

Akciğer Dışı Tüberkülozun Güncel Tanı ve Tedavisi

Alper Şener

*Onsekiz Mart Üniversitesi Tıp Fakültesi Enfeksiyon
Hastalıkları ve Klinik Mikrobiyoloji*

ÇANAKKALE

Sunum içeriđi

- Akciđer dıřı tüberkuloz (AD-TB) tanımı
- AD-TB epidemiolođisi
- AD-TB yaklaşım
- AD-TB tanı testleri
- Klinik Tablolar ve Tanı
- Tedavi

Ekstrapulmoner TB (EPTB)=Akciğer dışı TB (AD-TB)

Akciğer parenkimi dışında görülen TB

AD-TB

- AC+AC dıřı tutulum birlikte olduđu grup
 - Miliyer TB
 - Larenks TB
 - Plevra TB
- *DSÖ, AC –TB olarak tanımlıyor*
- *Türkiye SB; AD-TB olarak tanımlıyor , bildirimini Akciđer TB olarak yapıyor*

(Türkiye’de Verem Savaşı 2012 Raporu,2013 Ek-2 111)

AD-TB

'Omnes viae Romam ducunt'

Bütün yollar Roma'ya çıkar

DSÖ

- TB lenfadenit
- Kemik -Eklem TB
- GİS- TB
- SSS -TB
- GÜS ve Adrenal TB
- KVS -TB
- Kutanöz -TB
- Diğer; tiroid, göz

Türkiye

- Plevra
- İntratorasik lenfadenit
- Ekstratorasik lenfadenit
- Vertebra
- Vertebra dışı kemik/eklem
- Menenjit
- Menenjit dışı SSS –TB
- GÜS-TB
- GÜS dışı batın-TB, periton
- Miliyer

Primer enfeksiyon+ghon kompleksi



2-8 hf

Primer immünite



Yetersiz immünite



İyileşme ve kalsifikasyon
(Latent Enfeksiyon)

Yıllar sonra



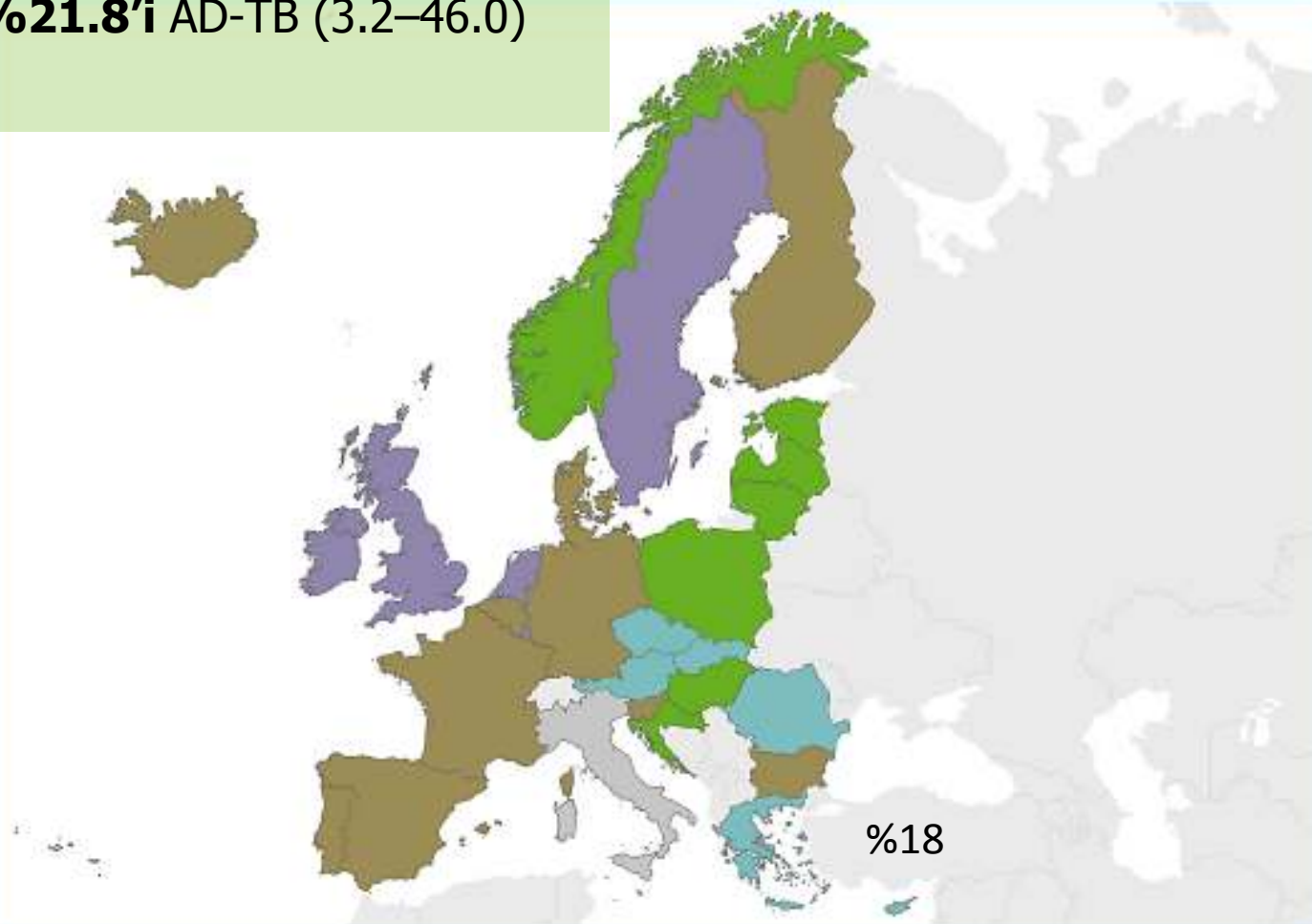
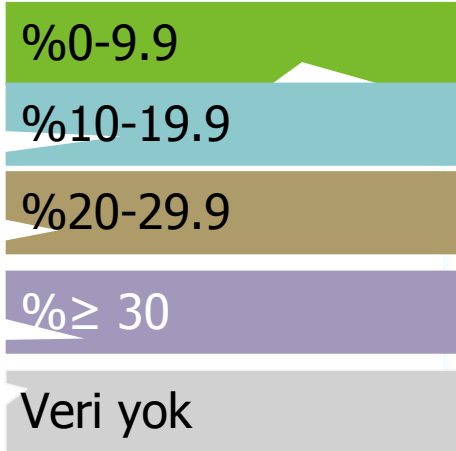
İmmün baskılanma ile reaktivasyon

Konsolidasyon/kollaps/effüzyon
+/-
miliyer yayılım

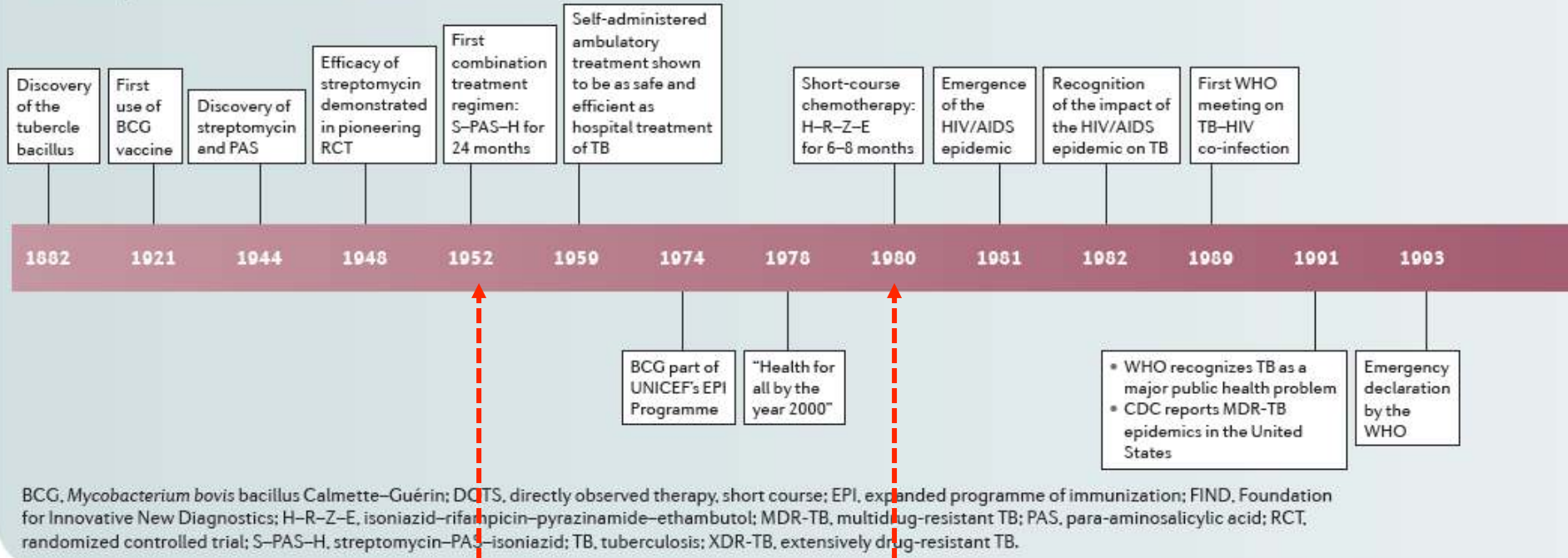
AD-TB

AD-TB sıklık

EU; TB olgularının **%21.8'i** AD-TB (3.2–46.0)



Timeline | Landmarks in TB control



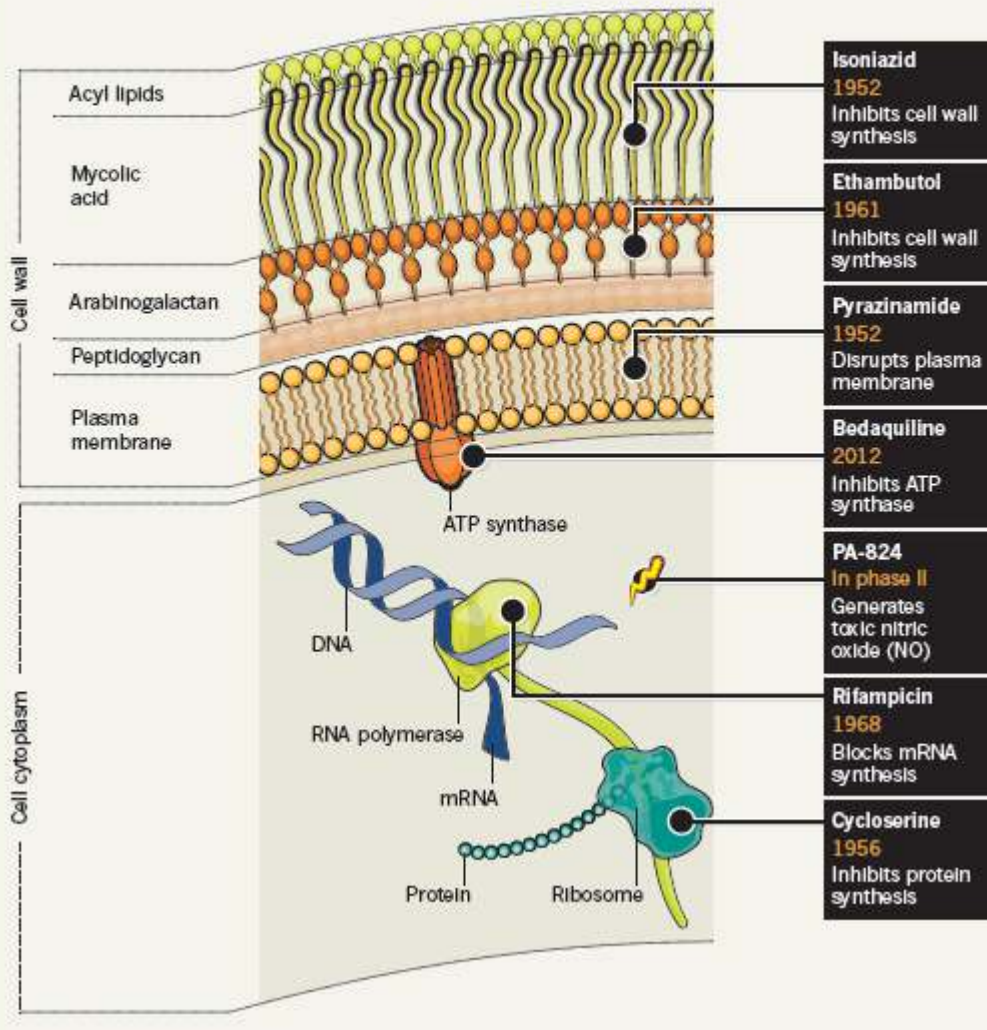
İlk kombinasyon tedavisi

HRZE/ RIPE

Tedavi protokolü ve tedavide kullanılan ilaçlar çok hızlı değişmeyen bir hastalık

HIT LIST

Anti-TB drugs attack *Mycobacterium tuberculosis* in different ways, so combining different drugs helps combat the bacterium developing ways to overcome a drug.



1968-Rifampicin
2012-Bedaquiline
2016(?) -PA-824 (PII)

AD-TB Yaklaşım

- Konak tanımı yapılmalı
- Sendrom tanımlanmalı
- Mikrobiyolojik ekten gösterilmeli
- Tedavi seçenekleri ve ek tedavi modaliteleri değerlendirilmeli

Konak Tanımı?

- İmmün durum- özellikler HIV durumu
 - Primer TB riski daha yüksek
 - AD-TB tutulumu yüksek
 - Mortalite yüksek
 - Dirençli etken (MDR-TB veya XDR-TB) riski
- Erişkin /çocuk/ gebelik/emzirme
- Yaşadığı yer (bakımevi, hapisane vs)
- Komorbid hastalık (DM, KBY, Bağ doku hastalığı vs)

Sendrom Tanımı-enfeksiyon yeri?

- Pnömoni var mı? AC grf veya ek bulgular? Miliyer tutulum?
- AD-TB aranır; diğer organ tutulumları...
- Sorular ve sorunlar
 - ? Aktif TB var mı; miliyer tutulum
 - ? Yeni TB mu veya reaktivasyon TB
 - ? İlaç dirençi riski var mı veya daha önce tedavi almış
- Tüm bunların yanıtına göre tedavi **kişiselleştirilir**

Mikrobiyolojik etken?

? Enfeksiyon mu veya enfeksiyon dışı enflamasyon mu

? Enfeksiyonsa TB dışında bir şey olabilir mi

İdeal TB-Mikrobiyoloji Testi?

AC ve AD-TB
ayrımı
yapabilmeli

HIV
durumundan
etkilenmemel
i

İlaç
direncini
gösterebil
meli

Aktif TB tanısı
(+)

Ucuz
olmalı

Erişkin / çocukta
uygulanabilmeli

Latent ve aktif TB ayrımı

Serolojik tanı testleri

- FDA onayı yok
- Güvenilirlik düşük,
- Sensitivite ve spesifite değişken
- Hatta yanlış tanı, gereksiz tedavi ile sonraki olası tedavileri etkiliyor (MDR/XDR TB)

Let Us Stop Malpractices in TB Diagnosis

Inaccurate Serological Blood Tests for Diagnosis of TB banned by the Government of India in Public Interest

MINISTRY OF HEALTH AND FAMILY WELFARE (Department of Health and Family Welfare) NOTIFICATION
New Delhi, 19th June, 2012

G.S.R. 432(1). - Whereas the Central Government is satisfied that the use of the serodiagnostic test kits for diagnosis of tuberculosis are giving inconsistent and imprecise results leading to wrong diagnosis and their use is likely to involve risk to human beings and whereas safer alternatives are available

And whereas the Central Government is satisfied that it is necessary and expedient to prohibit the manufacture, sale, distribution and use of the said test kits in public interest;

Now, therefore, in exercise of the powers conferred by Section 26A of the Drugs and Cosmetics Act, 1940 (25 of 1940), the Central Government hereby prohibits the manufacture for sale, distribution and use of the following test kits with immediate effect:

"Serodiagnostic test kits for diagnosis of tuberculosis"

Frequently asked questions on the notification

Q. What is the reason behind the ban?
ANS: There is proven scientific evidence that serodiagnostic tests for TB provide inconsistent and imprecise results despite high claims of its accuracy.

No More Deaths From TB Together We Can Make India TB Free
Free Diagnosis and Treatment for TB is Available
For More Details Please Contact Concerned District TB Officer

Q. What is the consequence of inconsistent and imprecise results?
ANS: The dependence on such unreliable tests can be harmful as many patients will end up undergoing TB treatment without any need for it as they are wrongly diagnosed as TB. At the same time, the test also misses many TB patients who require treatment at the right time. Such patients will continue to suffer and even spread the infection to other healthy individuals.

Q. What is meant by "serodiagnostic test kits" for tuberculosis?
ANS: Serodiagnostic tests for tuberculosis are tests that detect the antibody response to tuberculosis causing bacteria in blood samples of suspected tuberculous patients.

Q. Is the ban applicable to India as well as reported TB serodiagnostic kits?
ANS: Yes, the ban is applicable to all kits manufactured in India as well as all types of imported kits.

Q. How can TB be detected if all blood tests have been banned? Are there any alternative tests available?
ANS: Government of India has approved the following tests for diagnosis of TB:
• Sputum examination under microscope
• Culture tests
• Newer molecular tests.

Q. What are Interferon-gamma release assays (IGRAs)?
ANS: IGRAs are laboratory blood test that measure the cell-mediated immune response of TB in infected individuals.

Q. In which situation should IGRAs not be used?
ANS: IGRAs blood tests have limited use as they cannot differentiate between active pulmonary TB disease and latent TB infection. Hence IGRAs should not be used as stand alone tests to detect active TB disease.

REVISED NATIONAL TUBERCULOSIS CONTROL PROGRAM
Ministry of Health and Family Welfare, Government of India

RESEARCH ARTICLE

Interferon-gamma release assays for the diagnosis of extrapulmonary tuberculosis: a systematic review and meta-analysisLin Fan¹, Zhou Chen², Xiao-Hui Hao¹, Zhong-Yi Hu¹ & He-Ping Xiao¹

- IGRA Quantiferon-TB gold (Celestis -Australia) ve T spot (Oxford -immunotec -UK)
- 20 çalışma,1711 hasta

	sensitivite	spesifite
Quantiferon	72 (%95-CI %65-79)	82 (%95-CI %78-87)
T.spot	90 (%95-CI %86-93)	68 (%95-CI %64-73)

Az ve orta gelişmiş ülkelerde IGRA testlerinin AD-TB ayırıcı tanısında etkinliği kısıtlıdır

Moleküler testler

- Nükleik asid çoğaltma testleri
 - ARB (+) veya (-) örneklerde
 - BOS, idrar, doku, eklem sıvısında değişken sensitivite
- GeneXpert -MTB/RIF (Cepheid Sunnyvale CA)
 - M. tuberculosis* yakalar ve RIF direnci (*RpoB* gen)
 - Kalitatif MTB ARB (+) balgamda sensitivite % 98-100
 - ARB(-) balgamda sensitivite: % 57-83
 - Akciğer dışı sensitivite: % 53-95

Kemik eklem tutulumu

- Spondilodiskit (Pott Hastalığı)
- Artrit (kalça ve diz)
- Enflamatuvar süreç (Ponchet Hastalığı): simetrik poliartrit, TB basiline aşırı duyarlılık
- Protez enfeksiyonu
- Osteomyelit (uzun kemikler)

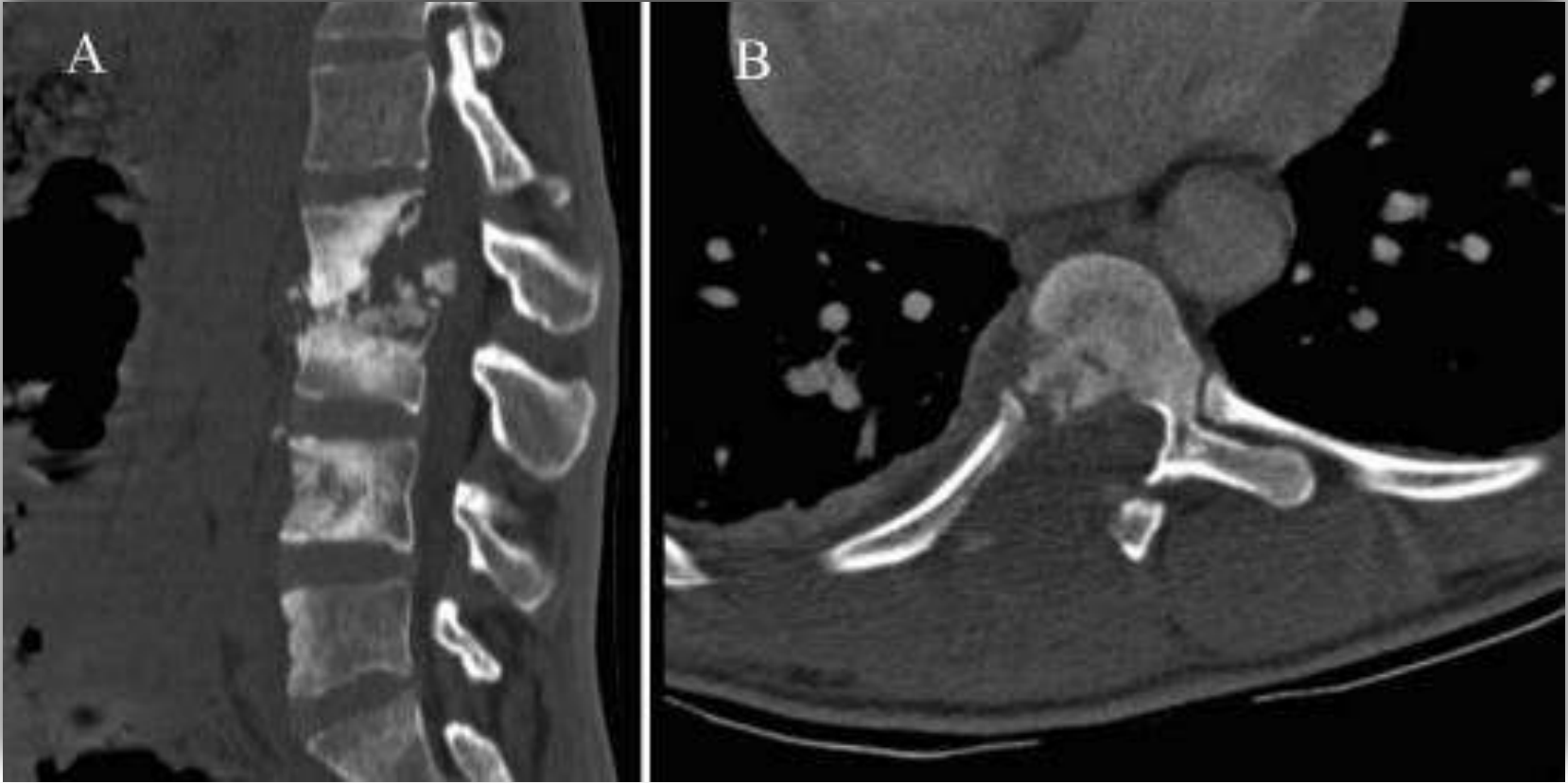
Pott Hastalığı

- Sırt ağrısı-süregen-yavaş ilerleme
- Spinal X-ray;
 - erken evrede: N
 - geç dönemde: disk dejenerasyonu (osteolizis)



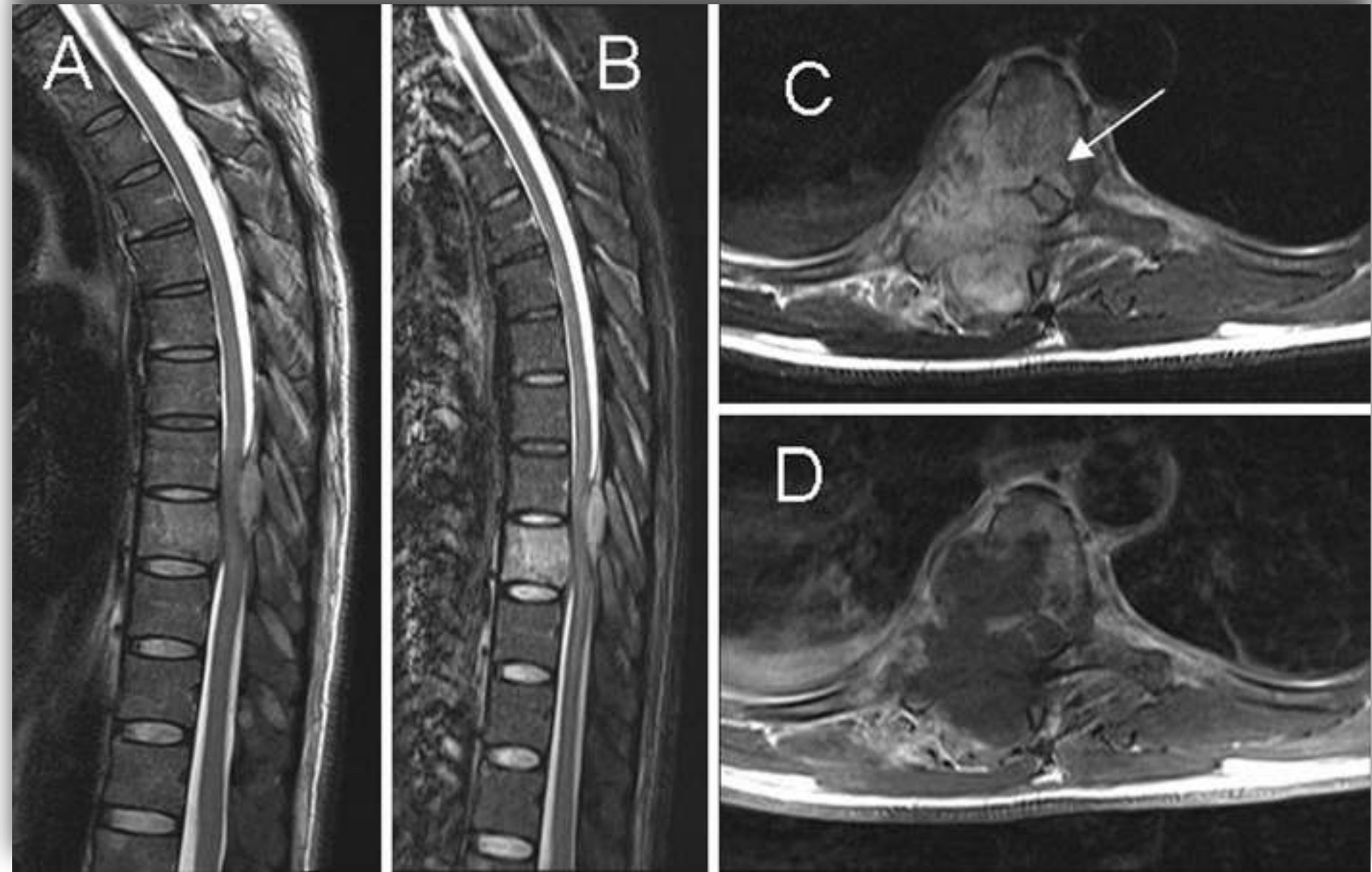
Pott Hastalığı

BT; aksiyel kesitte dejenerasyon iyi görülebilir



Pott Hastalığı

- MRG;
 - erken tanı için en iyi görüntüleme
 - disk aralığı değerlendirmede etkin,
 - basıyı iyi gösterir
 - özel işlemlerle STIR, FLAIR vb ile yağ doku baskılanması ve su baskılanması ile 'soğuk abse' görüntüsü
 - T1 ve T2 sekans değişimi ile hiperintens ve hipointens görünüm,



Tanı

- BT eşliğinde biyopsi
- Cerrahi materyelde (operasyon)
 - ARB(-) >%50
 - Kültür
- Tek seride (UK)
 - ARB pozitifliği %75 ve kültür pozitifliği %76
(olgu sayısı 20)
- PZR-alternatif mi?

Diagnosis of tuberculous vertebral osteomyelitis (TVO) in a developed country and literature review

D Wang^{*1}

¹*The National Spinal Injuries Centre (NSIC), Stoke Mandeville Hospital (SMH), Aylesbury, Buckinghamshire, UK*

- Olgu serisi ve Literatur derlemesi
- Vertebra osteomyelitli 10 olgu,
- Literatürde 188 makale derlenmiş,
- Hangisi daha iyi bir tanı metodu; radyoloji/ laboratuvar, mikrobiyoloji/ patoloji ilişkisi kurulan makaleler

Conclusion: Clinical manifestations, discrepancy between ESR and WBC, plain radiographs and PCR are keys to a correct diagnosis of TVO.

Spinal Cord (2005) 43, 531–542. doi:10.1038/sj.sc.3101753; published online 19 April 2005

Tedavi

Cerrahi vs İlaç (süre?)



Review

Drug treatment of multidrug-resistant osteoarticular tuberculosis: a systematic literature review

Inés Suárez-García^{a,*}, Arturo Noguerado^b

- 12 osteoartiküler TB
 - MDR-TB ,
 - 6 hasta spinal TB,
 - 6 hasta ekstra spinal TB,
 - 5 hastada cerrahi tedavisiz yanıt (+),
 - Toplam tedavi süreleri 18 ay ile 24 ay arasında değişiyor.
 - 1 hasta septisemiden ex

Conclusions: Osteoarticular MDR-TB is very infrequently reported in the literature. The few cases reviewed suggest that it is possible to achieve a good outcome with second-line anti-tuberculous drugs, and that surgery might be useful for cases in which an optimized medical treatment is not possible.

The treatment of spinal tuberculosis: a retrospective study

S. Ramachandran,* I. J. Clifton,* T. A. Collyns,† J. P. Watson,* S. B. Pearson*

- 1998-2002 arası İngiltere 42 kemik TB
 - 34 spinal TB, 8 diğer kemik TB
 - 38 (34 spinal TB, 4 kemik TB) hastanın kayıtlarına ulaşılmış,
 - 6 ay tedavi alanlarda (5/8)relaps
 - > 9 ay alan 30 hastada sıfır relaps

CONCLUSION: Six months of treatment, as currently recommended by the BTS, may be inadequate for bone TB, including spinal TB.

Cerrahi vs Medikal



The Spine Journal 5 (2005) 79–84

THE
SPINE
JOURNAL

Results of nonsurgical treatment of thoracic spinal tuberculosis in adults

Abhay Nene, MS (Orth), Shekhar Bhojraj, MS (Orth), FCPS (Orth), D Ortho*

The Spine Clinic, P.D. Hinduja National Hospital and Medical Research Centre, Veer Savarkar Road, Mahim, Mumbai 400 016, India

Received 15 January 2004; accepted 24 May 2004

- 1998-2000, retrospektif, 70 spinal TB; Cerrahi yapılmayan
 - 42 spinal (21'i epidural) abse,
 - 8 nörolojik kompresyon bulgusu
 - 9 ay tedavi, %98 (69/70), medikal tedavi başarısı
 - %74 residüel hasar yok
 - %23 kifoz gelişti
 - 40 ay bağımsız gözlemci izleminde relaps yok

Cerrahi vs Medikal

Hoffman EB, Allin J, Campbell JA, Leisegang FM, South Africa
Tuberculosis of the knee.
Clin Orthop Relat Res. 2002 May;(398):100-6.

1979-1999, Afrika, retrospektif;

- Diz TB, 52 çocuk, sinovit, kemik erozyonu yok, eklem aralığı normal (evre1,2)
- Sinoviyektomisiz, Anti TB tedavide; %93 başarı
- Tedavi süresi 9 ay

Eklem TB; cerrahi tedavisiz başarı daha yüksek

CASE REPORT

Glenohumeral joint tuberculosis with multiple cold abscesses: an uncommon cause of shoulder pain

Betul Kizildag,¹ Alper Sener,² Erkam Komurcu,³ Ozan Karatag,¹ Sule Kosar¹

TREATMENT

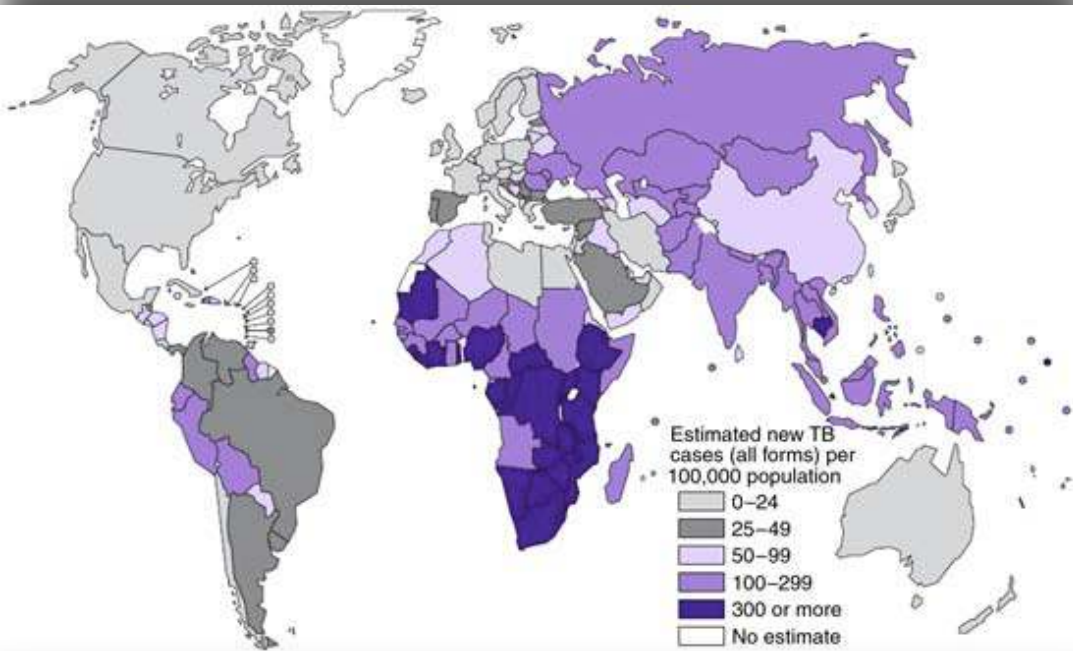
The patient was thought to have right shoulder tuberculous osteoarthritis and multiple cold abscess involving the right shoulder girdle muscles according to the MRI findings and anti-TB treatment was started. Isoniazid 300 mg, rifampicin 600 mg, ethambutol 1500 mg and morphazinamide hydrochloride 2500 mg were used for initial treatment. He was then hospitalised in the orthopaedic clinic for debridement on the 15th day after the start of treatment. Debridement was not considered due to the age of the patient and the cardiovascular risk. A total of 12 months of treatment with double anti-TB treatment was planned for the patient 2 months later.

Glenohumeral eklem TB+
multiple soğuk abse;
-Cerrahi yaşı nedeniyle
yapılamadı,
-2HRZE, 10HR; toplam 12 ay
-Tedavi sonrası izlemde
sorun yok

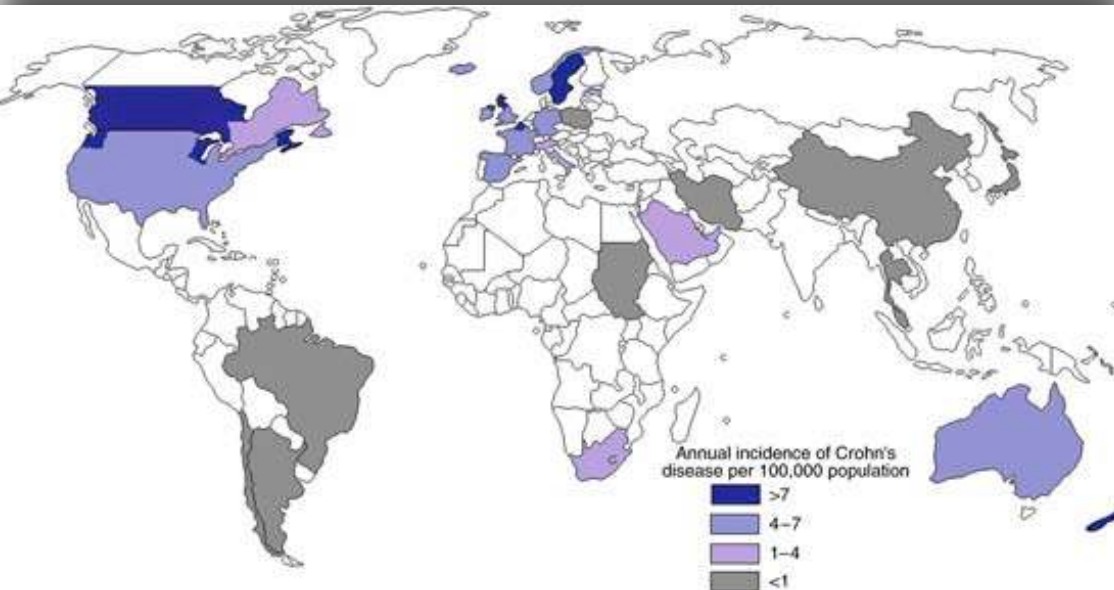
GİS

- TB enteriti (İlioçekal tutulum en sık)
 - Ülseratif(%60)
 - Hipertrofik (%10)
 - Ülserohipertrofik (%30)
- TB peritonit
- Hepatik tutulum (granülomatöz hepatit)
- Pankreatit (Miliyer TB varlığında)
- Kolesistit (Miliyer TB varlığında)

TB



Crohn



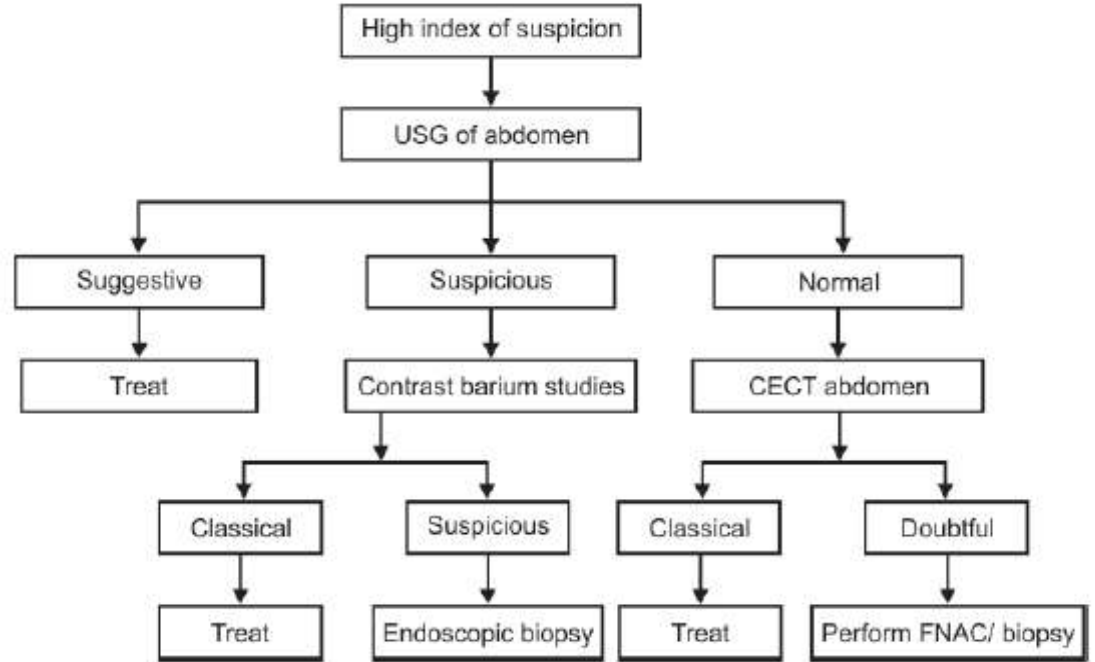
Tanı

- Görüntüleme(BT/ Baryum/ MRG)
 - Paraaortik LAP
 - Asimetrik barsak duvarı kalınlaşması
 - İleocaecal kalınlaşma
 - Serbest sıvı-ADA aktivitesi
- Endoskopi veya EUS
 - ARB %10-30 sensitivite
 - Kültür - gayta
 - Biyopsi
 - PZR
- IGRA testleri- net değil, takipte önerilebilir(?)

Tanı-algoritmi

- Yüksek olasılıklı semptomlar (karın ağrısı, rahatsızlık hissi, kilo kaybı)
- Görüntüleme şüphe
- Histopatolojik veya mikrobiyolojik kanıt ve/veya
- Anti TB tedaviye yanıt

Flow chart 1: Algorithmic approach to diagnosis of abdominal tuberculosis



Lingenfelser T, Zak J, Marks IN, et al. Abdominal tuberculosis; still a potentially lethal disease. *Am J Gastroenterol* 1993;88:744.

Tedavi

Cerrahi vs İlaç (KSD?)

Cerrahi

'Primum non nocere'
Öncelikle, zarar verme

- Fistül,
- Obstrüksiyon,
- Striktür,
- Adhezyon,
- Durum tesbiti (tanı koyma)

'Palyatif yaklaşım, major cerrahiden kaçınılmalı.'

Abdominal tuberculosis.Aston NO.World J Surg. 1997;21(5):492.

'Endoskopik balon dilastasyonu uygun vakalarda denenebilir'

Endoscopic balloon dilation of ileal stricture due to tuberculosis.

Bhasin DK, Sharma BC, Dhavan S, Sethi A, Sinha SK, Singh K.Endoscopy.
1998;30(3):S44.

Abdominal tuberculosis: a retrospective review of cases presenting to a UK district hospital

J.P. MAMO¹, S.O. BRIJ¹ and D.A. ENOCH²

- 2008-2011 arası Abd TB tanısı alan 17 hasta,
 - 4 hastada eş zamanlı AC TB var,
 - HRZE, tedavi 6-12 ay
 - 6 hastaya cerrahi girişim (psoas absesi, obstrüksiyon, rezeksiyon); tedavi sırasında gelişen durumlar ve mortalite (%50)
 - 9 hasta sadece medikal (mortalite %0)

CLINICAL ARTICLES

Corticosteroid Treatment of Peritoneal Tuberculosis

Abdulrahman A. Alrajhi, Magid A. Halim,
Abdullah Al-Hokail, Fahad Alrabiah, and
Kawther Al-Omran

*From the Section of Infectious Diseases, Department of Medicine, King
Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia*

- 1987-1996, Kral Faysal Hastanesi
 - 35 peritoneal TB; 9 anti TB+ KSD, 26 antiTB
 - HRZE (9 ay) -Ortalama 24 ay takip
- 26 antiTB;
 - 19 (%73)...abdominal ağrı
 - 7 (%27)...tekrarlayan bulantı-kusma, yapışıklık
 - 5(%19)...Akut batın, 4 laparotomi
 - 3 hasta ex (Bir hasta 9 ay sonra, bir hasta tedavinin 8. diğeri 10.haftası; intestinal obstrüksiyon ve sepsis
- KSD alan grupta; tedavi sorunsuz tamamlandı,

Tuberculous peritonitis – reports of 26 cases, detailing diagnostic and therapeutic problems

Kadir Demir^a, Atilla Okten^a, Sabahattin Kaymakoglu^a, Dinc Dincer^a,
Fatih Besisik^a, Ugur Cevikbas^b, Sadakat Ozdil^a, Güngör Bostas^a,
Zeynel Mungan^a and Yilmaz Cakaloglu^a

- 1995-1999, 26 TB peritonit, 25 hastaya laparoskopik örneklem,
 - Başlangıç; HZ+ streptomisin (40 gün) (R'siz tedavi rejimi), 2ay
 - Sonrasında;HE, 4 ay
 - 18 hasta, İlk bir ay prednisolon+anti TB
 - 1 hasta serebral ve KC'de granülom, R eklenip, 12 ay tedavi planlandı, HKP ex
 - 1 hasta Hbs Ag taşıyıcı, KCFT bozulması, tedaviyi sorunsuz tamamlıyor,
 - 24 hastada tedavi başarılı (24/26, %92)
 - KSD alan hastalarda klinik düzelme daha hızlı

Systematic review: tuberculous peritonitis – presenting features, diagnostic strategies and treatment

F. M. SANAI & K. I. BZEIZI

Division of Hepatology, Department of Internal Medicine, Riyadh, Saudi Arabia

Accepted for publication 27 July 2005

- 6HRZE, 9HRZE/12 HRZE aralarında fark yok
- Önceden mevcut KC hasarı/hastalığı (+), daha etkin
 - 6 RZE
 - 2HRE , 7HR
 - RE+florokinolon+ sikloserin, 12-18 ay
 - E+SM+florokinolon+II.kuşak ilaç, 12 ay
- KSD, erken dönemde (ilk 2 ay) yararlı

Intestinal tuberculosis

Helen D. Donoghue and John Holton

Centre for Infectious Diseases and International Health, Department of Infection, University College London, London, UK

Correspondence to Helen D. Donoghue, PhD, CIDII, Department of Infection, University College London, 46 Cleveland Street, London W11 4JF, UK
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Current Opinion in Infectious Diseases 2009, 22:490–495

Purpose of review

Intestinal tuberculosis (TB) is increasing due partly to the HIV pandemic. Its clinical presentation mimics inflammatory conditions such as Crohn's disease and malignancies, which are becoming more prevalent, so the diagnosis is problematic.

Recent findings

Greater awareness of intestinal TB is needed, both in countries where TB is endemic and developed countries with immigrant populations. Some strains of *Mycobacterium tuberculosis* are associated with more extrapulmonary disease and greater dissemination, thereby exacerbating the rise in HIV-associated extrathoracic TB. Recent

- 6HRZE veya 9 HRZE, DOTS'a göre daha başarılı,
- HAART tedavisi alanlarda R'siz rejim
- Anti –TNF alacaklarda öncesinde 3HR yada sırasında TB gelişirse 6HRZE,
- KSD, kullanımı net değil? Anti –TB tedaviye olumsuz etkisi yok
- Cerrahi tedavi üstünlük yok

Gelatin microspheres of rifampicin cross-linked with sucrose using thermal gelation method for the treatment of tuberculosis

ABDUS SAMAD¹, YASMIN SULTANA¹, ROOP K. KHAR¹, K. CHUTTANI²,
& A. K. MISHRA²

¹*Faculty of Pharmacy, Department of Pharmaceutics, Jamia Hamdard, Hamdard Nagar, New Delhi, India and*

²*Department of Radiopharmaceuticals, Institute of Nuclear Medicine and Allied Sciences (INMAS), Delhi, India*

(Received 10 July 2007; accepted 28 April 2008)

- Doğal jelatin ve Sükroz bağı içeren RIF
- GIS-TB'da hedef organda salınım ve yüksek MIC düzeyi elde etme çalışması
- Başarılı; dağılım ve doku konsantrasyonu diğerine göre yüksek,
- Klinik denemeye uygun,

Saaig M, Shah SA, Zubair M.

Abdominal tuberculosis: epidemiologic profile and management experience of 233 cases.

J Pak Med Assoc. 2012 Jul;62(7):704-7.

- 2003-2008 yılları arasında Abdominal TB
- Pakistan
- 233 hasta; 6 HRZE planlanmış, tedavi sırasında
 - Akut batın 157 (%67,38)
 - Per op striktür 161 (%69)
 - Mortalite 5 (%2,4)

- Cerrahi reserve olarak durmalı,
- Cerrahi komplikasyon tedavisi için daha uygun
- Obstrüksiyon ileri derecede olmadığı sürece beklenmeli,
- Unutulmamalı ki bu hastalarda cerrahi sonrası komplikasyon oranı daha yüksek
- Asıl tedavi prensibi; anti TB tedavi olmalı
- Cerrahi endikasyonlar;
 - Akut batın
 - Kanama (Durdurulamayan, Rektal, Özofagus)
 - Fistül
- * Major cerrahiden kaçınılmalı=rezeksiyon=anastomoz problemleri

SSS-TB

- TB-menenjit
- Tüberküloom
- Komminüke hidrosefali
- Spinal TB Araknoidit
- Proliferatif Araknoidit
- Vaskülit

TB-menenjit

- Evre-I: Prodromal faz; 2-3 hf, baş ağrısı, halsizlik, yorgunluk
- Evre-II: Menenjitik faz; meningismus, bulantı, kusma, kraniyel sinir tutulumu,
- Evre-III: Paralitik faz; konfüzyon, stupor, koma, konvülsüyon

Tanı

- ADA
 - tanıyı destekleyen en iyi test
 - lenfosit proliferasyonunu gösterir
 - sensitivitesi %99-100
 - spesifitesi cut off değerine bağlı (<11,39IU/L ise düşük)
- ADA aktivitesi aynı zamanda
 - SSS lenfomasında
 - Nörobrusellozda
 - Malaryanın SSS tutulumunda
 - CMV'nin SSS tutulumunda (HIV)
 - Kriptokok menenjitinde (HIV)

Cerebrospinal Fluid Research

Research

Open Access

Cerebrospinal fluid adenosine deaminase activity: A complimentary tool in the early diagnosis of tuberculous meningitis

Rajpal S Kashyap¹, Rani P Kainthla¹, Anju V Mudaliar¹, Hemant J Purohit², Girdhar M Taori¹ and Hatim F Daginawala*¹

Table 1: The mean ADA activity (with range) in the CSF of TBM patients (n = 117), non-TBM infectious meningitis patients (n = 60) and control patients with non-infectious neurological disorders (n = 104). The data are expressed as mean \pm SD

Patient groups	ADA activity (U/L/min) Mean \pm SD	Range
1. Tuberculous Meningitis (n = 117)	14.31 \pm 3.87	2.99–26.94
Culture positive (n = 27)	17.67 \pm 4.18	9.01–26.94
Clinically suspected (n = 90)	13.29 \pm 3.16	2.99–21.02
2. Non TBM infectious meningitis (n = 60)	9.25 \pm 2.14	4.99–13.96
Pyogenic meningitis (n = 41)	10.11 \pm 1.99	5.11–13.96
Viral meningitis (n = 19)	7.39 \pm 0.93	4.99–9.00
3. Non-infectious neurological disorders (n = 104)	2.71 \pm 1.96	0.00–7.68
Headache (n = 32)	0.98 \pm 0.19	0.11–1.20
Stroke (n = 29)	4.18 \pm 1.19	1.92–5.83
Venous sinus thrombosis (n = 13)	1.82–4.12	
Guillian-Barré syndrome (n = 12)	5.38 \pm 2.16	2.63–7.68
Epilepsy (n = 6)	2.36 \pm 0.79	1.01–3.18
Other neurological disorders (n = 12)	1.18 \pm 0.47	0.5–1.87

Cutt of değeri önemli >11,39 IU/L ise sensitivite %83 ve spesifite %82

Tanı

- ARB pozitifliği %5-30 tek incelemede
 - 2mL %95 alkol ilavesi ve santrifüj sonrası tüp dibinden bakılması; %71'e çıkartır
 - Yüksek volümde BOS alınması (10mL)
 - En az iki kişinin bakması
- Kültür (+)'liği %45-71'dir, HIV(+)'lerde >%88
- PZR %50 (hiç bir zaman kültür veya ARB yerine kullanılmaz)
- GeneXpert/RIF; WHO öneriyor,
- MTBDRplus(*rpoB* rifampin; *katG* and *inhA* for isoniazid rezistans) gündemde ?

1.Thwaites GE et al.Improving the bacteriological diagnosis of tuberculous meningitis.J Clin Microbiol. 2004;42(1):378.

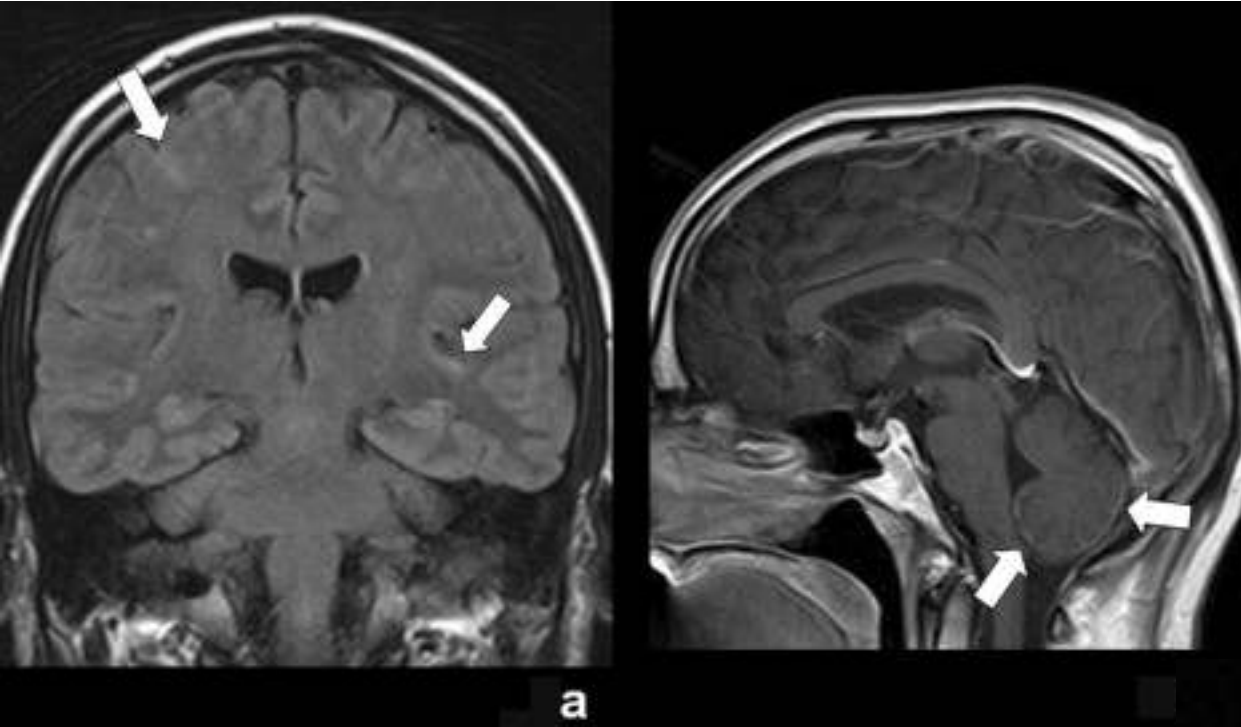
2.http://apps.who.int/iris/bitstream/10665/112472/1/9789241506335_eng.pdf

3.Barnard M et al. Rapid molecular screening for multidrug-resistant tuberculosis in a high-volume public health laboratory in South Africa.Am J Respir Crit Care Med. 2008;177(7):787.

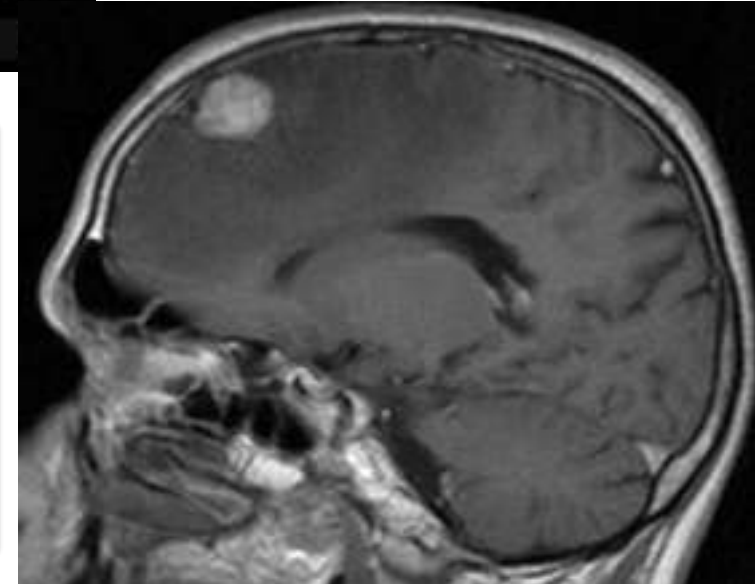
Tüberküloz

- SSS parenkimal lezyon
- Tek yada çoğul
- Meninks enflamasyonu yok
- Anti-TB tedavi ile geriler
- Kalsifiye kalır
- Genç erişkin ve çocuklarda; nöbet ve intrakraniyel basınç artışı

Tanı



- Granülomları göstermede en etkin MRG
- Bazal tutulum sık



Tedavi

ilaç –KBB sorunu?-süre?

KSD ?

Tüberküloz-Cerrahi?

Effect of Antituberculosis Drug Resistance on Response to Treatment and Outcome in Adults with Tuberculous Meningitis

Guy E. Thwaites,^{1,4*} Nguyen Thi Ngoc Lan,² Nguyen Huy Dung,² Hoang Thi Quy,² Do Thi Tuong Oanh,² Nguyen Thi Cam Thoa,² Nguyen Quang Hien,² Nguyen Tri Thuc,² Nguyen Ngoc Hai,² Nguyen Duc Bang,² Nguyen Ngoc Lan,² Nguyen Hong Duc,² Vu Ngoc Tuan,² Cao Huu Hiep,² Tran Thi Hong Chau,³ Pham Phuong Mai,³ Nguyen Thi Dung,³ Kasia Stepniewska,⁴ Nicholas J. White,^{1,4} Tran Tinh Hien,² and Jeremy J. Farrar^{1,4}

- 180 SSS-TB hastası;
 - 72(%40) en az bir anti TB ilaç dirençli
 - 10(%5,6) en az R veya H dirençli (MDR)
 - Klinik izlem, bakteriyel temizlenme, klinik yanıt, mortalite ve morbidite izlem, prospektif

Table 2. Nine-month outcome of tuberculous meningitis caused by *Mycobacterium tuberculosis* with different drug susceptibilities.

Drug resistance	No. dead (%)	No. severely disabled (%)	No. partially recovered (%)	No. completely recovered (%)
Fully sensitive (<i>n</i> = 108)	<u>31 (28.7)</u>	14 (13.0)	15 (13.9)	48 (44.4)
Resistant to INH only (<i>n</i> = 9)	2 (22.2)	4 (44.4)	1 (11.1)	2 (22.2)
Resistant to SM only (<i>n</i> = 24)	4 (16.7)	1 (4.2)	6 (25.0)	13 (54.1)
Resistant to INH and SM only (<i>n</i> = 28)	12 (42.9)	3 (10.7)	5 (17.9)	8 (28.6)
Resistant to RFP only (<i>n</i> = 1)	1 (100)
MDR (<i>n</i> = 10)	<u>10 (100)</u>

NOTE. INH, isoniazid; MDR, multidrug resistant (organisms resistant to at least INH and RFP); RFP, rifampicin; SM, streptomycin.

- Tedavinin 9. ayda tüm duyarlılarda dahi mortalite %28,7
- MDR'lilerin tamamı ex
- Tüm gruplarda mortalite %33,3 (60/ 180)
- Kombine R ve H direnci; kötü klinik gidişle direkt ilişkili
- H ve/veya S direnci; bakterinin BOS'tan temizlenmesi ile ilişkili ancak klinik seyire etkisi yok,

ORIGINAL ARTICLE

Dexamethasone for the Treatment of Tuberculous Meningitis in Adolescents and Adults

Guy E. Thwaites, M.R.C.P., Nguyen Duc Bang, M.D., Nguyen Huy Dung, M.D.,
Hoang Thi Quy, M.D., Do Thi Tuong Oanh, M.D., Nguyen Thi Cam Thoa, M.D.,
Nguyen Quang Hien, M.D., Nguyen Tri Thuc, M.D., Nguyen Ngoc Hai, M.D.,
Nguyen Thi Ngoc Lan, Ph.D., Nguyen Ngoc Lan, M.D., Nguyen Hong Duc, M.D.,
Vu Ngoc Tuan, M.D., Cao Huu Hiep, M.D., Tran Thi Hong Chau, M.D.,
Pham Phuong Mai, M.D., Nguyen Thi Dung, M.D., Kasia Stepniewska, Ph.D.,
Nicholas J. White, F.R.C.P., Tran Tinh Hien, M.D., and Jeremy J. Farrar, F.R.C.P.

- 545 hasta; >14y SSS-TB, Vietnam, prospektif, randomize
 - 275 hasta dexametazone
 - 271 hasta plasebo (KSD)
- 9 ay anti-TB tedavisi planlanmış
- Başlangıçta Dexametazone (eş zamanlı)
- Mortalite, morbidite, komplikasyon izlem

Table 1. Baseline Characteristics of the Study Population.

Variable	Dexamethasone (N=274)	Placebo (N=271)
Age — yr		
Median	36.0	35.0
Range	15–88	15–84
Male sex — no. (%)	168 (61.3)	163 (60.1)
Diagnosis at discharge — no. (%)		
Definite	98 (35.8)	89 (32.8)
Probable	130 (47.4)	131 (48.3)
Possible	44 (16.1)	47 (17.3)
Not tuberculous meningitis*	2 (0.7)	4 (1.5)
Duration of symptoms — days†		
Median	15	15
Range	4–90	2–90
Weight — kg		
Median	45.0	45.0
Range	25–75	30–70
Score on Glasgow coma scale‡		
Median	14	14
Range	3–15	3–15
Cranial nerve palsy — no. (%)	82 (29.9)	74 (27.3)
Hemiparesis — no. (%)	48 (17.5)	37 (13.7)
Paraparesis — no. (%)	28 (10.2)	11 (4.1)
MRC grade — no. (%)§		
I	90 (32.8)	86 (31.7)
II	122 (44.5)	125 (46.1)
III	62 (22.6)	60 (22.1)
HIV status — no. (%)		
Positive	44 (16.1)	54 (19.9)
Negative	227 (82.8)	209 (77.1)
Not tested	3 (1.1)	8 (3.0)
Lymphocyte count — per mm ³ ¶		
CD4 cells		
Median	64	66
Range	14–694	7–359
CD8 cells		
Median	606	386
Range	134–998	28–1001

•Grupların başlangıç özellikleri hemen hemen aynı

MRC: British Medical Consult Criteria, SSS-TB evresi
I-Nörolojik bulgu yok, GKS>15
II-GKS 11-15 (>15+nörolojik bulgu)
III-GKS<10

- Tedavi protokolü

- H (5mg/kg/g)+ R (10mg/kg/g) + Z (25mg/kg/g)+ S(1g/g); 3 ay

- PO nasogastrikten ve IM

- Sonrasında 6HRZ

- HIV (+)'lerde S'in E ile değiştirildi,

- Dexametazone (MRC II ve III);toplam 2 ay

1.hf- 0,4mg/kg/g

2.hf- 0,3mg/kg/g

3.hf-0,2mg/kg/g

4.hf-0,1mg/kg/g

IV

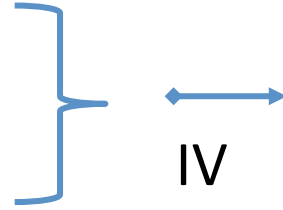


PO; 4 mg/g- 4 hf (her hf
1 mg doz azaltılarak

- Dexametazone (MRC I);toplam 2 ay

- 1.hf- 0,3mg/kg/g

-2.hf-0,2mg/kg/g



PO;

•0,1mg/kg/g (3.hf)

•3mg/g (hf'da 1mg azaltma)

- 1,2,6,9 ayda klinik gidiş ve sonrası skora
- GKS gerileme
- Ateşte çözülme
- 9 ayda bağımsız araştırmacı değerlendirilmesi

Table 2. Outcome Nine Months after Randomization, According to Disease-Severity Grade and HIV Status.*

Outcome and Group	Dexamethasone	Placebo	Relative Risk (95% CI)	P Value
	<i>no./total no. (%)</i>			
Death				
All patients	87/274 (31.8)	112/271 (41.3)	0.69 (0.52–0.92)	0.01
Grade				
I	15/90 (16.7)	26/86 (30.2)	0.47 (0.25–0.90)	0.02
II	38/122 (31.1)	50/125 (40.0)	0.71 (0.46–1.1)	0.11
III	34/62 (54.8)	36/60 (60.0)	0.81 (0.51–1.29)	0.38
Relative risk of death stratified according to grade†			0.68 (0.52–0.91)	0.007
HIV status				
Negative	57/227 (25.1)	67/209 (32.1)	0.72 (0.51–1.02)	0.07
Positive	27/44 (61.4)	37/54 (68.5)	0.86 (0.52–1.41)	0.55
Undetermined	3/3 (100)	8/8 (100)	1.16 (0.71–1.91)	0.71
Relative risk of death stratified according to HIV status‡			0.78 (0.59–1.04)	0.08
	Dexamethasone	Placebo	Odds Ratio	P Value
	<i>no./total no. (%)</i>			
Death or severe disability				
All patients	121/274 (44.2)	134/271 (49.4)	0.81 (0.58–1.13)	0.22
Grade				
I	19/90 (21.1)	30/86 (34.9)	0.50 (0.25–0.98)	0.04
II	57/122 (46.7)	61/125 (48.8)	0.92 (0.56–1.52)	0.74
III	45/62 (72.6)	43/60 (71.7)	1.05 (0.47–2.31)	0.91
Odds ratio stratified according to grade§			0.79 (0.56–1.13)	0.20
HIV status				
Negative	93/230 (40.4)	96/217 (44.2)	0.86 (0.59–1.25)	0.42
Positive	28/44 (63.6)	38/54 (70.4)	0.74 (0.32–1.72)	0.48
Undetermined	3/3 (100)	8/8 (100)	—	—
Odds ratio stratified according to HIV status¶			0.87 (0.62–1.24)	0.44

Dexametazone

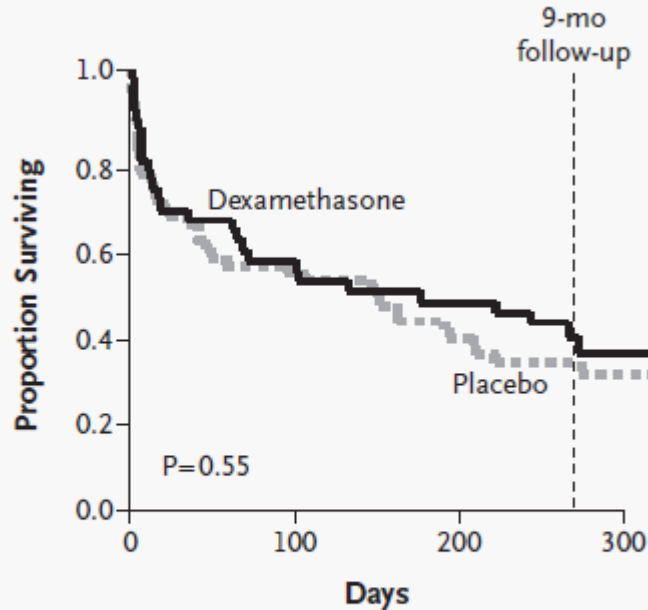
- Evre I'de mortaliteyi azaltıyor (%17 vs %30)
- Evre II-III'de azaltıyor ama p anlamlı değil

Table 3. Outcomes of 545 Patients Nine Months after Randomization.

Group	No. of Patients	Outcome			
		Good	Inter- mediate	Severe Disability	Death
Dexamethasone*	274	104 (38.0)	49 (17.9)	34 (12.4)	87 (31.8)
Placebo	271	95 (35.1)	42 (15.5)	22 (8.1)	112 (41.3)

- 9. ay değerlendirilmede -Steroid alan grupta kalıcı nörolojik hasarlar arasında fark yok - Mortalite azalmış ama anlamlı değil

C Patients Infected with HIV



No. at Risk

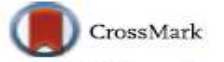
Dexamethasone	44	24	20	16	4
Placebo	54	29	21	17	5

- HIV (+) hastalarda dahi steroidin sağ kalım üzerine etkisi yok



Review

Tuberculoma of the central nervous system

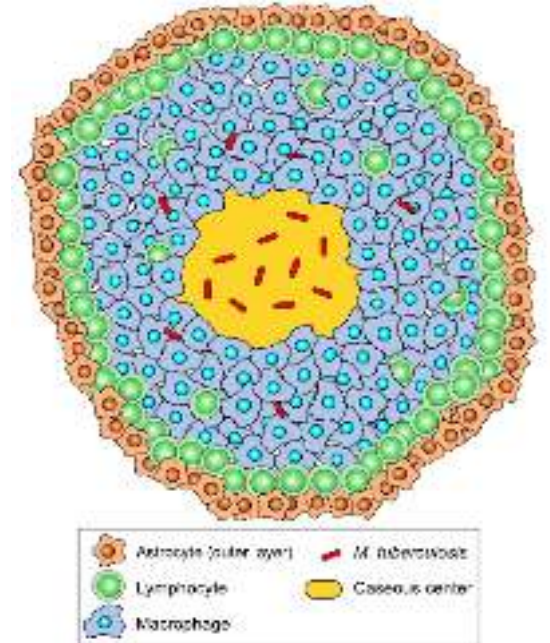


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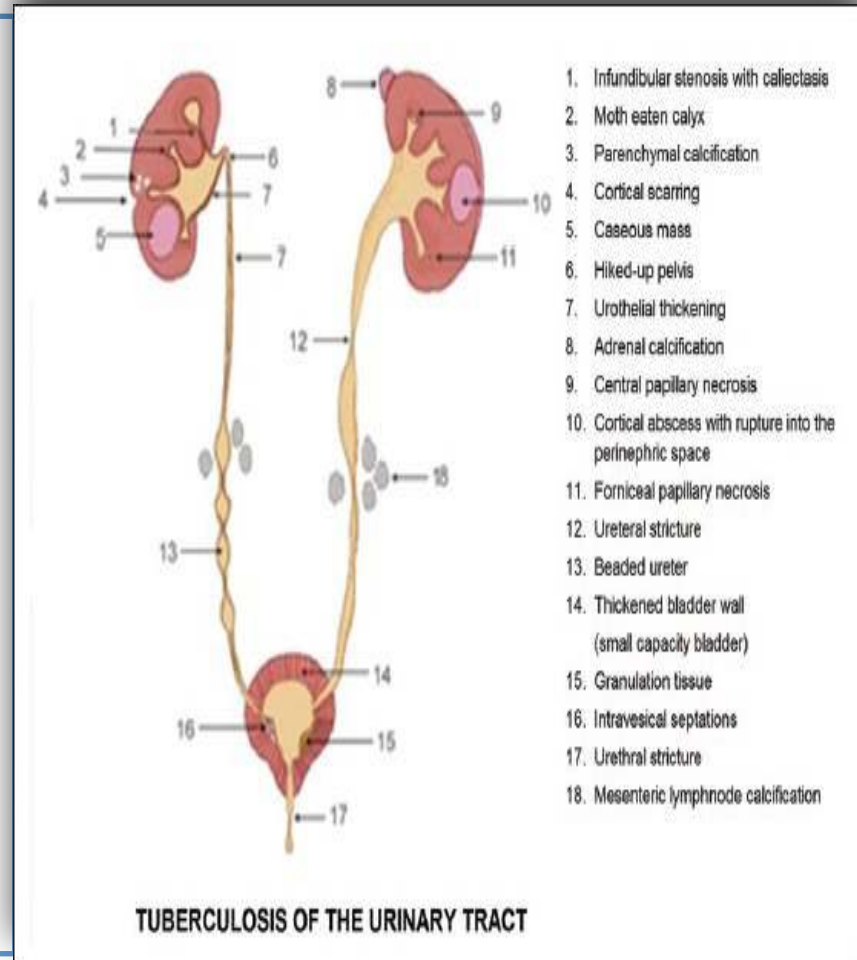
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- Bası etkisi oluşturan tüberküloom,
- Önlenemeyen Fokal/generalize nöbet
- Çapı > 20mm,
- Orta hatta kayma,
- Intrakraniyel basınç artışı (hidrosefali)



Üriner-TB

- Granülom formasyonu,
- İnterstisyum tutulumu,
- Progresif medullar hasar,
- Renal papillada destrüksiyon,
- Abse,
- Fibrosis-skar



GÜS-TB ilişkili Tablolar

- TB interstisyel nefriti
- TB glomerülonefriti
- Sekonder amilodozis
- Hiponatremi-SADH
- İlaç ilişkili nefrotoksisite
 - R; nefrotoksik, ABY yapabilir
 - E ve P; nefrotoksik değil ancak ürik asit atılımını azaltarak, hiperürisemi yapabilir,
- İnfravesikal BCG sonrası *M.bovis*

Tanı

- Görüntüleme (IV ürografi)
 - Üreteral darlık
 - Renal pelvis distorsiyonları
 - Mesane fibrozisi
- BT
 - Kalsifikasyon (%50)
 - Çeşitli seviyede darlıklar
 - Mesane duvarı kalınlaşması

Tanı

- İdrar ARB ve kültür
 - Sabah ilk idrar (3-6 kez)
 - >5000 basil/mL(+)
 - Sensitivite%11-88
- PZR
 - Değişken çalışmalar var,
 - Sensitivite %87-100
 - Spesifite %93-96
- GeneXpert/RIF (tek çalışma)
 - Sensitivite %100
 - Spesifite % 98,6

Urogenital Tuberculosis: Update and Review of 8961 Cases from the World Literature

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Table 1
Frequency of Tuberculosis-Affected Urogenital Organs

	Christensen, 1974 ¹⁴ (United States)	Garcia-Rodriguez et al, 1994 ¹⁸ (Spain)	Mochalova and Starikov, 1997 ²⁷ (Russia)
Total (N)	102	81	4298
Men (n)	72	51	2888
Kidney	60.8	93.8	100
Bilateral	29	14.5	83.4
Unilateral	71	85.5	16.6
Ureter	18.6	40.7	NR
Bladder	15.7	21	10.6
Prostate*	26.4	2	49.5
Epididymis*	22.2	11.8	55.5
Seminal vesicles	6.9	0	NR
Urethra	1.4	2	21.4

Values are percentages unless otherwise noted.

*In relation to male patients.

NR, not reported.

- Tüm üriner sistem tutulur ancak en sık böbrekler
- Renal tutulum tek/ çift taraflı olabilir

- Hastaların nerdeyse yarısı ilerleyen dönemde cerrahi geçiriyor
- Gelişmiş ülkelerde daha sık
- Cerrahi tipi nefrektomi yada palyatif cerrahi
- Mesanede fibrozis nedeniyle büyültme operasyonları en sık (%8)
- Cerrahi anti-TB tedavinin 4-6.hfsında yapılmalı

Cerrahinin yeri?

- Tedavi sırasında gelişen hidrops

** Primary genitourinary tuberculosis: rapid progression and tissue destruction during treatment. Psihramis KE, Donahoe PK. J Urol. 1986 May; 135(5):1033-6.*

** Urogenital tuberculosis: update and review of 8961 cases from the world literature. Figueiredo AA, Lucon AM. Rev Urol. 2008;10(3):207-17.*

- Üreteral striktür

** Renal tuberculosis. Becker JA. Urol Radiol. 1988;10(1):25.*

** Role of early endourologic management of tuberculous ureteral strictures. Shin KY, Park HJ, Lee JJ, Park HY, Woo YN, Lee TY. J Endourol. 2002 Dec;16(10):755-8.*

EAU Guidelines

**EAU Guidelines for the Management of Genitourinary
Tuberculosis**

Mete Çek*, Severin Lenk, Kurt G. Naber, Michael C. Bishop, Truls E. Bjerklund Johansen, Henry Botto, Magnus Grabe, Bernard Lobel, Juan Palou Redorta, Peter Tenke

the Members of the Urinary Tract Infection (UTI) Working Group of the European Association of Urology (EAU) Guidelines Office

Department of Urology, Taksim Teaching Hospital, Istanbul, Turkey

- Anti TB tedavi HRZE/S (2 ay), HR (4ay)
- Rekürrens, komplikasyon, HIV(+); 9-12 ay
- MDR-TB; duyarlılığa göre;>18 ay
- Cerrahi?

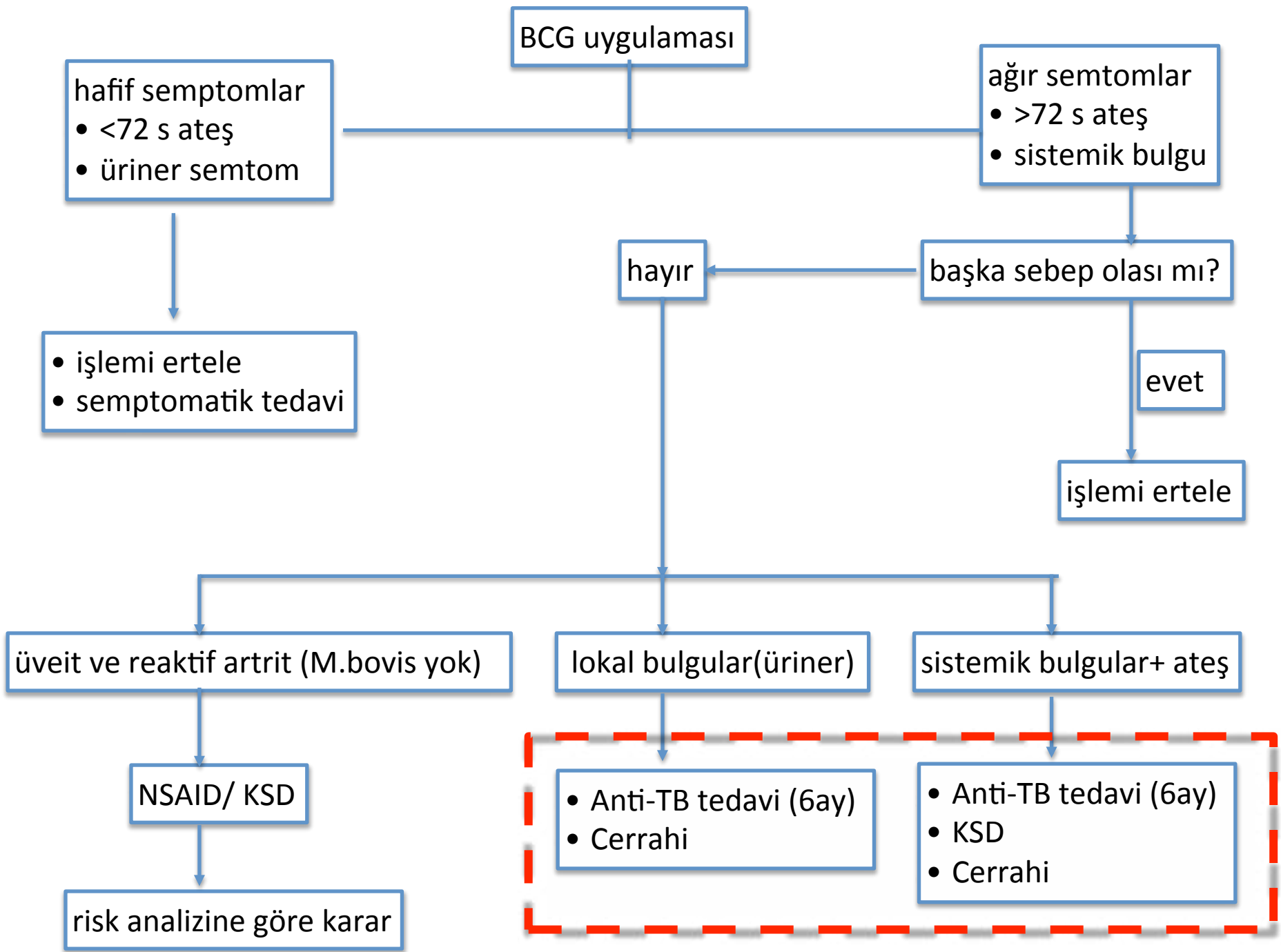
- Nefrektomi;
 - Nonfonksiyone böbrek (kalsifiye/değil)
 - Tüm böbrek tutulumu+HT/ üreteropelvik birleşke tutulumu,
 - Beraberinde renal karsinom
- Parsiyel nefrektomi
 - 6 hafta anti-TB tedaviye rağmen kalsifikasyon içeren polar lezyon,
 - Takiple büyüyen/ böbreğin genelini tehdit eden kalsifikasyon ,

- Abse drenajı
- Epidimektomi;
 - Anti TB tedaviye yanıt vermeyen kazefikiye abse,
 - Anti TB tedaviye rağmen sabit kalan yada büyüyen kitlesel lezyon
- Üreteral striktür
 - Ureteropelvik bileşke darlığı; double J kateter
 - Orta üreter darlığı;üreterostomi/ double J kateter
 - Alt ürter darlığı: anti-TB+KSD (<3 hf)+dilatasyon

nadir görülen bir tablo

'insanın yeter ki ters gitmesin işi muhallebi yerken kırılır dişi'

Mesane kanserinde immunoterapi
BCG (*M.bovis*) uygulaması sonrası TB?



KVS

- Perikardit
- Myokardit (nadir)
- Endokardit (en nadir)

Perikardit

- Konstrüktif perikardit
- Effüzyonun eşlik ettiği konstrüktif perikardit
- Kardiyak tamponat

Tanı

- Kardiyak silüet belirtisi (%40-60)
- EKG'de düşük voltaj
- EKO'da perikardiyel kalınlaşma-efüzyon
- BT/MRG'da perikardiyel kalınlaşma ve mediastinal trakeobronşiyal LAP



Perikardiyosentez

- Kanlı perikardiyel sıvı %80
- Eksüdatif, lenfosit hakimiyeti, perikardiyel lenfosit/nötrofil >1 (%86 sensitivite, %73 spesifite)
- ADA >30IU/L ise sensitivite %94, spesifite %68
- ARB (+) %40-60
- Kültür (+) %53-75
- PZR tanıya yardımcı

1. Cherian G. Diagnosis of tuberculous aetiology in pericardial effusions. Postgrad Med J. 2004 May;80(943):262-6

2. Reuter H et al. Diagnosing tuberculous pericarditis. QJM. 2006;99(12):827.

3. Maisch B, et al. S Task Force on the Diagnosis and Management of Pericardial Diseases of the European Society of Cardiology Guidelines on the diagnosis and management of pericardial diseases executive summary; The Task force on the diagnosis and management of pericardial diseases

4. Burgess LJ, et al. The use of adenosine deaminase and interferon-gamma as diagnostic tools for tuberculous pericarditis. Chest. 2002;122(3):900.

Cardiovascular Topics

Surgical management of effusive constrictive pericarditis

FUAT BUYUKBAYRAK, ERAY AKSOY, SERPIL TAS, KAAAN KIRALI

- Effüzyonlu konstrüktif perikardit
 - 12 hasta(5 idiyopatik, 4 TB, 3 malignite),
 - 10 hastaya perikardiyosentez başarısız,
 - 1 hasta acil, 9 hasta elektif perikardiektomi,
 - post op takip 3 ay-9 yıl,
 - mortalite 5 hasta (%41,6),

TABLE 5. RESULTS OF PERICARDIAL TISSUE BIOPSY AND FOLLOW-UP DATA

<i>Pat- ient</i>	<i>Aetiolo- gy</i>	<i>Date of opera- tion</i>	<i>Intensive care unit stay</i>	<i>Pericardial biopsy</i>	<i>Follow up (months)</i>	<i>Outcome</i>
1	ID	2004	8 days, LCOS, RF, RDS	Non-specific inflammation	4.04	Death from pneumonia + sepsis
2	TB	2004	1 day, uneventful	Granulomatous inflammation	95.0	NYHA class I
3	MG	2005	7 days, LCOS, RF, RDS	Neoplastic involvement [†]	2.9	Death from disease progression
4	MG	2005	2 days, uneventful	Neoplastic involvement [†]	19.7	Death from disease progression
5	TB	2006	8 days, re-operation for bleeding, RF, RD	Granulomatous inflammation	79.9	NYHA class III
6	ID	2006	6 days, re-operation for bleeding, RF, RD	Non-specific inflammation	25.7	Death from advanced HF
7	MG	2007	2 days, uneventful	Neoplastic involvement [§]	25.6	Death from disease progression
8	TB	2007	8 days, LCOS, RD	Non-specific inflammation	66.4	NYHA class II
9	ID	2007	1 day, uneventful	Non-specific inflammation	62.5	NYHA class I
10	ID	2008	5 days, low-dose inotrope	Non-specific inflammation	51.3	NYHA class I
11	TB	2008	2 days, uneventful	Granulomatous inflammation	48.2	NYHA class II
12	ID	2012	3 days, low-dose inotrope	Non-specific inflammation	8.9	NYHA class II

ID: idiopathic, TB: tuberculous, MG: malignancy, LCOS: low-cardiac output syndrome, RF: renal failure, RD: respiratory distress, NYHA: New York Heart Association, HF: heart failure.

[†]Neoplastic cell invasion without definitive diagnosis,

[‡]Pericardial involvement of malignant mesothelioma (epitolid type),

[§]Pericardial involvement of high-grade diffuse B-type cell lymphoma.

- TB hastalarında erken cerrahi sonuçları iyi,
- Anti TB tedavi yanında KSD tedavisi uygulanmamış,

Seminar

Pericarditis

Richard W Troughton, Craig R Asher, Allan L Klein

Bakteriyel enfeksiyonlar
içinde en sık ekten TB

Cause of acute pericarditis**Idiopathic****Infections**

Bacterial, tuberculous, viral (coxsackie, influenza, HIV, etc), fungal, rickettsial, mycoplasma, leptospiral, listeria, parasitic, and others

Vasculitis and connective-tissue disease

Rheumatoid arthritis, rheumatic fever, systemic lupus erythematosus, scleroderma, Sjögren's syndrome, Reiter syndrome, ankylosing spondylitis, Wegener's granulomatosis, giant-cell arteritis, polymyositis (dermatomyositis), Behçet's syndrome, familial Mediterranean fever, dermatomyositis, polyarteritis, Churg-Strauss syndrome, thrombohaemolytic thrombocytopenic purpura, leucoclastic vasculitis, and others

Diseases in adjacent structures

Myocardial infarction, aortic dissection, pneumonia, pulmonary embolism, empyema

Metabolic disorders

Uraemic, dialysis-related, myxoedema, gout, scurvy

Neoplastic disorders*Primary*

Mesothelioma, sarcoma, fibroma, lipoma, and others

Secondary (metastatic or direct spread)

Carcinoma, lymphoma, carcinoid, and others

Trauma*Direct*

Pericardial perforation (penetrating injury, oesophageal or gastric perforation) and cardiac injury (cardiac surgery, percutaneous procedures)

Indirect

Radiation, non-penetrating chest injury

Association with other syndromes

Postmyocardial and pericardial injury syndromes, inflammatory bowel disease, Löffler syndrome, Stevens-Johnson syndrome, giant-cell aortitis, hypereosinophilic syndromes, acute pancreatitis, others

Modified with permission from Spodick DH. Pericardial disease. In: Braunwald E, Zipes DP, Libby P, eds. Heart disease: a textbook of cardiovascular medicine, 6th edn. Philadelphia: WB Saunders, 2001 (reference 1).

Tedavi algoritminde

- 1) NSAİ ilk seçenek
- 2) Devam eden tablolarıda (TB gibi);ileri inceleme ve KSD
- 3) Komplikasyon varsa;
 - perikardiyosentez
 - perikardiyektomi

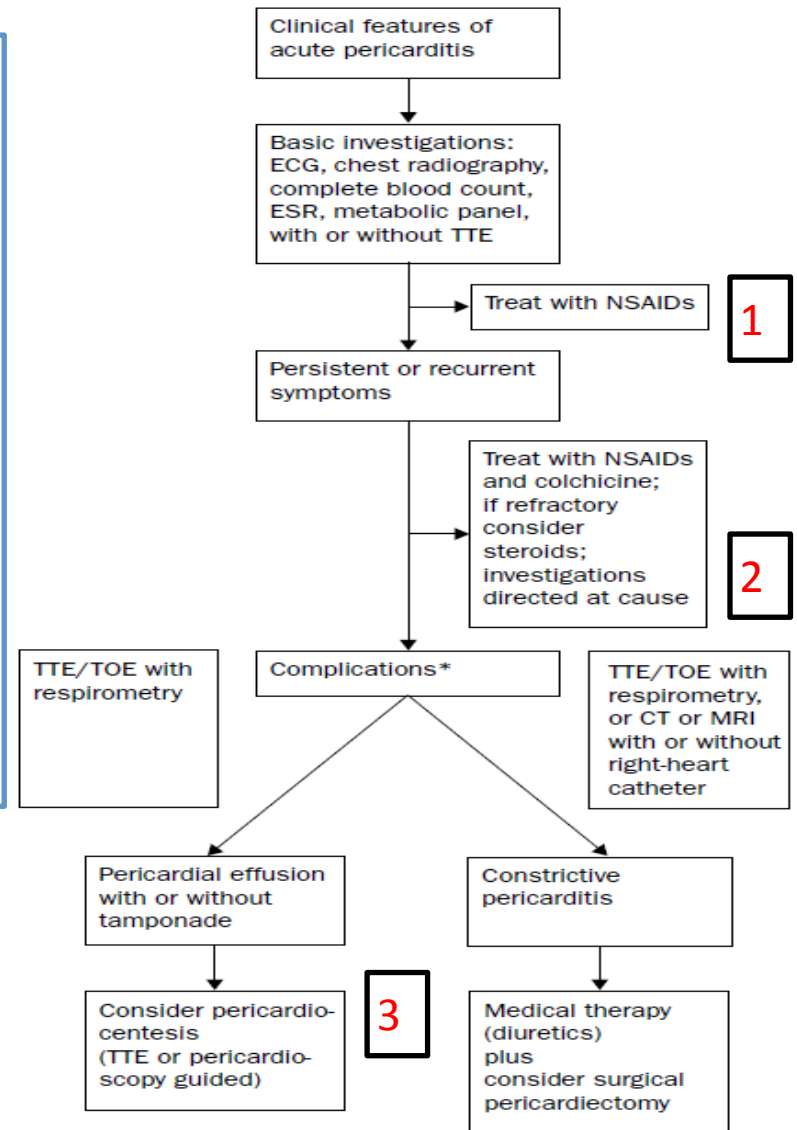


Figure 1: **Suggested approach to investigation and management of pericarditis and its complications**

TTE=transthoracic echo. TOE=transoesophageal echo. *Defined as haemodynamic instability, right-heart failure, volume overload, or both, or unexplained cardiovascular symptoms.

Rationale and design of the Investigation of the Management of Pericarditis (IMPI) trial: A 2 × 2 factorial randomized double-blind multicenter trial of adjunctive prednisolone and *Mycobacterium w* immunotherapy in tuberculous pericarditis

- TB Perikardit, Çok merkezli, çift randomize, çift körlü, prednisolon ve Mycobacterium W immunoterapi
- TB perikarditte mortalite ve kalıcı hasar %50'lerdedir,
- TB perikarditte efüzyon birikimini azaltıcı etkin olan KSD, immünoterapi (M. w) ile kıyaslanmıştır,
- TB perikardit tanılı/olası 1400 hasta,

Table I. Diagnostic criteria for TB pericarditis in a TB-endemic country or community²³

Diagnostic category	Criteria
Definite TB pericarditis	<ul style="list-style-type: none">● Tubercle bacilli are found in stained smear or culture of pericardial fluid; or● Tubercle bacilli or caseating granulomata are found on histologic examination of pericardium
Probable TB pericarditis	<ul style="list-style-type: none">● Evidence of pericarditis in a patient with TB demonstrated elsewhere in the body; or● Lymphocytic pericardial exudate with elevated adenine deaminase activity; or● A Tygerberg TB Pericarditis Diagnostic Index Score ≥ 6 in patients in whom pericardiocentesis is not feasible, and other causes of pericarditis have been excluded

TB tanı:

- Perikardiyel sıvıda TB basili
- Perikard biyopsisinde TB basili veya kazeifikasyon granülomu

TB olası:

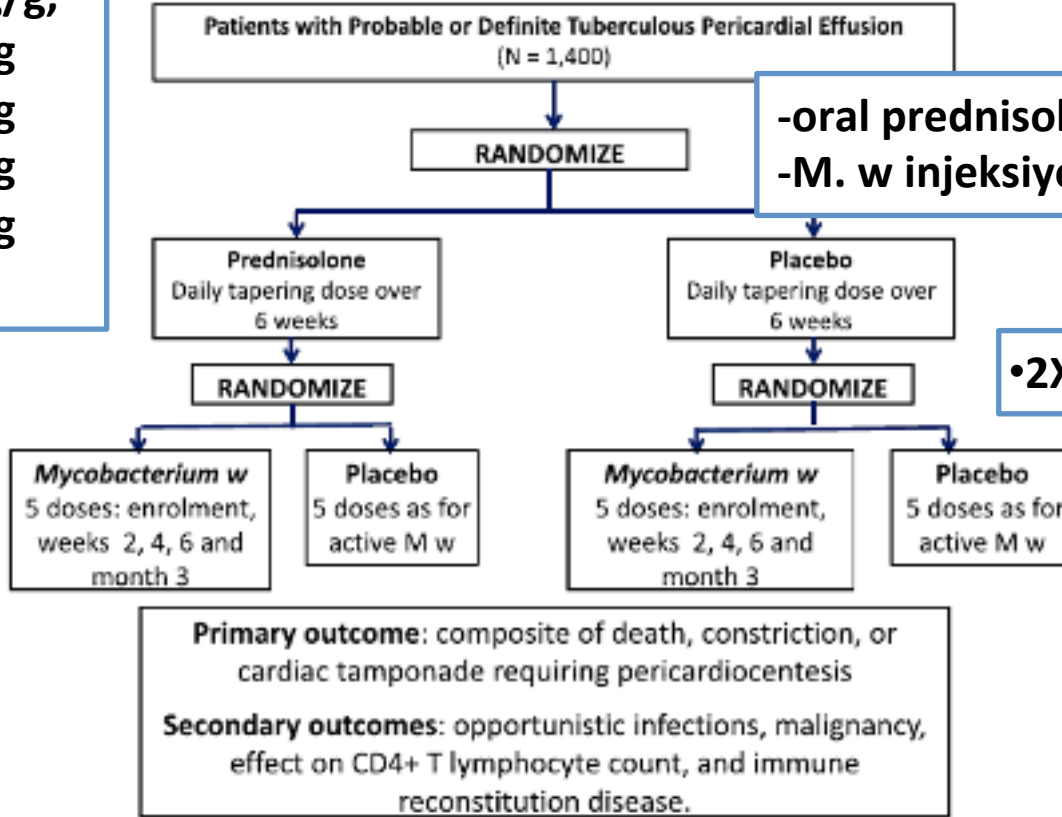
- Başka bir yerde TB tanısı konan perikardit veya
- Artmış lenfositik aktivite ile ADA pozitifliği
- Perikardiyosentez mümkün olmayan hastalarda Tygerberg skoru >6

Tygerberg TB perikardit Tanı Kriteri Puanı (>6)-perikardiyosentez yapılamayanlar

- Kilo kaybı (1)
- Gece terlemesi (1)
- Ateş (2)
- Serum globulin $>40\text{g/L}$ (3)
- BK sayısı $< 10 \times 10^9 / \text{L}$ (1)

- Prednisolon ve M. w immünoterapsinin tamponat ve perikardiyel drenaj gerektiren effüzyon gelişimi üzerine etkisi araştırıldı ve kıyaslandı,
- Randomize
 - oral prednisolon / plasebo (6 hf)
 - M. w injeksiyonu / plasebo (3ay)
- Takip
 - 2,4,6. hf
 - 3 ve 6. ay ve 6 aylık periyotlarla 4 yıl
- Primer sonlanım: ölüm/ perikardiyel kontrüksiyon/ perikardiyosentez gerektiren tamponat
- Sekonder sonlanım:immünmodülasyonun olumsuz etkileri fırsatçı enfeksiyon (herpes zooster vb) veya malignite (kaposi vb)

- 1.hf; 120 mg/g,
- 2.hf; 90mg/g
- 3.hf; 60mg/g
- 4.hf; 30mg/g
- 5.hf; 15mg/g
- 6.hf; 5mg/g



-oral prednisolon / plasebo (6 hf)
-M. w injeksiyonu / plasebo (3ay)

•2X2 (çift randomizasyon)

IMPI Trial study design.

Primer sonlanım: ölüm/ perikardiyel kontrüksiyon/perikardiyosentez gerektiren tamponat
Sekonder sonlanım:immünmodülasyonun olumsuz etkileri fırsatçı enfeksiyon (herpes zooster vb) veya malignite (kaposi vb)

4. Detectable RRR comparisons between the cell with double placebo versus each individual drug (2-tailed $\alpha = .0264$, 10% drop-out and 6% lost to follow-up)

Double placebo event rate	1200-patient study		1400-patient study		1600-patient study	
	n = 300 vs 300 cell comparison		n = 350 vs 350 cell comparison		n = 400 vs 400 cell comparison	
	80% power	90% power	80% power	90% power	80% power	90% power
35%	30.2%	34.0%	28.2%	31.8%	26.6%	30.0%
40%	28.9%	32.5%	27.0%	30.4%	25.4%	28.7%
45%	27.8%	31.3%	26.0%	29.3%	24.5%	27.6%

- Sonuç:
 - KSD ve M. w immünizasyonu TB perikarditte anti TB tedaviye yardımcıdır,
 - KSD'lerin etkisi daha erken çıkmaktadır,
 - İmmünoterapinin etkisi daha uzun sürmekte ve tekrarlayan effüzyona etkisi daha güçlüdür,

TB cilt tutulumu-sınıflama-I

- Eksojen kaynaktan inokülasyon
 - Primer cilt TB
 - Tuberculosis verrükosa cutis
- Otoinokülasyon veya endojen kaynaktan yayılım
 - Skrofuloderma
 - Tuberculosis cutis orificialis
 - Lupus vulgaris
- Hematojen yayılım
 - Lupus vulgaris
 - Akut miliyer TB
 - Metastatik TB absesi

TB cilt tutulumu sınıflama-II

'Usus magister est optimus'
Tecrübe en iyi öğretmendir

- Multibasiler (basil doku yada eksüdatta var)
 - Skrofuloderma
 - Tuberculosis cutis orificialis
 - Akut miliyer TB
 - TB absesi
- Paucibasiler (basil yok/ çok az)
 - Tuberculosis verrucosa cutis
 - Lupus vulgaris
- Tüberküloid (basil yok TB aglerine duyarlılık)
 - Papülonekroid tüberküloid(PNT)
 - Lichen scrafulosorum
 - Eritema endüratum Bazin (nodüler vaskülit)

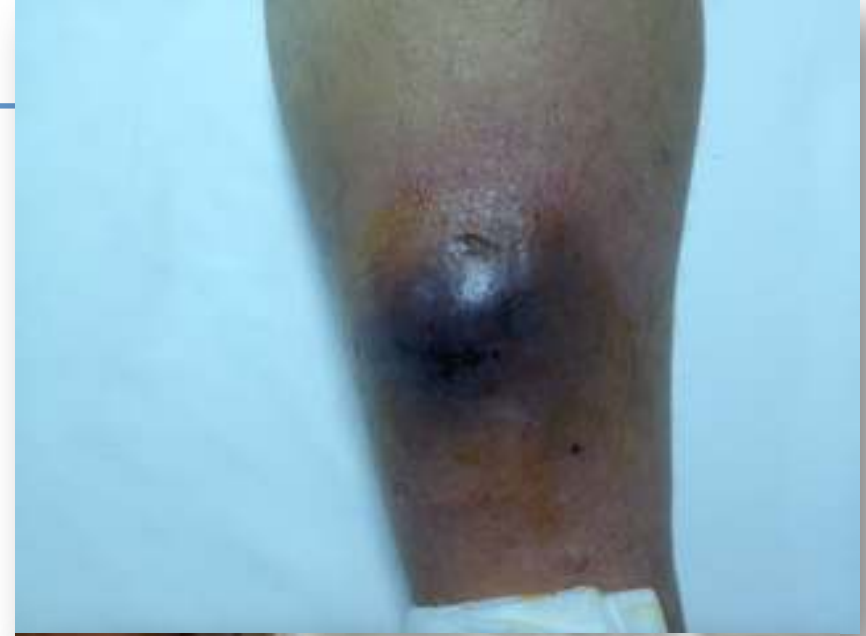
Nadir Görülen Bir Cilt Tüberkülozu: Tuberculosis Verrucosa Cutis

Alper Şener¹, Suzan Saçar¹, Sevilay Oğuz², Rıdvan Dumlu¹, Özlem Çakmak¹

Onsekiz Mart Üniversitesi Tıp Fakültesi Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji AD./ Çanakkale
Onsekiz Mart Üniversitesi Tıp Fakültesi Dermatoloji AD./ Çanakkale

Olgu:

- 67y E, çiftçi, oniki yıldır KOAH nedeniyle inhale kortikosteroid ve beta blokör kullanıyor.
- Sol bacak 1/3 distalinde üç haftadır devam eden ağrısız, fistülüze, üzeri yer yer nekrotik kurutlanma içeren ve pürülan akıntı sonrası tekrar kapanan yara (Resim 1).
- Farklı hekimlerce betalaktam ve beta laktamaz inhibitörü başlanmasına rağmen iyileşmiyor
- Aspirasyon direkt bakı ve kültüründe; her sahada bol lökosit ve eritrosit, gram negatif bakteri ve GSBL (+) *E.coli*
- Hastaya ertapenem 1x1 gr IV tedavi başlandı.
- Tedavinin üçüncü günü mikrobiyoloji laboratuvarından gelen sonuçlarda yara direkt bakısında 2-3 adet ARB basil görüldüğü bildirildi.
- HRZE, PO başlandı. Birinci ayda görünüm (Resim 2).



TB cilt tutulumu-tedavi

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Management of cutaneous tuberculosis

Table 1. Recommended dosage for initial treatment of cutaneous tuberculosis

Drug	Daily dose	Thrice-Weekly dose	Children ^a
Isoniazid	5 mg/kg, max 300 mg	15 mg/kg, max 900 mg	10-15 mg/kg daily; 20-30 mg/kg intermittent
Rifampicin	10 mg/kg, max 600 mg	10 mg/kg, max 600 mg	10-20 mg/kg
Pyrazinamide	20-25 mg/kg, max 2 g	30-40 mg/kg, max 3 g	
Ethambutol	15-20 mg/kg	25-30 mg/kg	

^aDosage for children is similar, except that some authorities recommend higher doses of isoniazid and rifampicin.

Source: Based on American Thoracic Society, Infectious Disease Society of America and Centers for Disease Control and Prevention.

HRZE başlangıç tedavisi (2 ay) ve HR (4 ay) (AC TB ile aynı)

TB cilt tutulumu-tedavi

Table 2. Treatment regimen for cutaneous tuberculosis

Chemotherapy	First-line drugs	Resistance to isoniazid	Resistance to isoniazid and rifampicin	Resistance to all first-line drugs
Initial or bactericidal phase	Rifampicin + isoniazid + pyrazinamide + streptomycin or ethambutol 2 months, daily	Rifampicin + pyrazinamide + ethambutol ^a	Pyrazinamide + ethambutol + quinolone antibiotic Streptomycin (or another injectable agent ^b)	1 injectable agent ^b + 3 of the following: ethionamide, cycloserine, quinolone antibiotic, para-aminosalicylic acid
Continuation or sterilizing phase	Rifampicin + isoniazid 4 months, daily 2/week or 3/week	Throughout (6 months)	Throughout (18-24 months)	Throughout (24 months)
Total duration of therapy	6 months at least	6 months	18-24 months	24 months

^aA fluoroquinolone may strengthen the regimen for patients with extensive disease.

^bAmikacin, kanamycin, or capreomycin. All agents should be discontinued after 2-6 months, depending upon tolerance and response.

- Toplam tedavi süresi 6 ay
- H direncinde; RZE, 6 ay
- HR direncinde; ZE+FQ / S, 18-24 ay
- Tüm birinci basamaklara direnç; S (enjektabl amikasin/kanamisin/kapreomisin)+ 3'lü (sikloserin, etionamid, FQ, PAS), 24 ay



MMWRTM

Morbidity and Mortality Weekly Report

Recommendations and Reports

June 20, 2003 / Vol. 52 / No. RR-11

Treatment of Tuberculosis

**American Thoracic Society, CDC, and Infectious
Diseases Society of America**

TABLE 2. Drug regimens for culture-positive pulmonary tuberculosis caused by drug-susceptible organisms

Regimen	Initial phase		Continuation phase			Range of total doses (minimal duration)	Rating* (evidence)†				
	Drugs	Interval and doses‡ (minimal duration)	Regimen	Drugs	Interval and doses‡§ (minimal duration)		HIV-	HIV+			
1	INH RIF PZA EMB	Seven days per week for 56 doses (8 wk) or 5 d/wk for 40 doses (8 wk)¶	1a	INH/RIF	Seven days per week for 126 doses (18 wk) or 5 d/wk for 90 doses (18 wk)¶	182–130 (26 wk)	A (I)	A (II)			
			1b	INH/RIF	Twice weekly for 36 doses (18 wk)				92–76 (26 wk)	A (I)	A (II)#
			1c**	INH/RPT	Once weekly for 18 doses (18 wk)				74–58 (26 wk)	B (I)	E (I)
2	INH RIF PZA EMB	Seven days per week for 14 doses (2 wk), then twice weekly for 12 doses (6 wk) or 5 d/wk for 10 doses (2 wk),¶ then twice weekly for 12 doses (6 wk)	2a	INH/RIF	Twice weekly for 36 doses (18 wk)	62–58 (26 wk)	A (II)	B (II)#			
			2b**	INH/RPT	Once weekly for 18 doses (18 wk)				44–40 (26 wk)	B (I)	E (I)
3	INH RIF PZA EMB	Three times weekly for 24 doses (8 wk)	3a	INH/RIF	Three times weekly for 54 doses (18 wk)	78 (26 wk)	B (I)	B (II)			
4	INH RIF EMB	Seven days per week for 56 doses (8 wk) or 5 d/wk for 40 doses (8 wk)¶	4a	INH/RIF	Seven days per week for 217 doses (31 wk) or 5 d/wk for 155 doses (31 wk)¶	273–195 (39 wk)	C (I)	C (II)			
			4b	INH/RIF	Twice weekly for 62 doses (31 wk)				118–102 (39 wk)	C (I)	C (II)

Definition of abbreviations: EMB = Ethambutol; INH = isoniazid; PZA = pyrazinamide; RIF = rifampin; RPT = rifapentine.

* Definitions of evidence ratings: A = preferred; B = acceptable alternative; C = offer when A and B cannot be given; E = should never be given.

† Definition of evidence ratings: I = randomized clinical trial; II = data from clinical trials that were not randomized or were conducted in other populations; III = expert opinion.

‡ When DOT is used, drugs may be given 5 days/week and the necessary number of doses adjusted accordingly. Although there are no studies that compare five with seven daily doses, extensive experience indicates this would be an effective practice.

§ Patients with cavitation on initial chest radiograph and positive cultures at completion of 2 months of therapy should receive a 7-month (31 week; either 217 doses [daily] or 62 doses [twice weekly]) continuation phase.

¶ Five-day-a-week administration is always given by DOT. Rating for 5 day/week regimens is AIII.

Not recommended for HIV-infected patients with CD4+ cell counts <100 cells/μL.

** Options 1c and 2b should be used only in HIV-negative patients who have negative sputum smears at the time of completion of 2 months of therapy and who do not have cavitation on initial chest radiograph (see text). For patients started on this regimen and found to have a positive culture from the 2-month specimen, treatment should be extended an extra 3 months.

5.2.1. Six-month regimens

The current minimal acceptable duration of treatment for all children and adults with culture-positive tuberculosis is 6 months (26 weeks). The initial phase of a 6-month regimen for adults should consist of a 2-month period of INH, RIF, PZA, and EMB given daily throughout (Regimen 1), daily for 2 weeks followed by two times weekly for 6 weeks (Regimen 2), or three times a week (Regimen 3). The minimum

•Optimum tedavi HRZE (2 ay), HR(4 ay) toplamda 6 ay (26hf) olmalı

5.2.2. Nine-month regimen

If PZA cannot be included in the initial regimen, or if the isolate is determined to be resistant to PZA (an unusual circumstance, except for *Mycobacterium bovis* and *M. bovis* var. BCG), a regimen consisting of INH, RIF, and EMB should be given for the initial 2 months (Regimen 4) followed by INH and RIF for 7 months given either daily or twice weekly (Regimens 4a and 4b).

•Eğer PZA başlanamıyorsa veya direnç varsa; HRE(2 ay) sonrasında HR (7 ay), toplamda 9 ay olmalı

8. Treatment in Special Situations

8.1. HIV Infection

Tuberculosis and HIV Infection

The treatment of tuberculosis in persons with HIV infection is essentially the same as for patients without HIV infection. There are two important exceptions to this generalization: 1) Once weekly INH–rifapentine in the continuation phase should not be used in any HIV-infected patient; and 2) twice weekly INH–RIF or rifabutin should not be used for patients with CD4⁺ lymphocyte counts less than 100/μl. Providers must be alert to the potential for interactions among many of the antiretroviral drugs and the rifamycins. Paradoxical reactions that mimic worsening of tuberculosis are more common in patients with HIV infection and may complicate therapy.

HIV (+)'lerde;
-INH-rifapentine /hf devamda kullanılmamalı
-INH-RIF/ rifabutin / 2kez /hf, 100<CD4 olanlarda kullanılmamalı

8.3. Extrapulmonary Tuberculosis

randomized controlled trials, suggests that 6- to 9-month regimens that include INH and RIF are effective (2–16). Therefore, among patients with extrapulmonary tuberculosis, a 6- to 9-month regimen (2 months of INH, RIF, PZA, and EMB followed by 4–7 months of INH and RIF) is recommended as initial therapy unless the organisms are known or strongly suspected of being resistant to the first-line drugs. If PZA cannot be used in the initial phase, the continuation phase must be increased to 7 months, as described for pulmonary tuberculosis.

The exception to the recommendation for a 6- to 9-month regimen is tuberculous meningitis, for which the optimal length of therapy has not been established, but some experts recommend 9–12 months.

Corticosteroid treatment is a useful adjunct in treating some forms of extrapulmonary tuberculosis, specifically meningitis and pericarditis caused by drug-susceptible organisms. Evidence-based recommendations on the duration of treatment for extrapulmonary tuberculosis and the use of corticosteroids are shown in Table 13.

AD-TB;

- 6-9 arası rejimler önerilir,
- 2 ay HRZE, 4-7 ay HR,
- PZA başlanamazsa; devam fazı 7 aya uzatılır,

TB-menenjitte toplam süre 9-12 ay olmalıdır

KSD tedavisi menenjit ve perikarditte anti TB tedaviye ek olarak önerilir.

TABLE 13. Evidence-based* guidelines for the treatment of extrapulmonary tuberculosis and adjunctive use of corticosteroids†

Site	Length of therapy (mo)	Rating (duration)	Corticosteroids‡	Rating (corticosteroids)
Lymph node	6	A1	Not recommended	DIII
Bone and joint	6–9	A1	Not recommended	DIII
Pleural disease	6	AII	Not recommended	DI
Pericarditis	6	AII	Strongly recommended	A1
CNS tuberculosis including meningitis	9–12	BII	Strongly recommended	A1
Disseminated disease	6	AII	Not recommended	DIII
Genitourinary	6	AII	Not recommended	DIII
Peritoneal	6	AII	Not recommended	DIII

* For rating system, see Table 1.

† Duration of therapy for extrapulmonary tuberculosis caused by drug-resistant organisms is not known.

‡ Corticosteroid preparations vary among studies. See Section 8.3 for specific recommendations.

KSD tedavisi konusunda bu iki tablo dışında yararını gösterir etkin çalışma yoktur

Tedavi süreleri açısından bakıldığında ;

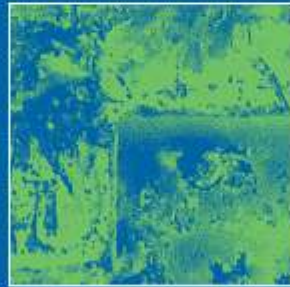
- Lenf nodu TB; 6 ay
- Kemik-eklem TB; 6-9 ay
- Perikardiyel TB; 6 ay
- Genitoüriner TB; 6 ay
- Peritoneal TB; 6 ay

SSS –TB açısından 9-12ay önerilen sürenin kanıt düzeyi daha düşük

TREATMENT OF TUBERCULOSIS

guidelines

FOURTH EDITION



World Health
Organization

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Treatment of extrapulmonary TB and of TB in special situations

Pulmonary and extrapulmonary disease should be treated with the same regimens (see Chapter 3).¹ Note that some experts recommend 9–12 months of treatment for TB meningitis (2, 3) given the serious risk of disability and mortality, and 9 months of treatment for TB of bones or joints because of the difficulties of assessing treatment response (3). Unless drug resistance is suspected, adjuvant corticosteroid treatment is recommended for TB meningitis and pericarditis (1–4). In tuberculous meningitis, ethambutol should be replaced by streptomycin.

- AC ve AD-TB'da tedavi seçenekleri aynıdır,
- Ana farklılıklar tedavi süresindedir,

- TB menenjitte ve kemik eklem TB'unda >9 ay tedavi süreleri önerilir,
- TB perikardit ve TB menenjitte ilaç dirençli TB şüphesi olmadığı sürece KSD tedavi eklenebilir,
- TB menenjitte ETM, Streptomisinle değiştirilmelidir,

TREATMENT OF TUBERCULOSIS: GUIDELINES

Although sometimes required for diagnosis, surgery plays little role in the treatment of extrapulmonary TB. It is reserved for management of late complications of disease such as hydrocephalus, obstructive uropathy, constrictive pericarditis and neurological involvement from Pott's disease (spinal TB). For large, fluctuant lymph nodes that appear to be about to drain spontaneously, aspiration or incision and drainage appear beneficial (3).

Tanı için bazen gerekli olsa da; cerrahinin yeri AD-TB'da sınırlıdır. Hidrosefali, obstüriktif üropati, konstriktif perikardit ve Pott hastalığı (spinal TB) nörolojik tutulumu için rezervde tutulmalıdır. Büyük lenf nodlarında da yararlıdır.



*National Institute for
Health and Clinical Excellence*

Issue date: March 2011

Tuberculosis

**Clinical diagnosis and management of
tuberculosis, and measures for its
prevention and control**



Eve Gidecek Mesajlar

'Sapientia est potentia'

Bilgelik güçtür

- AD-TB tedavisinde
 - İlaç duyarlı etken varlığında 6HRZE uygulanır,
 - Eğer başlangıçta Z başlanamıyorsa toplam tedavi 9 aya uzatılır,
 - İlaç dirençli etken varlığında duyarlılığa göre seçilir ve süre >18 ay,
 - KSD tedavisi sadece perikardit ve menenjit EII ve EIII'te yararlıdır,
 - SSS ve Kemik-Eklem TB tedavi süresi >9ay
 - SSS-TB'da E yerine S kullanılmalıdır

Eve Gidecek Mesajlar
'Sapientia est potentia'
Bilgelik güçtür

- Cerrahi tedavi sadece özel durumlarda uygulanır;
 - Hidrosefali,
 - Obstüriktif üropati,
 - Konstriktif perikardit,
 - Pott hastalığı (spinal TB) nörolojik bulgular varlığında,
 - Büyük lenf nodları(?)
 - Tüberküлом(?)