Bruselloz: Güncel Literatürler Eşliğinde Güncelleme

Dr. Tuba TURUNÇ

Başkent Üniversitesi Dr. Turgut Noyan Adana Uygulama ve Araştırma Merkezi
Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji

EKMUD Çukurova Günleri Konya 10/03/2018

Bir Konya’lı olarak

Bruselloz

- ‘Akdeniz ateşi gerek yayılımı gerekse kronikleşmesi nedeniyle en sık görülen ve inatçı seyreden bir illet olacaktır. Akdeniz ateşi geleceğin hastalığıdır’.

  Charles Nicolle

Quoted by Abela-Hyzler P., ‘Undulant fever in Malta. An analysis of a public health problem.’ Unpublished DPH thesis, London School of Hygiene and Tropical Medicine, London, 1964.

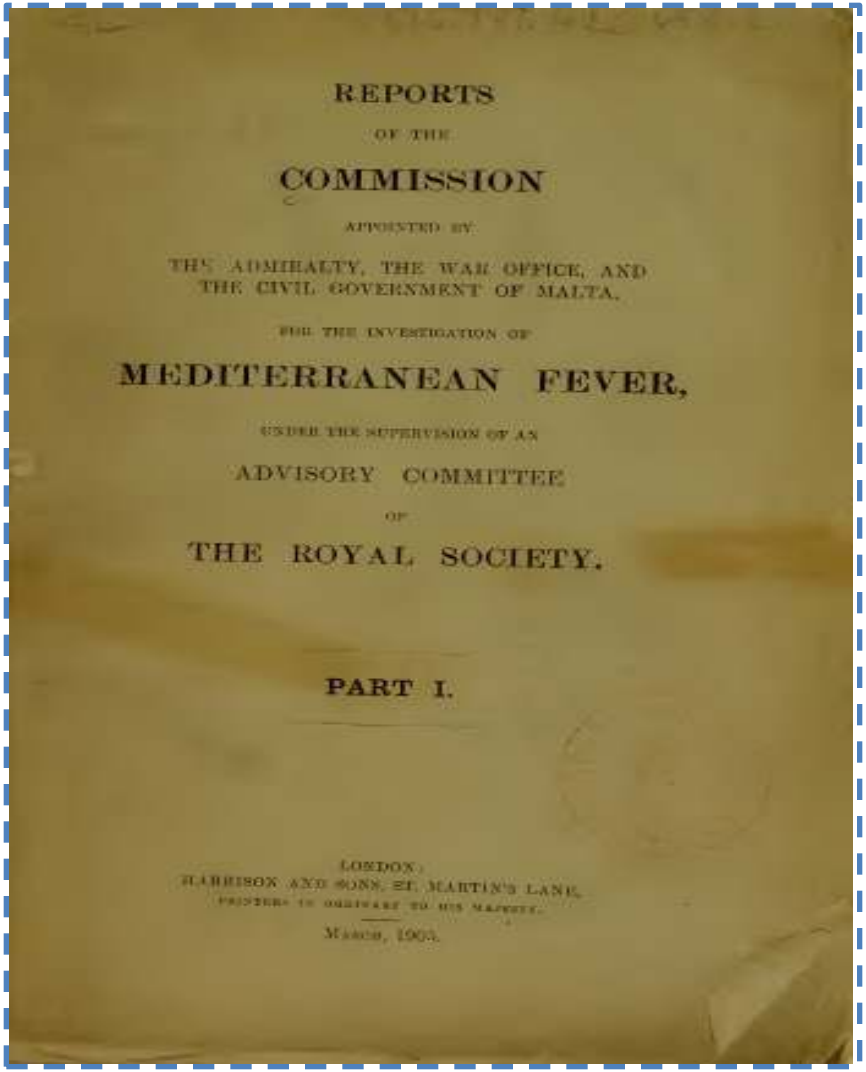
Sunum Planı

- Önemi
- Epidemiyoloji
- Klinik, Tanı ve Tedavide yeni ne var?

Tarihçe

1887 ölen asker otopsisi
X500 büyütmede mikrokoklar
mikroskopta dans ediyordu.
Micrococcus melitensis (melita: Malta)

Tarihçe



REPORTS

OF THE

COMMISSION

APPOINTED BY

THE ADMIRALTY, THE WAR OFFICE, AND THE CIVIL GOVERNMENT OF MALTA,

FOR THE INVESTIGATION OF

MEDITERRANEAN FEVER,

UNDER THE SUPERVISION OF AN

ADVISORY COMMITTEE

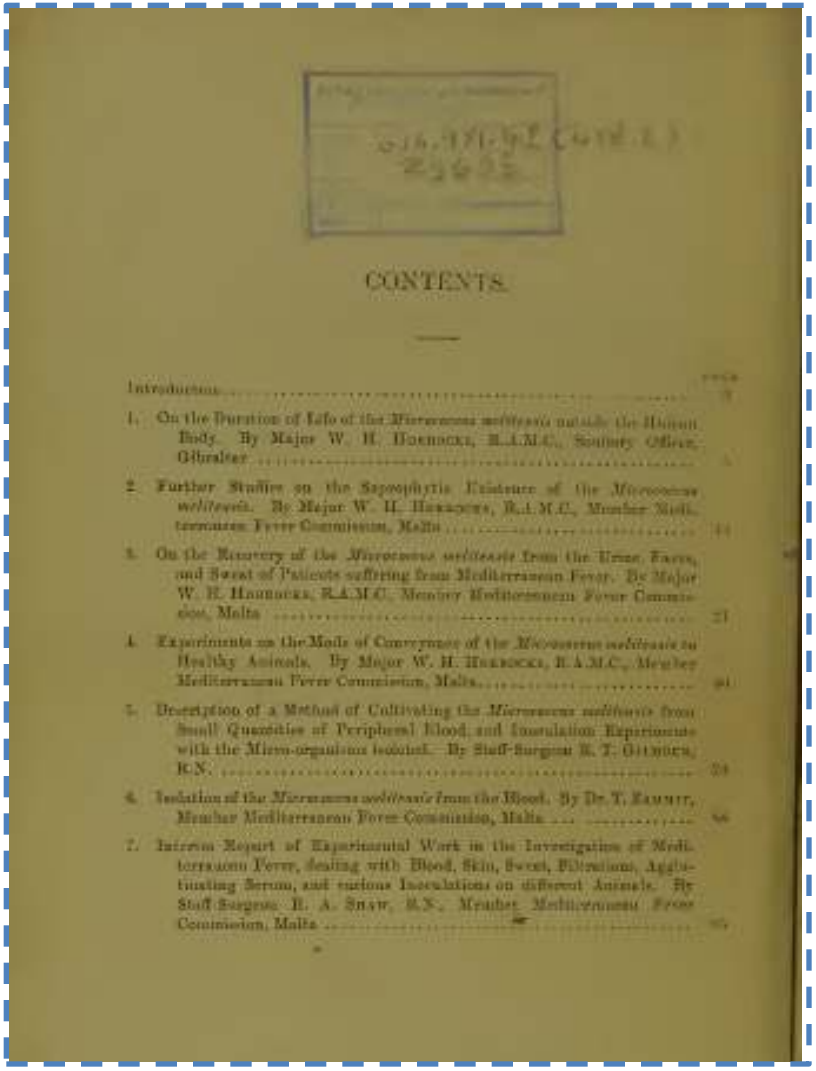
OF

THE ROYAL SOCIETY.

PART I.

LONDON:
HARRISON AND SONS, ST. MARTIN'S LANE,
PRINTERS IN ORDINARY TO HIS MAJESTY.

MDCCCC. 1905.



CONTENTS.

Önemi

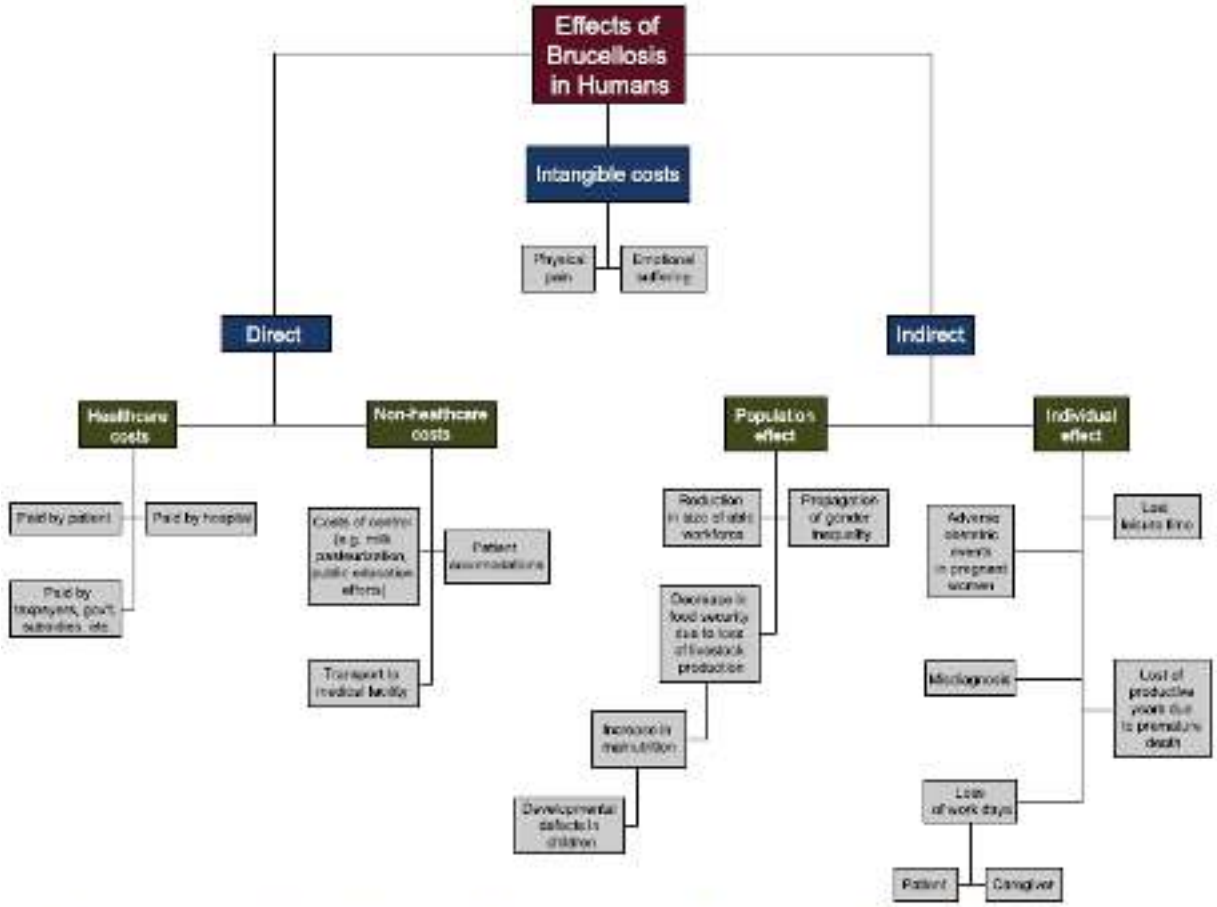


Fig. 2 Framework to assess the effects of human brucellosis in regions where the disease is endemic, adapted from Jay 2014

Franc et al. BMC Public Health (2018) 18:125

Önemi

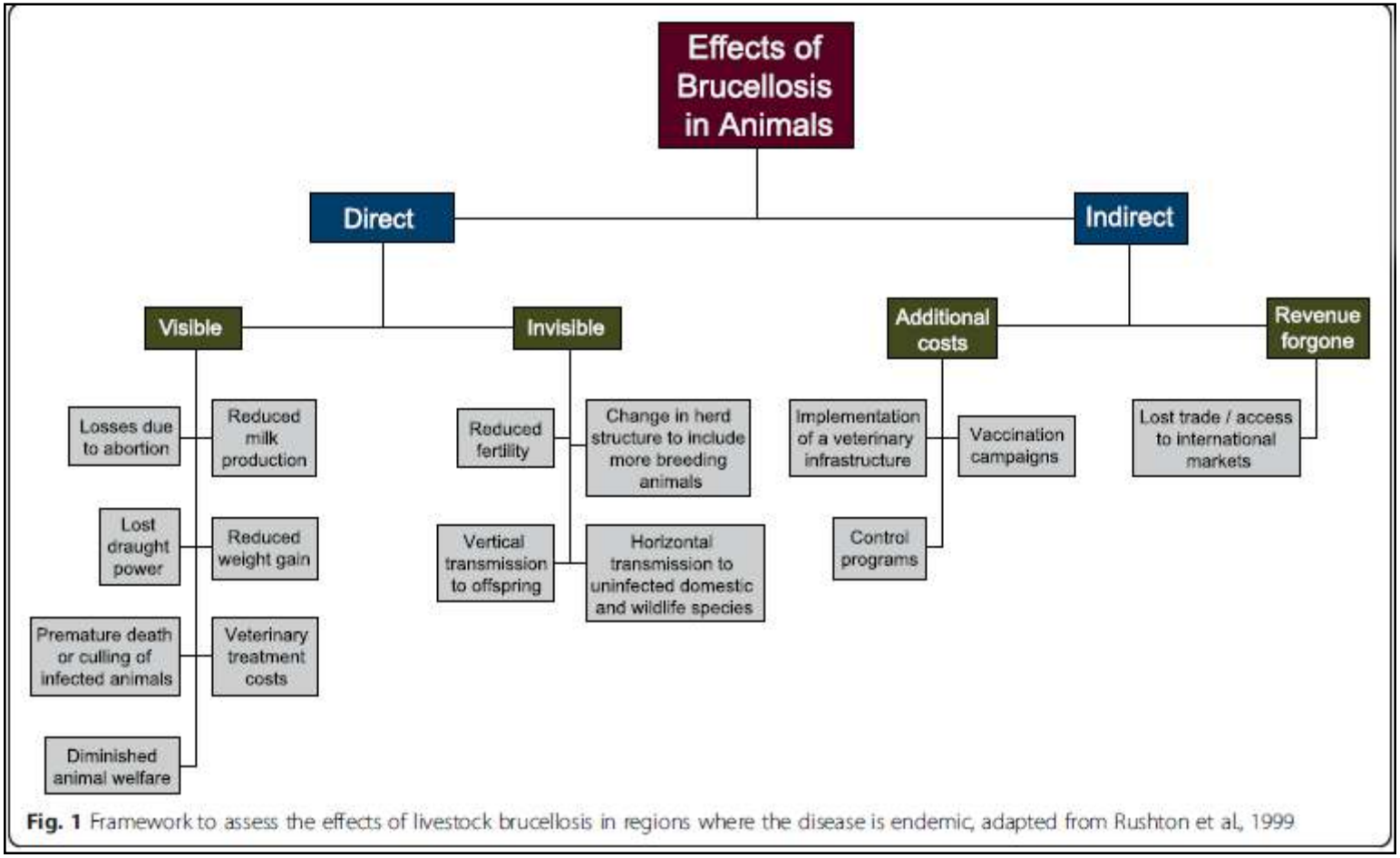


Fig. 1 Framework to assess the effects of livestock brucellosis in regions where the disease is endemic, adapted from Rushton et al., 1999

Franc et al. BMC Public Health (2018) 18:125

Ekonomik Yük Türkiye

Poliklinik	96,4
Lab	89,4
Görüntüleme	86,9
Yatış	1689,2
İlaç	544,5
Toplam	2506,4

Ekonomik Yük Türkiye

• Bruselloz insidansı	14/100.000 (Yılmaz, 2009)
• TUİK verilerine göre 2015 yılı nüfusu	78.741.053
• Bu durumda Bruselloz vakası	11024
• Bruselloz hastalığının ortalama toplam direkt maliyeti	27.632.511,40 TL

Bir Biyoterörizm Aracı Olarak Brusella

- 50 kg *B. suis'in iki kilometrelik bir hat*
- boyunca havaya bırakılması,
- 500 000 nüfuslu bir kentte
- 125 000 kişinin etkilenmesine,
- 500 kişinin ölmesine ve
- mikroorganimaya maruz kalan her 100 000 kişi için 477,7 milyon $'lık bir harcamaya mal olacaktır

Doganay GD, Doganay M. Recent Patents Anti-Infect Drug Disc. 2013;8(1):27–33.

Brucella Türlerinin Sınıflandırılması

Tür	Konak Hayvan	İnsanlarda hastalık
Eski türler		
B. melitensis	Keçi, koyun, deve	(+) En yaygın
B. abortus	Sığır, deve, buffalo, geyik	(+) 2. yaygın
B. suis	Domuz , yabani tavşan , ren geyiği, kemirgen	(+)
B. canis	Köpekgiller	(+)
B. ovis	Koyun	(-)
B. neotomae	Kemirgenler	(-)
Yeni türler		
B. ceti	Balina, yunus balığı, domuz balığı, fok	Nörobruselloz, spondilit ve laboratuvar kaynaklı
B. pinnipedialis	Ayı balığı	(+)
B. microti	Kırmızı tilki, tarla faresi	(-)
B. inopinata	Bilinmiyor	Prostetik meme implant infeksiyonu

Pappas G. Int J Antimicrob Agents 2010

Journal of Infection and Public Health (2016) 9, 675–678

http://www.elsevier.com/locate/jiph

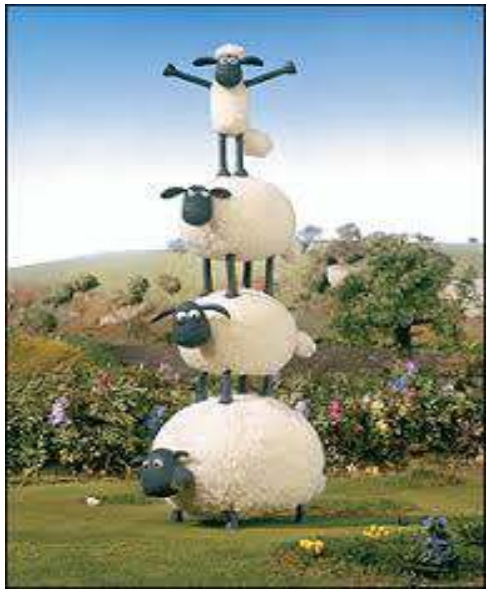
SHORT COMMUNICATION

The first report of *Brucella suis* biovar 1 isolation in human in Turkey

Murat Kutlu[a,*], Nural Cevahir[b], Sevil Erdenliğ-Gürbilek[c], Şerife Akalın[a], Mehmet Uçar[a], Selda Sayın-Kutlu[a]

Epidemiyoloji

- Brusellozis, Birlesmis Milletler Gıda ve Tarım Teskilatı (FAO), Dünya Saglık Örgütü (WHO) ve Uluslar Arası Salgın Hastalıklar Ofisi (OIE) tarafından dünyada en yaygın zoonozlardan biri olarak kabul edilmektedir



Her yıl yaklaşık 500.000 yeni olgu bildirilmektedir

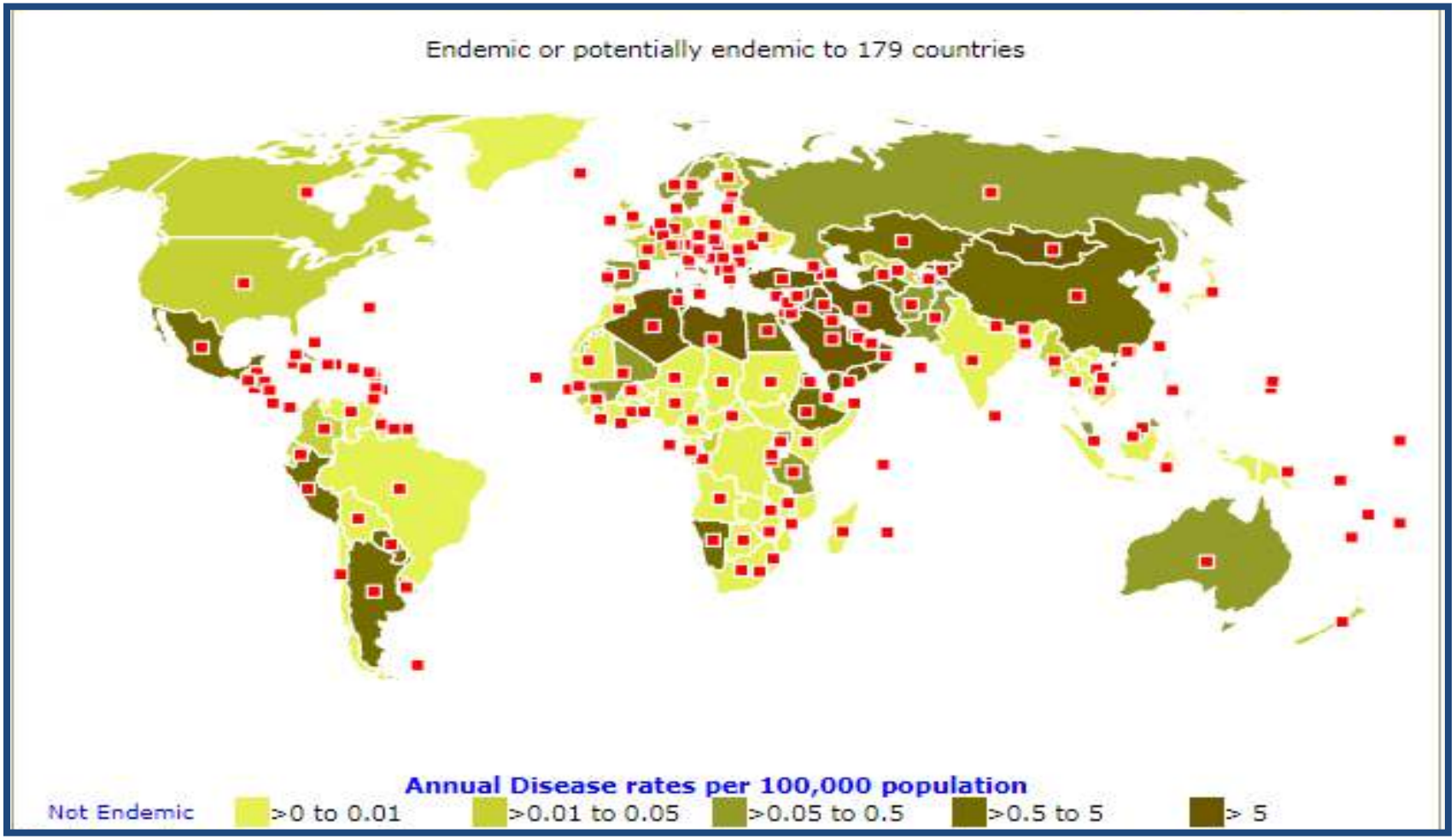
Nicoletti, P. 2010. Section of Medical Science. XXXI: 21-32.

Epidemiyoloji

Bildirilen

Gerçek x30 kat

Epidemiyoloji



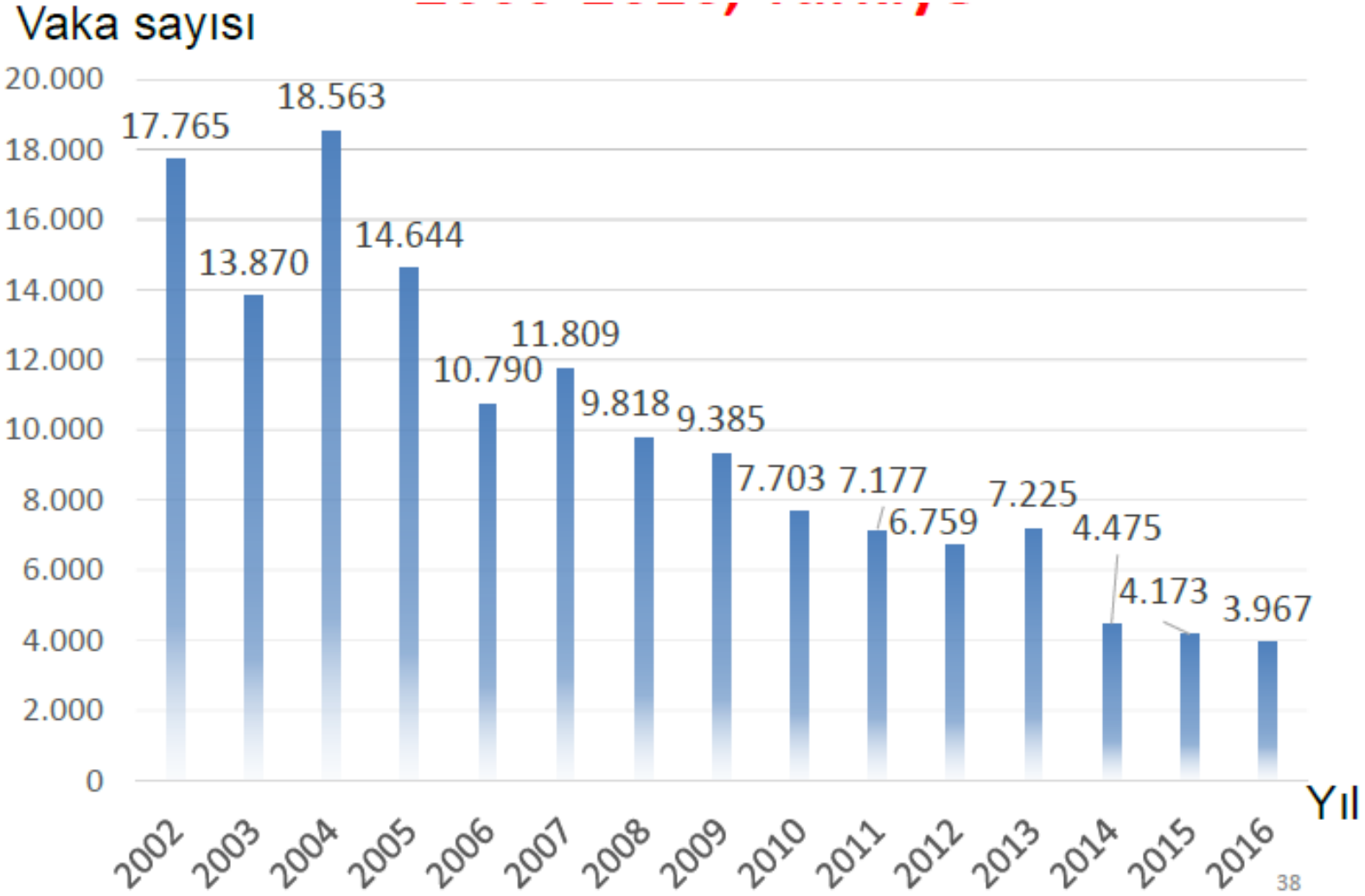
GIDEON,2018

Epidemiyoloji

- **Brusellozun Eradike Edildiği Ülkeler**
- Son 5 yıl içinde vaka bildirilmemesi
- Avustralya
- Kanada
- Kıbrıs
- Danimarka
- Finlandiya
- Hollanda
- Norveç
- İsveç
- İngiltere
- Yeni Zelenda

Franc et al. BMC Public Health (2018) 18:125

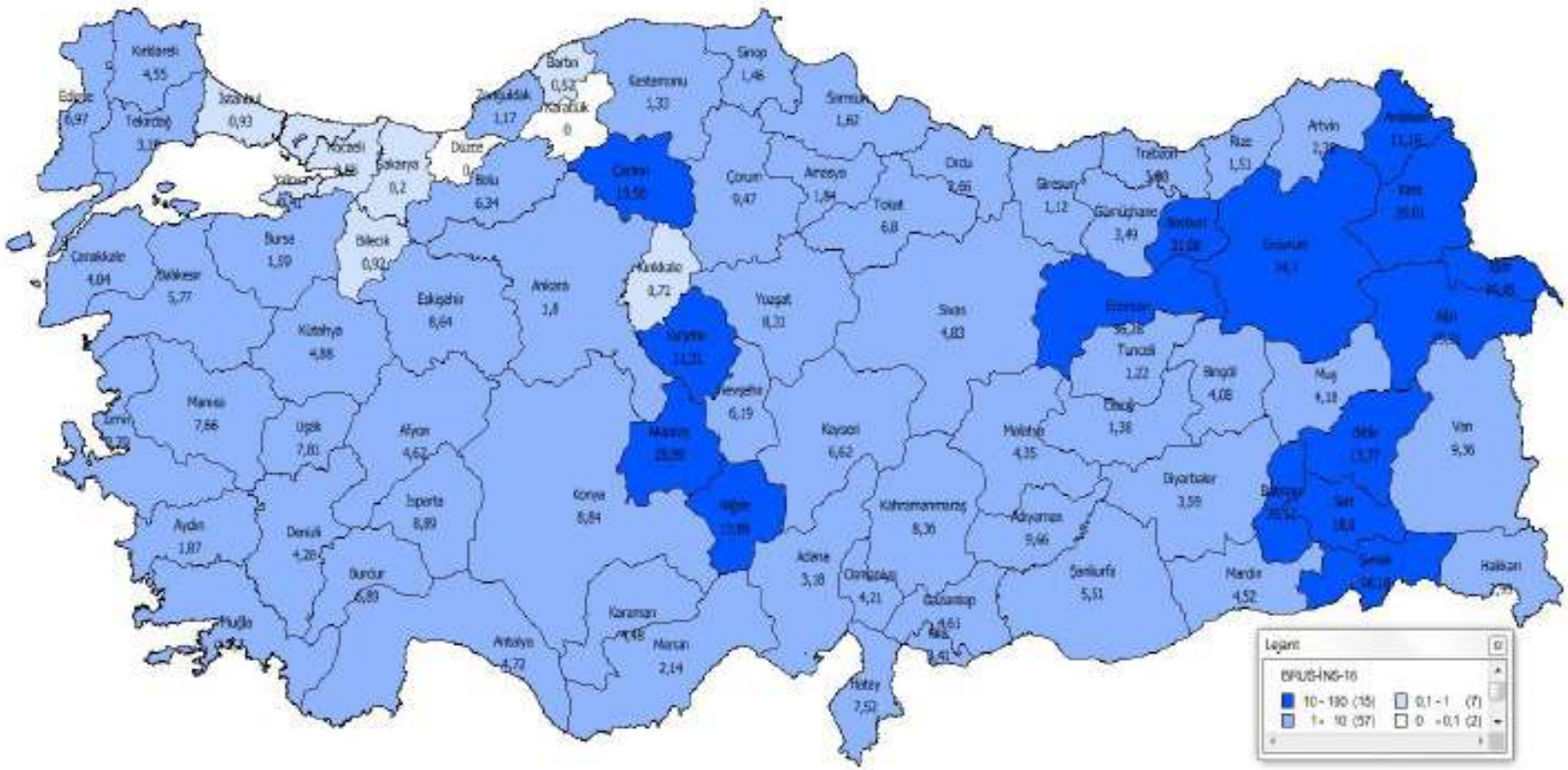
İnsan Bruselloz Vakaları Türkiye 2000-2016



Bruselloz İnsidans Haritası, 2014

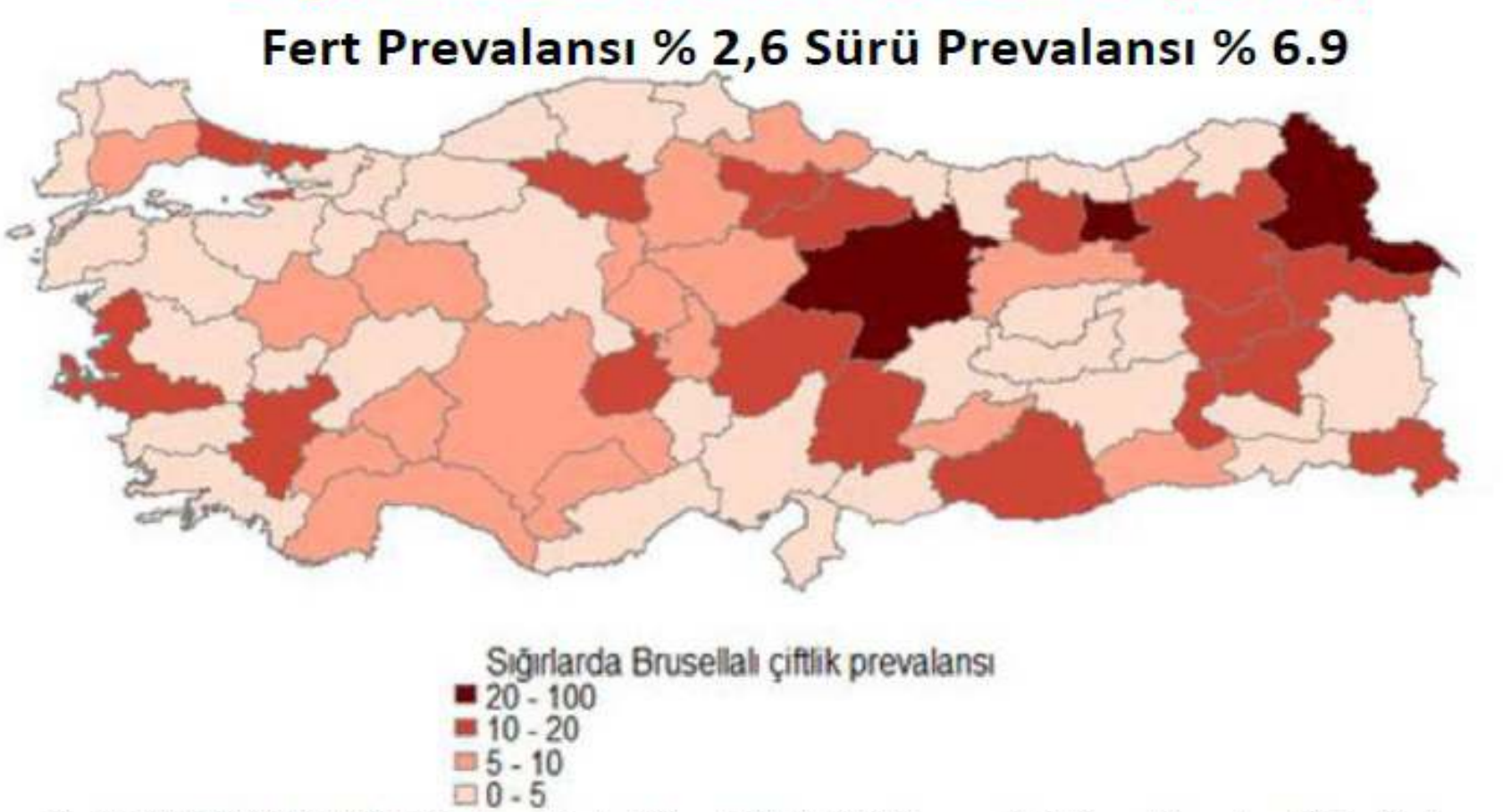
Sağlık Bakanlığı THSK verisidir.

Bruselloz İnsidans Haritası, 2016



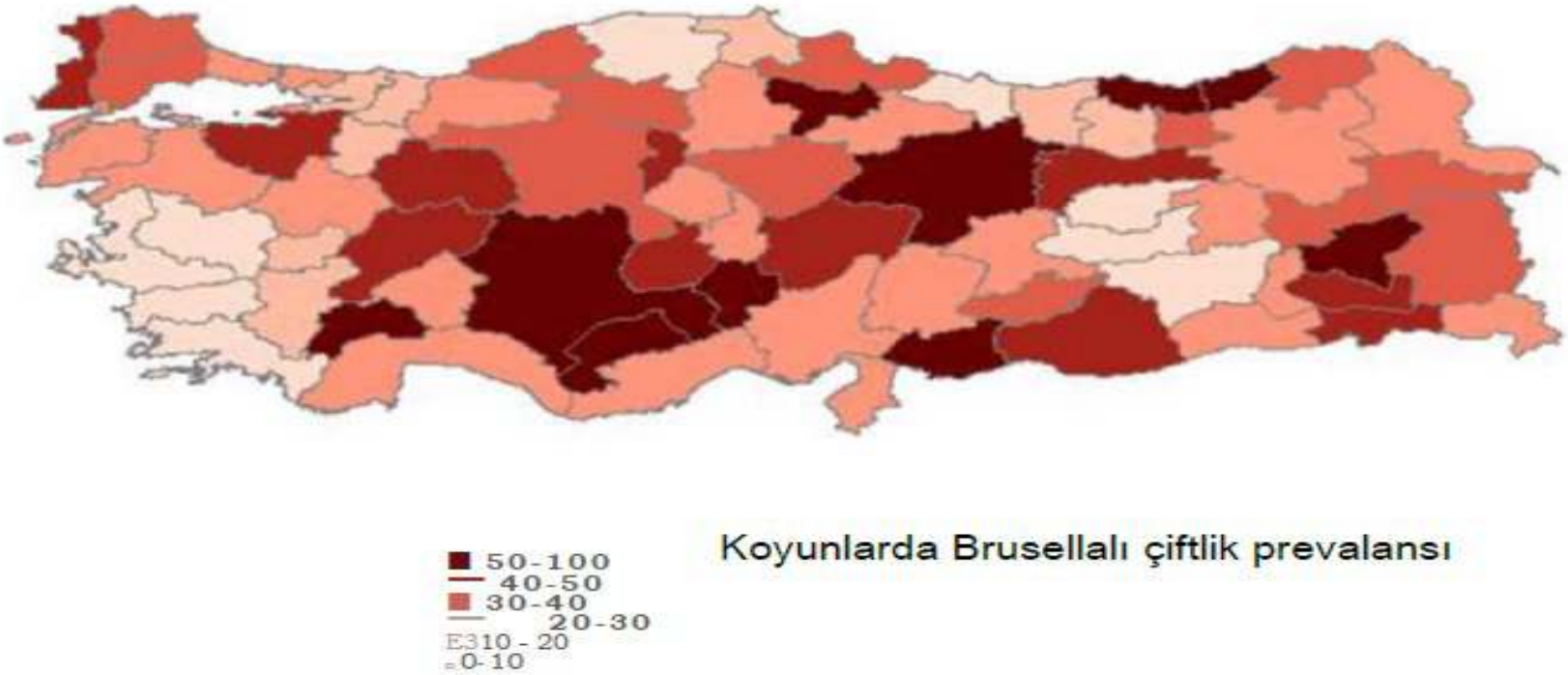
Sağlık Bakanlığı THSK verisidir.

Eradikasyon Programı Öncesinde Sığırlarda Brusella Prevelansı (2011)



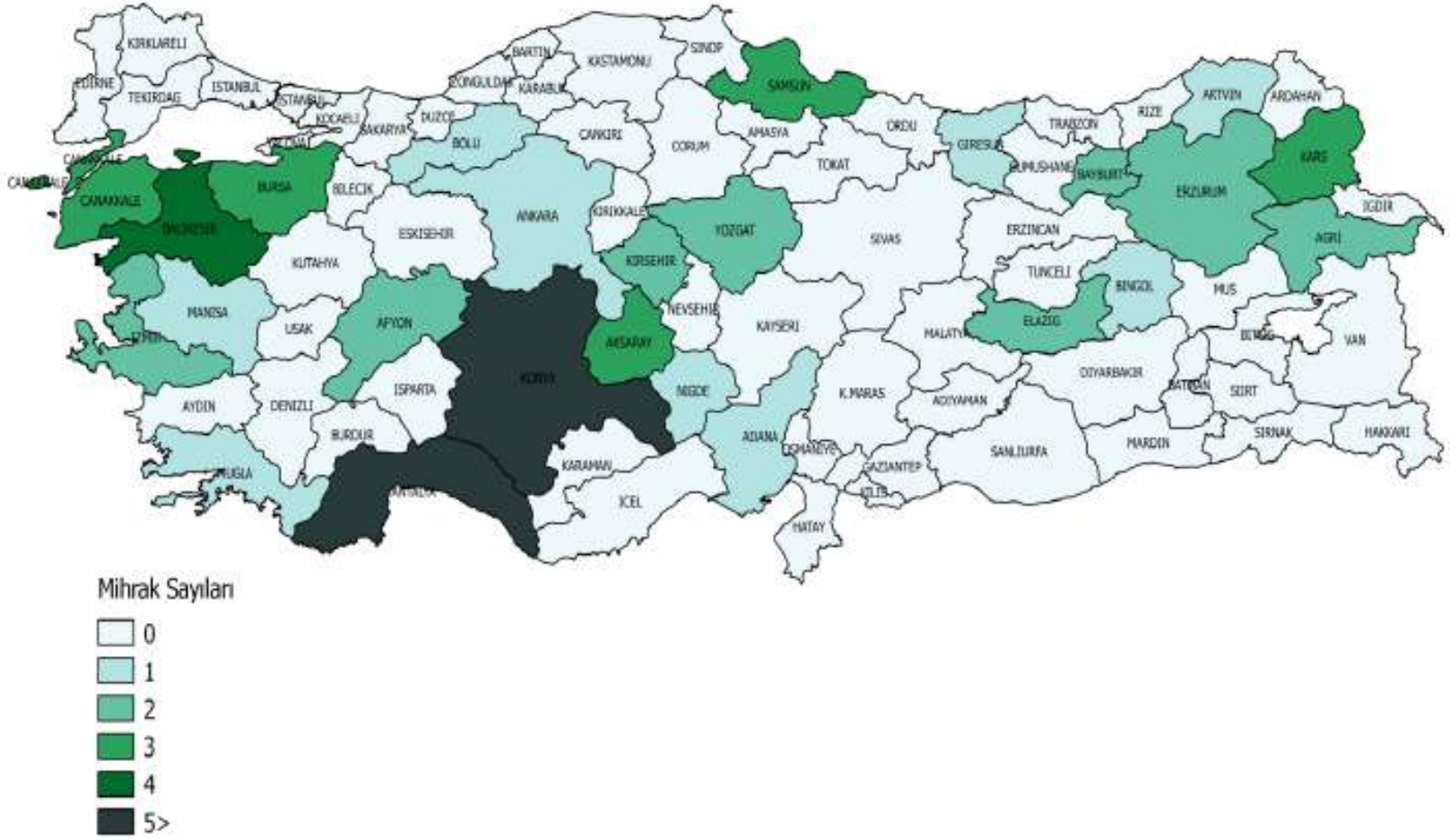
Koyun ve Keçilerde Prevelans,2011

Fert Prevalansı % 4,7
Sürü Prevalansı % 30



Dr. N. YAZICIOĞLU GTHB Gıda ve Kontrol Genel Müdürlüğü Hayvan Sağlığı ve Karantina Daire Başkanı
V.Türkiye Zoonotik Hastalıklar Sempozyumu-24/25 Ekim 2014-Erzurum

Koyun ve Keçilerde Bruselloz Mihrakları,2016 (76)



Bruselloz Olgu Sayıları Akdeniz Bölgesi

	2014		2015		2016		2017*	
IL	Vaka	Ölüm	Vaka	Ölüm	Vaka	Ölüm	VAKA	ÖLÜM
ADANA	92	0	117		77	0	115	0
ANTALYA	57	0	36		111	0	89	0
BURDUR	62	0	17		18	0	26	0
HATAY	83	0	65		117	0	184	0
ISPARTA	63	0	25		39	0	105	0
MERSİN	24	0	31		40	0	54	0
KAHRAMANMARAŞ	57	0	61		93	0	116	0
OSMANİYE	20	0	14		22	0	66	0
Bölge Toplamı	458	0	366	0	517	0	755	0

Komşularda Bruselloz

Ülke	İnsan (/100.000)	Koyun/Keçi (%)	Sığır (%)
İran	23.9	10.2	17.5
Irak	27.9	15	3
Suriye	160	3	3.1
Türkiye	9.6	3.4	2.7
Yunanistan	0.81		
Bulgaristan	0.03		
Avrupa Birliği	0.07		

Zeki Yumuk Z, O'Callaghan D. Int J Infect Dis 2012
European Centre for Disease Prevention and Control. Annual Epidemiological Report 2013
Erganiş O. IV. Zoonotik Hastalıklar Sempozyumu Kitabı, 2012

Farkında mıyız?

Gümüşhane Üniversitesi Sağlık Bilimleri Dergisi / Gümüşhane University Journal of Health Sciences: 2012;1(4)

HAYVAN YETİŞTİRİCİLERİNİN İŞLETME BÜYÜKLÜĞÜNE GÖRE, BRUSELLA HASTALIĞI HAKKINDAKİ BİLGİ DÜZEYLERİNİN ARAŞTIRILMASI*

Handan ÖZCAN[1], Mitat ŞAHİN[2]

- Mart 2009 - Temmuz 2009
- Kars, 11 köy,
- 350 kişi
- Sürülerdeki hayvan sayısı: 6313

	Sayı	Yavru atan (%)	Kısır (%)
Küçükbaş	789	53 (6.7)	30 (3.8)
Büyükbaş	5524	561 (10.2)	627 (11.4)

Farkında mıyız?

Atık yapan hayvanlarınıza neler yaparsınız?	Sayı	%
Sürüde saklarım	92	51,1
Satarım	77	42,8
Keserim	9	5
Kasaba veririm	2	1,1
Toplam	180	100,0

Atık olduğu zaman nerelere haber verir siniz?	Sayı	%
Kimseye haber vermem	274	78,28
Veteriner hekime	72	20,57
İl tarıma	4	1,14
Toplam	350	100,0

ÖZCAN H, ŞAHİN M. Gümüşhane Üniv Sağlık Bil Derg 2012

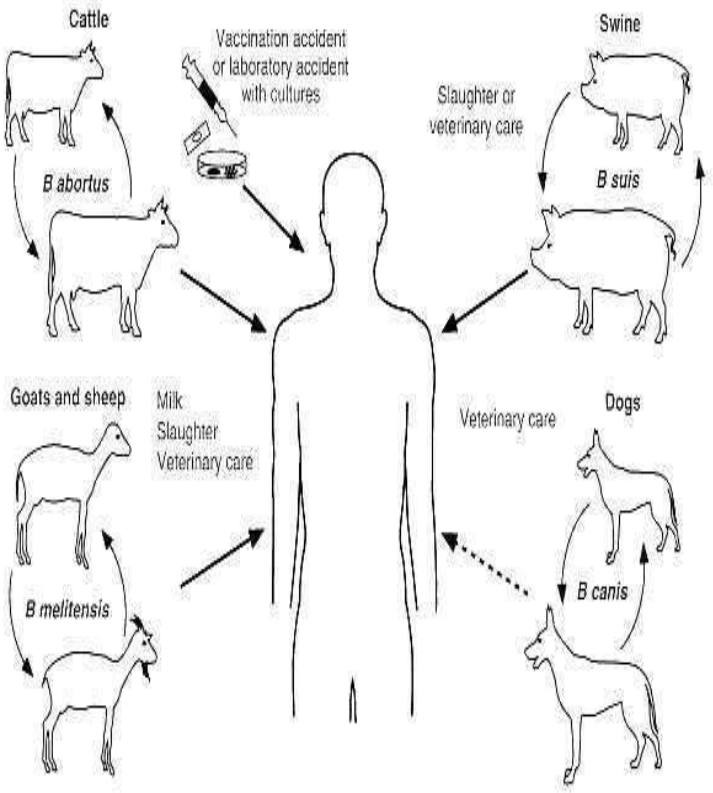
Farkında mıyız?

Yaptığınız peynirleri nasıl tüketir siniz?	Sayı	%
Taze olarak tüketirim	144	41,15
Salamura yaparak tüketirim	128	36,57
Tuluma koyup 3 ay bekleterek tüketirim	78	22,28
Toplam	350	100,0

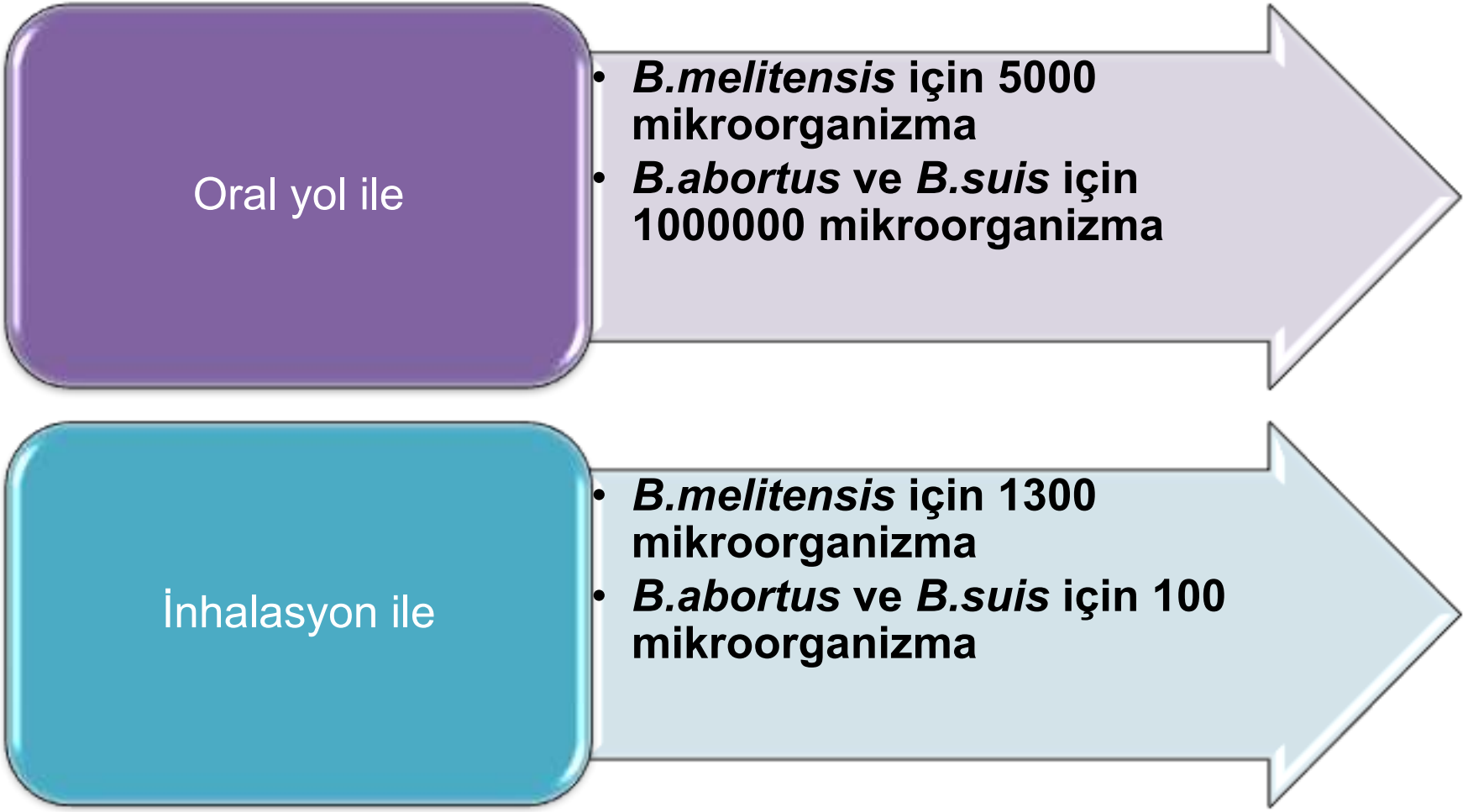
Doğum sonrası çıkan zar ve sıvıları nasıl imha edersiniz?	Sayı	%
Dışarı atarak	130	72,2
Toprağa gömerek	40	22,2
Köyden uzak yere atarak	7	3,8
Diğer	3	1,8
Toplam	180	100,0

ÖZCAN H, ŞAHİN M. Gümüşhane Üniv Sağlık Bil Derg 2012

Bulaş Yolları



İNFEKTİF DOZU NEDİR?



Doganay GD, Doganay M. Recent Patents Anti-Infect Drug Disc. 2013;8(1):27–33.

Bulaş Yolu Türkiye Verileri

Bulaş Yolu (%)	Hatipoğlu Ankara (n=202)	Taşova Adana (n=238)	Koşar Isparta (n=280)	Taşbakan İzmir (n=109)	Gür Diyarbakır (n=283)	Demirdağ Elazığ (n= 146)
Çiğ süt ve süt ürünü kullanımı	94.6	53	30	67.9	72	76.7
Hayvancılık, mesleksel temas	70.3	31	90	29.4	47	-
Laboratuvar teması	-	-	1	3.3	6	-
Bilinmeyen	2.4	16	13	-	36	

Laboratuvar Kaynaklı Bruselloz

Kutlu S.J Hospital Infect 2012 Apr;80(4):326-30

Laboratuvar Kaynaklı Bruselloz

1982-2007

28 olgu raporu

167 temaslı laboratuvar çalışanından, 71 olguda LKB gelişmiş

Temas şekli	En sık sorumlu etken	İnkübasyon süresi
%18 laboratuvar kazası %88 aerosellerin inhalasyonu %1 bilinmeyen	%80 *B. melitensis*	Ortalama 8 hafta

Traxler RM et al. J Clin Microbiol. (2013)

Laboratuvar Kaynaklı Bruselloz

TABLE 3 Comparison of *Brucella* postexposure follow-up recommendations

Procedure	CDC recommendations, 2008 (23)	Modifications to recommendations[a]
Antimicrobial PEP	High risk: doxycycline (100 mg) twice daily and rifampin (600 mg) once daily for 3 weeks; TMP-SMZ should be considered for patients with contraindications for doxycycline	Doxycycline (100 mg) twice daily and rifampin (600 mg) once daily for 3 weeks; TMP-SMZ or another antimicrobial agent effective against *Brucella* should be selected for persons with contraindications to doxycycline or rifampin; regimen and dosing should be chosen in consultation with the person's HCP; pregnant women should consult an obstetrician
	Low risk: discuss with HCP; consider if patient is immunocompromised or pregnant	No change
Serologic monitoring[b]	Baseline, 2, 4, 6, 24 weeks after last known exposure	Sequential serologic testing at baseline, 6, 12, 18 and 24 weeks post exposure *(after last known exposure)*
Symptom surveillance	Regular (e.g., weekly) symptom watch for febrile illness through 24 weeks after last known exposure	Regular (e.g., weekly) symptom watch and daily self temp checks through 24 weeks post-exposure *(after last known exposure)*

[a] These modifications are based on the above case reports and a review of the literature (24).

[b] Obtain baseline and periodic serum samples from all workers exposed to *Brucella*, unless they have been exposed to *B. abortus* strain RB51 or *B. canis*, which do not elicit a measurable serologic response in available *B. abortus* antigen-based assays.

CDC. 2008. Laboratory-acquired brucellosis—Indiana and Minnesota, 2006. MMWR Morb. Mortal. Wkly. Rep. 57:39–42.

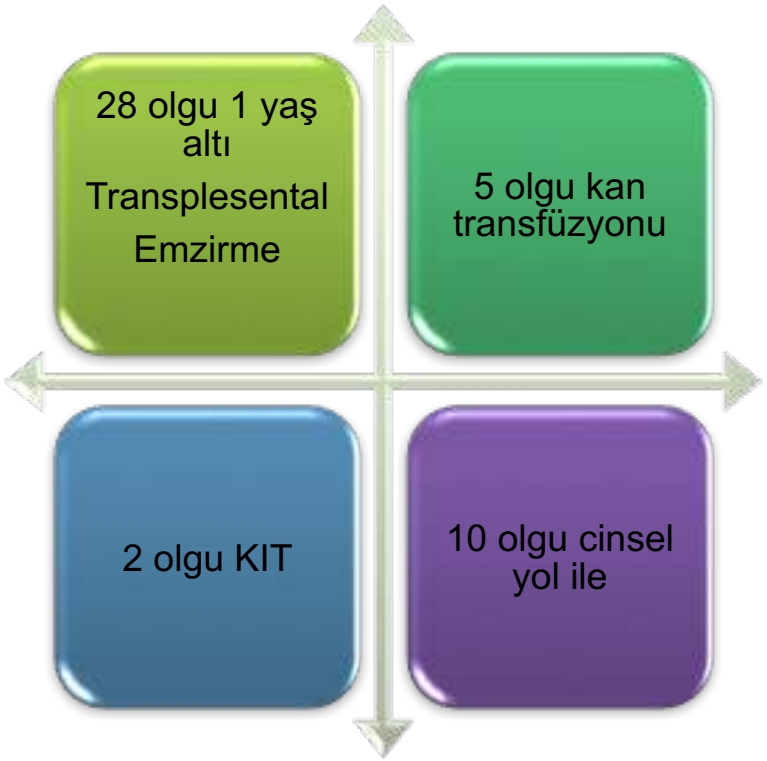
İnsandan İnsana Bulaş

Tropical Medicine and International Health doi:10.1111/tmi.12856
VOLUME 22 NO 5 PP 539–546 MAY 2017

Systematic Review

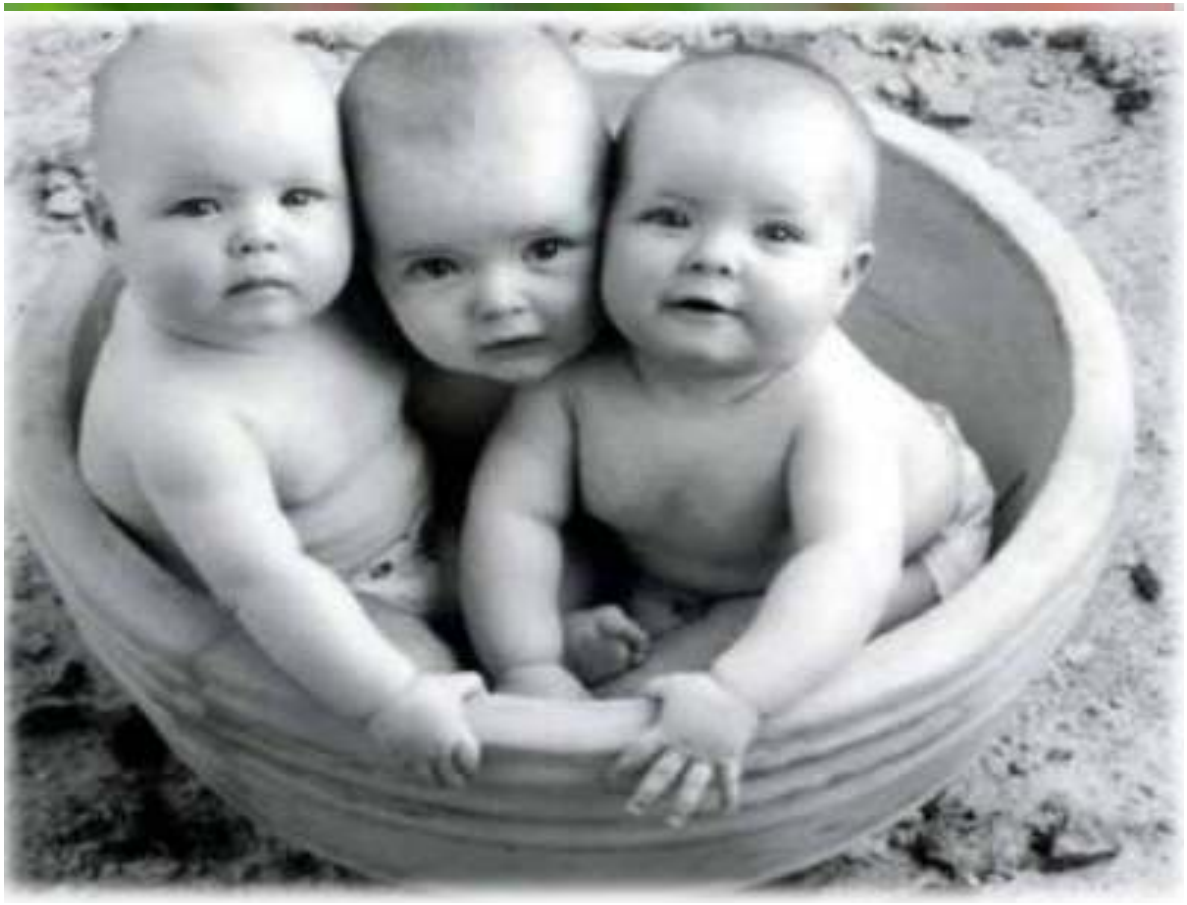
Human-to-human transmission of *Brucella* – a systematic review

Felipe F. Tuon[1,2], Regina B. Gondolfo[1] and Natacha Cerchiari[2]



2016 yılına kadar 35 yayın toplam 45 olgu

Bruselloz Klinik



Her hastalığı taklit edebilir

B.melitensis,B.abortus ve *B. suis*

Klinikleri birbirine çok benzer

Bruselloz Klinik

INTERNAL MEDICINE

Characteristic	n (%)
Mean age	48 year (15-86)
Female	261 (58.4%)
Male	186 (41.6%)
Living in a rural area	96 (21.5%)
Consumption of non-pasteurized milk or dairy products	362 (81%)
Family history of Brucellosis	54 (12%)
Personal history of Brucellosis	73 (16.3%)
Occupation	
Livestock/sheep-farming	88 (20%)
Veterinarian	7 (1.7%)
Laboratory staff	1(0.2%)
Slaughter staff	2 (0.4%)
Butcher	2 (0.4%)
Other*	347 (77.3%)
Clinical diagnosis	
Acute	304 (68%)
Subacute	101 (22.6%)
Chronic	42 (9.4%)

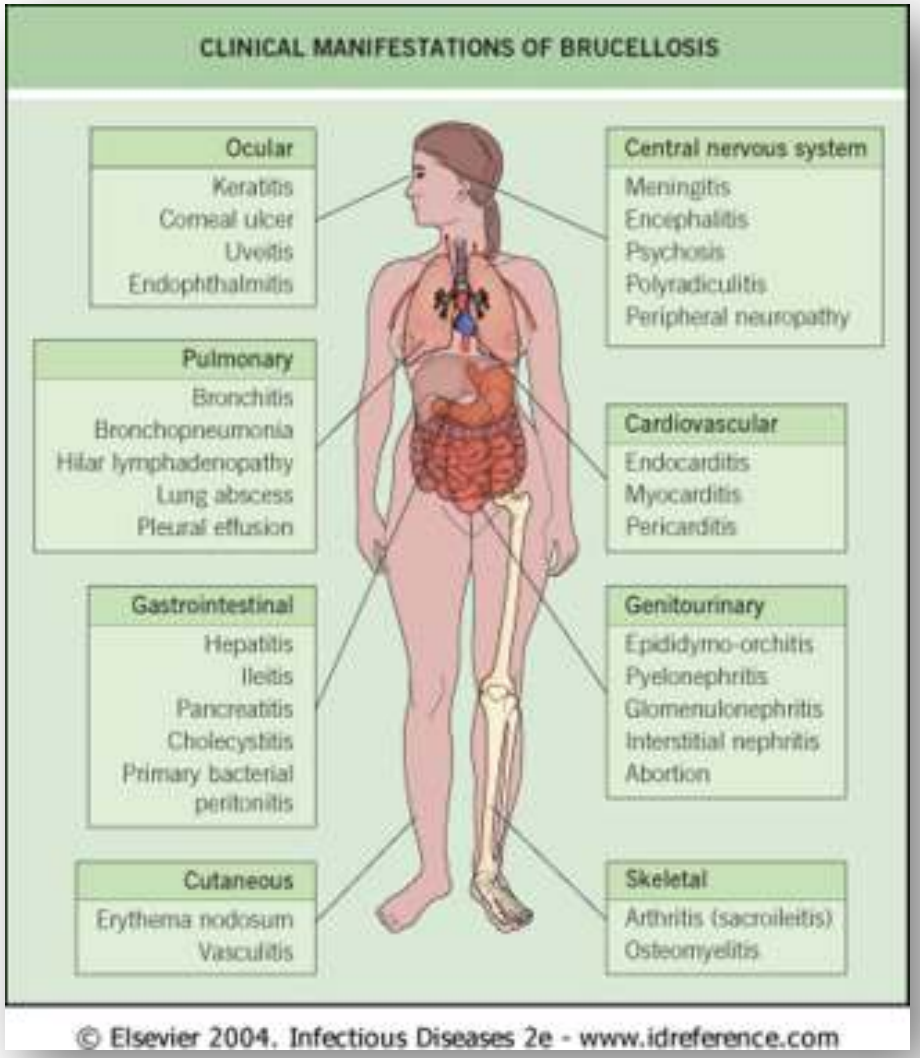
* Housewife, retired, student, self-employed and unoccupied.

	Diseases form		
Characteristics	**Acute**	**Subacute**	**Chronic**
Patient	304	101	42
Mean age (min-max)	48 (15-86)	51 (16-79)	52 (18-81)
Leukocyte (K/mm^3), mean (min-max)	7,565 (1,120-27.100)	7,150 (1,030-18.900)	7,620 (2,850-12.200)
CRP (mg/L), mean (min-max)*	25 (1-242)	8.8 (2.7-178)	6.1 (3-82)
ESR (mm/h), mean (min-max)*	29 (1-178)	25 (2-130)	23 (4-92)
Blood culture, n (%)*	130 (42.8%)	30 (29.7%)	2 (4.8%)
Spondylodiscitis, n (%)	55 (18.1%)	24 (23.8%)	6 (14.3%)
Sacroiliitis, n (%)	22 (7.2%)	10 (9.9%)	3 (7.1%)
Peripheral arthritis, n (%)	9 (3%)	5 (5%)	2 (4.8%)
Neurobrucellosis, n (%)	19 (6.3%)	4 (4%)	1 (2.4%)
Genitourinary system involvement, n (%)**	13/14 (9.7%)	1/14 (2.4%)	0/14 (0%)
Hepatomegaly, n (%)	33 (4.5%)	9 (13.8%)	1 (4.2%)
Splenomegaly, n (%)	55 (24.2%)	15 (23.1%)	2 (8.7%)
Fever complaint, n (%)*	243 (79%)	65 (64%)	23 (54%)
Arthralgia, n (%)	253 (83.2%)	74 (73%)	34 (81%)
Loss of appetite, n (%)	218 (71.7%)	57 (56.4%)	27 (64.3%)
High fever, n (%)*	67 (22%)	2 (2%)	0 (0%)
Relapse, n (%)*	25 (8.2%)	9 (8.9%)	1 (2.4%)

Pearson's chi-square test was used.*$p<0.05$, **Male patients only (n:14)

Intern Med 52: 745-750, 2013

Bruselloz Klinik



TÜBİTAK

Original Article

Turk J Med Sci
2011; 41 (3): 549-555
© TÜBİTAK
E-mail: medsci@tubitak.gov.tr
doi:10.3906/sag-0911-404

Human brucellosis in Turkey: a review of the literature between 1990 and 2009

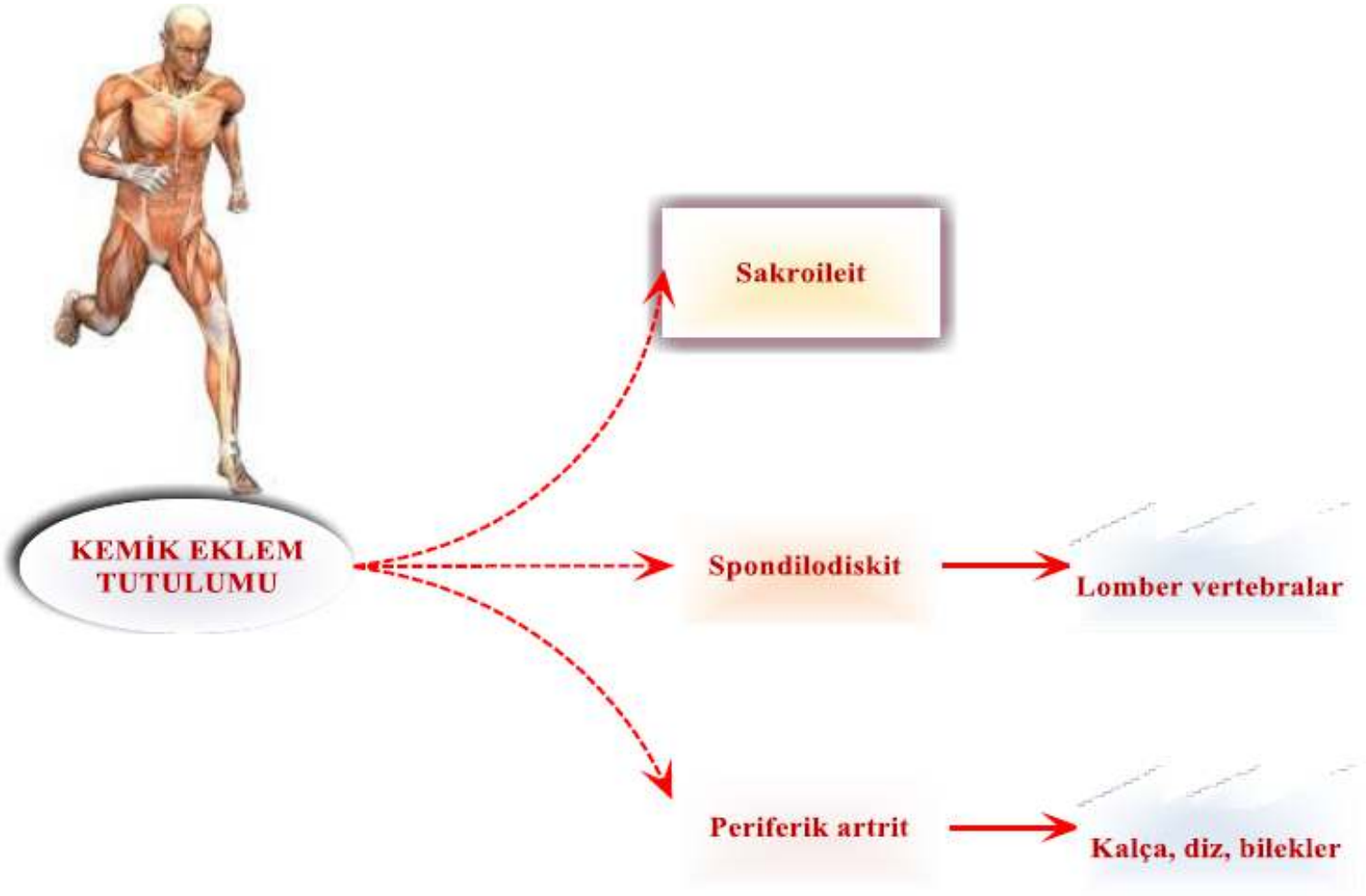
Şebnem ÇALIK[1], Ayşe Deniz GÖKENGİN[2]

Data for 4204 patients with brucellosis were obtained from 306 reports (287 published articles and 19 congress abstracts). Sex (male/female) and median patient age could not be evaluated because they were not reported in some papers. Case reports were published from 38 provinces in Turkey. Ankara, İstanbul, and Van were the most frequently reporting cities for brucellosis.

The most common involvement was osteoarticular in 1839 patients (43.74%) followed by the hematopoietic system in 1401 (33.32%) patients. In decreasing order, nervous, gastrointestinal, urogenital, skin/mucous membrane, cardiovascular, respiratory system, and ocular involvement were reported in 413 (9.82%), 182 (4.32%), 171 (4.06%), 146 (3.47%), 67 (1.59%), 46 (1.09%), and 12 (0.28%) patients, respectively (Tables 1-9). Other, less frequent involvements are shown in Table 10.

Osteoarticular system	n	%
Sacroiliitis	723	17.19
Spondylodiscitis	546	12.98
Osteoarthritis	541	12.86
Osteomyelitis	8	0.19
Bursitis	8	0.19
Psoas abscess	5	0.11
Dactylitis	2	0.04
Spontaneous bone fracture	2	0.04
Tendinitis	1	0.02
Myositis	1	0.02
Intramedullary dermoid cyst abscess	1	0.02
Gluteal abscess	1	0.02
Total	**1839**	**43.74**

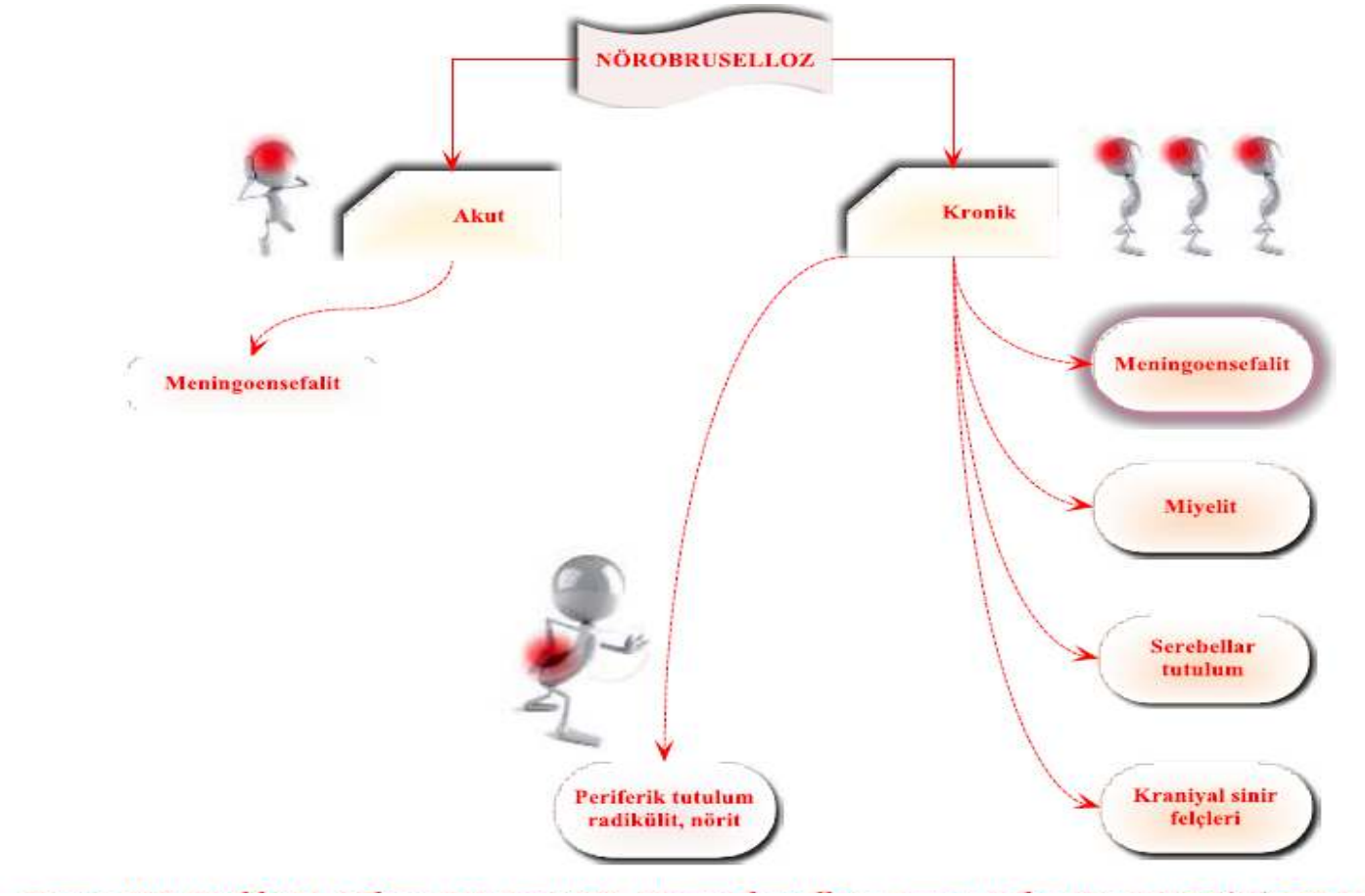
Brusellozda Kemik Eklem Tutulumu



Vertebra Tutulumu

Ulu-Kılıç A. CMI 2014;20(2):075-82

Nörobruselloz



Demiroğlu YZ,Turunç T. Mikrobiyol Bul; 2011:45(3):401-10

Meningoensefalit

187 olgu, Türkiye

En sık yakınmalar

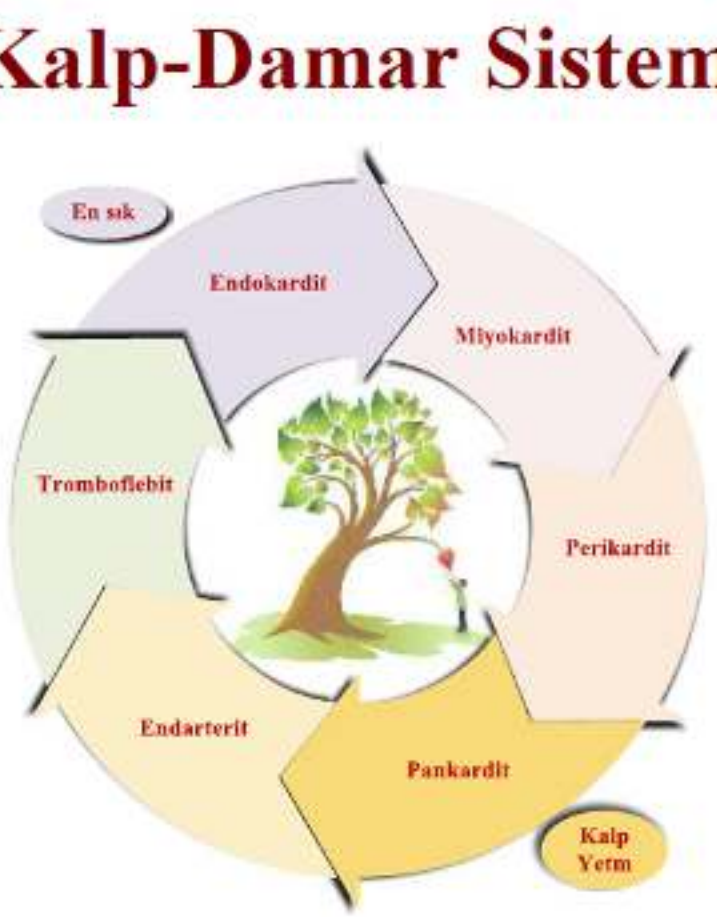
- Başağrısı, % 57
- Ateş, % 57
- Terleme, % 30
- Sırt ağrısı, % 28

En sık bulgular

- Ense sertliği, % 37
- Konfüzyon, % 18
- Karaciğer büyüklüğü, % 15
- Hipoestezi, % 12

Gul HC. Int J Infect Dis 2009:13(6):339-43

Kardiyovasküler Bruselloz



Endokardit

Endokardit, Mortalite

- Tedaviye rağmen % 13
  - Perikardiyal efüzyon ↗
  - KKY ↗

Koruk ST. Int J Antimicrob Agents 2012;40 (2)145-50

Akciğer Tutulumu

- Diğer TGP' lere benzer
- % 10, YBU gereksinimi
  - Ort. 4 gün
  - Standart tedaviye yanıt tam…
- Selim bir tablo

Erdem H. Chest 2014;145(1):87-94

Özel Durumlarda Bruselloz Gebelik

International Journal of Infectious Diseases 38 (2015) 95–100

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

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

Brucellosis in pregnancy: clinical aspects and obstetric outcomes

Gustavo Vilchez [a,b,*], Miguel Espinoza [a], Guery D'Onadio [a], Pedro Saona [a,c], Eduardo Gotuzzo [a,d]

Table 5
Obstetric outcomes after brucellosis complicating pregnancy (N = 101[a])

Obstetric outcome	Normal		Adverse							
	Full term delivery (n = 50), n (%)		Spontaneous abortion (n = 16), n (%)		Spontaneous preterm delivery (n = 12), n (%)		Fetal death (n = 7), n (%)		Congenital malformation (n = 1), n (%)	
Clinical stage										
Acute	36	(72.0)	5	(31.3)	8	(66.7)	3	(42.9)	1	100.0)
Subacute	13	(26.0)	9	(56.3)	3	(25.0)	3	(42.9)	0	(0.0)
Chronic	1	(2.0)	2	(12.5)	1	(8.3)	1	(14.3)	0	(0.0)
Trimester										
First	17	(34.0)	14	(87.5)	3	(25.0)	4	(57.1)	0	(0.0)
Second	8	(16.0)	2	(12.5)	4	(33.3)	2	(28.6)	1	(100.0)
Third	25	(50.0)	0	(0.0)	5	(41.7)	1	(14.3)	0	(0.0)
Severity of disease										
Mild	29	(58.0)	8	(50.0)	7	(58.3)	2	(28.6)	1	(100.0)
Moderate	18	(36.0)	7	(43.8)	4	(33.3)	4	(57.1)	0	(0.0)
Severe	3	(6.0)	1	(6.3)	1	(8.3)	1	(14.3)	0	(0.0)
Treatment status										
Before treatment	11	(22.0)	13	(81.3)	4	(33.3)	6	(85.7)	1	(100.0)
After treatment	39	(78.0)	3	(18.8)	8	(66.7)	1	(14.3)	0	(0.0)

[a] Fifteen of the 101 cases did not have follow-up at the study institution, leaving 86 cases.

Nephrol Dial Transplant (2008) 23: 2344–2349
doi: 10.1093/ndt/gfm925
Advance Access publication 4 January 2008

Original Article

NDT
Nephrology Dialysis Transplantation

Brucellosis in cases of end-stage renal disease

Tuba Turunç[1], Yusuf Ziya Demiroğlu[1], Hikmet Alişkan[2], Şule Çolakoğlu[2], Funda Timurkaynak[1], Nurhan Özdemir[3] and Hande Arslan[1]

	Group 1		Group 2	
Symptoms	*N*	Percentage	*n*	Percentage
Joint pain	7	100	132	87.4
Malaise	7	100	130	86.1
Fever	3	42.8	120	79.5
Sweating	3	42.8	118	78.1
Low back pain	2	28.5	107	70.9
Lack of appetite	6	85.7	85	56.3
Headache	3	42.8	78	51.7
Nausea	2	28.5	22	14.6

Table 5. Characteristics of patients with end-stage renal diseases accompanied by brucellosis

Cases	Age/Sex	Dialysis type	Clinical presentation	Blood culture	SAT	Complications
1	53/F	Haemodialysis	Fever, low back pain	*B. melitensis*	1/1280	Epidural abscess spondylodiscitis
2	24/M	CAPD	Fever, joint pain	*B. melitensis*	Negative	No complications
3	54/M	Haemodialysis	Joint pain, malaise	*B. melitensis*	1/1280	No complications
4	52/M	Haemodialysis	Diplopia, headache	No yielded	1/320	Neurobrucellosis
5	46/M	Haemodialysis	Low back pain, fever	*B. melitensis*	1/1280	Paravertebral abscess spondylodiscitis
6	70/M	Haemodialysis	Joint pain, malaise	No yielded	1/1280	No complications
7	64/F	Haemodialysis	Joint pain	No yielded	1/640	Peripheral arthritis

HIV VE BRUSELLOZ

ORIGINAL ARTICLE

Osong Public Health Res Perspect 2017;8(4):282–288
https://doi.org/10.24171/j.phrp.2017.8.4.09
eISSN 2233-6052

Seroprevalence of Brucellosis in Human Immunodeficiency Virus Infected Patients in Hamadan, Iran

Fariba Keramat[a], Mohammad Mehdi Majzobi[a], Jalal Poorolajal[b], Zohreh Zarei Ghane[c], Maryam Adabi[a]

Table 3. Distribution of HIV-positive patients with seropositive brucellosis according to the history of brucellosis infection

Test	History of brucellosis in patients with HIV				*p*-value
	Positive (n = 5)		Negative (n = 152)		
	Negative serology	Positive serology	Negative serology	Positive serology	
Wright	5	0	149	3	0.951
Coombs Wright	5	0	147	5	0.919
2ME test	5	0	152	0	-

HIV, human immunodeficiency virus; 2ME test, 2-mercaptoethanol *Brucella* agglutination test.

HIV VE BRUSELLOZ

International Journal of Infectious Diseases 14 (2010) e904–e906

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

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

Brucellosis serology in HIV-infected patients

Alireza Abdollahi [a,*], Afsaneh Morteza [b], Omid Khalilzadeh [b], Mehrnaz Rasoulinejad [c]

[a] Division of Pathology, Imam Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran
[b] Endocrinology and Metabolism Research Center, Vali-Asr Hospital, Tehran University of Medical Sciences, Tehran, Iran
[c] Division of Infectious Diseases, Imam Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran

Table 1
Patient characteristics

	Participants		p-Value
	HIV-negative (n = 100)	HIV-positive (n = 90)	
Age (years)	34.8 ± 0.71	36.5 ± 1.03	NS
Males, n (%)	55 (55%)	68 (75.6%)	0.003
Brucellosis infection, n (%)			
Positive serology	30 (30%)	66 (73.3%)	0.003
Negative serology	70 (70%)	24 (26.7%)	
CD4 count (cells/μl)	-	297.65 ± 14.68	
Hemoglobin (mg/dl)	14.35 ± 0.11	11.93 ± 0.12	<0.001
Red blood cell count ($\times 10^{12}$/l)	4.63 ± 0.06	4.14 ± 0.09	<0.001
White blood cell count ($\times 10^{9}$/l)	6.83 ± 0.21	4.61 ± 0.16	<0.001
Platelet count ($\times 10^{9}$/l)	266.430 ± 6.89	253.000 ± 7.44	NS

Variables are expressed as mean ± standard error, unless otherwise stated.
NS, not significant.

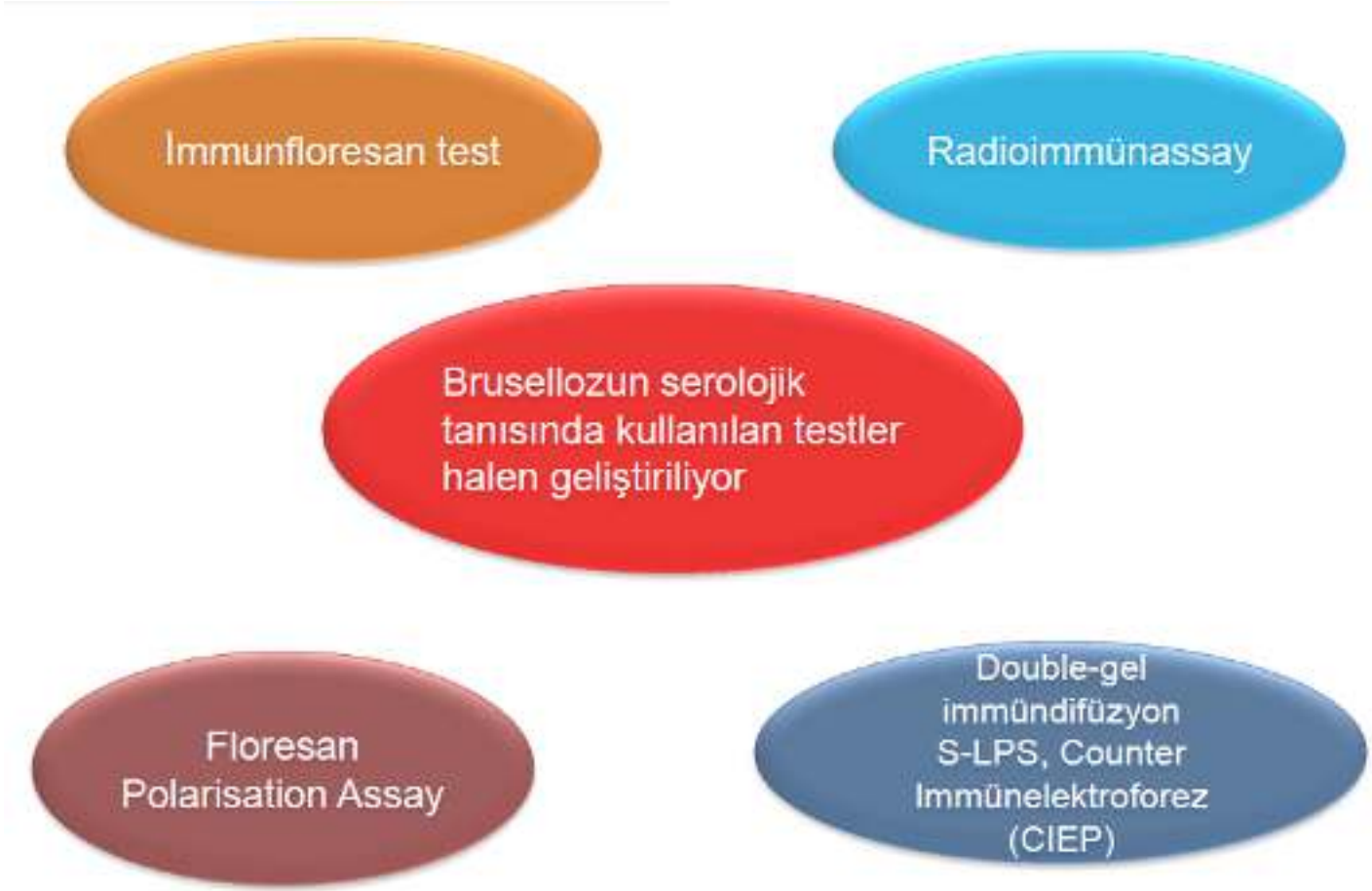
Tanı


Bakteriyolojik
Yöntemler
(DİREKT)
Serolojik
Yöntemler
(İNDİREKT)
Moleküler
Tanı
Yöntemleri
(DİREKT)

Tanı


Spot Test
Standart Tüp Aggl. Testi
Rose Bengal
Brusellozun serolojik tanısı ilk olarak 1897'de basit bir aglütinasyon testi ile başladı……
ELISA
Kompleman Fiksasyon Testi
BRUCELLACAPT
Dot-immunobinding (DIA) ve Dipstict testi

Tanı


İmmunfloresan test
Radioimmünassay
Brusellozun serolojik tanısında kullanılan testler halen geliştiriliyor
Floresan Polarisation Assay
Double-gel immündifüzyon S-LPS, Counter Immünelektroforez (CIEP)

Tanı

510 laboratuvarın %71.7‟si bruselloz tanısı için en az bir yöntem kullanmakta

Laboratuvarların yarıdan fazlasında STA testi, yaklaşık dörtte birinde de *Brucella kültürü yapılabilmektedir*

Ancak STA veya kültür yapabilen laboratuvarların %15-20‟sinde tanının geçerli prosedürlere dayanmadığı dikkati çekmektedir

Tanı- PCR

- Kültüre alternatif bir yöntem
- Nörobruselloz ve lokalize enfeksiyonlarda ön plana çıkmaktadır
- Daha fazla sayıda moleküler marker kullanımı sensitivite ve spesifiteyi artırır

Real-time/multiplex PCR (Sensitivite:%100 Spesifite:%93)

Tanı- PCR

REAL TIME PCR DUYARLILIK ORANLARININ KAN KÜLTÜRÜ İLE KARŞILAŞTIRILMASI

Klinik bulgular	Hasta sayısı (%)	Pozitif Test Sonuçları	
		Kan Kültürü (%)	RT-PCR (%)
Akut bruselloz	34 (68)	13 (38.2)	31 (91.2)
Kronik Bruselloz	6 (12)	1 (16.7)	4 (66.7)
Fokal organ tutulumu	10 (20)	4 (40)	9 (90)
Menenjit	4 (8)	1 (16.7)	4 (100)
Epididimoorşit	4 (8)	2 (50)	3 (75)
Osteomyelit	1 (2)	1 (100)	1 (100)
Spinal epidural abse	1 (2)	0	1 (100)
Toplam	50 (100)	18 (36)	44 (88)

Surucuoglu S, et al. Pol J Microb 2009;58:15-9

Yeni Tanı Testleri

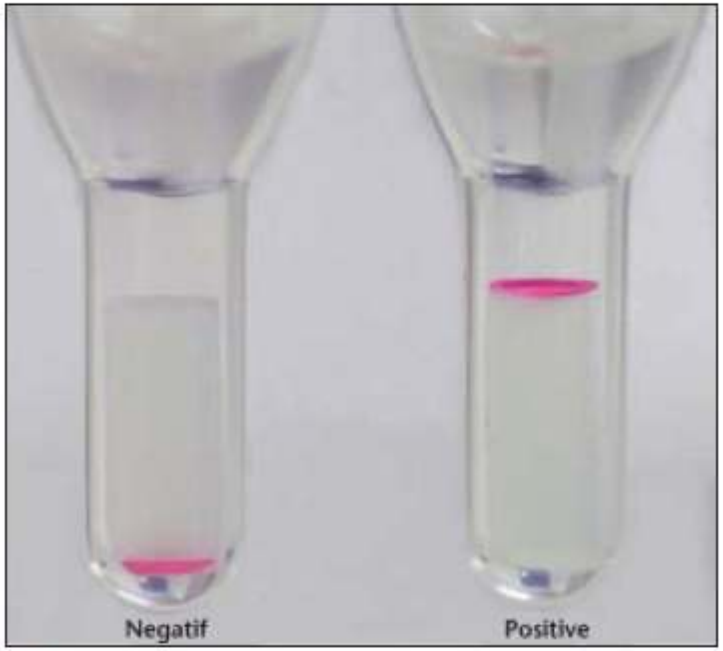
Özgün Çalışma/Original Article | Mikrobiyol Bul 2015; 49(2): 181-187

Brusellozun Serolojik Tanısında Yeni ve Hızlı Bir Yöntem Olan Brucella Coombs Jel Testi ile Diğer Yöntemlerin Karşılaştırılması

Comparison of a New and Rapid Method, Brucella Coombs Gel Test With the Other Methods in the Serological Diagnosis of Brucellosis

Arzu İRVEM[1], Fatma Muhterem YÜCEL[1], Sabahat AKSARAY[2], Emire BOR[3]

Brucella Coombs Jel Testi



Resim 1. *Brucella Coombs jel testinde negatif ve pozitif sonuçların görünümü.*

Tablo III. Yöntemler Arasındaki Uyum (Kappa Analizi)

Yöntemler	PKD	NKD	Doğruluk	Kappa*
CAB ile BCGT	96.88	100.0	99.00	0.977
ICA ile BCGT	90.63	98.53	96.00	0.907
CAB ile ICA	93.33	95.71	95.00	0.887

* κ= 0.81-0.99, mükemmel uyum olarak değerlendirilmiştir[10]. CAB: Coombs anti-Brucella testi; BCGT: *Brucella* Coombs jel testi; ICA: *Immunocapture* aglütinasyon testi; PKD: Pozitif kestirim değeri; NKD: Negatif kestirim değeri.

Uygulaması kolay
Kısa sürede sonuç veriyor
Görsel açıdan değerlendirmesi kolay

Duyarlılık

Jpn. J. Infect. Dis., 70, 235-238, 2017

Original Article

Clinical and Diagnostic Aspects of Brucellosis and Antimicrobial Susceptibility of *Brucella* Isolates in Hamedan, Iran

Fatemeh Torkaman Asadi[1,2], Seyyed Hamid Hashemi[1,3*], Mohammad Yousef Alikhani[1], Abbas Moghimbeigi[1], and Zahra Naseri[2]

[1]*Brucellosis Research Center, Hamedan University of Medical Sciences, Hamedan;*
[2]*Blood Transfusion Research Center, High Institute for Research; Education in Transfusion, Hamedan; and*
[3]*Division of Infectious Diseases, Sina Hospital, Hamedan, Iran*

Table 2. Minimum inhibitory concentration (MIC) values of antibiotics against 57 *Brucella* isolates

Antibiotic agent	MIC (μg/ml)			CLSI breakpoint for *Brucella* (μg/ml)		
	Range	MIC_{50}	MIC_{90}	S	I	R
trimethoprim-sulfamethoxazole (SXT)	0.012–0.750	0.250	0.500	≤ 0.5	1–2	≥ 4
doxycycline (DOX)	0.016–0.640	0.470	0.470	≤ 4	8	≥ 16
ciprofloxacin (CIP)	0.094–0.750	0.250	0.380	≤ 1[1)]	–	–
moxifloxacin (MXF)	0.032–0.750	0.190	0.500	≤ 1[1)]	–	–
streptomycin (STR)	0.125–2.000	1.000	1.500	≤ 8	–	–
gentamicin (GEN)	0.094–0.750	0.380	0.750	≤ 4	–	–
rifampin (RIF)	0.500–3.000	1.000	2.000	≤ 1[1)]	2[1)]	≥ 4[1)]

[1)]: Refer to CLSI breakpoints for slow-growing bacteria (*Haemophilus* spp.).
S, susceptible; I, intermediate; R, resistant.

DUYARLILIK

Table 2. Summary of Brucella antimicrobial susceptibility test results of Turkish studies.

Researcher		Akova et al.	Bodur et al.	Baykam et al.	Kose et al.	Sengoz et al.	Yamazhan et al.	Ayaslioglu et al.
Region		Ankara	Ankara	Ankara	İzmir	İstanbul	İzmir	Kırıkkale
Isolate #		43	41	42	11	43	44	46
B. melitensis		43	41	37	11	43	44	46
(biotype 3)		(ND)	(39)	(29)	(10)	(ND)	(ND)	(45)
B. abortus		0	0	5	0	0	0	0
Method		Microdilution	E test	E test	E test	E test	Agar dilution	E test
MIC_{90} (mg/l)	DOX	< 0.125	0.064	0.064	0.047	0.090	0.50	0.25*
	STR	2.0				0.75		0.50
	SXT		0.38	1.5	1.0			
	CRO		0.38	0.50	0.50			
	RIF	2.0	0.75	1.0	0.75	1.0		1.0
	CIP	2.0	0.25	0.19	0.25	0.38	2.0	0.25
	AZM	1.0					32.0	1.0

DOX: doxycycline; STR: streptomycin; SXT: trimethoprim/sulfamethoxazole; CRO: ceftriaxone; RIF: rifampin; CIP: ciprofloxacin; AZM: azithromycin.
ND: not determined.
*E strip for tetracycline was used.

Tedavi

OPEN ACCESS Freely available online

PLoS MEDICINE

Policy Forum Ariza J. 2007

Perspectives for the Treatment of Brucellosis in the 21st Century: The Ioannina Recommendations

Javier Ariza, Mile Bosilkovski, Antonio Cascio, Juan D. Colmenero, Michael J. Corbel, Matthew E. Falagas, Ziad A. Memish, Mohammad Reza Hasanjani Roushan, Ethan Rubinstein, Nikolaos V. Sipsas, Javier Solera, Edward J. Young, Georgios Pappas*

Brucellosis is probably the commonest anthropozoonotic infection worldwide [1–3], but remains in various aspects an enigma in the 21st century [4]. *Brucella melitensis* remains the major cause of human disease worldwide, followed by *B. abortus* and *B. suis*, while rare but persisting cases of *B. canis* human infection and disease by novel *Brucella* pathogens of marine mammals have also emerged. The disease is re-emerging as a significant cause of travel-related disease [5] and represents an index of poor socioeconomic status (Figure 1). Its treatment is largely based even today on the principles applied half a century ago by pioneer researchers [6] and few modifications have been made in the

Summary Points

- Brucellosis remains the commonest anthropozoonosis worldwide, and its treatment remains complex, requiring protracted administration of more than one antibiotic.
- In November 2006, a consensus meeting aimed at reaching a common specialist statement on the treatment of brucellosis was held in Ioannina, Greece under the auspices of the International Society of Chemotherapy and the Institute of Continuing Medical Education of Ioannina.
- The author panel suggests that the optimal treatment of uncomplicated brucellosis should be based on a six-week regimen of doxycycline combined either with streptomycin for

Competing Interests: ER has received research grants from Daiichi, Bayer, and Theravance and has served as a consultant to Pfizer, Theravance, Bayer, Wyeth, Rosetta, and Biondvax. The other authors have declared that they have no competing interests.

Citation: Ariza J, Bosilkovski M, Cascio A, Colmenero JD, Corbel MJ, et al. (2007) Perspectives for the treatment of brucellosis in the 21st century: The Ioannina recommendations. PLoS Med 4(12): e317. doi:10.1371/journal.pmed.0040317

Abbreviations: DOX-GENT, doxycycline-gentamicin; DOX-RIF, doxycycline-rifampicin; DOX-STR, doxycycline-streptomycin; MRI, magnetic resonance imaging; TMP-SMX, trimethoprim-sulfamethoxazole; WHO, World Health Organization

Javier Ariza is with the Servicio de Enfermedades Infecciosas, Hospital de Bellvitge, Universidad de

Tedavi

Table 2. The recommendations of Ioannina on the Optimal Treatment of Brucellosis Without Serious Complications in Adults

Treatment Regimen	Dose	Recommendation Validation	Comments
DOX-STR	DOX: 100 mg twice daily orally for 6 weeks; STR: 15 mg/kg daily intramuscularly for 2–3 weeks	AI	Considered the "gold standard."
DOX-RIF	DOX: as above; RIF: 600–900 mg daily for 6 weeks, one morning dose	AI	Convenience of the regimen overcomes slight drawbacks concerning the pharmacokinetics of the combination and the overall outcome.
DOX-GENT	DOX: as above; GENT: 5 mg/kg daily parenterally in 1 dose for 7 days	BI	May be considered the preferred alternative regimen. Duration of GENT administration may need modification for optimal result (different studies suggest that it may be shortened to 5 days or extended to 14 days).
TMP-SMX-containing regimens	TMP-SMX: 800 + 160 mg twice daily for 6 weeks	CII	Recommendation referring to three-drug regimens containing DOX.
Quinolone-containing combination regimens	Ofloxacin: 400 mg twice daily for 6 weeks; ciprofloxacin: 500 mg twice daily for 6 weeks	CII	Ofloxacin or ciprofloxacin may be used alternatively as second or third agents in combination regimens containing DOX.

Tedavi

RESEARCH ARTICLE

Rifampicin versus streptomycin for brucellosis treatment in humans: A meta-analysis of randomized controlled trials

Fanjie Meng[1]*, Xiangpo Pan[2], Wenzhen Tong[1]

ground regimen. We systematically searched PubMed, EmBase, and the Cochrane Library from their inception up through December 2016. We included studies with a randomized controlled design that evaluated the effect of streptomycin compared with rifampicin in human brucellosis patients who received doxycycline therapy as background regimen. The overall failure and relapse were summarized using random-effects model. Our meta-analysis included 1,383 patients with brucellosis from 14 trials. We found that patients who received rifampicin therapy had a higher risk of overall failure (RR: 2.36; 95% CI: 1.72–3.23; P<0.001) and relapse (RR: 2.74; 95% CI: 1.80–4.19; P<0.001) compared with streptomycin. Results of the sensitivity analysis were consistent with the overall analysis. Subgroup analysis indicated that mean age of the patients and percentage of male participants might influence the treatment effects. Furthermore, no publication bias was detected. The findings of this study indicated that rifampicin therapy significantly increased the risk of overall failure and relapse compared with streptomycin. Hence, it can be recommended to patients with human brucellosis receiving streptomycin therapy.

PLOS ONE | https://doi.org/10.1371/journal.pone.0191993 February 20, 2018

Bruselloz İle Mücadele ve Hastalığın Kontrol Altına Alınması

- En etkili yöntem hayvanlarda hastalığın kontrol altına alınmasıdır
- Hayvanların aşılanması ve işletmelerin ari kılınması çok önemlidir
- 2012 yılında Sağlık Bakanlığı desteği ile Bruselloz Eradikasyon Programı uygulamaya konmuştur

Bruselloz Eradikasyon Programı

Hayvanlarda Aşılama

- Sığırlar *B.abortus* S19, koyun ve keçiler *B.melitensis* Rev 1 konjüktival aşıları
- Yeterli bağışıklama için hayatları boyunca bir kez aşılanmaları yeterli
- 2014 yılından itibaren ergin hayvanlarda aşılama tamamlandı

Teşekkür ederim