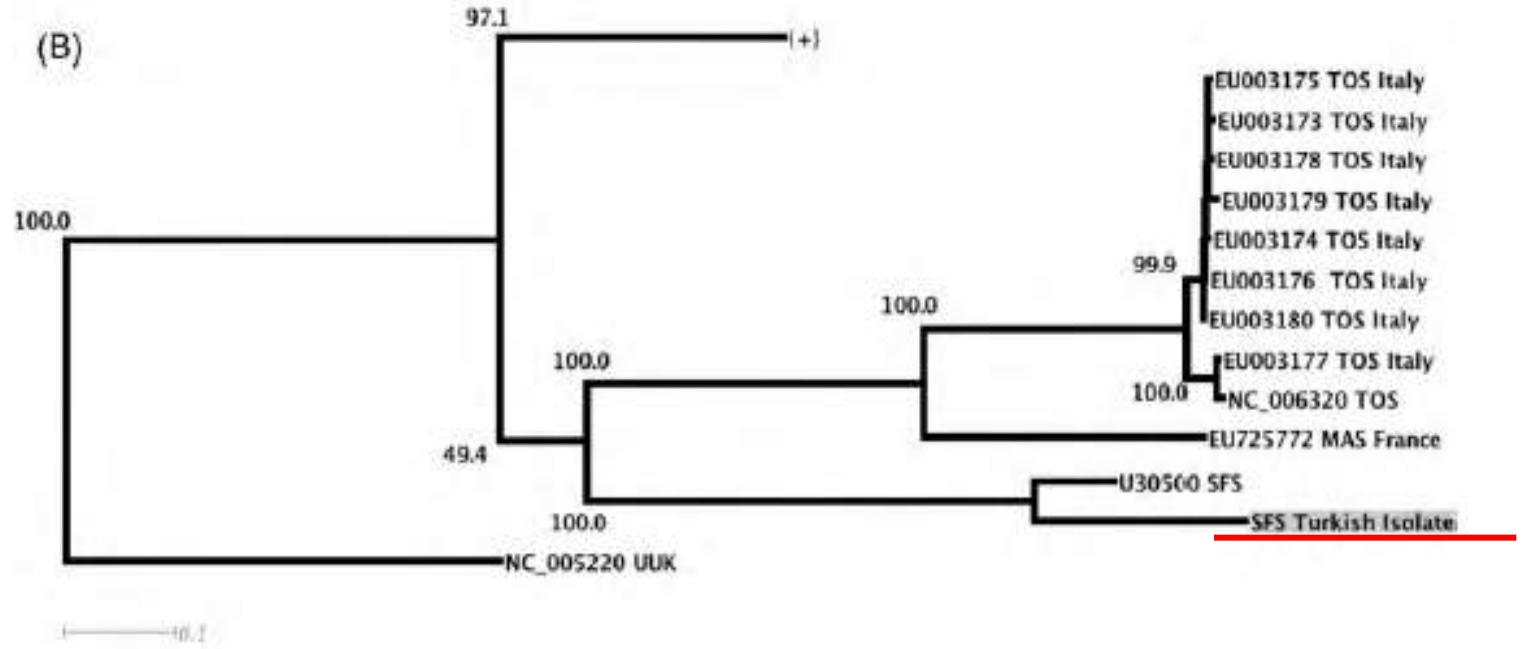


Fig. 2. Bootstraped dendrogram of Phlebovirus nucleotide sequence alignments (Clustal W, 1000 bootstraps) (A) S-segment sequences, (B) M-segment sequences, (C) L-segment sequences, (D) partial 201 nt L-segment sequence alignment. Dendrogramms (A, B, and C) respectively include 71 RVF S-, M- and L-segment sequences ((+) subtree collapsed). All dendrograms are respectively rooted to the S-, M-, L-segment sequence of the tick transmitted Phlebovirus Uukuniemi (UUK). Bootstrap values are given in percent. Sequences are given with their respective accession numbers and country association where available. The Turkish isolate sequence SFT is highlighted in grey. TOS = Toscana virus, SFS= sandfly fever Sicilian virus, SFN= sandfly fever Naples virus, PTV= Punta Toro virus, MAS= Massila virus.

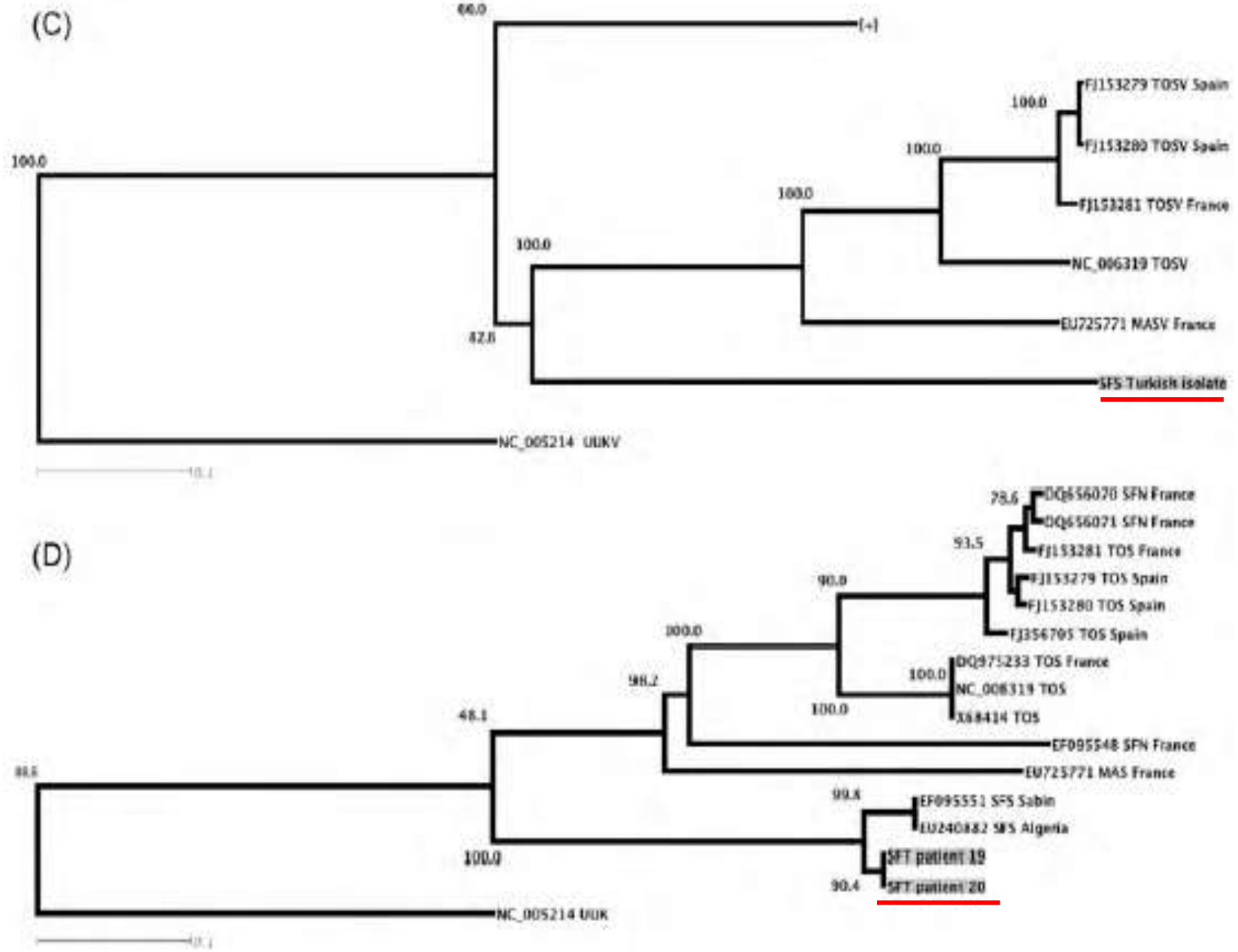

(C)
66.0
100.0
100.0
100.0
100.0
42.0
FJ153279 TOSV Spain
FJ153280 TOSV Spain
FJ153281 TOSV France
NC_006319 TOSV
EU725771 MASV France
SFS Turkish isolate
NC_005214 UUKV
(D)
78.6
93.5
90.0
100.0
98.2
100.0
100.0
48.1
88.6
99.8
100.0
90.4
DQ656070 SFN France
DQ656071 SFN France
FJ153281 TOS France
FJ153279 TOS Spain
FJ153280 TOS Spain
FJ356705 TOS Spain
DQ971233 TOS France
NC_006319 TOS
368414 TOS
EF095548 SFN France
EU725771 MAS France
EF095551 SFS Sabin
EU240882 SFS Algeria
SFT patient 19
SFT patient 20
NC_005214 UUK

Table 1
SFV case characteristics, sample types and analysis results.

Province	Region	Patient no.	Gender[a]	Age	Onset of disease (days)	Sample type[b]	SFCV IgM[c]	SFCV IgG	SFSV IgM	SFSV IgG	SFNV IgM	SFNV IgG	TOSV IgM	TOSV IgG	L-PCR	TQ-PCR	VI	Acute disease
Adana	Kozan	4	M	26	n.d.	S, P	–	–	–	–	–	–	–	–		+	–	
Izmir	Karaburc	20	M	12	2	S, P	–	–	–	–	–	–	–	–	+	+	–	+
Izmir	Karaburc	21	F	13	2	S	(+)	–	–	–	–	–	–	–	–	+	–	+
Izmir	Karaburc	22	F	38	2	S	–	–	–	–	–	–	–	–	–	+	–	+
Ankara	Mamak	7	F	56	3	S	–	–	–	–	–	–	–	–	–	–	v.n.	
Ankara	Mamak	10	M	46	3	S	–	–	–	–	–	–	+	–	–	–	v.n.	
Ankara	Mamak	6	M	29	4	S	+++	+++	+	–	–	–	(+)	–	–	–	v.n.	
Izmir	Merkec	23	M	37	4	S	–	–	–	–	–	–	–	–	–	–	v.n.	
Ankara	Mamak	5	M	22	5	S	–	–	–	–	–	–	–	–	–	–	v.n.	
Izmir	Comlekci	11	F	58	5	S, P	–	+	++	+	–	+	(+)	+	–	–	v.n.	
Izmir	Karaburc	15	F	56	5	S	++	–	–	–	–	–	(+)	–	–	–	v.n.	+
Izmir	Cayagzi	17	F	39	6	S	–	(+)	–	(+)	–	(+)	–	–	–	–	v.n.	+
Izmir	Karaburc	19	F	58	6	S, P	–	–	–	–	–	–	–	–	+	+	+	+
Izmir	Cayagzi	18	M	60	7	S	+	+++	–	+	–	–	–	–	–	–	v.n.	+
Izmir	Comlekci	12	M	51	8	S	+++	+++	–	+++	–	–	–	–	–	–	v.n.	
Izmir	Karaburc	16	F	37	9	S	++	+++	–	+++	–	–	–	–	–	–	v.n.	+
Ankara	Mamak	9	F	45	10	S	–	–	–	–	–	–	–	–	–	–	v.n.	
Izmir	Comlekci	13	M	15	10	S, P	+++	+++	–	+++	–	++	–	++	–	–	v.n.	
Adana	Kozan	1	M	26	11	S	+++	+++	+	–	–	–	(+)	–	–	–	v.n.	
Izmir	Comlekci	14	M	36	11	S, P	+++	+++	–	+++	–	+	–	+	–	–	v.n.	
Adana	Kozan	2	F	30	12	S	+++	+++	+	–	–	–	–	–	–	–	v.n.	
Adana	Kozan	3	F	22	12	S, P	++	++	++	+	–	–	–	–	–	–	v.n.	
Ankara	Mamak	8	M	59	14	S	–	–	–	–	–	–	–	–	–	–	v.n.	

The samples are sorted according to days from onset of disease. VI= virus isolation, v.n. = virus isolation not attempted; n.d.= no data.

[a] F= female, M= male.

[b] S=serum, P= plasma.

[c] (+) slight reaction, + positive, ++ strong positive, +++ very strong positive.

T.C. Sağlık Bakanlığı

Refik Saydam Hıfzıssıhha Merkezi Başkanlığı

TATARCIK HUMMASI (SANDFLY FEVER)

SEMPOZYUMU

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Characterization of a sandfly fever Sicilian virus isolated during a sandfly fever epidemic in Turkey

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ABSTRACT

Background: Phleboviruses cause sandfly fever but isolates are rare.
Objectives: To analyse samples from concurrent outbreaks of suspected sandfly fever in the Mediterranean provinces of Adana, Izmir and the central province of Ankara, Turkey.
Study design: Samples from acute cases were analysed by immunofluorescence assay (IFA). Virus isolation was attempted and pyrosequencing performed.
Results: In IFA 38% of 106 samples tested scored IgM positive for sandfly fever Sicillian virus (SFSV), 12% for SFSV/sandfly fever Cyprus Virus (SFCV) and only 4% for SFCV. A sandfly fever Sicilian type virus designated sandfly fever Turkey virus (SFTV) was isolated. The S-segment sequence of SFTV had a homology of 98% to that of SFCV. The M-segment sequence showed a 91.1% homology to the only SFSV sequence available. The L-segment sequence showed a homology of 58% and 60.3% to Toscana virus and Rift Valley Fever virus sequences, a partial 201 nt sequence showed 95.5% homology to the SFSV Sabin strain.
Conclusion: A new phlebovirus related to sandfly fever Sicilian virus, SFTV was isolated and characterized from acute patient material. The sandfly fever Sicilian virus activity seems to be changing in Turkey. Entomological studies are needed.

SANDFLY FEVER TURKEY VIRUS:
CLASSICAL VIROLOGICAL CHARACTERIZATION OF A PHLEBOVIRUS FROM AN EPIDEMIC IN TURKEY 2008

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Tomographic reconstruction of the two alternative ways of SFTV maturation

Romanowsky-Giemsa staining

References

Frey et. Al. 2010

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Tomographic reconstruction of the two alternative ways of SFTV maturation

Fig.1: Section of a reconstructed tomogram of the two ways of SFTV maturation (pink arrows).

Fig.2: Visualisation of the reconstructed tomogram of virus form by budding in the Golgi apparatus.

Fig.3: 3D-model of the Golgi apparatus.

Fig.4: Visualisation of the reconstructed tomogram of virus maturation at the plasma membrane.

Fig.5: 3D-model of a virus budding at the plasma membrane.

Romanowsky-Giemsa staining

References

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Fig. 4

Romanowsky-Giemsa staining

Fig. 7: Cytopathic effects in Vero B4 cells were investigated using Romanowsky Giemsa staining. Vacuolisation of the cytoplasm was observed (red arrows). A: control, 100x; B: 24 h p.i, 400x; C: 30 h p.i., 400x; D: 48 h p.i., 400x.

Tomographic reconstruction of the two alternative ways of SFTV maturation

Fig.1: Section of a reconstructed tomogram of the two ways of SFTV maturation (pink arrows).

Fig. 1

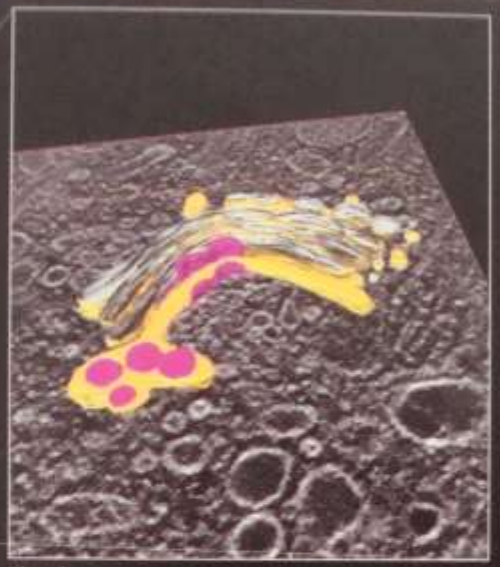

Fig. 2

Fig. 3

Fig.2: Visualisation of the reconstructed tomogram of virus form by budding in the Golgi apparatus.

Fig.3: 3D-model of the Golgi apparatus.

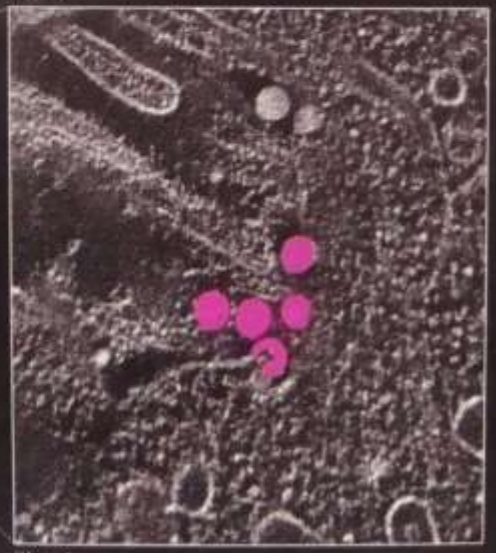

Fig. 4

Fig. 5

Fig.4: Visualisation of the reconstructed tomogram of virus maturation at the plasma membrane.

Fig.5: 3D-model of a virus budding at the plasma membrane.

Transmission electron microscopy

Sections of infected Vero B4 cells prepared by high pressure freezing and freeze substitution[2] sh

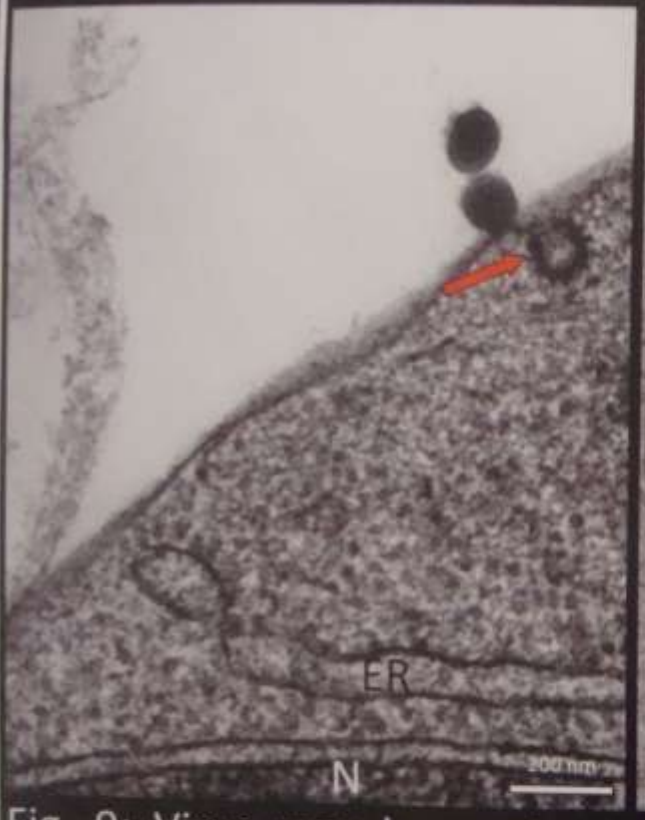

Fig. 9: Virus may bee entry by receptor mediated endocytosis. This picture shows a possible entry of SFTV in a cell (red arrow).

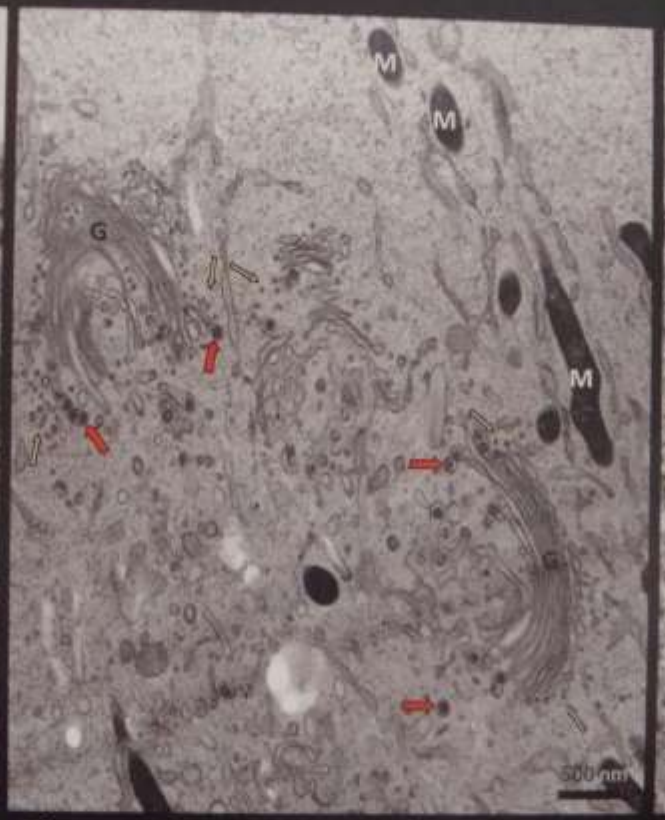

Fig. 10: Virus factory is characterised by an arrange-ment of mitochondria and small vesicles (yellow arrows) around the Golgi.

Fig. 11: Viral particles form by budding in the Golgi apparatus (red arrows).

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Sandfly Fever Virus Activity in Central/Northern Anatolia, Turkey: First Report of Toscana Virus Infections.

Ergünay K, Saygan MB, Aydoğan S, Lo MM, Weidmann M, Dilcher M, Sener B, Hasçelik

Abstract

Abstract Sandfly Fever Viruses (SFVs) cause febrile diseases as well as aseptic meningitis/encephalitis and include serotypes Sandfly Fever Sicilian Virus (SFSV), Sandfly Fever Naples Virus (SFNV) and Toscana Virus (TOSV). Infections are endemic in the Mediterranean basin and data on SFV activity in Turkey are limited. In this study, sera from 1533 blood donors from **Ankara, Konya, Eskisehir and Zonguldak** provinces of Turkey were evaluated for SFV exposure by indirect immunofluorescence test (IIFT) and confirmed by virus neutralization test (VNT). One hundred and two patients with central nervous system (CNS) infections of unknown etiology were also tested via IIFT and real-time reverse-transcription PCR for SFV/TOSV. Rate of overall IgG reactivity in IIFT was 32.9% (505/1533) among blood donors. TOSV exposure was confirmed by VNT in all study regions. Exposure to the **recently-identified serotype Sandfly Fever Turkish virus, as evaluated by VNT, was revealed in Konya and Ankara.** ~~SFNV exposure was identified~~ in Konya and SFSV was observed to be present in all regions except Zonguldak. TOSV RNA was detected in 15.7% (16/102) and was accompanied by TOSV IgM in 25% (4/16) of the patients. Partial L and S sequences suggested that TOSV circulating in Turkey can be grouped into TOSV genotype A strains. Exposure to TOSV and other SFV serotypes were revealed in blood donors and CNS infections by TOSV were identified for the first time in Turkey. Infections are observed to be endemic in Central Anatolia and should be considered as etiologic agents in cases/outbreaks of fever and meningoencephalitis.

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Özgün Çalışma/Original Article Mikrobiyol Bul 2010; 44: 431-439

KIRIKKALE İLİNDE SAPTANAN TATARCIK HUMMASI SALGINI

SANDFLY FEVER OUTBREAK IN A PROVINCE AT CENTRAL ANATOLIA, TURKEY

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ÖZET

Tatarcık humması virusu (Sandfly fever virus; SFV), *Bunyaviridae* ailesi, *Phlebovirus* cinsinde sınıflandırılmakta olup Ortadoğu'da ve Akdeniz havzasında görülmektedir. SFV'nin, Sicilya (SFSV), Kıbrıs (SFCV), Napoli (SFNV) ve Toskana virus (TOSV) olmak üzere dört serotipi mevcuttur. Başta *Phlebotomus* spp. olmak üzere çeşitli tatarcık türleri ile bulaşan hastalık, ani ateşle başlar ve üç gün içinde sona erer. En sık görülen klinik bulgular baş ağrısı, iştahsızlık ve kas ağrısıdır. Bu çalışmada, Temmuz 2009 tarihinde Kırıkkale ilinde ortaya çıkan tatarcık humması salgını sırasında tanımlanan hastaların klinik ve laboratuvar bulgularının sunulması amaçlanmıştır. Kırıkkale ilinin değişik mahallelerinde ikamet eden 20 hasta, sinek sokması hikayesi ve ateş, kas-eklem ağrısı, baş ağrısı, gözlerde kızarıklık ve ishal, bulantı-kusma gibi sindirim sistemi şikayetleri ile Kırıkkale Devlet Hastanesi, Enfeksiyon Hastalıkları Kliniğine başvurmuştur. Hastalar, hastaneye yatırılarak izlenmiş ve benzer klinik ve laboratuvar bulgularının olması, şikayetlerinin özellikle temmuz ayında görülmesi ve sinek sokması hikayesinin bulunması, bir tatarcık humması salgınını düşündürmüştür. Her mahalleden başvuran ilk hastalar "indeks olgu" olarak kabul edilmiş ve bu şekilde toplam 11 hastanın serum örnekleri Refik Saydam Hıfzıssıhha Merkezi Başkanlığı, Viroloji Referans ve Araştırma Laboratuvarına gönderilmiştir. Örneklerin analizi; SFSV, SFCV, SFNV ve TOSV'ye karşı oluşan IgG ve IgM antikorlarını saptamak için hazırlanmış ticari bir mozaik immünofloresans testi (IFT) (Euroimmun, Almanya) ile yapılmıştır. On bir hastanın 8'inde SFV-IgM pozitifliği saptanmış (5'inde Napoli, 3'ünde Sicilya serotipine karşı), hastaların hiçbirisinde IgG varlığı tespit edilmemiştir. Pozitiflik saptanan 8 hastanın ikisi kadın altısı erkek olup, yaş ortalaması 30.7 (yaş aralığı: 16-53) yıldır. Beş olguda tatarcık humması tanısı, olguların ilk serum örneklerinde saptanan tek başına IgM pozitifliği ile; 3 olguda ise 6 gün sonra alınan ikinci örneklerdeki IgM serokonversiyonu ile konulmuştur. Klinik olarak, seropozitif 8 hastanın hepsinde ateş ve miyalji; 7'sinde ishal ve bulantı-kusma; 5'inde baş ağrısı ve birinde konjunktivada kızarıklık mevcuttur. Laboratuvar bulguları olarak; hastaların hepsinde lökopeni (1800-3800 hücre/µl), 7'sinde trombositopeni (69.000-140.000 hücre/µl), 7'sinde yüksek AST (42-271 IU/L), 5'inde yüksek ALT (46-173 IU/L), 6'sında yüksek CK (185-1560 U/L) ve 5'inde yüksek CRP (5.18-83.6 mg/L) düzeyleri izlenmiştir. Semptomatik tedavi uygulanan hastalarda herhangi bir sekel izlenmemiş, tüm hastalar şifa ile taburcu edilmiştir. So-

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