

Extrapulmonale Tuberkulose

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Infektiologie / Spitalhygiene
Kantonsspital Olten

**KURZREPETITORIUM DER INNEREN
MEDIZIN....
...& ETWAS MEHR**

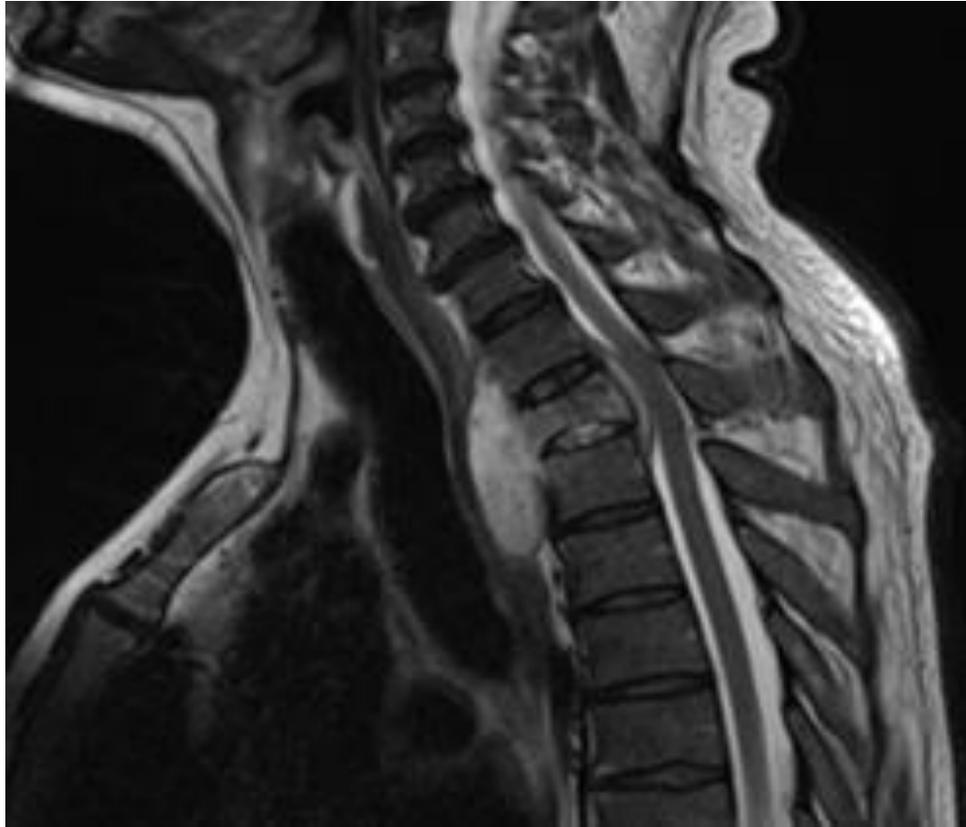
- 28 J, w, Eritrea, CH seit 1½ J.
- Schwellung zervikal
- Kein Fieber, kein Nachtschweiss
- Keine respirat. Symptome
- Dg.: Mumps
- Im Verlauf Progredienz:
 - beginnend fluktuierend



- 55 J., m., CH
- Lastwagenfahrer, vermehrte Pollakisurie
- „Feierabendbier“ (2-3 Glas ?)
- Im Verlauf Makrohämaturie & Urge-Symptomatik
- Dg.: HWI
- Kein Beschwerdebesserung,
unter Bactrim persistierende Lukozyturie



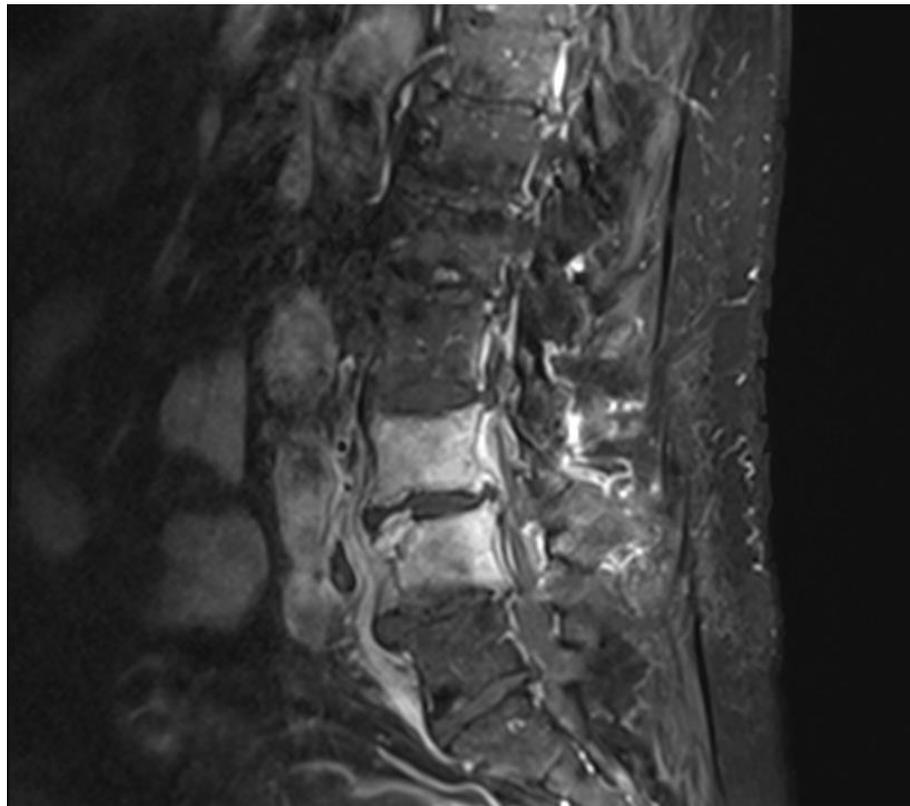
- 32 J., M, Äthiopien
- Thorakale Rückenschmerzen nach Sport
- Keine Besserung auf NSAR >2 Mt.
- Im Verlauf subfebril



- 42 J., w., Südafrika
- Persistierende Bauchschmerzen seit >6 Mt.
- zunehmender Bauchumfang seit wenigen Wochen
- Allg. Abgeschlagenheit, neu subfebril
- Sonographisch Aszites
- CA-125 2x positiv (fluktuierend)
- Dg.: V.a. Ovarial-Ca



- 88 J., CH, m
- Rückenschmerzen lumbal seit 1 Mt.
- Gewichtsverlust, alg. Abgeschlagenheit
- Keine Besserung auf Paracetamol, Opiate

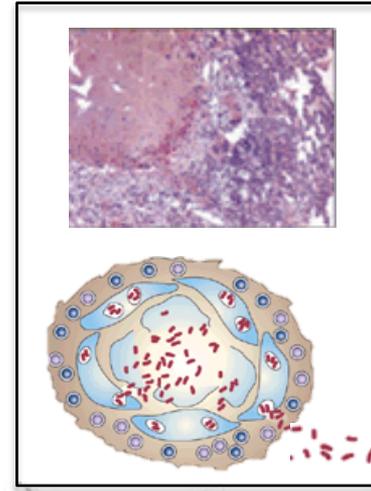
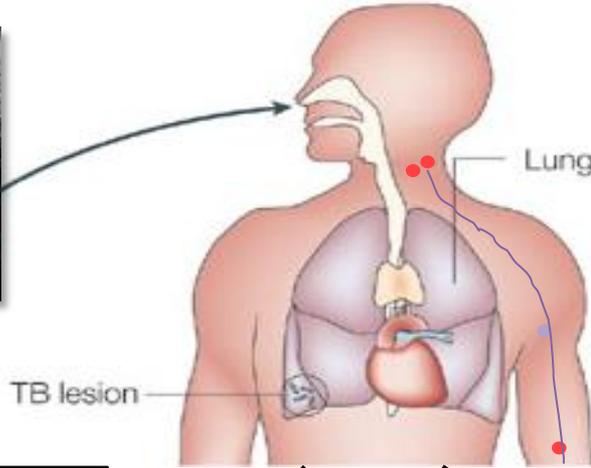


- PA: Urothel-Ca,
- St.n. BCG Instillationen, letztmals vor 3 Mt.

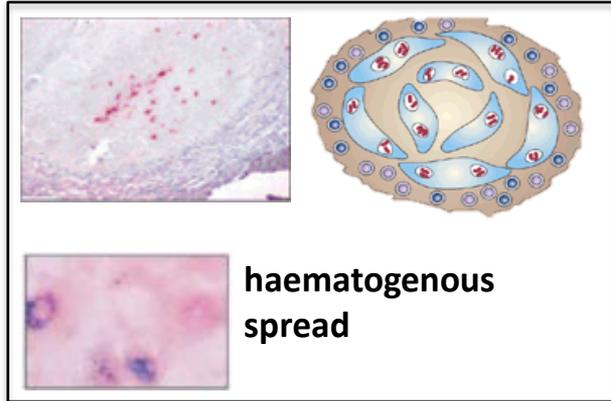
HINTERGRUND



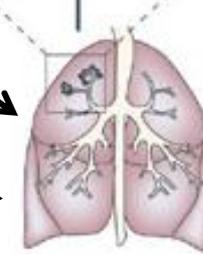
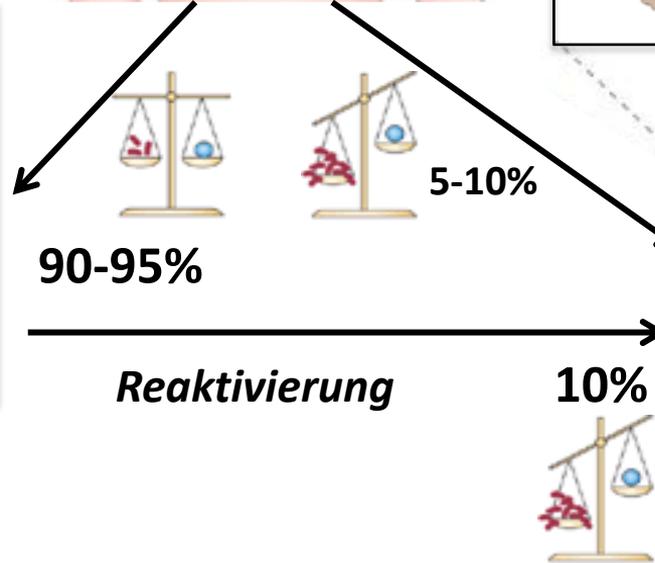
Tuberkulosekontakt



Aktive Tuberkulose



Latente Tuberkulose (LTBI)



Bacillarity at autopsy in pulmonary tuberculosis

Mycobacterium tuberculosis is often disseminated

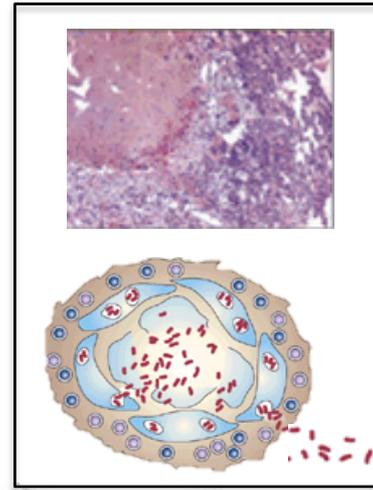
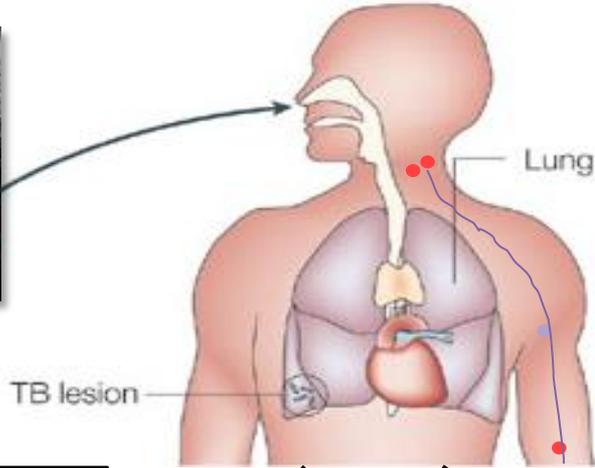
TABLE 2. Days of treatment; initial bacillarity while still alive in sputum or gastric lavage; and bacillarity at autopsy in lung, spleen, liver, and kidney in 98 patients with culture-positive pulmonary tuberculosis

Days of treatment	N	Initial bacillarity	Bacillarity at autopsy				
			Lung N-B	Spleen N-B	Liver N-B	Kidney N-B	Total pos. N (%)
0	5	3.4	5-4	5-2.2	5-2	2-1.5	5 (100.0)
1-9	22	3.5	20-3	11-1.4	6-1.3	5-1.4	20 (90.9)
10-19	8	3.3	7-2.1	2-1	1-1	0	7 (87.5)
20-29	5	3.2	4-3	1-1	0	0	4 (80.0)
30-49	4	3.0	2-2.5	0	0	1-1	2 (50.0)
50-99	7	2.4	2-1	0	0	0	2 (28.6)
			Good compliance				
100+	35	3.0	4-2	2-1	1-2	1-1	5 (14.3)
			Poor compliance				
100+	12	3.8	4-2	1-1	0	1-2	6 (50.0)

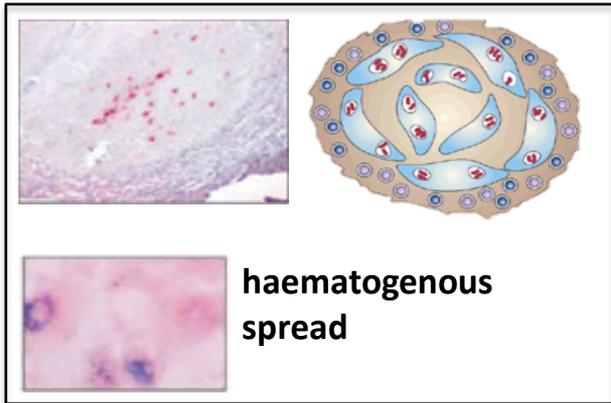
N=number of patients; B=average bacillarity (1=1-5 colonies, 2=6-25 colonies, 3=26-100 colonies, 4=more than 100 colonies); Total pos.=total number of examined patients with a positive culture at autopsy.



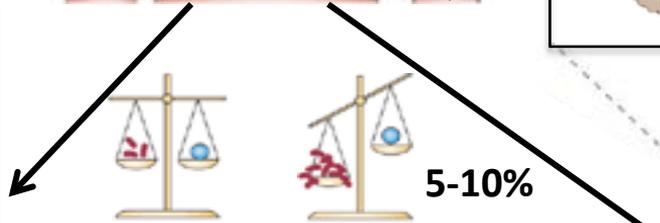
Tuberkulosekontakt



Aktive Tuberkulose



Latente Tuberkulose (LTBI)



90-95%

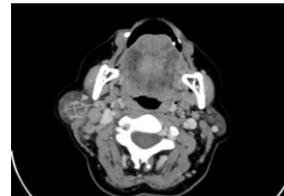
5-10%

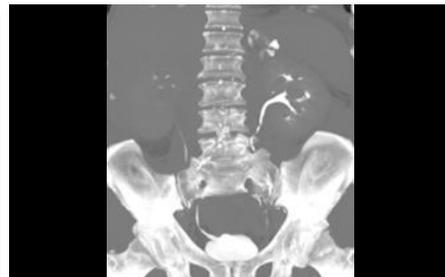
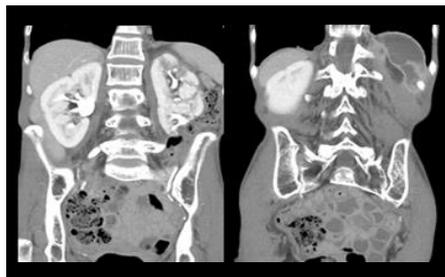
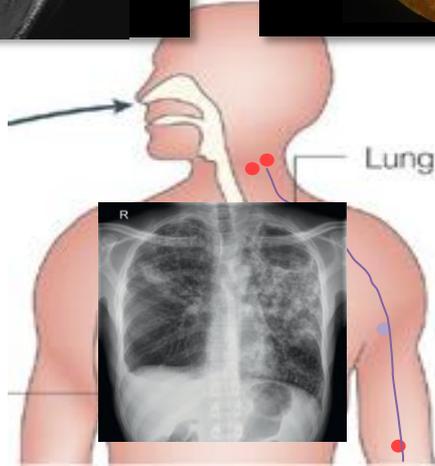
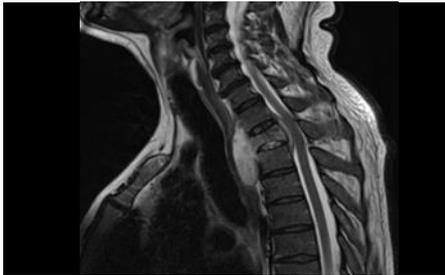
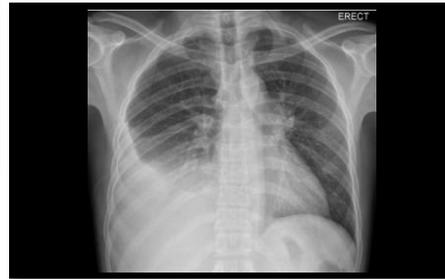
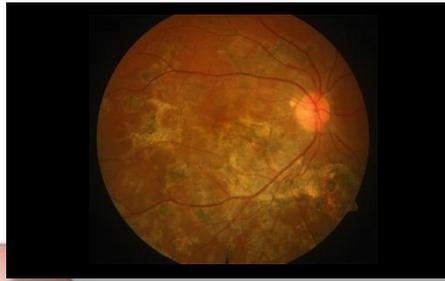
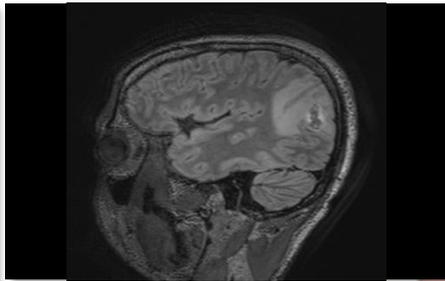
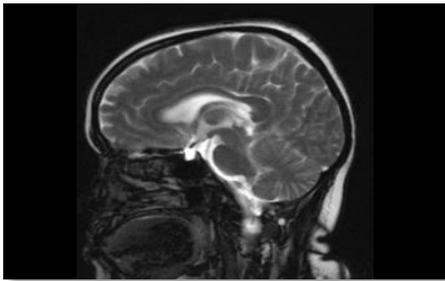


Reaktivierung

10%

Extrapulmonale TB





HIV
(CD4 <100/uI)



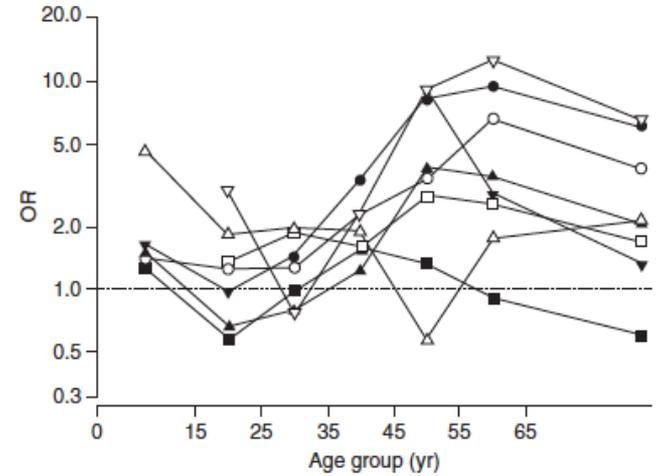
50% HIV+

TNF- α Blocker



>50% TNF- α Tx

Alter



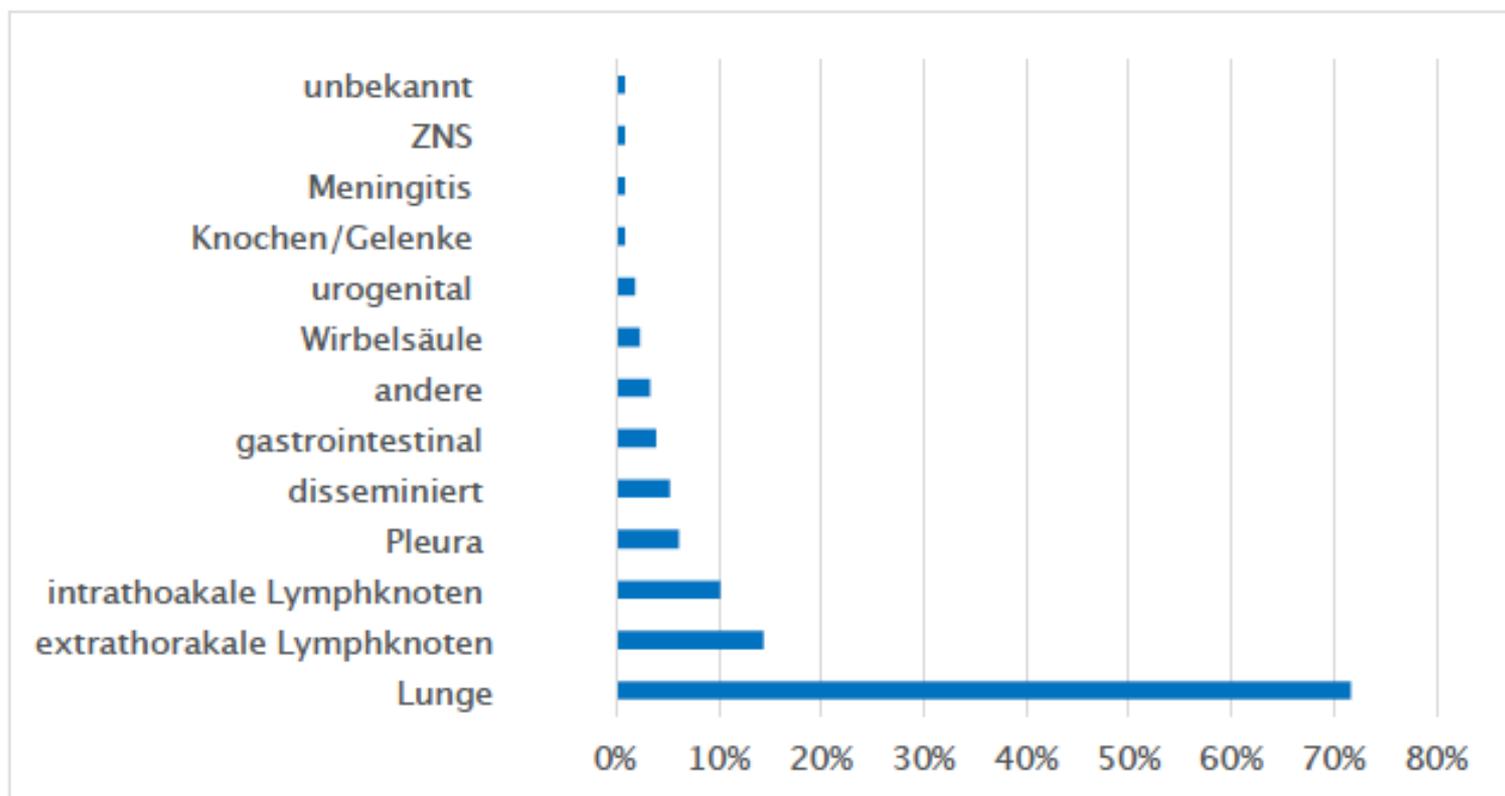
Forssohm et al., Eur Resp 2008

Abbildung 4:

Tuberkulose in der Schweiz 2014, Organbefall (Mehrfachnennungen sind möglich)

9. November 2015

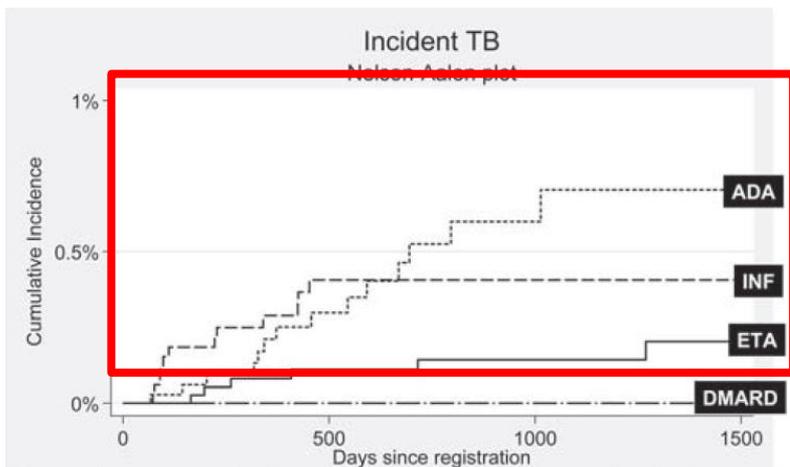
Bulletin 46



ZNS = Zentralnervensystem

Disseminiert: miliare TB oder Befall von mehr als 2 Organen

Drug-specific risk of tuberculosis in patients with rheumatoid arthritis treated with anti-TNF therapy: results from the British Society for Rheumatology Biologics Register (BSRBR)



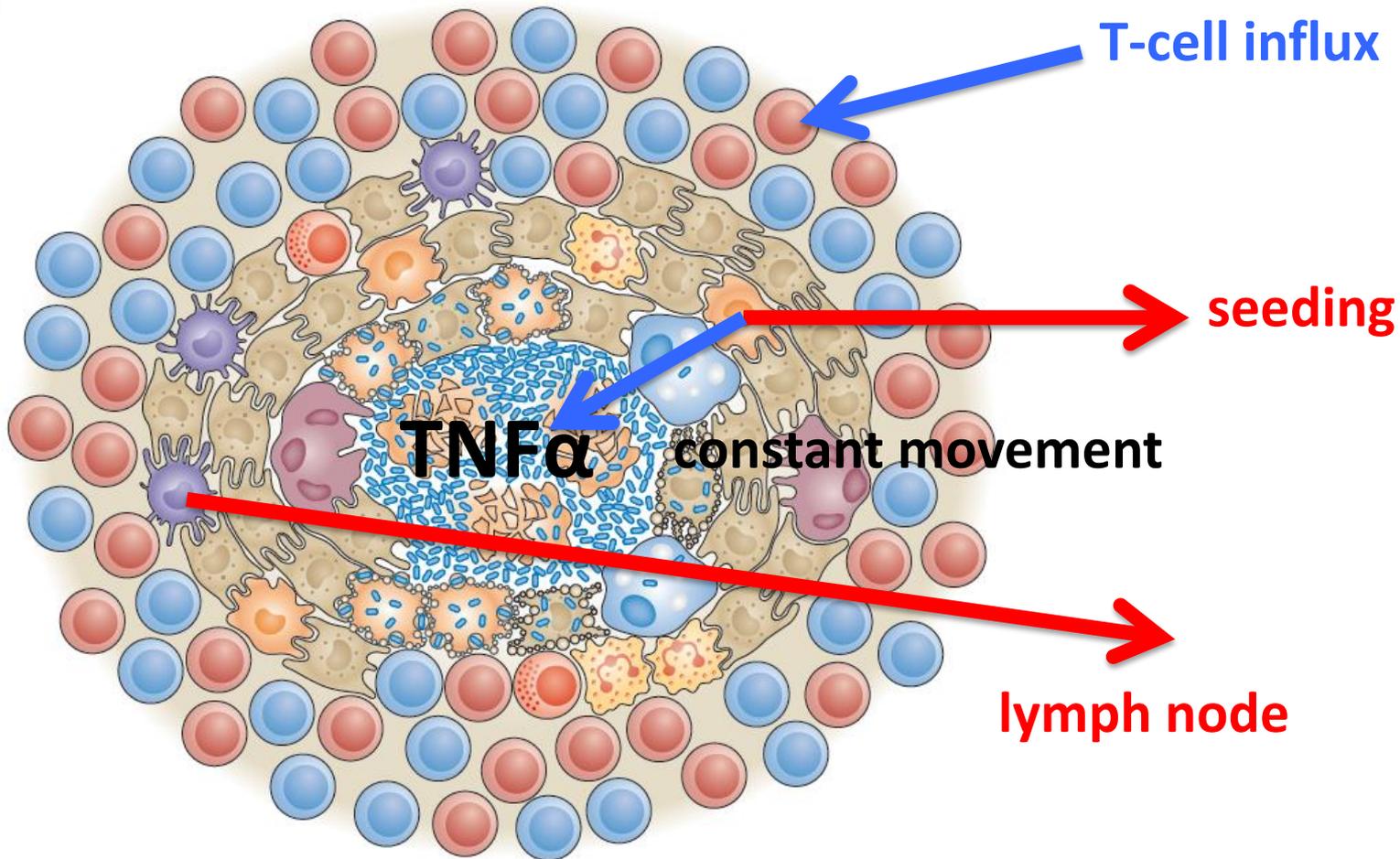
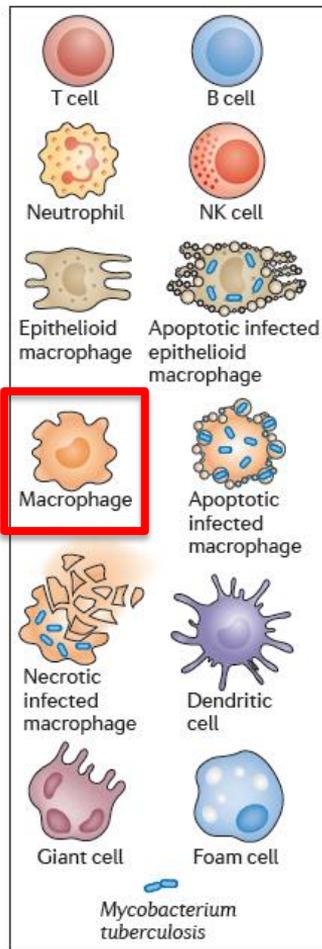
3 J.

	ETA n = 8 {5}	INF n = 12 {11}	ADA n = 20 {11}	All anti-TNF n = 40 {27}
Pulmonary, n = 15 (38% total)				
Lower respiratory tract	4 {2}	2 {2}	6 {3}	12 {7}
Pleural	–	2 {2}	1 {1}	3 {3}
Total pulmonary	4 {2}	4 {4}	7 {4}	15 {10}
Extra-pulmonary (including disseminated), n = 25 (62% total)				
Bone and joint	1 {1}	–	–	1 {1}
Gastrointestinal	–	3 {3}	–	3 {3}
Lymph node	2 {2}	2 {2}	2 {2}	6 {6}
Central nervous system	–	1 {1}	2 {1}	3 {2}
Pharyngeal wall	–	–	1 {1}	1 {1}
Disseminated	1 {0}	2 {1}	8 {3}	11 {4}
Total extrapulmonary	4 {3}	8 {7}	13 {7}	25 {17}

62%

Numbers represent number of cases attributable to most recent drug {number of cases while “on drug”}.

ADA, adalimumab; ETA, etanercept; INF, infliximab; TB, tuberculosis; TNF, tumour necrosis factor.

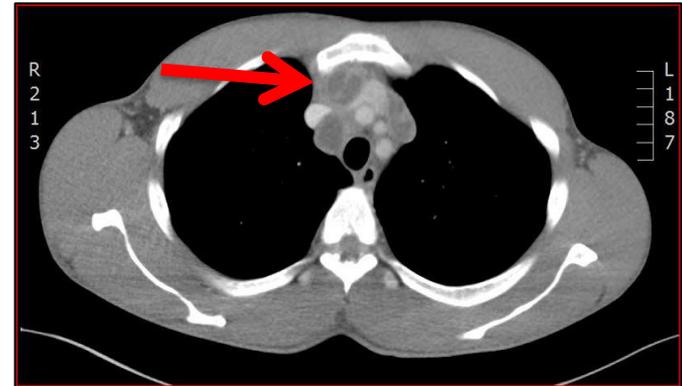


KLINIK



- **Häufigste extrapulmonale Manifestation**
 - v.a. zervikal = Scrofula (c.a. 70%)
- **Immigranten:**
 - >3 J. nach Immigration, Alter 20 – 40

Geldmacher H. et al. Chest 2002; 121:1177.

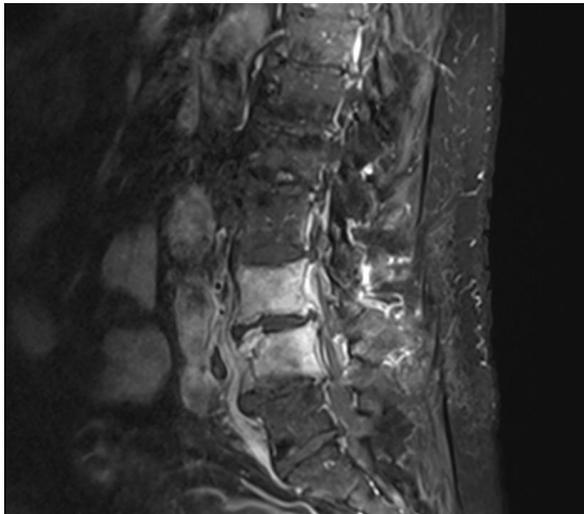




Pott's disease: Spondylodiszitis



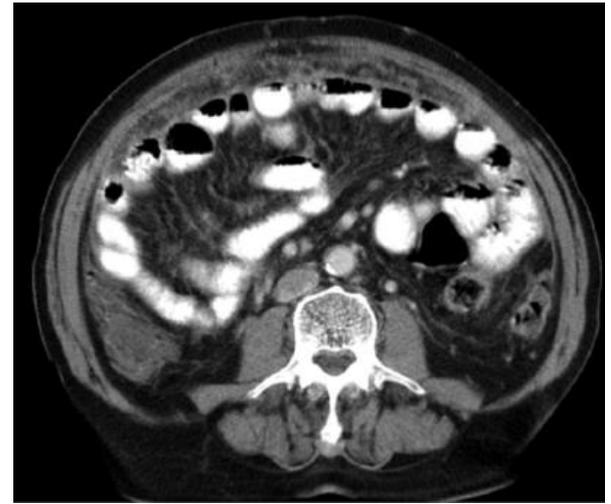
Arthritis (Knie, Hüfte)

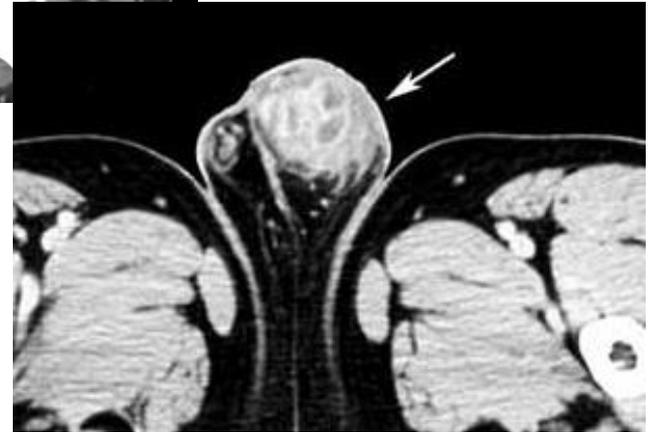
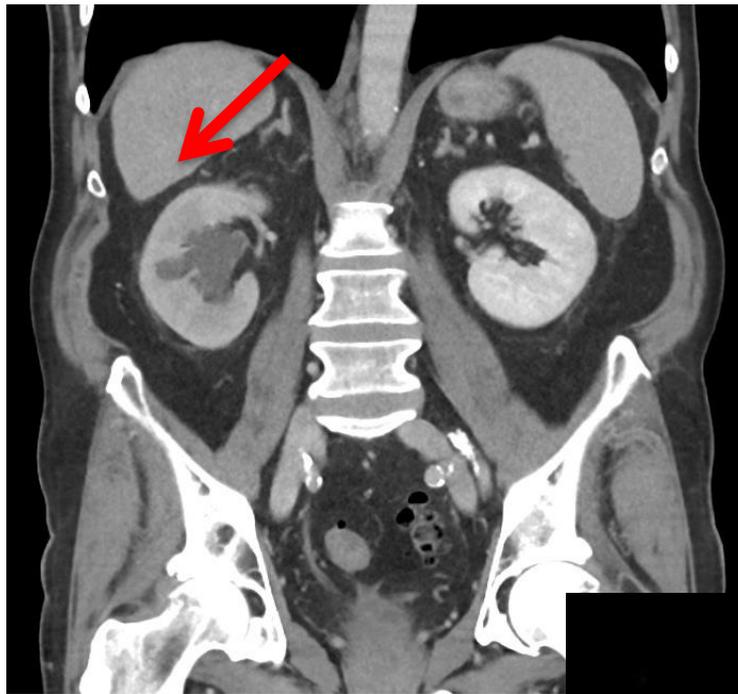


**Osteomyelitis
(„kalter“ Abszess)**

N Engl J Med 2018; 379:1161

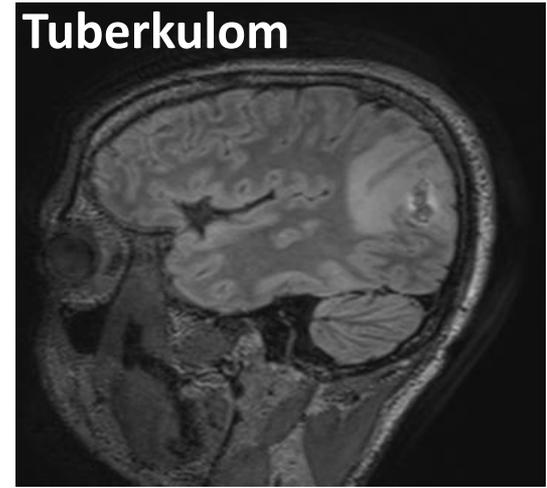
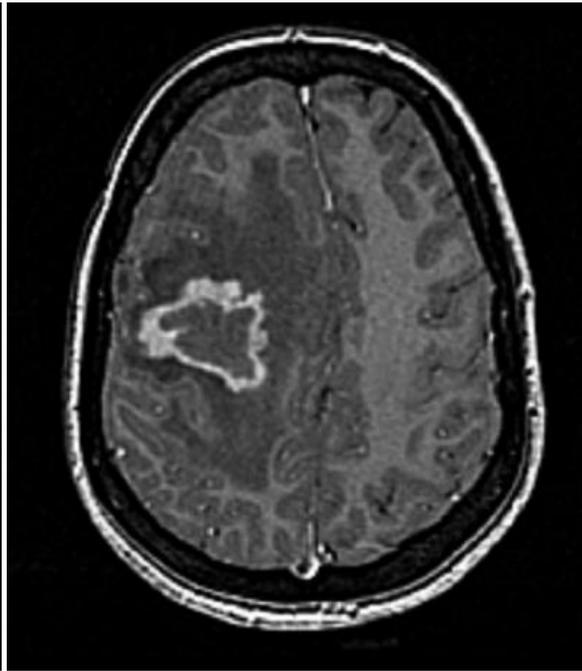
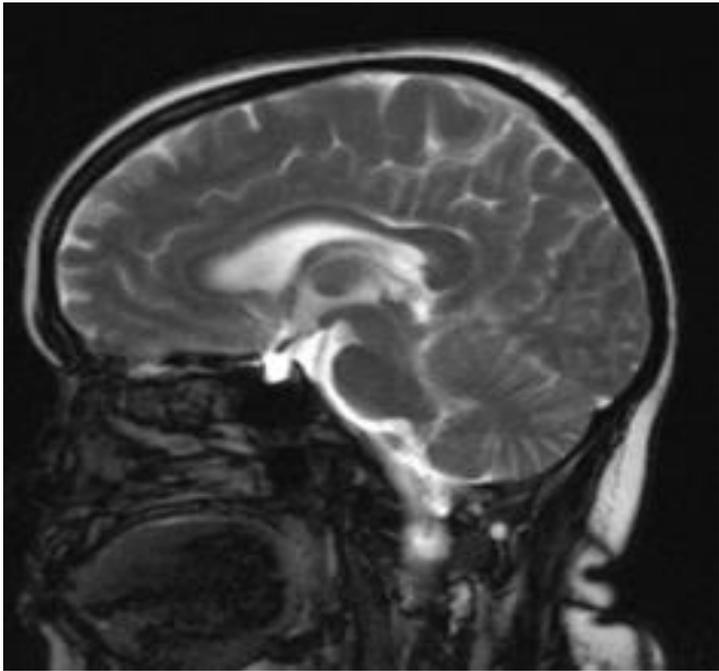






- **Ableitende Harnwege; (Glomerulonephritis)**
 - Prostatitis (subklinisch 40-50%)
- **Epididymitis**

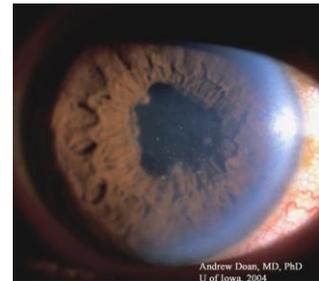
Interstitielle Nephritis (DD RIF!)

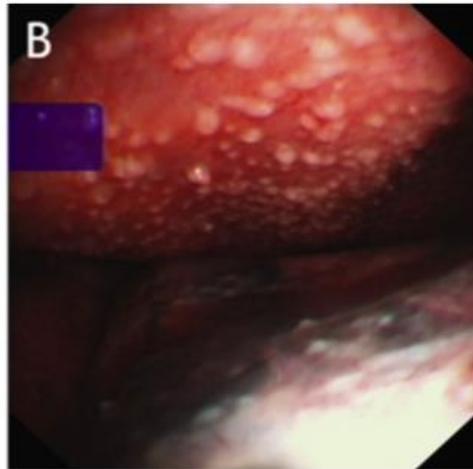
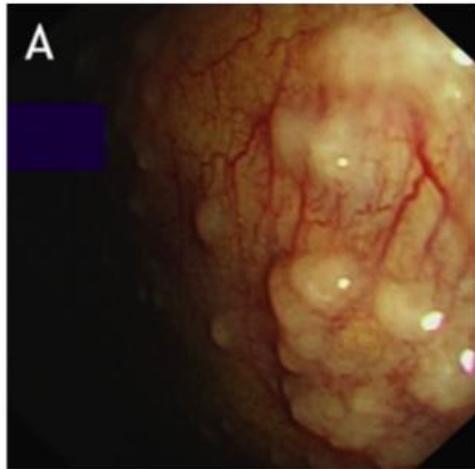
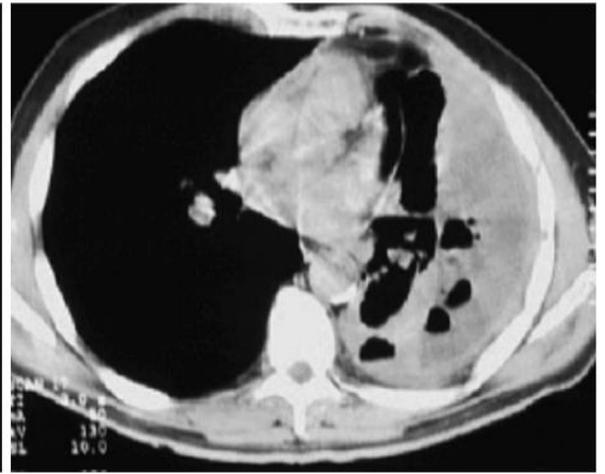
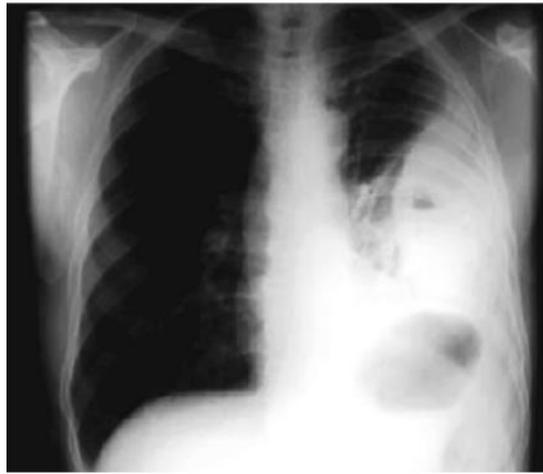
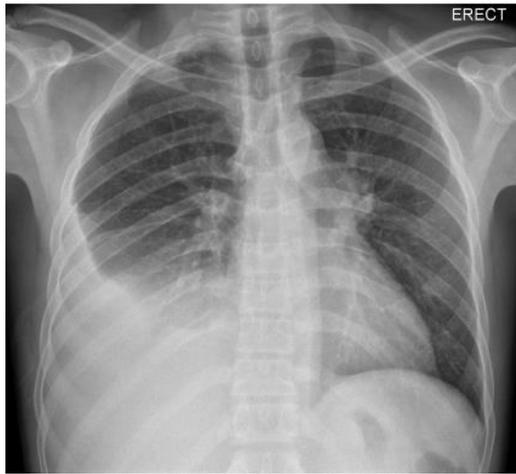


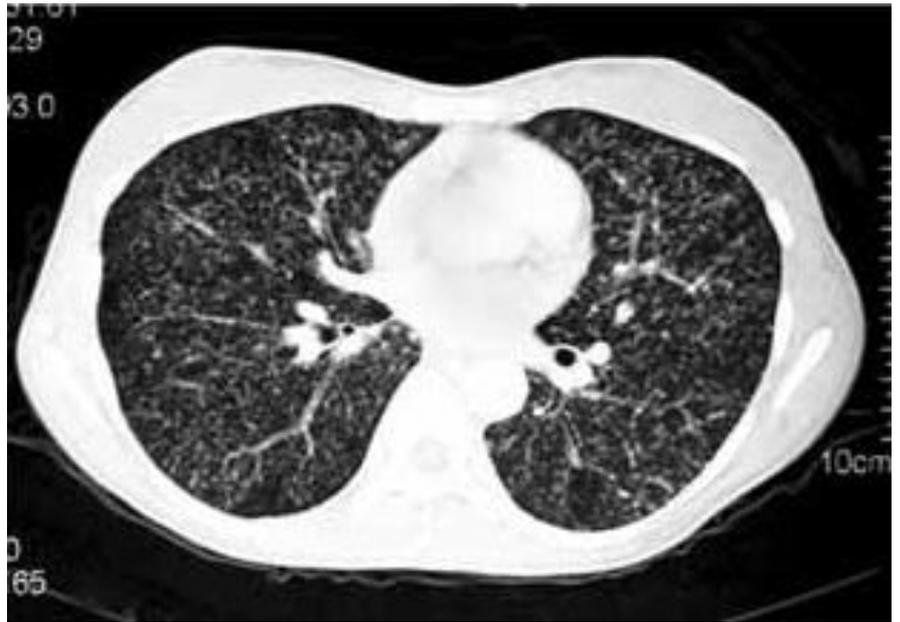
(basale) Meningitis

- 1/3 offene TB (!!)

- HIV <100 CD4/ μ l







Häufiger unter Immunsuppression

- HIV + pulm. TB: 10%
- HIV + extrapulm. TB: 38%



Tuberculosis verrucosa cutis



Gumma



Erythema induratum Bazin



**Lupus vulgaris
tuberculosa**

Leo F, et al. Dtsch Arztebl Int 2018; 115: 428.

DIAGNOSTIK



Anamnese und Klinik „daran denken“!!



Herkunft / Alter
St.n. TB? TB-Therapie?
Immunsuppression?
Konstitutionelle Symptome?
BCG Instillationen? (BCGitis)

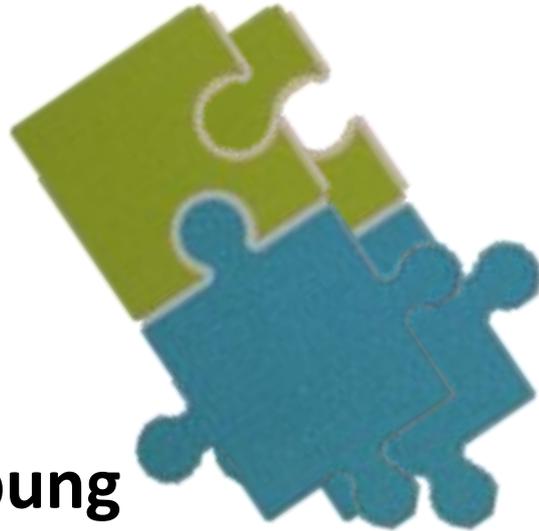


Symptomorientierte Diagnostik:

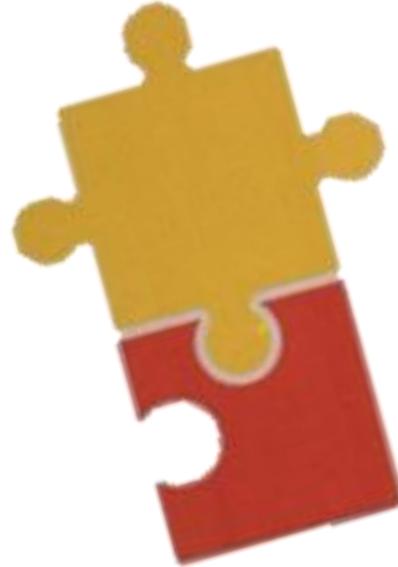
- **Bildgebung**
- **Biopsie (chirurgisch!) / LP / Punktion (Aszites, Pleura, (LK))**
- Heparin-Blutkultur
- PCR (Xpert RIF)
- **Kultur (IMMER!!)**
- **Rx-Thorax ev. (induziertes) Sputum**
- **HIV-Test**

Mikrobiologie / Histologie

Anamnese



Bildgebung

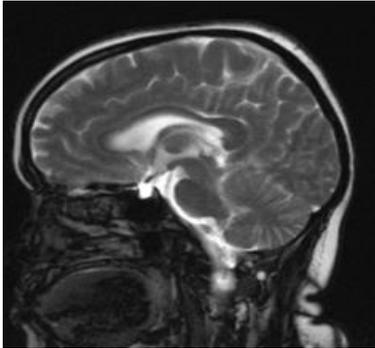


Klinik



Aspiration: Sensitivität 62%

→ **LK Exzision** (Histologie, Kultur [in NaCl 0,9%])



Lumbalpunktion (keine Zeitverzögerung)

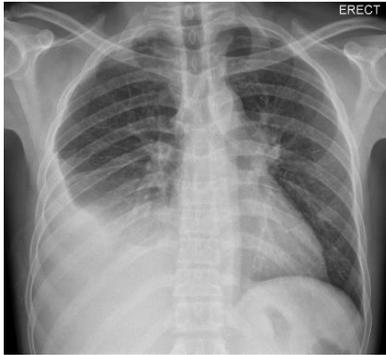
- lympho-monozytär; 25 – 1'000 / ul
- Protein 45 – 500 mg/dl
- Glucose 10 – 45 mg/dl (leicht erniedrigt)
- Chlorid ↓



(Morgen)Urin >40ml – Kultur!

CAVE: falsch-neg. nach Chinolonen

- Bildgebung: Strikturen 80%, Hydronephrose



Punktion, meist unlat. Erguss

- lympho-monozytär
- Exsudat, pH ↓, Glukose ↓, (ADA >40)

➔ **Pleurabiopsie**



Aszitespunktion

- Mikroskopie Sensitivität ↓↓

➔ **Laparoskopie und Biopsie**

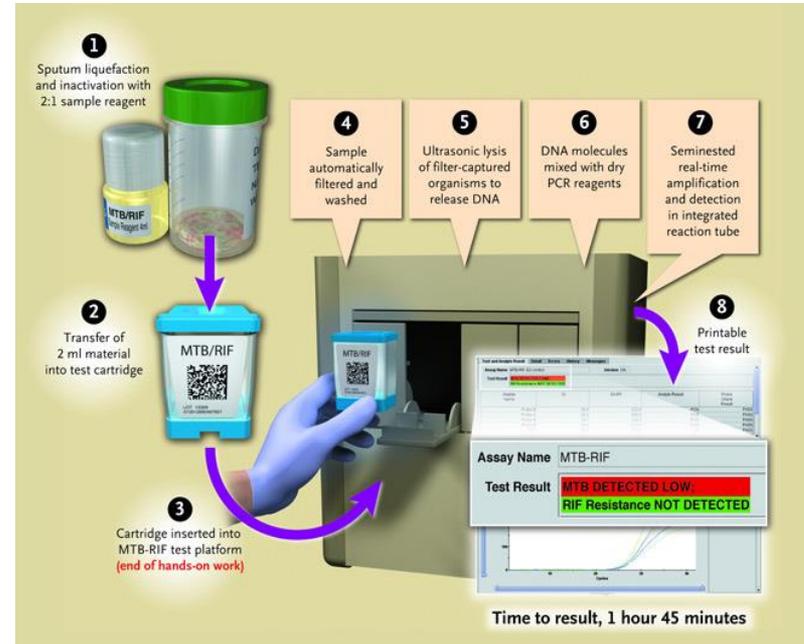
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

SEPTEMBER 9, 2010

VOL. 363 NO. 11

Rapid Molecular Detection of Tuberculosis and Rifampin Resistance



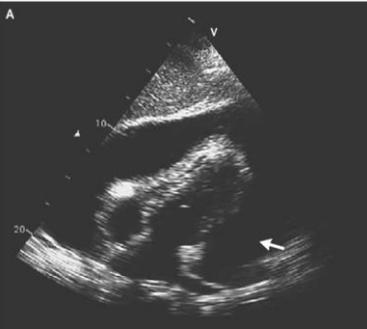
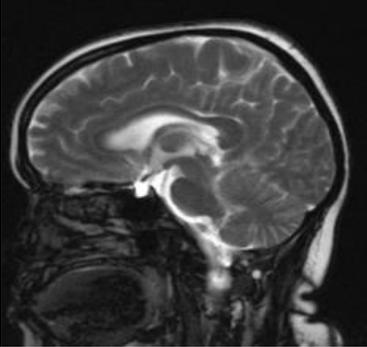
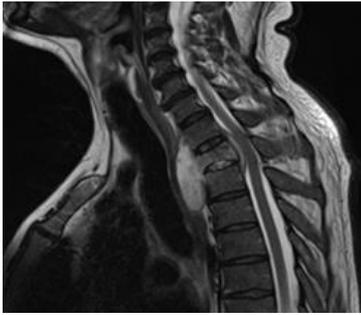
Setting	Sensitivity	Specificity
Pulmonary TB, smear pos. ¹	100%	98-99%
Pulmonary TB, smear neg.		
- 3 samples ¹	90%	
- 1 sample ^{2,4}	67%	
Pulmonary TB w/o smear (replacement) ₂	89%	
TB meningitis ^{3,5}	(55)-80%#	
Lymph node (aspirate) ^{3,4}	83-96%	
Pleural fluid ^{3,4}	37-46%	
Pericardial fluid ⁶	52%	
Aszites	? (70%)	

- 1 Boehme CC et al. N Engl. J Med 2010
- 2 Steingart et al. CHOCRANE review 2014
- 3 Denkinger et al. Eur Respir J 2014;
- 4 Maynard-Smith BMC Infect Dis 2014
- 5 Rufai et al., J Infect 2017
- 6 Zeka et al., J Clin Microbiol 2001
- 7 Rufai et al., J Lab Physician 2017

Anreicherung x2 vor Xpert
erhöht Sensitivität!

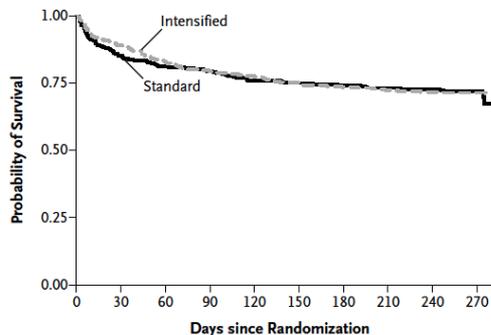
THERAPIE

HRZE2 + HR4



- **Therapie: mit RIF!**
 - **HRZE2 + HR4-7**
(6 Mt.: 62% Relapse) Ramachandran S et al. Int J Tuberc Lung Dis 2005; 9:541
 - **ohne RIF: 9 Mt., Chinolon?**
- TP möglich
- **Therapie: HRZE2 + HR7-10 ?**
 - + **Chinolon (bei INH Resistenz)**
 - + **Aminoglykosid?**
- **Steroide (Hyperimmunsyndrom!)**
Prasad K et al. Cochrane Database Syst Rev 2016; 4:CD002244
Cantier et al. Critical Care (2018) 22:210
- **Pericarditis constrictiva**
 - + **Steroide**

A All Patients



No. at Risk

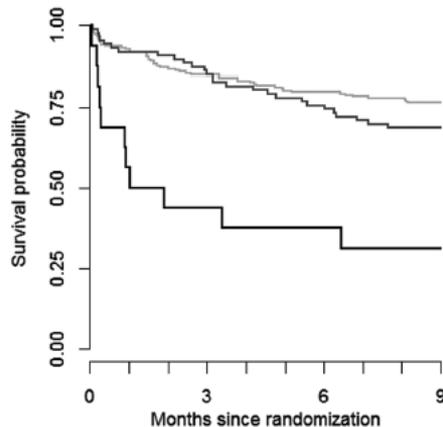
Standard	409	342	322	315	298	293	290	286	284	222
Intensified	408	353	328	313	305	295	288	283	379	225

Heemskerk AD et al. N Engl J Med 2016; 374:2

HRZE3 + HR6 (Standard)

HRZE3 + HR6 + Levoflox(20mg/kgKG) & R(15mg/kgKG) 8 weeks

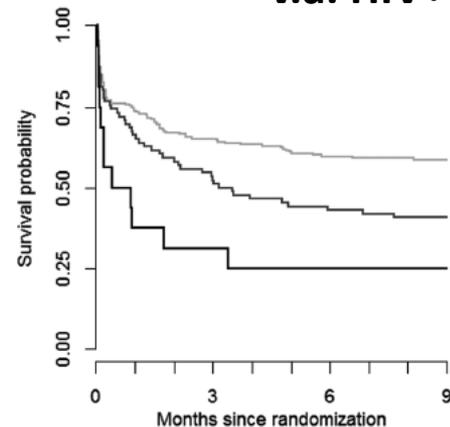
A



No. at risk

No INH or RIF resistance	220	183	169	17
INH resistant	86	73	65	5
MDR or RIF resistant	16	7	6	2

B v.a. HIV+



No. at risk

No INH or RIF resistance	220	142	129	15
INH resistant	86	45	37	3
MDR	16	5	4	2

Heemskerk AD et al. Clin Infect Dis 2017; 65:20

Tabelle 2:

Tuberkulose in der Schweiz 2014, Empfindlichkeit gegenüber Rifampicin und Isoniazid

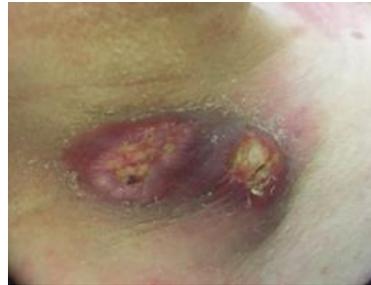
	Rifampicin		Total der Getesteten
	Sensibel	Resistent	
Isoniazid			
Sensibel	391	5	396
Resistent	11	13	24
Total	402	18	420

Therapiemonitoring / -ansprechen

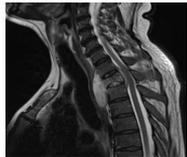
Klinik!



Fistel



paradoxe Reaktion
1-4 Mt. unter Tx.



keine Bildgebung



innert Wochen regredient
CA-125? (Evidenzlevel level X)



Poncet-Disease :
symmetrische Polyarthrits
assoziiert mit aktiver TB

Erkol İnal E, Keskin D, Bodur H. Turk
J Phys Med Rehab 2015;61:77-9

Zusammenfassung

- „Daran denken“
- Anamnese
- Biopsie – Histologie / Kultur
- Therapie nach Klinik
- Evidenzlage eingeschränkt



Danke