Toksoplazmoz

Dr. Öğr. Üyesi Kerem YAMAN

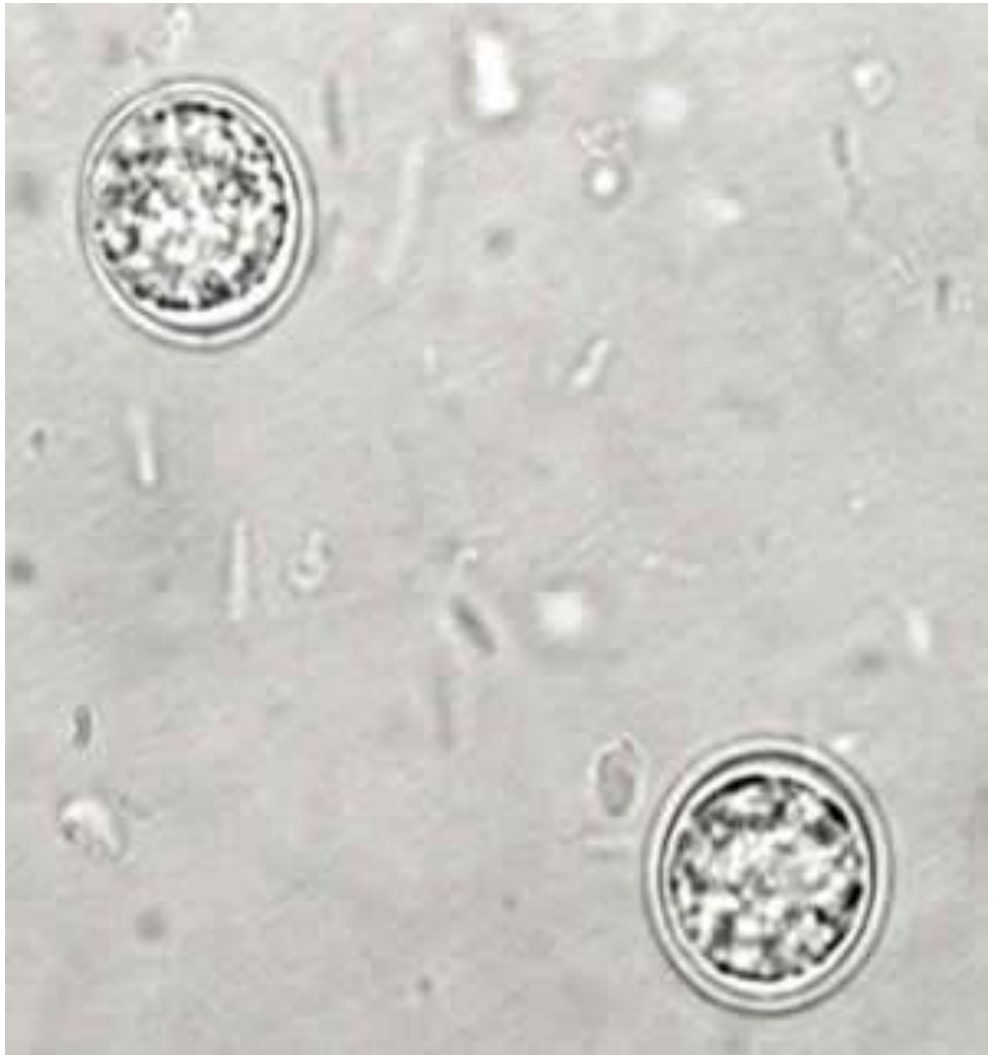
Bolu Abant İzzet Baysal Üniversitesi Tıp Fakültesi Tıbbi Parazitoloji AD.

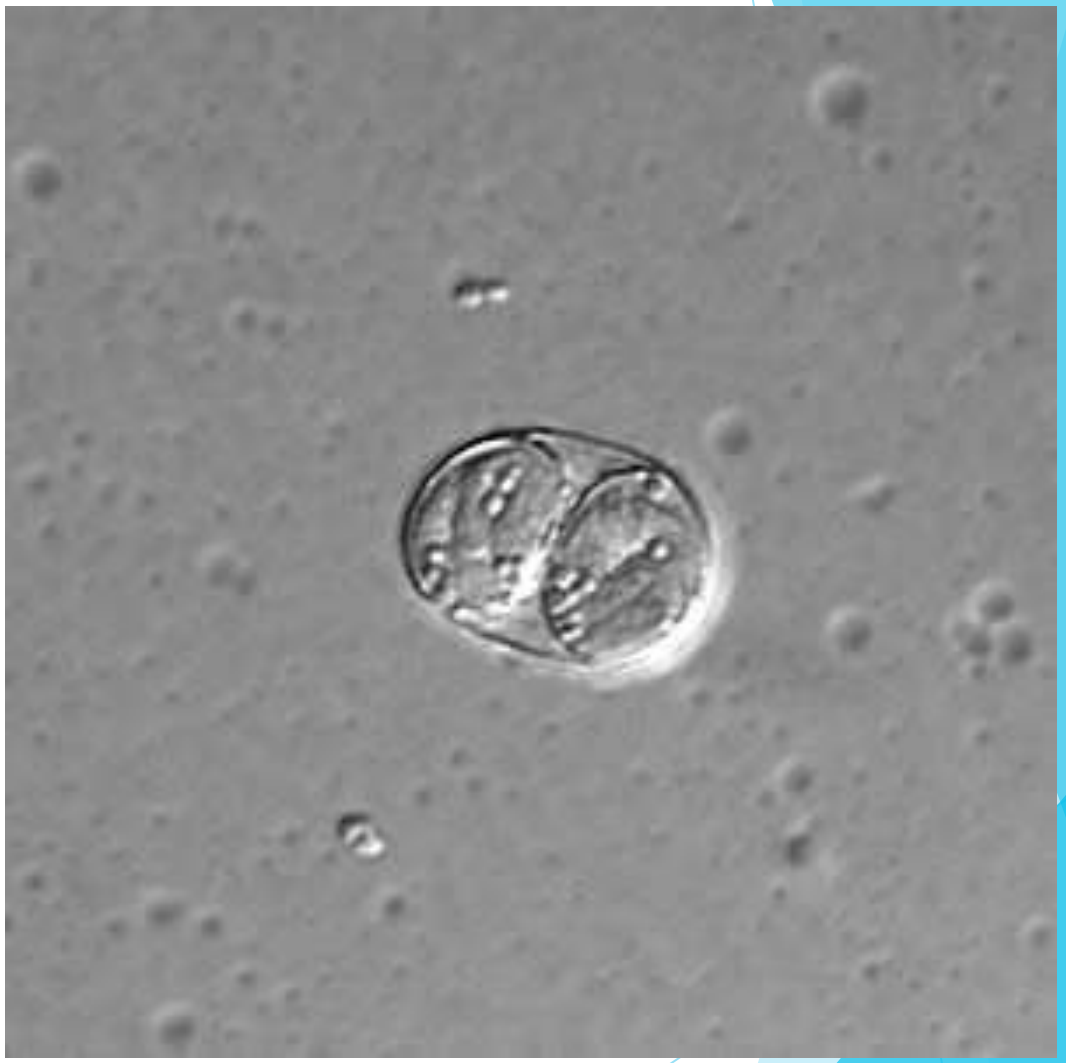
- Giriş- genel bilgiler
- Bulaşma yolları
- Epidemiyolojik veriler
- Tanı yöntemleri
- Klinik belirtiler
- Tedavi
- Korunma yolları
- Aşı çalışmaları

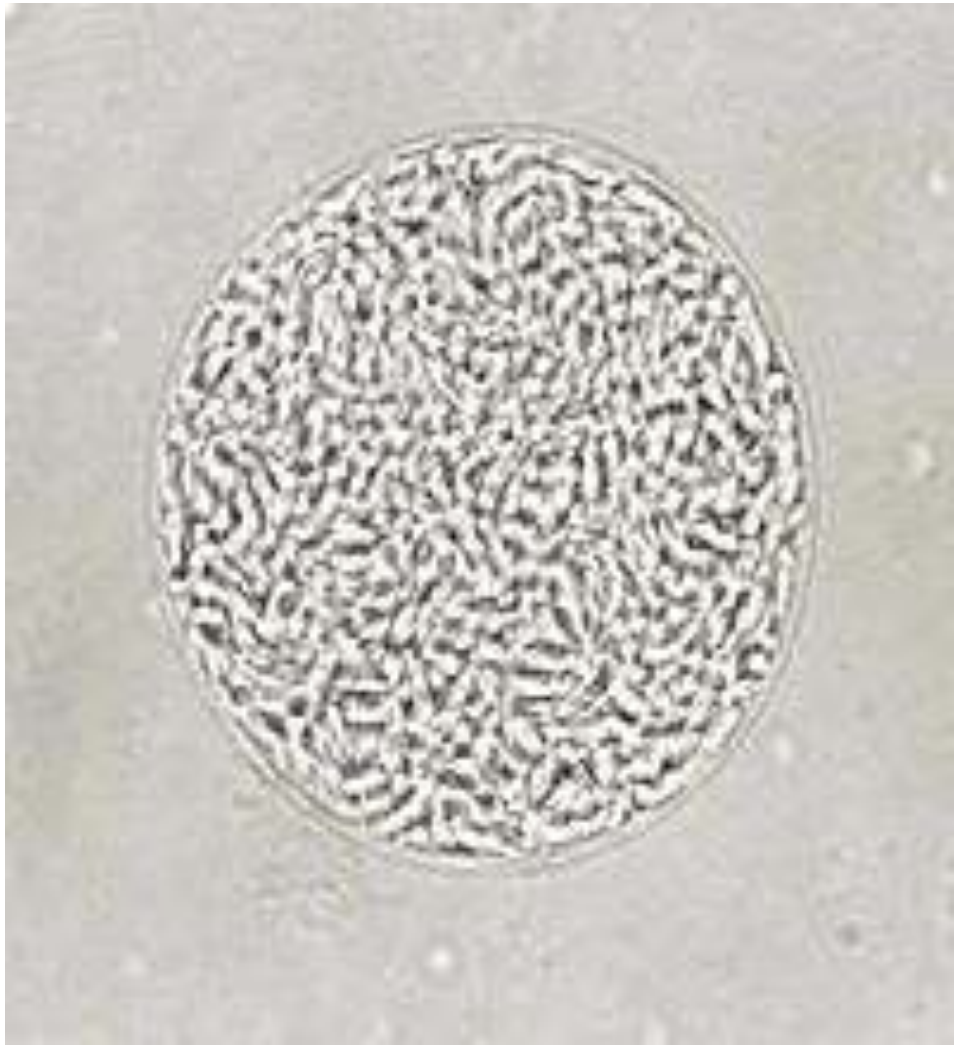
Giriş- Genel Bilgiler

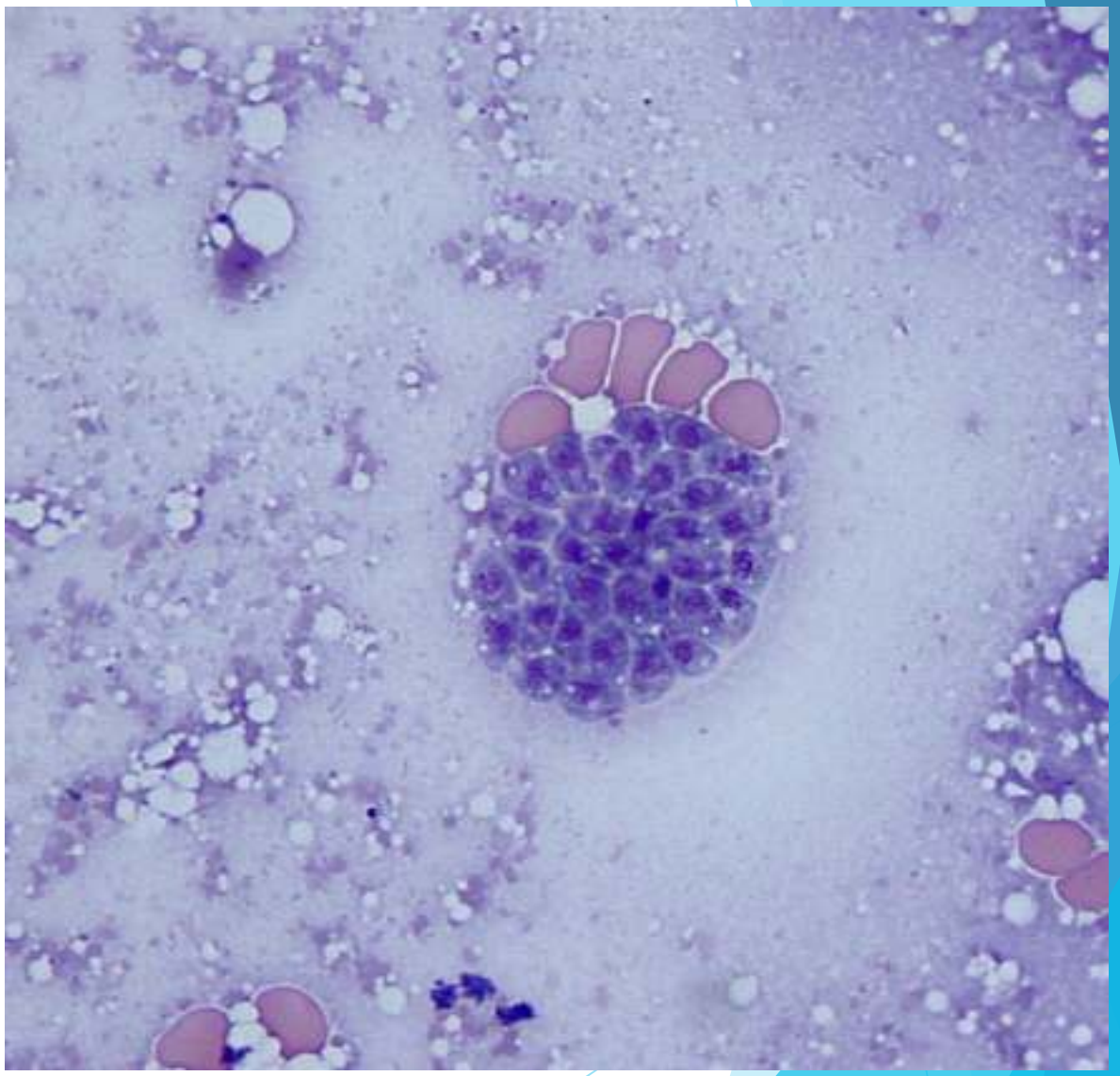
- Toksoplazmoz, Toxoplasma gondii adlı protozoon parazit tarafından oluşturulan kozmopolit bir enfeksiyon hastalığıdır
- Son konağı kedigiller (Felidae) ailesinin üyeleridir
- Özgüllük gözetmeden, tüm sıcak kanlı canlıları enfekte edebilir
- Parazitlik yaptığı konaklarında intrasellüler yerleşmektedir

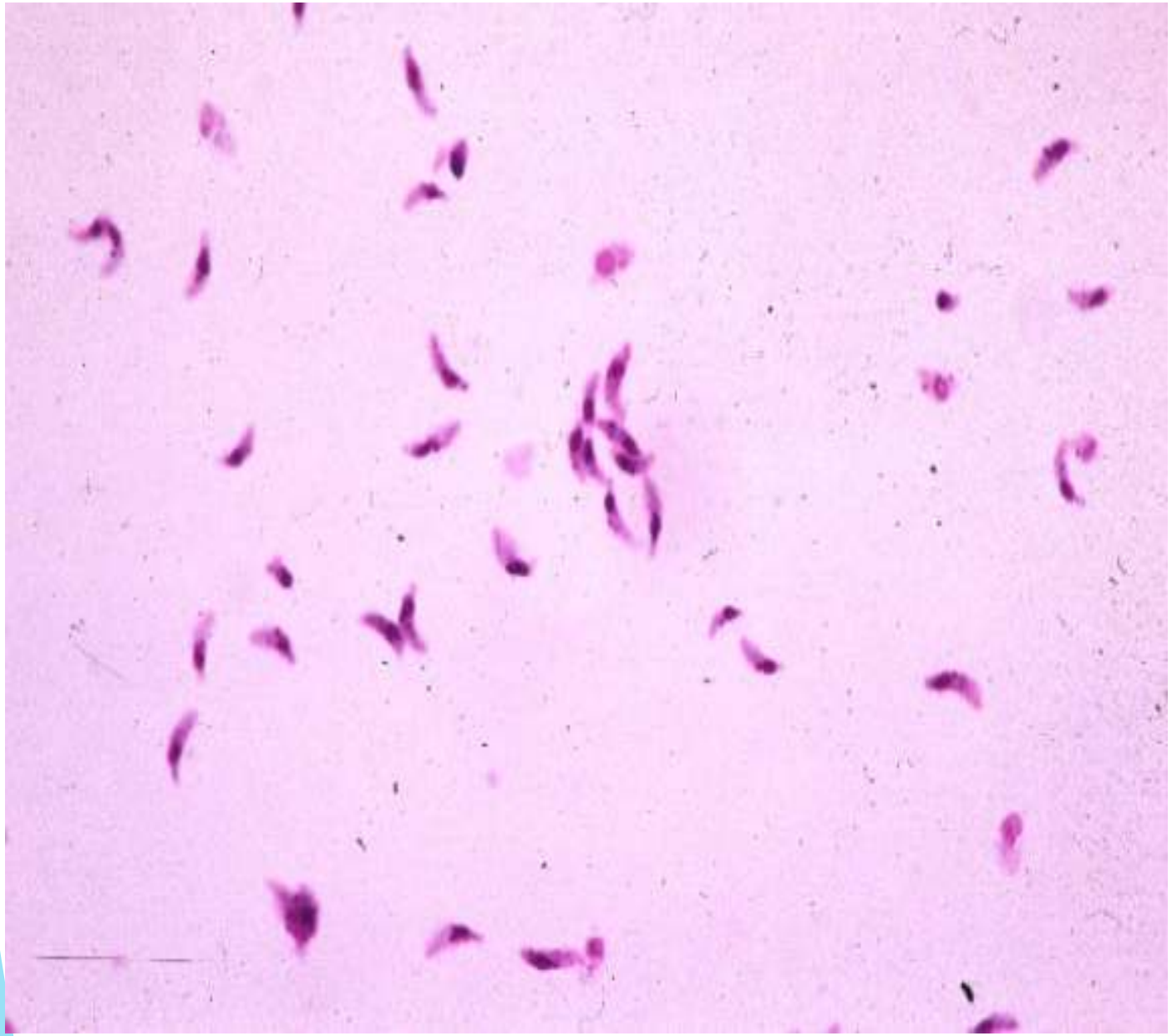
- Yaşam döngüsünde üç farklı formu bulunmaktadır
- Kedigillerin bağırsak epitel hücrelerinde oluşan ookist formu
- Ara konakların çeşitli dokularında latent halde kalan ve doku kisti oluşturan bradizoit formu
- Ara konaklarda aktif olarak çoğalan takizoit formu

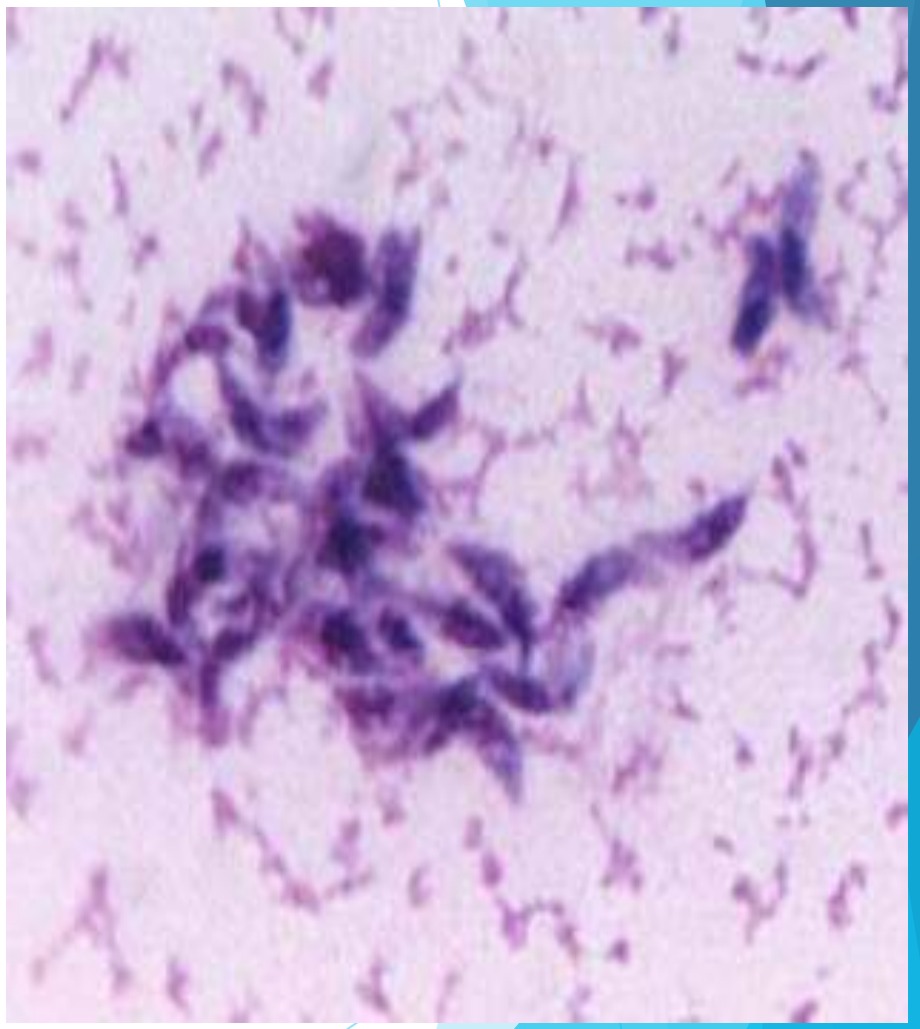


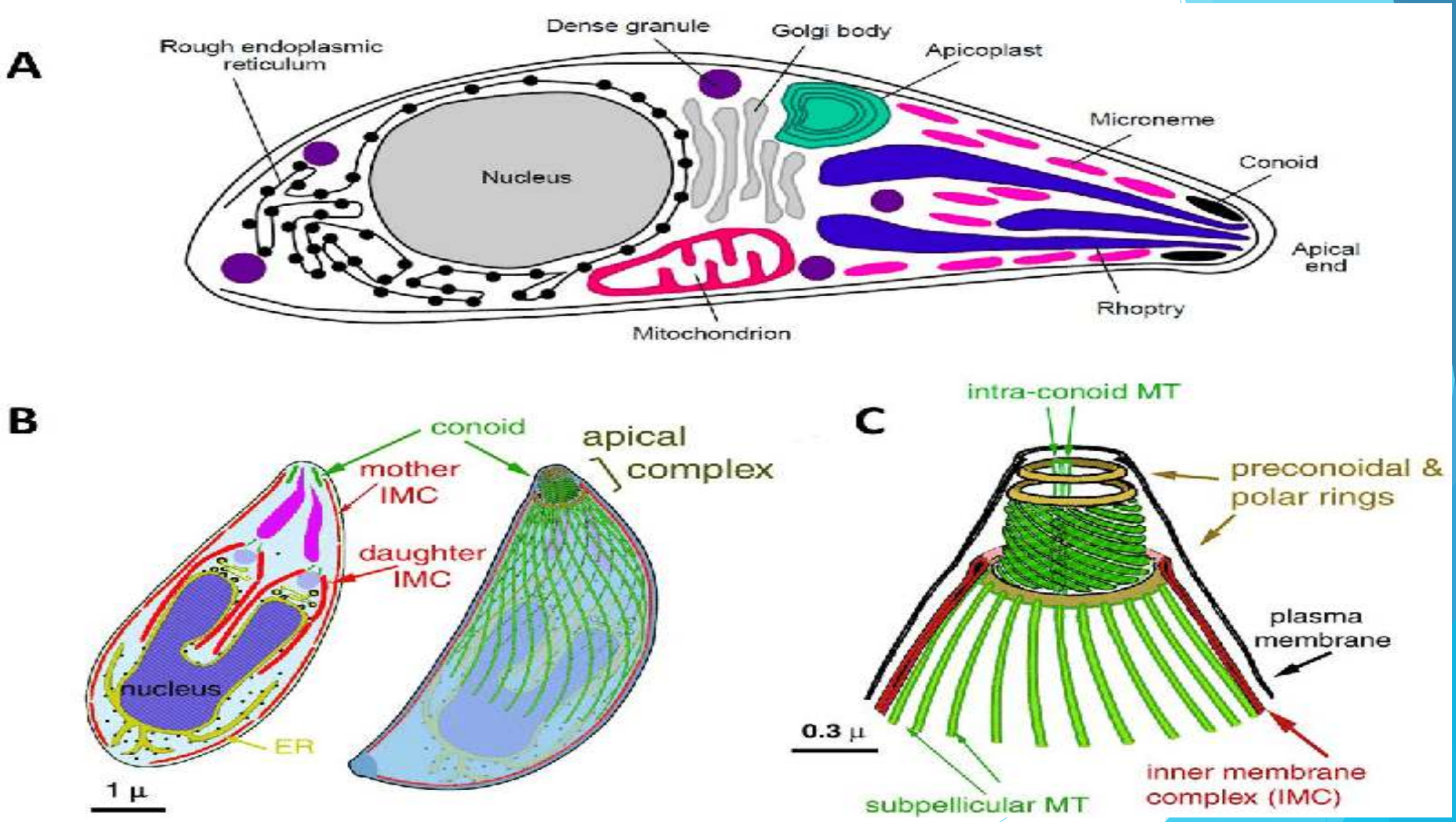




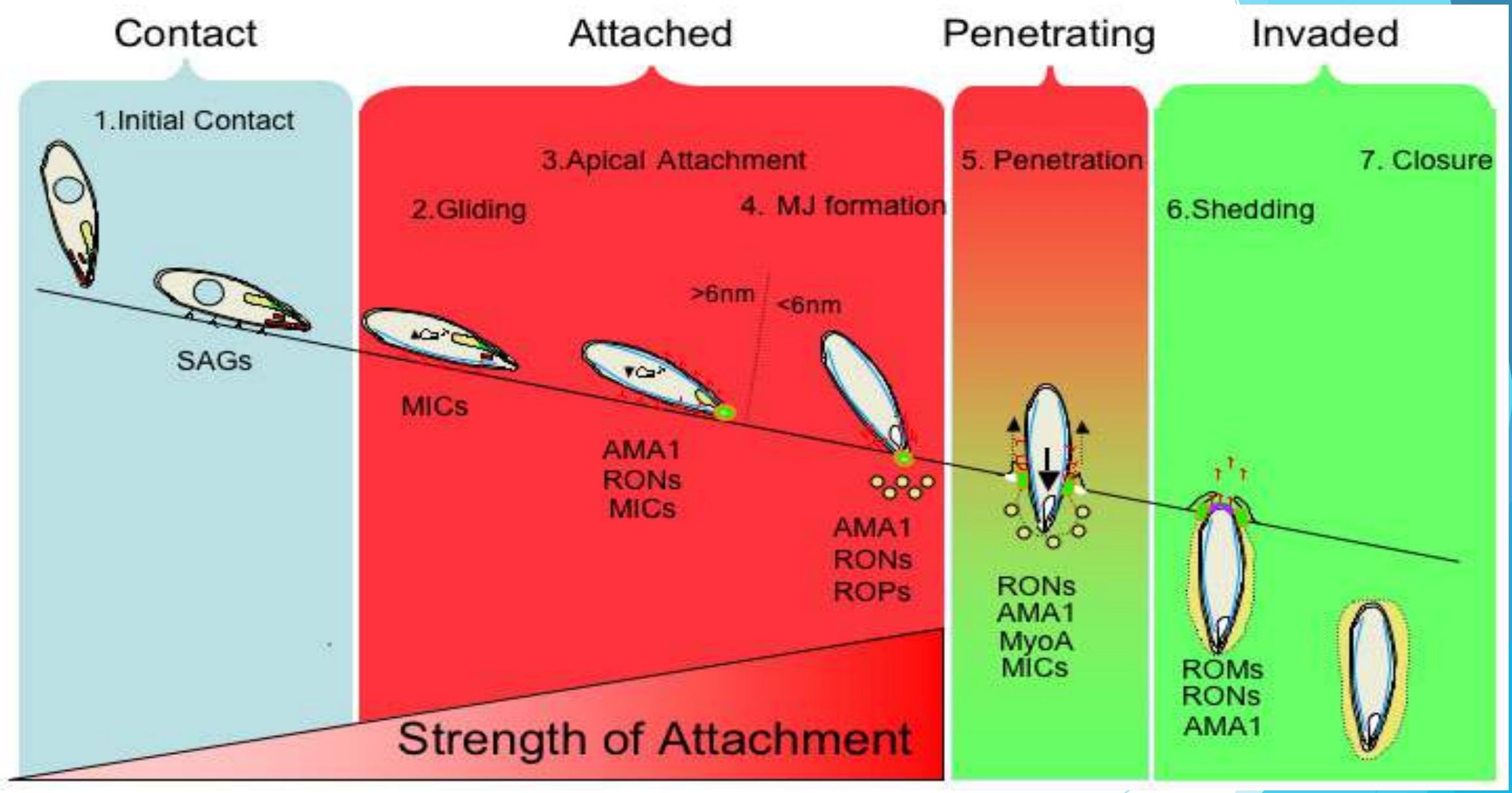


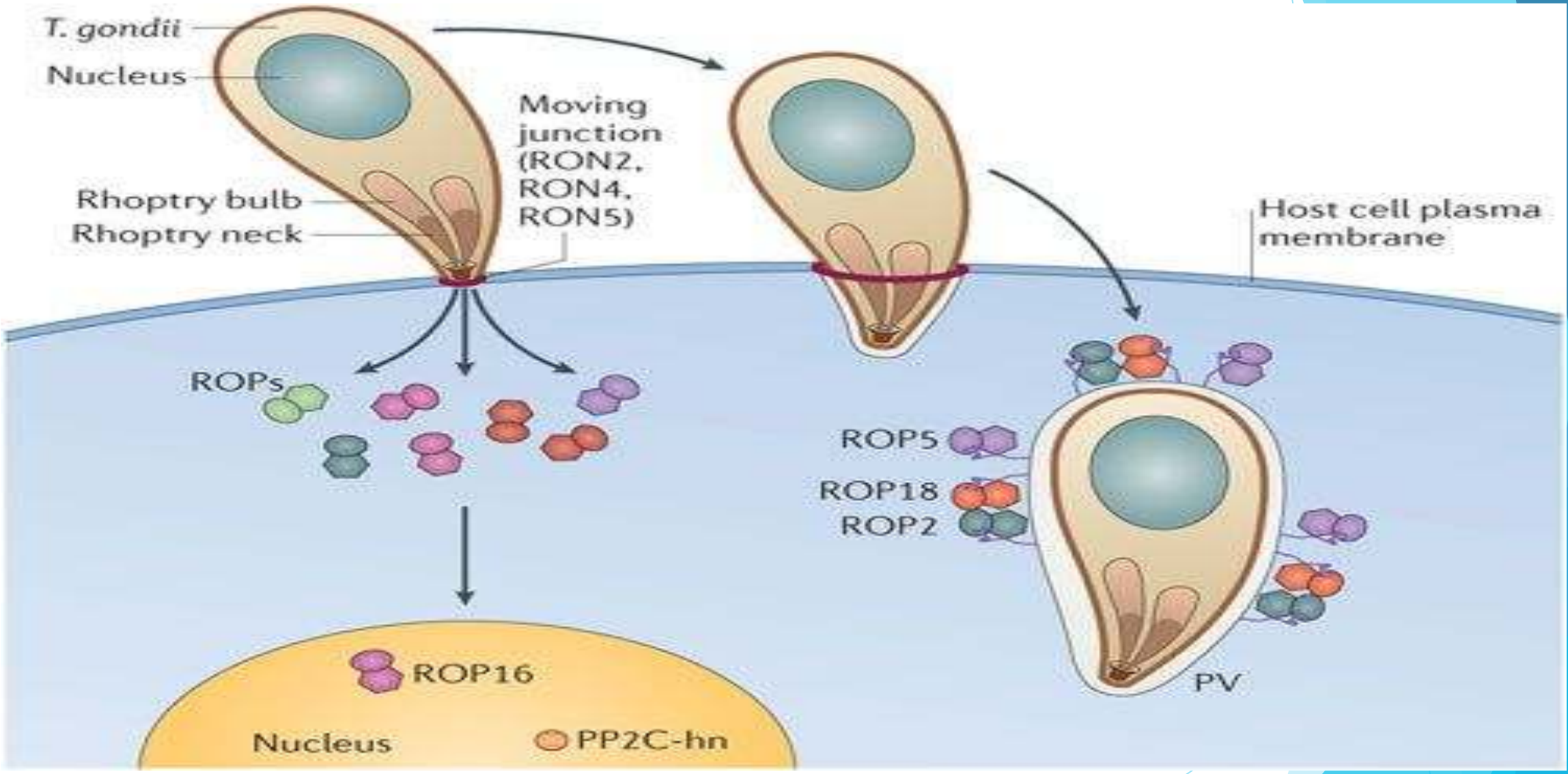





A
Rough endoplasmic reticulum
Dense granule
Golgi body
Apicoplast
Nucleus
Microneme
Conoid
Apical end
Rhoptry
Mitochondrion
B
conoid
apical complex
mother IMC
daughter IMC
nucleus
ER
1 µ
C
intra-conoid MT
preconoidal & polar rings
plasma membrane
0.3 µ
inner membrane complex (IMC)
subpellicular MT

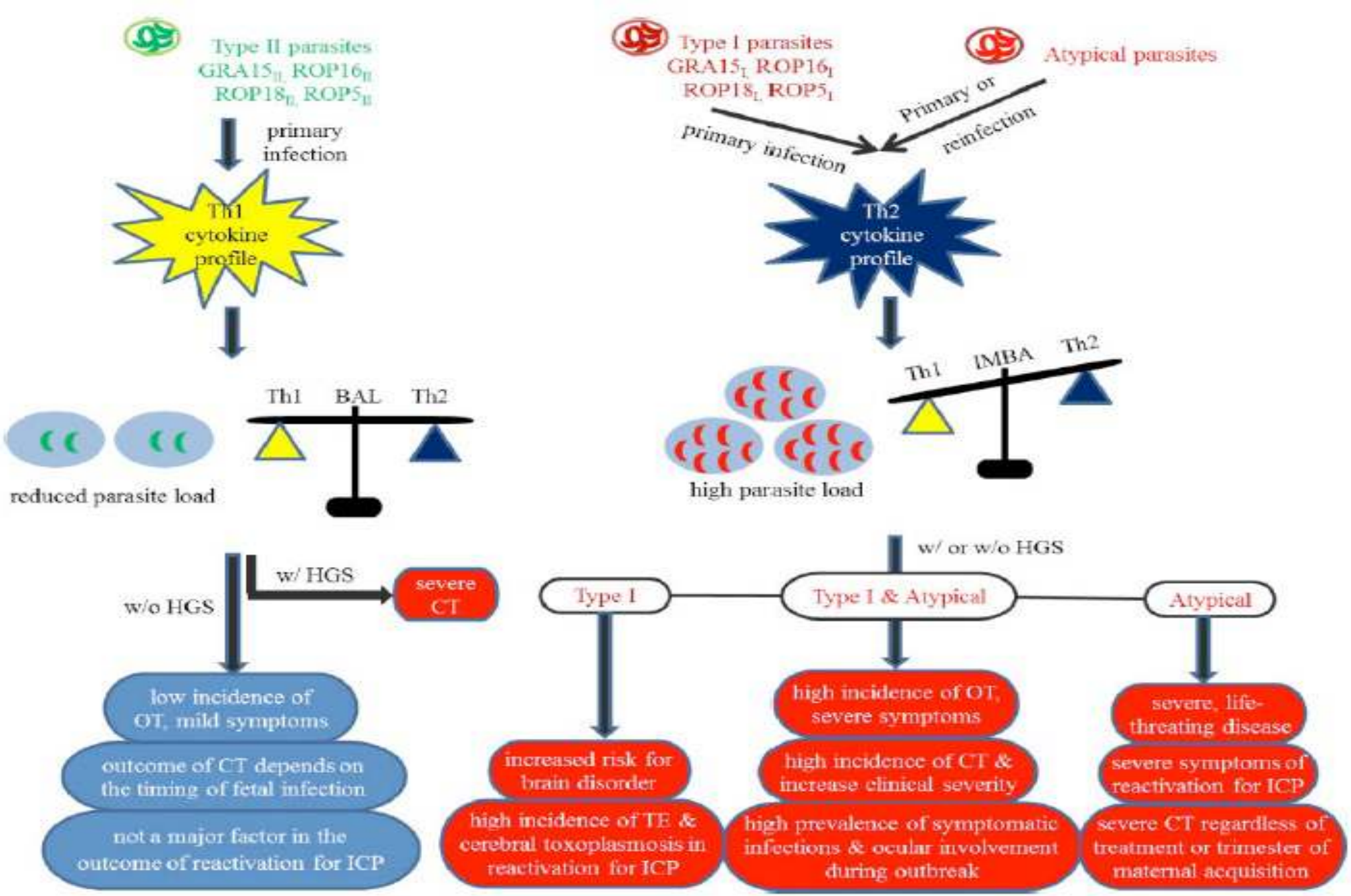
- Apikompleksan parazitlere özgü olan organellere sahiptir
- Roptriler
- Mikronemler
- Dens granüller (Yoğun granüller)
- Bu organellere ait olan protein yapıda salgılar, antijen görevi görüp konak hücre invazyonunda rol oynamaktadır


Contact
Attached
Penetrating
Invaded
1.Initial Contact
SAGs
2.Gliding
3.Apical Attachment
4. MJ formation
MICs
>6nm
<6nm
AMA1
RONs
MICs
AMA1
RONs
ROPs
5. Penetration
RONs
AMA1
MyoA
MICs
6.Shedding
7. Closure
ROMs
RONs
AMA1
Strength of Attachment


T. gondii
Nucleus
Moving junction (RON2, RON4, RON5)
Rhoptry bulb
Rhoptry neck
Host cell plasma membrane
ROPs
ROP5
ROP18
ROP2
ROP16
Nucleus
PP2C-hn
PV

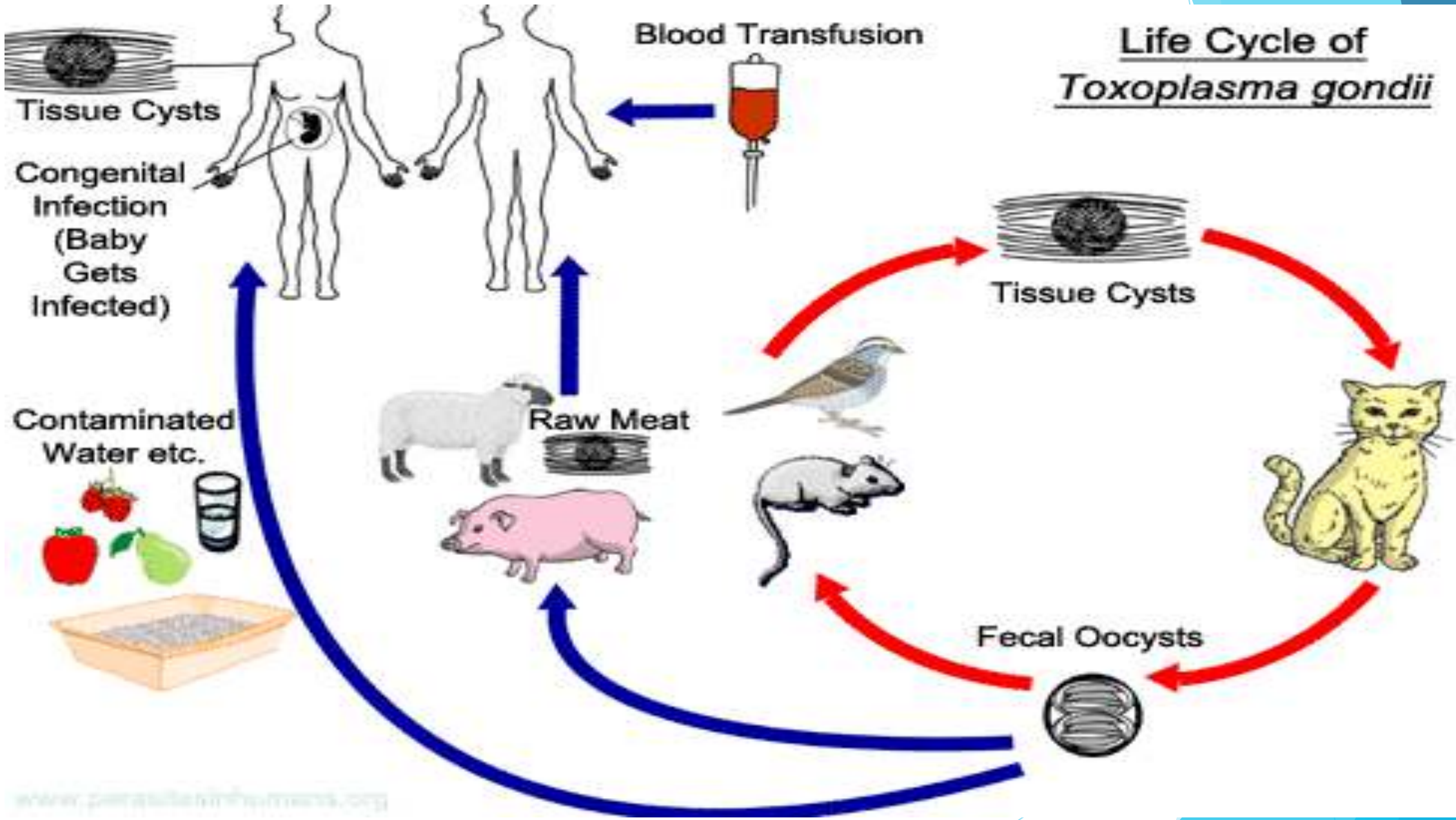
- T.gondii’nin tanımlanmış 950’nin üstünde suşu bulunmaktadır
- Bu suşlar farklı coğrafi dağılımlara ve karakterlere sahiptir
- Üç farklı genotipte sınıflandırılmışlardır
- Sınıflandırmaya girmeyenler atipik veya son dönemlerde tip IV olarak adlandırılmışlardır
- İlk üç tipe giren suşlar daha sık Avrasya ve Kuzey Amerika’da bulunurken , atipik olanlar ise daha çok Güney Amerika’da bulunmaktadır

- Genotiplerin önemi aralarındaki virulans farklılıklarından kaynaklanmaktadır
- Tip I suşlar virulanken, tip II ve tip III suşlar avirulan olarak kabul edilir ve latent halde kalıp, doku kisti oluşturmaya meyillidir


Type II parasites
GRA15II, ROP16II
ROP18II, ROP5II
primary infection
Th1 cytokine profile
Th1 BAL Th2
reduced parasite load
w/o HGS
w/ HGS
severe CT
low incidence of OT, mild symptoms
outcome of CT depends on the timing of fetal infection
not a major factor in the outcome of reactivation for ICP
Type I parasites
GRA15I, ROP16I
ROP18I, ROP5I
Atypical parasites
primary infection
Primary or reinfection
Th2 cytokine profile
Th1 tMBA Th2
high parasite load
w/ or w/o HGS
Type I
Type I & Atypical
Atypical
increased risk for brain disorder
high incidence of TE & cerebral toxoplasmosis in reactivation for ICP
high incidence of OT, severe symptoms
high incidence of CT & increase clinical severity
high prevalence of symptomatic infections & ocular involvement during outbreak
severe, life-threating disease
severe symptoms of reactivation for ICP
severe CT regardless of treatment or trimester of maternal acquisition

Bulaşma Yolları

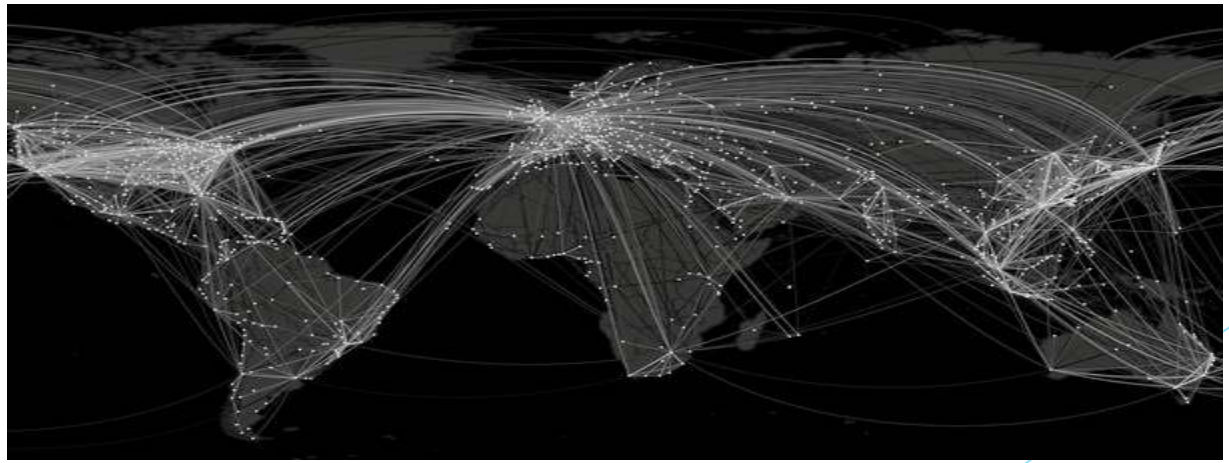
- Konaklarına üç farklı formuyla da bulaşabilmektedir
- En sık insanların tüketime sunulan et ve et ürünlerinde bulunan doku kistlerinin çiğ veya az pişmiş olarak alınmasıyla bulaşmaktadır


Life Cycle of
Toxoplasma gondii
Blood Transfusion
Tissue Cysts
Congenital Infection (Baby Gets Infected)
Tissue Cysts
Contaminated Water etc.
Raw Meat
Fecal Oocysts

- Sporlanmış ookistlerin doğrudan alınması veya kontamine olan gıdaların suyun tüketilmesiyle
- Nadir olarak takizoitlerin alınmasıyla bulaş meydana gelmektedir

Epidemiyolojik Veriler

- Toxoplasma gondii seropozitiflik oranları yüksek olan paraziter hastalıklardan birisidir
- Bulaşma yollarına bakıldığında, dünyada yaygın görülen bir parazit olmasına rağmen prevalans değerlerinin farklı coğrafyalarda birbirlerinden farklı bulunmasın da pek çok faktörün rol oynadığı anlaşılmalıdır



- Ülkemizden örnekler

Ankara Üniversitesi Tıp Fakültesi Tıbbi Parazitoloji Bilim Dalı Laboratuvarında 1997-2007 Yılları Arasında Yapılan Sabin-Feldman Test Sonuçlarının Değerlendirilmesi

Evaluation of Sabin-Feldman Test Results of Ankara University Medical Faculty Medical Parasitology Laboratory Between 1997-2007

Gülay Aral Akarsu, Kerem Yaman, Çiğdem Güngör, Kürşat Altıntaş

Ankara Üniversitesi Tıp Fakültesi, Tıbbi Parazitoloji Bilim Dalı, Ankara, Türkiye

Tablo 1. Yıllara ve cinsiyete göre SFT sonuçları

Yıl	Cinsiyet	Pozitif örnekler (%)	Negatif örnekler (%)	Toplam
1997	K	41 (71.93)	16 (28.07)	57
	E	7 (50)	7 (50)	14
1998	K	72 (43.64)	93 (56.36)	165
	E	23 (64.86)	14 (35.14)	37
1999	K	34 (44.74)	42 (55.26)	76
	E	5 (27.78)	13 (72.22)	18
2000	K	14 (38.89)	22 (61.11)	36
	E	3 (25)	9 (75)	12
2001	K	11 (36.67)	19 (63.33)	30
	E	4 (23.53)	13 (76.47)	17
2002	K	9 (36)	16 (64)	25
	E	2 (20)	8 (80)	10
2003	K	9 (47.37)	10 (52.63)	19
	E	5 (50)	5 (50)	10
2004	K	15 (53.57)	13 (46.43)	28
	E	8 (42.11)	11 (57.89)	19
2005	K	20 (58.82)	14 (41.18)	34
	E	6 (46.15)	7 (53.85)	13
2006	K	12 (50)	12 (50)	24
	E	3 (30)	7 (70)	10
2007	K	13 (72.22)	5 (27.78)	18
	E	2 (28.57)	5 (71.43)	7
Toplam	K	250 (48.82)	262 (51.18)	512
	E	68 (40.96)	98 (59.04)	166
	K+E	318 (46.90)	360 (53.10)	678

Tablo 2. SFT sonuçları: Anti-Toxoplasma antikor titreleri

	1:16	1:64	1:256	1:1024	1:1024+
Kadın	71	104	43	23	9
Erkek	22	30	10	5	1
Toplam	93	134	53	28	10

Çiğ Köftenin Yaygın Tüketildiği Şanlıurfa İlinde Kadınlarda *Toxoplasma gondii* Seroprevalansı

Fikret TEKAY[1], Erdal ÖZBEK[2]

[1]Şanlıurfa Kadın Hastalıkları ve Doğum Hastanesi, Mikrobiyoloji Laboratuvarı, Şanlıurfa,
[2]Dicle Üniversitesi Tıp Fakültesi, Mikrobiyoloji Anabilim Dalı, Diyarbakır, Türkiye

Tablo 1. Chemiluminescence Immunoassay yöntemi ile saptanan *Toxoplasma gondii* IgM ve IgG aAntikorlarının dağılımı

(n=2.586)	IgM (+) (%)	IgM (-) (%)	Toplam
IgG (+) (%)	75 (%2,9)	1.723 (%66,6)	1.798 (%69,5)
IgG (-) (%)	3 (%0,1)	785 (%30,4)	788 (%30,5)
Toplam	78 (%3,0)	2.508 (%97,0)	2.586 (%100)

Muğla Sıtkı Koçman Üniversitesi Eğitim ve Araştırma Hastanesi Mikrobiyoloji Laboratuvarı'nda 2012-2013 Yılları Arasında Çalışılan *Toxoplasma* Serolojik Test Sonuçlarının Retrospektif Olarak Değerlendirilmesi

The Retrospective Analysis of *Toxoplasma* Serology Results from Muğla Sıtkı Koçman University Training and Research Hospital between 2012 and 2013

Funda Sankur[1], Şeniz Ayturan[1], Erdoğan Malatyalı[2], Burak Ekrem Çitil[3], Hatice Ertabaklar[2], Sema Ertuğ[2]

[1]Muğla Sıtkı Koçman Üniversitesi Eğitim ve Araştırma Hastanesi, Mikrobiyoloji Laboratuvarı, Muğla, Türkiye
[2]Adnan Menderes Üniversitesi Tıp Fakültesi, Tıbbi Parazitoloji Anabilim Dalı, Aydın, Türkiye
[3]Muğla Sıtkı Koçman Üniversitesi Tıp Fakültesi, Tıbbi Mikrobiyoloji Anabilim Dalı, Muğla, Türkiye

Tablo 1. Cinsiyete, yaş gruplarına, yıllara ve bölümlere göre anti-*Toxoplasma* IgG seropozitifliğinin değerlendirilmesi

	Pozitif		Negatif		Toplam		
Cinsiyet	**n**	**%**	**n**	**%**	**n**	χ^2	**p**
Erkek	16	17,6	75	82,4	91	0,583	0,445
Kadın	138	21	518	79	656		
Yaş grupları							
<16	4	9,5	38	90,5	42	18,567	0,001
16-24	29	18,8	125	81,2	154		
25-34	70	18,3	312	81,7	382		
35-49	37	27	100	73	137		
>49	14	43,8	18	56,3	32		
Dönem							
2012	55	22,9	185	77,1	240	1,144	0,285
2013	99	19,5	408	80,5	507		
Bölüm							
Dahili	63	24,5	194	75,5	257	3,800	0,150
Cerrahi	3	15	17	85	20		
Kadın hastalıkları ve doğum[1]	88	18,7	382	81,3	470		
Toplam	154	20,6	593	79,4	747		

[1]Risk grubu olduğu için ayrıca değerlendirilmiştir.

Tablo 2. Cinsiyete, yaş gruplarına, yıllara ve bölümlere göre anti-*Toxoplasma* IgM seropozitifliğinin değerlendirilmesi

	Pozitif		Negatif		Toplam		
Cinsiyet	**n**	**%**	**n**	**%**	**n**	χ^2	**p**
Erkek	2	2	99	98	101	0,094	1,000
Kadın	25	2,5	986	97,5	1011		
Yaş grupları							
<16	0	0	44	100	44	6,636	0,156
16-24	11	4,3	242	95,7	253		
25-34	13	2,2	574	97,8	587		
35-49	3	1,6	190	98,4	193		
>49	0	0	35	100	35		
Dönem							
2012	8	2,8	275	97,2	283	0,255	0,614
2013	19	2,3	810	97,7	829		
Bölüm							
Dahili	14	5,1	258	94,9	272	11,412	0,003
Cerrahi	0	0	17	100	17		
Kadın hastalıkları ve doğum[1]	13	1,6	810	98,4	823		
Toplam	27	2,4	1085	97,6	1112		

[1]Risk grubu olduğu için ayrıca değerlendirilmiştir

Kilis Devlet Hastanesi Kadın Doğum Polikliniğine Başvuran Doğurgan Çağdaki Kadınlarda *Toxoplasma gondii* Seropozitifliğine Etki Eden Risk Faktörlerinin Araştırılması

Investigation of the Risk Factors Affecting *Toxoplasma gondii* Seropositivity in Women of Reproductive Age Applying to the Maternity Clinic of Kilis State Hospital

Tuğba Demiroğlu[1], Zübeyda Akın Polat[2], Cem Çelik[3]

[1]Kilis 7 Aralık Üniversitesi, Sağlık Hizmetleri Meslek Yüksekokulu, Kilis, Türkiye
[2]Cumhuriyet Üniversitesi, Parazitoloji Anabilim Dalı, Sivas, Türkiye
[3]Cumhuriyet Üniversitesi, Mikrobiyoloji Anabilim Dalı, Sivas, Türkiye

Tablo 1. Hastaların sosyo-demografik özellilerine göre *Toxoplasma*- IgG ve IgM sonuçlarının dağılımı

Demografik Özellik	Demografik Alt Özellik	IgG				IgM			
		Pozitif		Negatif		Pozitif		Negatif	
		Hasta Sayısı (n)	Yüzde (%)	Hasta Sayısı (n)	Yüzde (%)	Hasta Sayısı (n)	Yüzde (%)	Hasta Sayısı (n)	Yüzde (%)
Medeni Durum	Evli	188	63,3	109	36,7	13	4,4	284	95,6
	Bekâr	16	64,0	9	36,0	0	0	25	100,0
Yaş Grupları	15-19	14	46,7	16	53,3	1	3,3	29	96,7
	20-24	50	51,0	48	49,0	3	3,1	95	96,9
	25-29	52	65,8	27	34,2	6	7,6	73	92,4
	30-34	37	62,7	22	37,3	1	1,7	58	98,3
	35-39	21	80,8	5	19,2	0	0	26	100,0
	40-44	20	100,0	0	0	1	5,0	19	95,0
	45-49	10	100,0	0	0	1	10,0	9	90,0
Gelir Durumu	İyi	30	60,0	20	40,0	4	8,0	46	92,0
	Orta	123	63,1	72	36,9	8	4,1	187	95,9
	Düşük	32	66,7	16	33,3	0	0	48	100,0
	Çok Düşük	19	65,5	10	34,5	1	3,4	28	96,6
Eğitim Durumu	Yok	29	85,3	5	14,7	3	8,8	31	91,2
	İlkokul	97	63,8	55	36,2	4	2,6	148	97,4
	Ortaokul	38	57,6	28	42,4	6	9,1	60	90,9
	Lise	21	53,8	18	46,2	0	0	39	100,0
	Üniversite	19	61,3	12	38,7	0	0	31	100,0

IgG: Immunoglobulin G, IgM:Immunoglobulin M

Abant İzzet Baysal Üniversitesi Eğitim Araştırma Hastanesine Başvuran Hastalarda 6 Yıllık *Toxoplasma gondii* Seropozitifliğinin Araştırılması

Investigation of a 6-year seropositivity of *Toxoplasma gondii* in Abant Izzet Baysal University Educational Research Hospital

Şule Aydın Türkoğlu[1], Şeyda Karabörk[2], Mücahit Çakmak[3], Hayriye Orallar[4], Kerem Yaman[5], Erol Ayaz[5]

[1]Abant İzzet Baysal Üniversitesi Tıp Fakültesi, Nöroloji Anabilim Dalı, Bolu, Türkiye
[2]Abant İzzet Baysal Üniversitesi Tıp Fakültesi, Tıbbi Mikrobiyoloji Anabilim Dalı, Bolu, Türkiye
[3]Abant İzzet Baysal Üniversitesi, Deney Hayvanları Uygulama ve Araştırma Merkezi, Bolu, Türkiye
[4]Abant İzzet Baysal Üniversitesi, Ziraat ve Doğa Bilimleri Fakültesi, Bolu, Türkiye
[5]Abant İzzet Baysal Üniversitesi Tıp Fakültesi, Tıbbi Parazitoloji Anabilim Dalı, Bolu, Türkiye

Tablo 2. Tetkik istenen olguların antikor varlığının cinsiyete göre dağılımı

IgG	Negatif	Pozitif	IgM	Negatif	Pozitif
Erkek (n=460)	333 (%72,4)	127 (%27,6)	Erkek (n=514)	504 (%98,1)	10 (%1,9)
Kadın (n=3514)	2796 (%79,6)	718 (%20,4)	Kadın (n=12998)	12846 (%98,8)	152 (%1,2)
Bebek (n=74)	56 (%75,7)	18 (%24,3)	Bebek (n=93)	93 (%100)	0
Toplam (n=4048)	3185 (%78,7)	863 (%21,3)	Toplam (n=13605)	13443 (%98,8)	162 (%1,2)
Toplam			**Negatif**	**Pozitif**	**Grayzone**
IgG		n=4079	%78	%21	%08
IgM		n=13671	%98	%1.2	%05

Tablo 5. Nöroloji kliniğine başvuran IgG ve IgM pozitif hastaların başvuru şikayetleri ve yaş ortalaması

Nöroloji n=478			
IgG 130 (%27)	**Yaş Mean(±SS)**	**IgM 4 (%0,8)**	**Negatif 348 (%72,8)**
Nöropsikiyatrik bulgular n=14	52 (±15)	n=1 yaş: 18	
Genç inme-vaskülit n=55	45 (±10)		
AF+İnme n=25	72 (±12)		
Nörodejeneratif Hastalıklar n=13	66 (±9)		
Epilepsi n=16	45 (±18)	n=3 yaş:65 (30-69)	
Trigeminal Nevralji n=4	49 (±23)		
AIDP n=3	51 (±11)		

Investigation of Anti-*Toxoplasma gondii* Antibodies in Water Buffaloes *(Bubalus bubalis)* in Samsun and Afyon Provinces

Samsun ve Afyon yörelerindeki Mandalarda *(Bubalus bubalis)* Anti-*Toxoplasma gondii* Antikorlarının Araştırılması

Yunus Emre Beyhan[1], Cahit Babür[1], Oktay Yılmaz[2]

[1]National Reference Laboratory of Parasitology, Institution of Public Health, Ankara, Turkey
[2]Department of Obstetrics and Gynecology, Faculty of Veterinary Medicine, Afyon Kocatepe University, Afyon, Turkey

Table 2. Sabin-Feldman Dye Test (SFDT) results with provinces and titers

Titers / Provinces	1:16	1:64	1:256	1:1024	Negative	Total
Samsun	36	29	7	2	11	86
Afyon	24	12	2	1	5	45
Total	60	41	9	3	16	131

Ankara Yöresindeki Kedilerde 2016 Yılında Sabin-Feldman Dye Testi (SFDT) ile Anti-*Toxoplasma gondii* Antikorlarının Araştırılması

Investigation of Anti-Toxoplasma gondii Antibodies in Cats Using Sabin-Feldman Dye Test in Ankara in 2016

Banuçiçek Yücesan[1], Cahit Babür[1], Nafiye Koç[2], Figen Sezen[3], Selçuk Kılıç[1], Yüksel Gürüz[4]

[1]Halk Sağlığı Genel Müdürlüğü, Mikrobiyoloji Referans Laboratuvarları ve Biyolojik Ürünler Dairesi Başkanlığı Ulusal Parazitoloji Referans Laboratuvarı, Ankara, Türkiye

[2]Ankara Üniversitesi Veteriner Fakültesi, Parazitoloji Anabilim Dalı, Ankara, Türkiye

[3]Halk Sağlığı Genel Müdürlüğü, Sağlık Tehditleri, Erken Uyarı ve Cevap Dairesi Başkanlığı, Ankara , Türkiye

[4]Ege Üniversitesi Tıp Fakültesi, Parazitoloji Anabilim Dalı, İzmir, Türkiye

Tablo 2. Kedilerde Sabin-Feldman boya testi seropozitifliğinin risk faktörlerine göre değerlendirilmesi (n=129)

Özellikler	Test Sonuçları (SFDT)		İstatistiksel Analiz
	Pozitif	Negatif	
	Sayı (%)	Sayı (%)	
Cinsiyet			
Dişi	42 (65,6)	22 (34,4)	P=0,803
Erkek	44 (67,7)	21 (32,3)	
Yaş			
<1	14 (66,7)	7 (33.3)	P=0,991
1-2	39 (67,2)	19 (32.8)	
>2	33 (66,0)	17 (34.0)	
Yaşam Alanı			
Ev	48 (55,2)	39 (44,8)	P<0,001
Ev/Sokak	6 (66,7)	3 (33,3)	
Sokak	32 (97,0)	1 (3,0)	
Beslenme			
Doğal beslenme	34 (89,5)	4 (10,5)	P<0,001
Ticari kuru mama	47 (55,3)	38 (44,7)	
Avlanma			
Evet	34 (91,9)	3 (8,1)	P<0,001
Hayır	48 (55,2)	39 (44,8)	

SFDT: Sabin-Feldman boya testi

Continuous Decline of *Toxoplasma gondii* Seroprevalence in Hospital: A 1997–2014 Longitudinal Study in Paris, France

*Nicolas Guigue[1], Lucie Léon[2], Samia Hamane[1], Maud Gits-Muselli[1,3], Yann Le Strat[2], Alexandre Alanio[1,3] and Stéphane Bretagne[1,3]**

[1] Laboratoire de Parasitologie-Mycologie, AP-HP, Groupe Hospitalier Saint-Louis, Lariboisière, Fernand-Widal, Paris, France, [2] Santé Publique France, French National Public Health Agency, Saint-Maurice, France, [3] Université Paris Diderot, Sorbonne Paris Cité, Paris, France

TABLE 1 | Prevalence of anti-*Toxoplasma gondii* antibodies (%) by year and sex.

Year	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
Male patients (N)	993	724	743	625	657	720	625	685	704	708	662	709	681	670	704	710	674
Prevalence (%)	67.0	69.6	68.9	71.4	66.4	64.4	63.7	62.5	59.2	62.4	59.7	59.0	59.8	61.2	58.2	58.2	54.2
Female patients (N)	639	636	599	561	605	618	533	534	569	575	484	483	513	535	526	583	493
Prevalence (%)	60.6	63.5	60.1	62.7	61.5	62.8	54.4	54.5	54.3	56.3	53.7	55.5	51.7	51.4	51.5	50.4	55.4
All patients (N)	1632	1360	1342	1186	1262	1338	1158	1219	1273	1283	1146	1192	1194	1205	1230	1293	1167
Prevalence (%)	64.5	66.8	65.0	67.3	64.0	63.7	59.4	59.0	57.0	59.7	57.2	57.6	56.3	56.8	55.4	54.7	54.7

Prevalence and Risk Factors of *Toxoplasma gondii* Infection among Pregnant Women in Hormozgan Province, South of Iran

Seyedeh Zahra KHADEMI [1,2], *Fatemeh GHAFFARIFAR [1], ABDOLHOSSEIN Dalimi [1], Parivash DAVOODIAN [3], Amir ABDOLI [4,5]

1. *Department of Parasitology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran*
2. *Department of Biology, Payam Noor University, Tehran, Iran*
3. *Infectious and Tropical Disease Research Center, Hormozgan Health Institute, Hormozgan University of Medical Sciences, Bandar Abbas, Iran*
4. *Department of Parasitology and Mycology, School of Medicine, Jahrom University of Medical Sciences, Jahrom, Iran*
5. *Zoonosis Research Center, Jahrom University of Medical Sciences, Jahrom, Iran*

Table 1: *T. gondii* serological findings in pregnant women in 5 cities of Hormozgan province, southern Iran

City	*Bandar Abbas (N=190) (%)*	*Minab (N=40) (%)*	*Haji Abad (N=40) (%)*	*Bastak (N=40) (%)*	*Qeshm (N=50) (%)*	*Total (%)*
IgG positive	46(24. 2)	10(25)	6(15)	13(32. 5)	25(50)	100(27. 8)
IgM Positive	0(0)	1(2. 5)	1(2. 5)	1(2. 5)	0(0)	3(0. 36)

HIV/AIDS Hastalarında *Toxoplasma gondii* IgG Seroprevalansı

Toxoplasma gondii IgG Seroprevalence in Patients with HIV/AIDS

Sevtap Şenoğlu, Zuhal Yeşilbağ, Özlem Altuntaş Aydın, Hayat Kumbasar Karaosmanoğlu, Kadriye Kart Yaşar

Bakırköy Dr. Sadi Konuk Eğitim ve Araştırma Hastanesi, Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji, İstanbul, Türkiye

Tablo 1. Demografi ve CD4 T lenfosit sayılarına göre *T. gondii* seroprevalansı

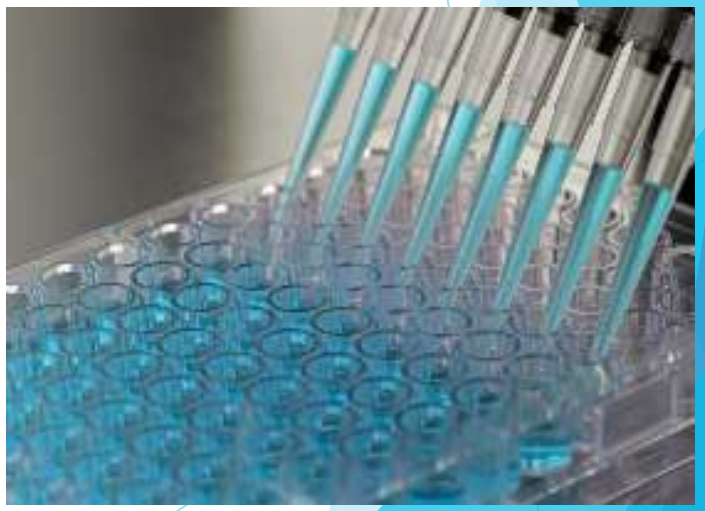
	T. gondii Ig G (+) (n/%)	*T. gondii* Ig G (-) (n/%)	Toplam
Cinsiyet			
Erkek	232 (44)	296 (56)	528
Kadın	35 (40,7)	51 (59,3)	86
Bulaş yolu			
Heteroseksüel temas	162 (48,4)	173 (51,6)	335
Homoseksüel temas	105 (37,6)	174 (67,4)	279
CD4 sayısı			
<100	46 (53,5)	40 (46,5)	86
100-200	29 (42)	40 (58)	69
200-350	64 (44)	81 (56)	145
350-500	54 (41)	78 (59)	132
>500	73 (40,3)	108 (59,7)	181
Yaş			
18-24	20 (24,7)	61 (75,3)	81
25-30	56 (34)	109 (66)	165
31-35	43 (35)	79 (65)	122
26-40	32 (43,2)	42 (56,8)	74
41-45	43 (56,6)	33 (43,4)	76
46-50	37 (74)	13 (26)	50
>50	49 (66,2)	25 (33,8)	74
Tanı yılı			
2006-2011	106 (47)	120 (53)	226
2012-2017	161 (41,5)	227 (58,5)	388
Eğitim			
Okuryazar değil	3 (75)	1 (25)	4
İlkokul	116 (47)	131 (53)	247
Lise	77 (46)	94 (54)	168
Lisans/Yüksek Lisans	71 (37)	120 (73)	191

Tablo 3. HIV/AIDS hastalarında Dünya'da farklı coğrafi bölgelerde yapılmış *T. gondii* seropozitifliğini gösteren çalışmalar

Çalışma	Şehir, Ülke	Hasta sayısı	Tanı metodu	Seroprevalans
Nissapatorn et al (5), 2007	Kuala Lumpur, Malaysia	693	Serum, ELISA	%43,85
Altuntaş Aydın et al. (10), 2010	İstanbul, Türkiye	164	Serum, ELISA	%52,0
Uneke et al. (15), 2005	Jos, Nigeria	219	Serum, ELISA	%38,8
Lago et al. (16), 2009	Rio Grande do Sul, Brazil	168 HIV enfekte gebe	Serum, ELISA	%72,0
Daryani et al. (17), 2011	Sari, İran	62	Serum, ELISA	%77,4
Machala et al. (18), 2009	Prague, Czech Republic	626	CFT*	%32,2
Millogo et al. (19), 2000	Burkino Faso, France	1828	Serum, ELISA	%25,4
Çalışmamızda	İstanbul, Türkiye	614	Serum, ELISA	%43,5
CFT: Complement Fixation Test				

Tanı Yöntemleri

- Toksoplazmoz tanısı doğrudan veya dolaylı tanı olabilir
- Çoğunlukla dolaylı olan serolojik yöntemler kullanılmaktadır
- ELISA
- IFA
- IHA
- Altın standart olan Sabin Feldman boya testi



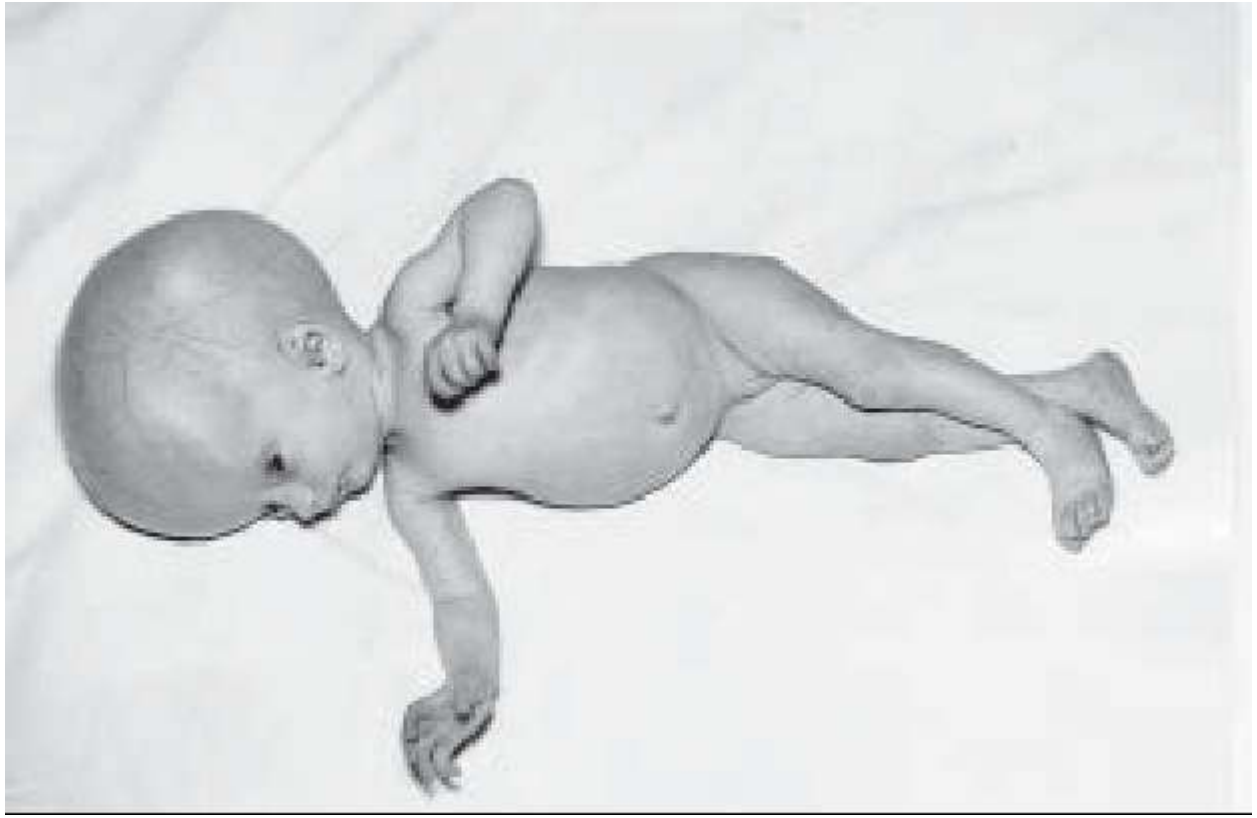
- Sabin Feldman boya testinde canlı parazit gerektirdiğinden dolayı sayılı merkezde uygulanmaktadır
- Kompleman antikor birleşmesini takiben membranları hasarlanan parazitlerin metilen mavisi ile boyanmaları ilkesine dayanmaktadır
- Laboratuvarda konfokal mikroskop varsa metilen mavisi kullanmadan, parlak görünüm canlı parazit- mat görünüm ölü parazit şeklinde de uygulanabilir

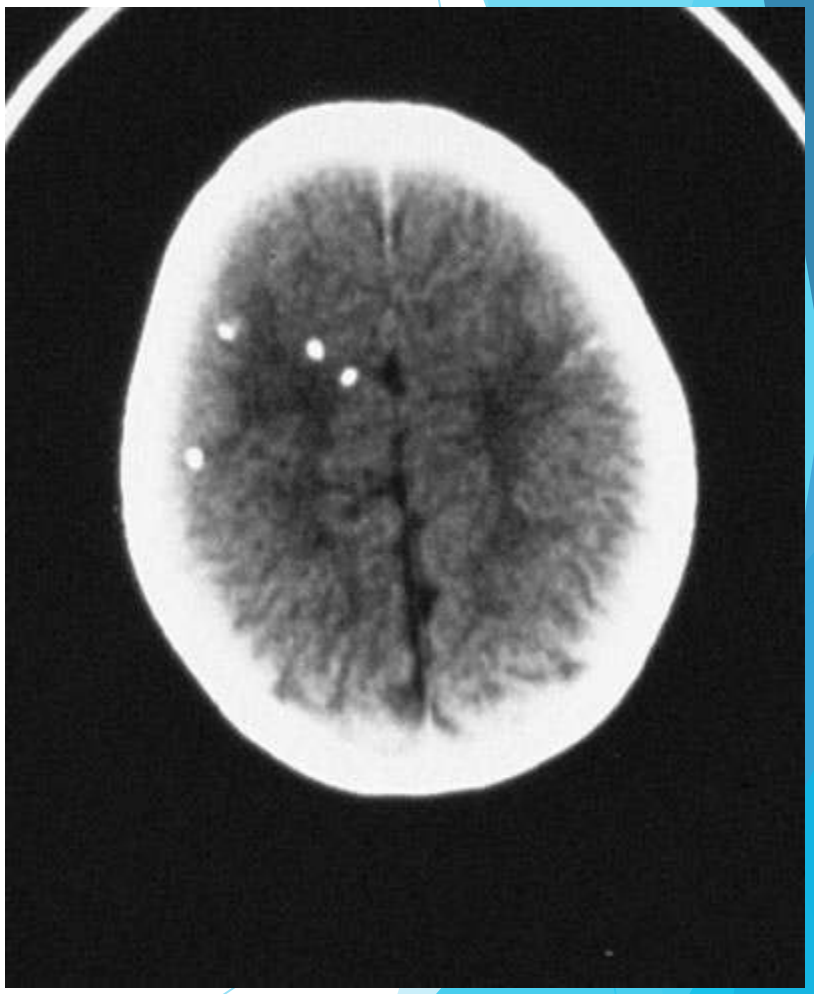
- Direk yöntemler ise PCR temelli moleküler yöntemler ve BOS, amniyon sıvısı gibi örneklerde ya da biyopsilerde etkenin kendisinin gözlenmesidir
-

Klinik Belirtiler

- Toksoplazmoz bağışıklık sistemi sağlıklı çalışan bireylerde sıklıkla asemptomatik seyreder
- Bu noktada parazitin suşu, alınan parazit yükü ve bulaşan form da önem taşımaktadır
- Toksoplazmozu klinik anlamda iki tabloya ayırabiliriz
- Doğumsal (konjenital) toksoplazmoz
- Edinsel tokosplazmoz

- Gebelikte trimestir ilerledikçe, parazitin bulaşma olasılığı artar ancak meydana getireceği klinik tablo ciddiyeti azalır
- Konjenital toksoplazmozun klasik üç belirtisi vardır
- İntraserebral kalsifikasyon
- Hidrosefali
- Korioretinit

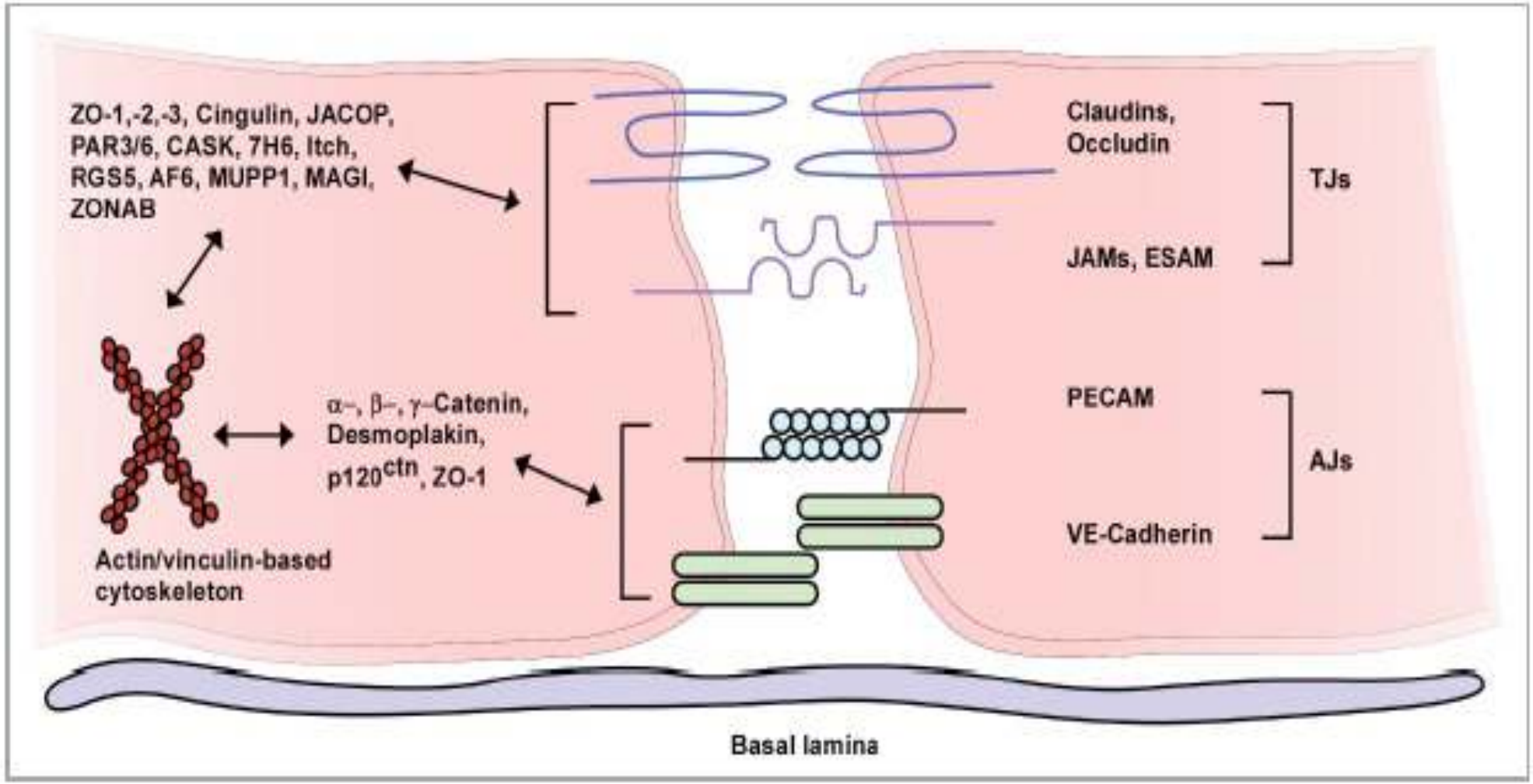


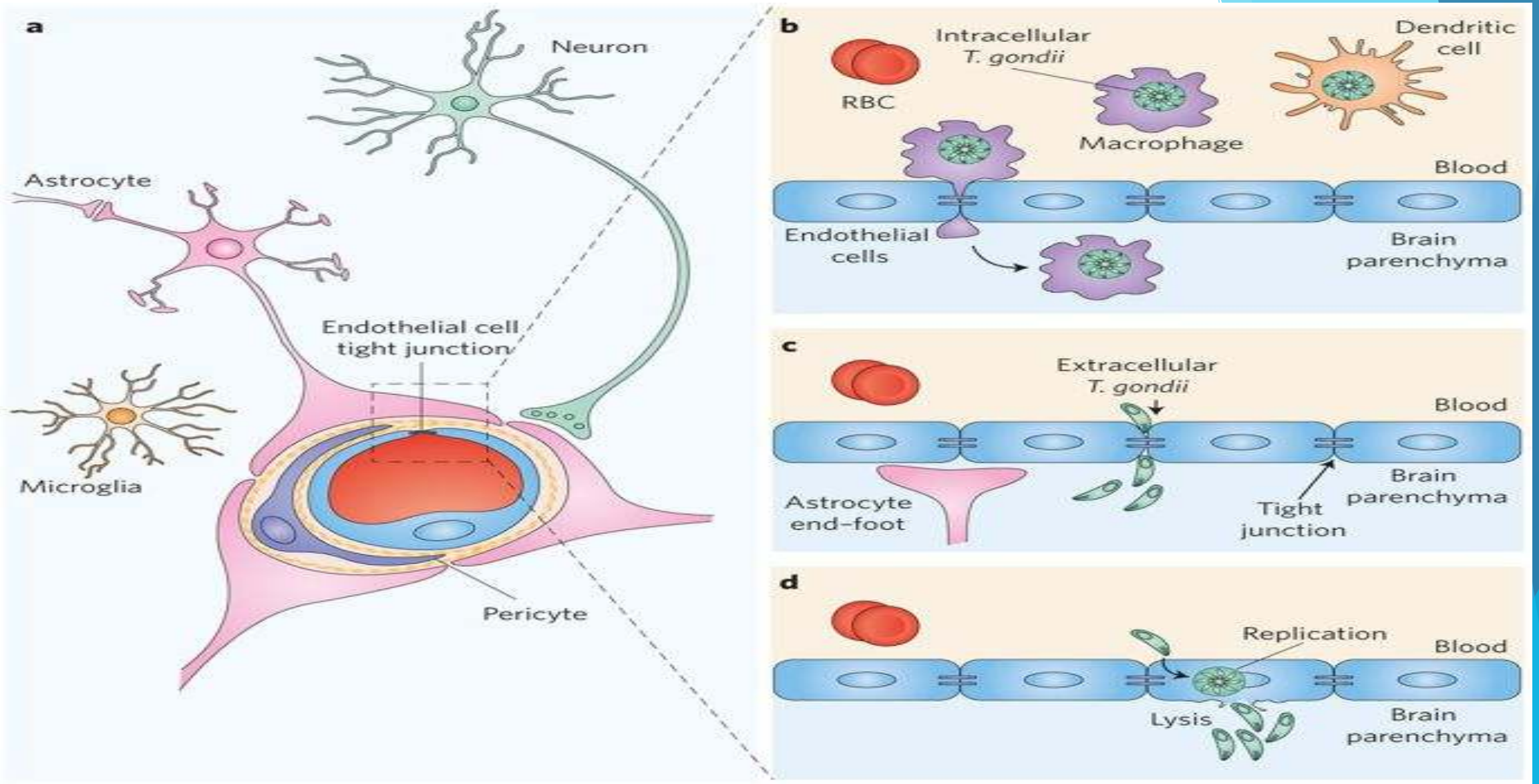


- Edinsel toksoplazmoz, konak çoğunlukla herhangi bir belirti göstermez
- Özgül olmayan ve soğuk algınlığını andırır
- Servikal LAP görülebilir
- Enfeksiyoz mononükleoza benzeyen tablo oluşabilir
- Nadir olarak poliadenopatili form söz konusu olabilir

- Etken parazit bazı dokulara tropizm gösterir
- MSS dokuları
- Göz
- Gebelerde plasenta
- Kalp kası

- Bazı nörolojik rahatsızlıkların alt yapısında T.gondii olduğuna dair çalışmalar vardır
- Epilepsi
- Şizofreni
- Alzheimer
- Parkinson


ZO-1,-2,-3, Cingulin, JACOP,
PAR3/6, CASK, 7H6, Itch,
RGS5, AF6, MUPP1, MAGI,
ZONAB
Claudins,
Occludin
TJs
JAMs, ESAM
α–, β–, γ–Catenin,
Desmoplakin,
p120ctn, ZO-1
PECAM
AJs
VE-Cadherin
Actin/vinculin-based
cytoskeleton
Basal lamina


a
Neuron
Astrocyte
Endothelial cell
tight junction
Microglia
Pericyte
b
Intracellular
T. gondii
Dendritic
cell
RBC
Macrophage
Blood
Endothelial
cells
Brain
parenchyma
c
Extracellular
T. gondii
Blood
Brain
parenchyma
Astrocyte
end-foot
Tight
junction
d
Replication
Blood
Lysis
Brain
parenchyma

Tedavi

- Toksoplazmozda her seropozitif olguda, antimikrobiyal tedavi uygulanmamaktadır
- Gerekli olduğu takdirde uygulanacak, antimikrobiyal tedavi protokollerini üç gruba ayırabiliriz
- İmmunkompetan olgularda tedavi
- İmmunsuppresif olgularda tedavi
- Gebelerde ve yenidoğanda tedavi

Drug	Target
Pyrimethamine	Folic acid synthesis, dihydrofolate reductase (C)
Sulfonamide	Folic acid synthesis, dihydropteroate synthetase (C)
Trimethoprim	Folic acid synthesis, dihydrofolate reductase (C)
Azithromycin	Protein translation, 23S rRNA (AP)
Clindamycin	Protein translation, 23S rRNA (AP)
Spiramycin	Protein translation, 23S rRNA (AP)
Clarithromycin	Protein translation, 23S rRNA (AP)
Atovaquone	Mitochondrial electron transport, cytochrome bc1 complex (Mi)
Dapsone	Folic acid synthesis, dihydropteroate synthetase (C)

TABLE 1 Treatment of toxoplasmosis in immunocompetent patients[a]

Regimen[b]	Comments
Pyrimethamine (100 mg daily for 1 or 2 days and then 25–50 mg daily) plus sulfadiazine (1g every 6 h [q6h]) plus folinic acid (10–20 mg daily)	Blood counts, creatinine, and liver function should be monitored regularly Adequate hydration should be ensured to prevent renal damage from crystalluria
Pyrimethamine plus folinic acid (dosing as described above) plus clindamycin (300 mg q6h)	Blood counts should be monitored regularly Clindamycin may cause diarrhea, including *Clostridium difficile* infection
TMP-SMX (5/25–10/50 mg/kg/day in divided doses)	Blood counts, creatinine, and liver function should be monitored regularly Adequate hydration should be ensured to prevent renal damage from crystalluria
Atovaquone (1,500 mg twice daily) ± pyrimethamine plus folinic acid (dosing as described above)	Blood counts and liver function should be monitored regularly Atovaquone should be taken with a high-fat diet
Pyrimethamine plus folinic acid (dosing as described above) plus azithromycin (250–500 mg daily[c])	Blood counts should be monitored regularly Azithromycin may cause hearing problems and a prolonged QT interval
Intravitreal clindamycin (1 mg) plus dexamethasone (400 μg)	Only for ocular toxoplasmosis; may need to be repeated 1 or 2 times if response is suboptimal

TABLE 2 Treatment of toxoplasmosis in immunocompromised patients

Induction therapy	Maintenance therapy	Comments
For those with body wt of ≥60 kg, pyrimethamine (200 mg once and then 75 mg daily) plus sulfadiazine (1.5 g q6h) plus folinic acid (10–50 mg daily)	Pyrimethamine (50 mg daily) plus sulfadiazine (1 g q6h) plus folinic acid (10–25 mg daily)	Blood counts, creatinine, and liver function should be monitored regularly Adequate hydration should be ensured to prevent renal damage from crystalluria
For those with body wt of <60 kg, pyrimethamine (200 mg once and then 50 mg daily) plus sulfadiazine (1 g q6h) plus folinic acid (10–50 mg daily)	Pyrimethamine (25 mg daily) plus sulfadiazine (0.5 g q6h) plus folinic acid (10–25 mg daily)	Blood counts, creatinine, and liver function should be monitored regularly Adequate hydration should be ensured to prevent renal damage from crystalluria
Pyrimethamine plus folinic acid (dosing as described above) plus clindamycin (600 mg q6h)	Pyrimethamine plus folinic acid (dosing as described above) plus clindamycin (600 mg q8h)	Blood counts should be monitored regularly Clindamycin may cause diarrhea, including *Clostridium difficile* infection
TMP-SMX (10/50 mg/kg/day[a] in divided doses)	TMP-SMX (5/25 mg/kg/day in divided doses)	Blood counts, creatinine, and liver function should be monitored regularly Adequate hydration should be ensured to prevent renal damage from crystalluria
Atovaquone (1,500 mg twice daily) ± pyrimethamine plus folinic acid (dosing as described above)	Atovaquone (750–1,500 mg twice daily) ± pyrimethamine plus folinic acid (dosing as described above)	Blood counts and liver function should be monitored regularly Atovaquone suspension should be taken with a high-fat diet to optimize bioavailability
Atovaquone plus sulfadiazine (dosing as described above)	Atovaquone plus sulfadiazine (dosing as described above)	Blood counts, creatinine, and liver function should be monitored regularly Atovaquone suspension should be taken with a high-fat diet to optimize bioavailability
Pyrimethamine plus folinic acid (dosing as described above) plus azithromycin[b] (1,000 mg daily)	Pyrimethamine plus azithromycin not recommended due to a high relapse rate; one of the above regimens should be used instead	Blood counts should be monitored regularly Azithromycin may cause hearing problems and a prolonged QT interval

TABLE 3 Treatment of acute toxoplasmosis in pregnant women and newborns

Infection stage	Regimen	Comments
Maternal infection at <14 weeks of gestation, no fetal infection	Spiramycin (1 g [3 million units] every 8 h until delivery)	Spiramycin is not effective for treating established fetal infection and hence should be used only for prevention of vertical transmission Amniocentesis and fetal ultrasound should be performed when feasible to rule out fetal infection
Maternal infection at >14 weeks of gestation[a]	Pyrimethamine (100 mg daily for 2 days and then 50 mg daily) plus sulfadiazine (1 g q8h [body wt of <80 kg] or 1 g q6h [body wt of ≥80 kg]) plus folinic acid (10–20 mg daily pending fetal USG and amniocentesis)	Pyrimethamine is teratogenic and should not be used in early pregnancy
	If fetus is confirmed to be infected (abnormal USG and/or positive amniotic fluid PCR), continue pyrimethamine plus sulfadiazine plus folinic acid until delivery	Serial fetal USG and amniotic fluid PCR should be performed at 18 weeks of gestation
	If fetus is not infected (e.g., negative USG and amniotic fluid PCR), pyrimethamine plus sulfadiazine plus folinic acid may be switched to spiramycin Alternatively, pyrimethamine plus sulfadiazine plus folinic acid can be continued until delivery or alternated with spiramycin on a monthly basis	
Congenital infection in newborns	Pyrimethamine (1 mg/kg q12h for 2 days and then 1 mg/kg/day for 2–6 mo and then 1 mg/kg/day 3 times a week) plus sulfadiazine (50 mg/kg q12h) plus folinic acid (10 mg 3 times a week)	Treatment should be started as soon as feasible after birth and continued for at least 1 year

[a]The 14-week cutoff period for starting pyrimethamine and sulfadiazine in pregnant women may vary in different countries.

Table 1 Summary of in vitro studies that evaluated the anti-*Toxoplasma* activity of drugs/compounds against tissue cysts

No.	Drug	Strain	Cell/medium	Culture	Evaluation	Main results	Effectivity	Ref
1	Compound 566C80	ME49	RPMI	24 and 72 h	Inoculation "'"'"into mice (IP)	None of the mice were infected with cysts	Effective	(Araujo et al. 1991)
2	Arprinocid-N-oxide, azithromycin and the hydroxynaphthoquinone 566C80	ME49	RPMI	24 and 72 h	Inoculation into mice (IP)	The most active compounds against the cyst form were arprinocid-N-oxide, azithromycin, and hydroxynaphthoquinone 566C80	Effective	(Huskinson-Mark et al. 1991)
3	Hydroxynaphthoquinone 566C80	ME49	RPMI	3 or 6 days	Inoculation into mice (IP)	Loss of viability of the cysts	Effective	(Huskinson-Mark et al. 1991)
4	CAMP PYR MTX	ME49	Peritoneal macrophages	1, 3, 5, and 10 days	[3H]-Uracil uptake assay and Giemsa stain	CAMP and PYR: the number of pseudocysts were decreased but the size was not changed. MTX: no effect was noted	Effective Effective Ineffective	(Choi et al. 1994)
5	Monensin	PLK, 76 K	Vero	6 or 48 h	Immunofluorescence assay, electron microscopy, and inoculation into mice	Significant cytological alterations of the monensin-treated bradyzoites were seen. Mice inoculated with cysts were treated 6 or 48 h; no antibodies and no cysts were recovered from their brains	Effective	(Couzinet et al. 2000)
6	PHNQ6 alone and combined with sulfadiazin	EGS	DMEM	24 or 48 h	Inoculation into mice (IP)	Infectivity of bradyzoites treated with PHNQ6 alone or combined with sulfadiazine was inhibited after in vitro incubation	Effective	(Ferreira et al. 2006)
7	Tetrapeptide FR235222	PRU	HFF	24, 48, and 72 h	Immunofluorescence assay (IFA)	100% altered cysts 24 h after treatment with the lowest concentration (30 nM) of FR235222	Effective	(Maubon et al. 2010)
8	New naphthoquinones (QUI-11, QUI-6, and QUI-5) and liriodenine	EGS	DMEM	24 and 48 h	Inoculation into mice (IP)	In vitro incubation with QUI-6, QUI-11, and liriodenine inhibited the infectivity of the bradyzoites. None of the surviving animals had detectable cysts in the brain	Effective	(Ferreira et al. 2012)
9	Spiramycin coadministered with metronidazole	ME49	Vero E6 cells	1 week	Counting the number of cysts	Spiramycin reduced the numbers of cysts 44 and 42%. Coadministration of drugs reduced the numbers of cysts (68 and 58% reductions)	Effective	(Chew et al. 2012)
10	Atovaquone and 3-bromopyruvate	RH	LLC-MK2	24 or 48 h, or 6 days	Indirect immunofluorescent assays	Atovaquone and 3-bromopyruvate in combination led to fewer parasite-infected cells with no evidence of cystogenesis	Atovaquone, effective	(de Lima et al. 2015)
11	Guanabenz	PRU	HFF	32 h	Stained with Diff-Quick and evaluated by light microscopy	4 and 15% of cysts were abnormal in the guanabenz and salubrinal	Effective	(Benmerzouga et al. 2015)
12	Tanshinone IIA and hydroxyzine	PLK/DLUC1C9	HFF	3 days	Dual-Glo luciferase assay	Both compounds reduced the bradyzoite number	Effective	(Murata et al. 2017)
13	Aureobasidin A and compound 20	PRU	HFF	3 days	ED_{50} determination	Aureobasidin A demonstrated slightly higher efficacy (ED_{50} 2·51, μg/ml) than compound 20 (ED_{50} 3·74, μg/ml)	Effective	(Alqaisi et al. 2017)

IP intraperitoneal, *PYR* pyrimethamine, *MTX* methotrexate, *PHNQ6* 2-hydroxy-3-(1'-propen-3-phenyl)-1,4-naphthoquinone

Korunma yolları- aşı çalışmaları

- Toxoplasma gondii'den korunmak için tüketime sunulan gıdalarda ve suda çeşitli işlemlerin uygulanması tercih edilmekte ve etkenin biyolojik döngüsünün kırılması için çeşitli aşı adayları araştırılmaktadır
- Günümüzde ticari olarak satılan tek toksoplazmoz aşısı Toxovax adlı attenüe S48 suşundan elde edilen aşıdır

Table 1. Selected List of Attenuated Live Vaccines Tested against Experimental *Toxoplasma gondii* Infection

Targeted gene	Parasite strain	Dosage	Animal model	Spectrum of protective efficacy	Refs
CPSII	RH	10^7 tachyzoites	BALB/c, C57BL/6 mice	Acute and chronic infection	[11,77]
MIC1-3	RH	20 tachyzoites	Swiss OF1 mice	Acute, chronic, and congenital infection	[78]
OMPDC	RH, Pru	10^7 tachyzoites	C57BL/6 mice	Acute and chronic infection	[79,80]
AMA1	RH	10^6 tachyzoites	BALB/c, C57BL/6, CD-1 mice	Acute and chronic infection	[81]
PTS	RH	5×10^3 tachyzoites	C57BL/6 mice	Acute and chronic infection	[82]
GRA17	RH	5×10^4 tachyzoites	Kunming mice	Acute, chronic, and congenital infection	[83]
CDPK2	Pru	5×10^2 tachyzoites	Kunming mice	Acute, chronic, and congenital infection	[84]
MIC1-3	RH	10^5 tachyzoites	Sheep	Congenital infection	[85]

Table 2. Summary of effects of thermal methods to inactivation of *T. gondii* and its infectious forms.

Type of methods	Temperature(s) (°C)	Time (min/h/day)	Main finding	Ref.
Heating	50	2.5 min	Sporulation of *Toxoplasma* oocysts inhibited.	[65]
	50	30 min	Infectivity of sporulated oocysts disappears.	[65]
	55	30 min	Tissue cysts are destroyed.	[66]
	58	30 min	No evidence of parasites in infected murine brains.	[67]
	58	15 min	Sufficient to inactivate all oocysts.	[67]
	61	3.6 min	Tissue cysts were generally rendered nonviable.	[75]
	60 or 100	1 min	No viable *T. gondii* infective stages isolated from meat samples.	[76]
	63	30 min	*T. gondii* tachyzoites RH strain die in pasteurized milk.	[77]
	75	1 h	Heat treatment like boiling water can inactivate *T. gondii* oocysts.	[78]
Cooking	63, 71, 82	–	Beef, lamb and veal roasts and steaks should be cooked to at least 63°C. Pork, ground meat and wild game should be cooked to 71°C before eating. Whole poultry should be cooked to 82°C in the thigh to ensure doneness.	[27]
	67	–	Tissue cysts in meat are killed by heating meat throughout.	[61]
	50	1 h	Heating inactivates tissue cysts.	[73]
	67	0.01–96 min	Kills tissue cysts in meat.	[79]
	66	-	Heating meat throughout to reach a temperature is sufficient to kill cysts in meat.	[80]
Freezing and low temperature	−12.37	11.2 day	Nonviable *T. gondii* tissue cysts in pork upon freezing.	[61]
	−20	1–2 day	Tissue cysts stored at −20°C could infection after 24 and 48 h of storage.	[81]
	−21	1 1/2 h	After 1 1/2 h of exposure to −21°C, many cysts seem to lose their infectivity.	[62]
	−10 or −20	3 day	Freezing of meat at −10°C for 3 days or at −20°C for 2 days killed parasite and cysts could not recover.	[76]
	−7	4 day	Inactivation of T *gondii* tissue cysts was achieved by freezing at −7°C for 4 days.	[82]
	−20	21 day	Sporulated oocysts were inactivated by freezing.	[82]
	−20	2 day	Freezing for 2 days at −20°C was sufficient to inactivate parasite.	[72]
	−25	6–35 day	Experiments with meat from pigs fed with *T. gondii* infected mice showed that all meat samples were rendered non-infectious.	[83]
	−7–12	4 day	Parasites in meat from experimentally infected pigs did not survive.	[82]
	−20	3 day	Temperature and time required to inactivate isolated tissue cysts.	[81]

Table 3. Summary of effects of non-thermal methods to inactivation of *T. gondii* and its infectious forms.

Type of methods	Experimental Conditions	Main finding	Ref.
High Pressure Processing	400 or 300 MPa to 30, 60, or 90 sec	No mice inoculated with tissue cysts exposed to 400 or 300 MPa became infected.	[104]
	340 MPa to 1 min	Use of HPP at 340 MPa for 60 sec required to render oocysts spot inoculated on raspberries non-infectious for mice.	[104]
	550 MPa, 480 MPa, 400 MPa, or 340 MPa to 1 min	*T. gondii* oocysts in HBSS (without calcium or magnesium) or distilled water treated with HPP at 550, 480, 400 or 340 MPa for 60 sec were rendered noninfectious for mice.	[105]
Ionizing Irradiation	Gamma (70 krad)	Use of 70 krad gamma radiation was minimum effective dose for fresh pork.	[93]
	Gamma (40 krad)	*T. gondii* in tissue cysts killed by exposure to 40 krad of gamma irradiation.	[93]
	Gamma (50 krad or more)	Tissue cysts irradiated with 40 krad were infectious when inoculated in mice, but when irradiated with 50 krad or more, tissue cysts were not detected.	[107]
	Gamma (70 krad or 100 krad)	Tissue cysts in murine brains and edible pig flesh irradiated with 30 and 50 krad doses were not effective, whereas irradiation with 70 or 100 krad did not infect cats or mice in bioassay.	[108]
	Gamma (20 krad)	Irradiation treatments at doses as low as 20 krad effectively inactivated *T. gondii* oocysts on blueberry surfaces with minimal impact on texture, color, or anthocyanin content of treated berries.	[109]
	Gamma (60 krad and 45 krad)	The minimal effective dose for Chinese NT strain and the American ME-49 and TS-2 strains of *T. gondii* cysts in mouse and pig tissues was 60 krad. The infectivity for mice of NT strain bradyzoites irradiated at 45 krad decreased 10,000-fold.	[95]
	Ultraviolet (>20 mJ/cm^2)	A 4-log inactivation of the oocyst/sporozoite infectivity was obtained for UV fluence.	[110]
	Ultraviolet (4 mJ/cm^2 and 10 mJ/cm^2)	The results from the animal bioassay show that 1- and 3-log10 inactivation was achieved with 4 mJ/cm^2 UV and 10 mJ/cm^2 low-pressure UV, respectively.	[94]
	Ultraviolet (40 mJ/cm^2)	A 2-log10 reduction of *T. gondii* oocyst infectivity was achieved at 40 mJ/cm^2.	[111,112]
	Ultraviolet (>500 mJ/cm^2)	Inactivation of *T. gondii* oocysts occurred with exposure to pulsed and continuous UV radiation, as evidenced by mouse bioassay. Even at >500 mJ/cm^2, some oocysts retained their viability.	[113]
	Ultraviolet (1 min UV exposure)	Using 1 min UV light at 3689.04 μJ/cm^2/sec powers for a total energy exposure, tachyzoites were unable to replicate in vitro or produce parasite cysts in vivo.	[96]

		tachyzoites were unable to replicate in vitro or produce parasite cysts in vivo.	
Curing	3.9% NaCl, 25 mg/kg nitrate, and 3 mg/kg nitrite; 14 months	The last curing salt concentration of 3.9% NaCl, 25 mg/kg nitrate and 3 mg/kg nitrite for a duration of curing of 14 months inactivated *T. gondii*.	[114]
	2.5% of sodium nitrite; 14 days	About 2.5% of initial amount of sodium nitrite was effective for killing *T. gondii* cysts in 14 days.	[115]
	7% nitrates, 4% nitrites, sodium ascorbate, and sodium chloride; 9–12 months	The viability of *T. gondii* was higher in hams cured for 9 months compared to those cured for 12 months.	[116]
	2.0% NaCl or 1.4% or higher lactate-based salt solutions; 8 h	The injection of 2.0% NaCl or 1.4% or higher lactate-based salt solutions into pork loins containing infective tissue cysts within 8 h prevented transmission of *T. gondii*.	[103]
	salt and sugar for 64 h at 4°C; smoking at 50°C to 24–28 h	Curing of lamb meat with salt and sugar for 64 h at 4°C or smoking salt-injected meat at temperatures not exceeding 50°C for 24 to 28 h was effective for killing *T. gondii*.	[110]
	6% NaCl; 4–20°C; 3–56 days	In various time intervals and all temperatures examined, tissue cysts were killed in 6% NaCl solution.	[101]
	2.0 and 2.5% of salt; 48 hours	Pig sausage experimentally inoculated with *T. gondii* showed that salt in concentrations of 2.0 and 2.5% inactivated the parasite within 48 h of onset of curing.	[117]
	3% table salt; 3–7 days	About 3% table salt after 3–7 days killed *T. gondii* tissue cysts.	[118]
	2.5 and 3.0%, NaCl and 0.5% nitrite; 1–8 day	The cysts lost their infectivity in concentrations of 2.5 and 3.0% NaCl after 1 day. NaCl plus 0.5% nitrite had a stronger effect on *T. gondii* cysts than common table salt.	[119]

Table 4. Effect of some disinfectants on *T. gondii* Oocysts.

Disinfections	Concentration	Treatment time (min/h/day)	Effective	Ref.
Formalin	10%	48 hr	No	[121]
Sulfuric acid +dichromate	63/7%	30 min	No	[66]
Ethanol +acetic acid	95/5%	1 hr	No	[66]
	95/5%	24 hr	Yes	
Ammonium hydroxide	5.0%	10 min	No	[66]
	5.0%	30 min	Yes	
Sodium hyporchlorite (Purex)	6.0%	24 hr	No	[66]
Sodium lauryl sulfate	0.1%	24 hr	No	[66]
Cetyl trimethyl ammonium	0.1%	24 hr	No	[66]
Tween 80	0.1%	24 hr	No	[66]
Ammonia, liquid	5.5%	1 hr	No	[78]
	5.5%	3 hr	Yes	
Tincture of iodine	2.0%	10 min	No	[78]
	2.0%	3 hr	Yes	
	7.0%	10 min	Yes	
Aldesol (contains benzalchoniumchloride, glutaraldehyde, and gloxal)	33%	24 hr	No	[129]
Tincture of hibisept (contains chlorhexidine gluconate in ethanol)	-	24 hr	No	[129]
Izosan-G (contains sodium dichloroizicyanurate-dihydrate in granulate)	.02%	24 hr	No	[129]
Lomasept	1%	1 hr	No	[121]
		3 hr	Yes	
Neo Kurehasol	5%	24 hr	No	[121]
Paracetic acid	5%	48 hr	Yes	[121]
Sodium chloride +potassium or sodium lactate	2% and ≥1.4% respectivily	14 days at 4°C	yes	[103]
Chlorination of water	100 mg/L	24 hr	No	[126]
Ozone treatment of water	6 mg/L	12 min	No	[126]
Ozone treatment of water	9.4 mg/L	20 min	No	[110]

Table 5. In vitro and in vivo studies on anti-toxoplasmosis effects of herbal medicine.

Plants and essential oils	Concentration	Result	Ref.
Satureja khuzestanica essential oil	0.2 and 0.3ml/kg	Mortality rate of infected mice was 8 days after oral administration of EO at 0.2 and 0.3 ml/kg.	[133]
Bunium persicum (Boiss) Essential Oil	0.05 and 0.1 mL/kg	Potential of Boiss EO for production of new preventive agent against toxoplasmosis.	[134]
Zingiber officinale (Ginger) extract	500 µg/ml	GE/F1 (fraction 1 obtained from GE) induced anti-*T. gondii* effects inactivating apoptotic proteins in infected host cells through the direct inhibition of *T. gondii* and has antiparasitic properties which inhibited inflammatory cytokine secretion in vivo.	[135]
Myristica Fragrans Houtt. Essential Oil	24.45 µg/mL	In vitro anti-*T. gondii* assay, oil extract caused significant inhibition with EC50 of 24.45 µg/mL.	[136]
Thymus broussonetii Boiss essential oil	20 µg/animal orally	Total absence of intracerebral cysts in mice who received EO of thyme, which appear to block appearance of cysts. No abnormality observed in control mice who received the EO of thyme.	[131]
Psidium guajava L. essential oil	3.94 ± 0.39 µg/mL	In vitro anti-*T. gondii* assay showed that guava leaf EO showed promising EC of 3.94 ± 0.39 µg/mL, as compared to the standard drug clindamycin (EC50 = 6.24 ± 0.53 µg/mL).	[137]
Curcuma longa water extracts	100 and 200 mg/kg/day	Most effective extract was *Curcuma longa* ethanol extract which showed a 98.6 and 99.2% inhibition of growth of *T. gondii* tachyzoites in 100 and 200 doses, respectively, compared to control.	[138]
Curcumin from the plant *Curcuma longa*	12.9 ± 0.5 µM and 38.3 ± 0.9 µM	Curcumin at the tested doses inhibited the enzymatic activity of recombinant TgGlo1 amplified from *T. gondii* cDNA and parasitic propagation of in vitro cultured *T. gondii*. Ki and IC50 were 12.9 ± 0.5 µM and 38.3 ± 0.9 µM, respectively.	[139]
N. sativa oil (NSO) +Pyrimethamine (PYR)	PYR (12.5mg/kg) and NSO (5 ml/kg) body weight/day	NSO+PYR combination markedly improved the antioxidant capacity of *T. gondii* infected mice compared to infected untreated controls. In total, combination of NSO and PYR had synergistic effect in treatment of toxoplasmosis.	[132]