Actualització en malalties infeccioses en Atenció Primària. Tuberculosi.

Anna Ferrer Traid

Carmen Ros Bertomeu

Novetats:
Tractament de la infecció tuberculosa latent.
Malaltia Tuberculosa
Covid – TB

Tractament de la infecció tuberculosa latent

- ✓ Qualsevol individu exposat a un malalt amb TB contagiosa i/o en situació de risc i de desenvolupar una tuberculosi per la seva patologia de base.
- ✓ Que tingui un resultat positiu en les proves de cribratge.
- ✓ Que NO tingui malaltia tuberculosa en el moment d'iniciar el tractament (ni clínica ni signes radiològics compatibles).
- ✓ Que estigui disposat a completar el tractament.
- ✓ Que no tingui contraindicacions a la medicació.

Tractament de la infecció tuberculosa latent

Grup A. **Realitzar sempre el cribratge sistemàtic**	• Persones infectades pel VIH. • Adults i nens en contacte amb malalts amb TB pulmonar • Pacients que inicien teràpia biològica • Malalts en teràpia renal substitutiva • Persones que es preparen per rebre transplantaments d'òrgans sòlids o hemàtics • Pacients amb silicosi
Grup B. **Considerar cribratge sistemàtic en funció de l'epidemiologia local i els recursos disponibles**	• Interns a les presons • Personal sanitari • Immigrants procedents de països amb alta carrega de TB • Persones sense sostre • Consumidors de drogues il·legals
Grup C. **No CAL realitzar el cribratge sistemàtic***	• Diabètics • Persones amb consum d'alcohol de risc • Fumadors • Persones amb pes insuficient (IMC????)

Tractament de la infecció tuberculosa latent

Esquema farmacológico	Dosis por kg de peso corporal	Dosis máxima
Isoniacida sola diariamente durante seis o nueve meses	Adultos: 5 mg Niños: 10 mg (amplitud: 7–15 mg)	300 mg
Rifampicina sola diariamente durante tres o cuatro meses	Adultos: 10 mg Niños: 15 mg (amplitud: 10–20 mg)	600 mg
Isoniacida diariamente en combinación con rifampicina durante tres o cuatro meses	Isoniacida: Adultos: 5 mg Niños: 10 mg (amplitud: 7–15 mg) Rifampicina: Adultos: 10 mg Niños: 15 mg (amplitud: 10–20 mg)	Isoniacida:300 mg Rifampicina: 600 mg
Rifapentina semanalmente en combinación con isoniacida durante tres meses (12 dosis)	Mayores de 12 años: 15 mg de isoniacida De 2 a 11 años: 25 mg de isoniacida Rifapentina: 10,0–14,0 kg = 300 mg 14,1–25,0 kg = 450 mg 25,1–32,0 kg = 600 mg 32,1–50,0 kg = 750 mg > 50 kg = 900 mg	Isoniacida: 900 mg Rifapentina: 900 mg

Tractament de la infecció tuberculosa latent

TABLE 3. Recommendations for regimens to treat latent tuberculosis infection

Priority rank*	Regimen	Recommendation (strong or conditional)	Evidence (high, moderate, low, or very low)
Preferred	3 mos isoniazid plus rifapentine given once weekly	Strong	Moderate
Preferred	4 mos rifampin given daily	Strong	Moderate (HIV negative)†
Preferred	3 mos isoniazid plus rifampin given daily	Conditional	Very low (HIV negative)
		Conditional	Low (HIV positive)
Alternative	6 mos isoniazid given daily	Strong§	Moderate (HIV negative)
		Conditional	Moderate (HIV positive)
Alternative	9 mos isoniazid given daily	Conditional	Moderate

Abbreviation: HIV = human immunodeficiency virus.

* *Preferred:* excellent tolerability and efficacy, shorter treatment duration, higher completion rates than longer regimens and therefore higher effectiveness; *alte*
excellent efficacy but concerns regarding longer treatment duration, lower completion rates, and therefore lower effectiveness.

† No evidence reported in HIV-positive persons.

§ Strong recommendation for those persons unable to take a preferred regimen (e.g., due to drug intolerability or drug-drug interactions).

Guidelines for the Treatment of Latent Tuberculosis Infection: Recommendations from the National Tuberculosis

Controllers Association and CDC, 2020 . *Recommendations and Reports* / February 14, 2020 / 69(1);1–11

Tractament de la infecció tuberculosa latent

Clinical Infectious Diseases

MAJOR ARTICLE

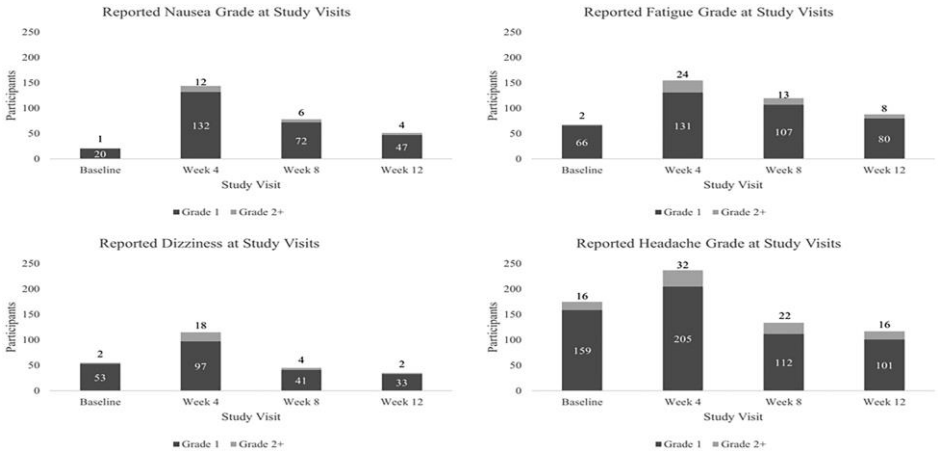
Symptoms and Systemic Drug Reactions in Persons Receiving Weekly Rifapentine Plus Isoniazid (3HP) Treatment for Latent Tuberculosis Infection

Claire Sadowski[1,2,3], Robert Belknap[4], David P. Holland[5], Ruth N. Moro[6,7*], Michael P. Chen[8*], Alicia Wright[9], Joan Pau Millet[10, 11, 12], Joan A. Cayla[12], Nigel A. Scott[2], Andrey Borisov[2], Neel R. Gandhi[1,]

Symptoms and Systemic Drug Reactions in Persons Receiving Weekly Rifapentine Plus Isoniazid (3HP) Treatment for Latent Tuberculosis Infection | Clinical Infectious Diseases | Oxford Academic (oup.com)

Tractament de la infecció tuberculosa latent

Figure 1. Reported grade of commonly reported symptoms at each study visit (includes newly reported and persistent ...



1002 pacients

77% refereixen símptomes:768 pers.

-81% durant les visites de seguiment

-149 no acaben la pauta i expliquen:

- 43% cefalea,
- 40% astenia, nausea 40%,
- 31% debilitat.

-111 pacients tenen Efectes Adversos

Clin Infect Dis, ciad083, https://doi.org/10.1093/cid/ciad083

Tractament de la infecció tuberculosa latent

EA

111 pacients

Supplementary Table 1: Comparison of Systemic Drug Definitions in PREVENT TB and iAdhere

TBTC Study 26 (PREVENT TB) SDR Definition[1]	TBTC Study 33 (iAdhere) SDR Definition[2]	
a) Hypotension (<90 systolic BP), urticaria, angioedema, or conjunctivitis that occurred in relation to study drug; or b.) ≥4 of the following (one of which had to be ≥grade 2: weakness, fatigue, nausea, vomiting, headache, fever, aches, sweats, dizziness, shortness of breath, flushing, or chills	Category 1	Category 2
	Any of the following: hives (grade 2 or higher), bronchospasm/wheezing (grade 3 or higher), angioedema, conjunctivitis/red eyes (grade 2 or higher), or hypotension (as determined by principal investigator	Four or more of the following symptoms reported concurrently (one of which grade 2 or higher): weakness, fatigue, nausea, vomiting, headache, fever, aches (muscle, bone, or joint), sweats (excessive sweating or night sweats), dizziness, shortness of breath, flushing, or chills

[1]Definition applied to reportable adverse events only. Excluded participants that were able to complete treatment.

[2]Definition applied to monthly scheduled treatment evaluations and reportable adverse events.

- Grade 1 Mild AE
- Grade 2 Moderate AE
- Grade 3 Severe AE
- Grade 4 Life-threatening or disabling AE
- Grade 5 Death related to AE

Tractament de la infecció tuberculosa latent

PULMONARY PERSPECTIVE

Latent Tuberculosis: Two Centuries of Confusion

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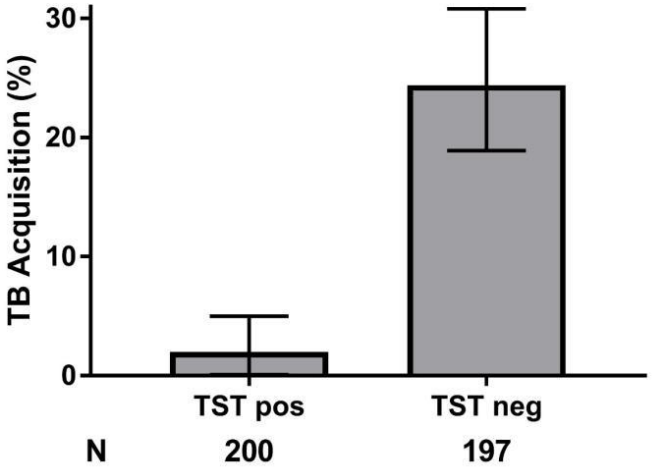
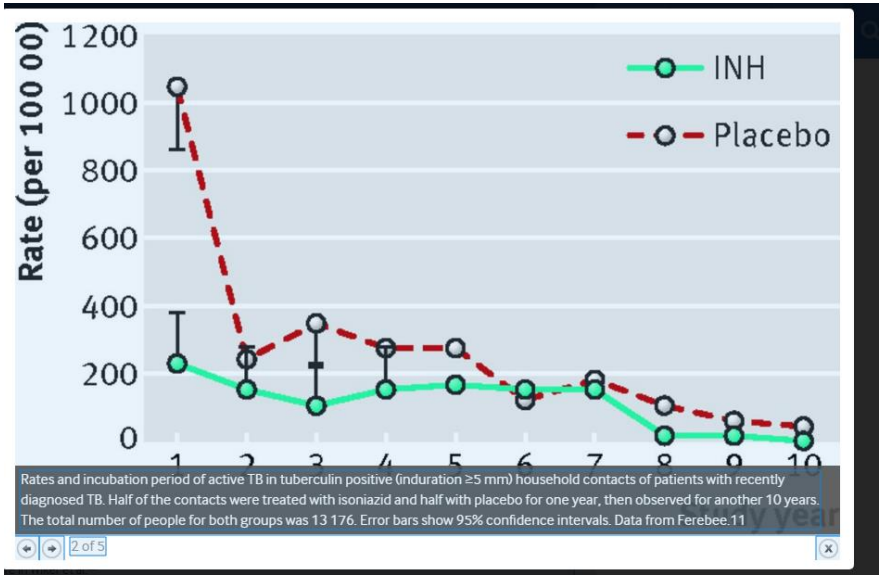
Tractament de la infecció tuberculosa latent

Existeix la infecció latent?

Rates of tuberculosis acquisition in nursing students after three years of exposure to patients with tuberculosis during their training period, by pre-exposure tuberculin skin test result. Error bars show 95% confidence intervals. Data from Heimbeck 28





Tractament de la infecció tuberculosa latent

Suggested simplified terms

Tuberculous reactivity—***Indirect evidence*** of present or past infection with *Mycobacterium tuberculosis* as inferred by a detectable adaptive immune response to *M tuberculosis* antigens (on tuberculin skin test or interferon gamma release assay) in an **asymptomatic person.**

Primary infection—Evidence of new tuberculous infection, obtained with a tuberculin skin test conversion or a new positive interferon gamma release assay, which may be asymptomatic or accompanied by transient fever, erythema nodosum, elevated erythrocyte sedimentation rate or characteristic roentgenographic abnormalities.

Active tuberculosis—Evidence of disease of the lung and/or other organs generally accompanied by a positive culture for *M tuberculosis* and/or roentgenographic findings and/or histopathology consistent with TB.

Malaltia tuberculosa. Tractament.

2 HRZE /4 HR

H: 5 mg/kg/dia
R: 10 mg/kg/dia
Z: 30 mg/kg/dia
E: 15-25 mg/kg/dia

Dosi ÚNICA, DIÀRIA, en dejú Associació a dosi FIXES. Rimstar®
Diari almenys en fase intensiva. Si intermitent en fase de continuació almenys tres cops per setmana.

Malaltia tuberculosa. Tractament.

RESEARCH ARTICLE

Impact of adverse drug reactions on the outcomes of tuberculosis treatment

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Estudi de cohorts prospectiu 2010-2016

550 malalts de TB inicien tt.

35% eren HIV coneguts: 7 moren, cap per reacció adversa al tractament.

78% dels pacients, experimenten algun efecte advers, la majoria lleus...1,64% foren grau IV, cap letal.

Els pacients HIV pateixen més hepatotoxicitat (EA grau III i IV).

Malaltia tuberculosa. Tractament.

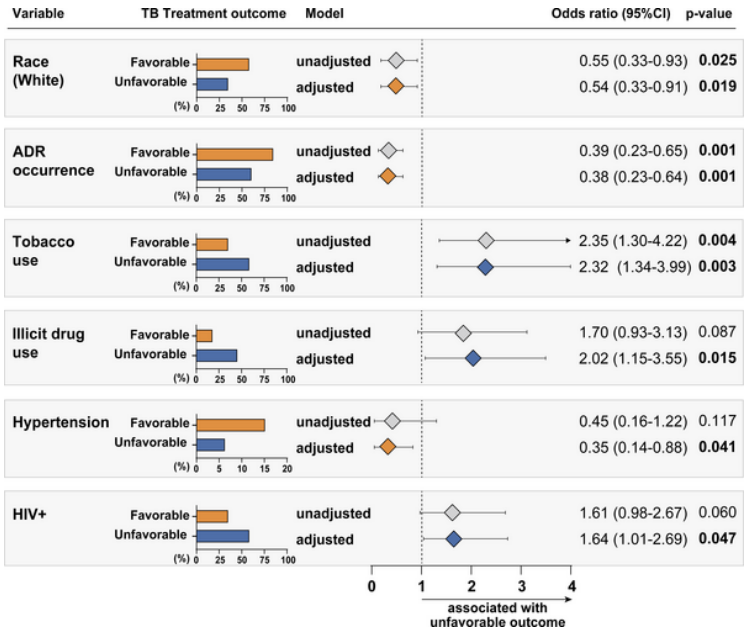
	Tots			
WHO ART classification, n (%):				**0.207**
Central and peripheral nervous system disorders	**45 (6.47)**	**43 (6.85)**	**2 (2.99)**	
Gastro-intestinal system disorder	**151 (21.7)**	**135 (21.5)**	**16 (23.9)**	
Liver and biliary system disorders	**54 (7.77)**	**44 (7.01)**	**10 (14.9)**	
Metabolic and nutritional disorders	**171 (24.6)**	**156 (24.8)**	**15 (22.4)**	
Musculo-skeletal disorders	**63 (9.06)**	**56 (8.92)**	**7 (10.4)**	
Other	**46 (6.62)**	**45 (7.17)**	**1 (1.49)**	
Skin and appendages disorders	**125 (18.0)**	**113 (18.0)**	**12 (17.9)**	

Data are shown as median and interquartile (IQR) range or number and frequency (percentage). Data were compared between the clinical groups using the Mann–Whitney U test (continuous variables) or the Pearson's χ 2 tests (for data on frequency). Bold in p-value indicates $p < 0.05$.

https://doi.org/10.1371/journal.pone.0269765.t002

No acaben el ... 7 pacients

Malaltia tuberculosa. Tractament.



Pitjors resultats: homes, fumadors, Usuaris drogues, pobra escolarització.

HIV: alcoholisme, ús d'ART previ

Eadv sobretot en la fase intensiva i NO suposen abandonament del tt.

Fig 2. Association between clinical characteristics and tuberculosis treatment outcomes among tuberculosis patients.

Sant´Anna FM, Araújo-Pereira M, Schmaltz CAS, Arriaga MB, Andrade BB, et al. (2023) Impact of adverse drug reactions on the outcomes of tuberculosis treatment. PLOS ONE 18(2): e0269765. https://doi.org/10.1371/journal.pone.0269765
https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0269765

Malaltia tuberculosa. Tractament.

Respiration

Thematic Review Series

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New and Repurposed Drugs for the Treatment of Active Tuberculosis: An Update for Clinicians

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Jakko van Ingen[f] Saskia Kuipers[f] Cecile Magis-Escurra[a] Jelmer Raaijmakers[f]
Elin M Svensson[e, g] Martin J Boeree[a]

Malaltia tuberculosa. Tractament.

- Fàrmacs nous, alguns ja s'apliquen en tuberculosi multiresistent (badaquilina, linezolid).
- Fàrmacs "optimitzats": rifampicina a dosi de 20 mg/kg durant dos mesos o 40mg/kg durant dues setmanes és segura i efectiva. AC fase II.
- **Shorter treatment for minimal tuberculosis in children: main findings from the SHINE trial** The Union; 2020. Dosi en nens JA és de 15 mg/kg "The results of the SHINE trial showed that with the revised WHO doses of all drugs a 4-month treat-ment regimen was noninferior to a 6-month treatment regimen in children with regard to efficacy ".

TB-Covid.

Joint Guidance on COVID-19 Vaccination and Osteoporosi Management.

1. Bifosfonats orals → cap canvi
2. Zolendronat → espaiar 7 dies la vacunació i el tractament
3. SERMs → cap canvi
4. Denosumab → espair 4-7 dies
5. Teriparatida → cap canvi
6. Romosozumab → espair 4-7 dies

TB-Covid.

Timing of TST or IGRA and COVID-19 vaccination or post COVID-19 infection. Decem

A TST or IGRA may take place at any time before, after or at the same visit as a COVID-19 vaccination.

Rationale: There is a theoretical risk that mRNA or viral vector vaccines could temporarily affect cell mediated immunity, resulting in false-negative TST or IGRA test results. However, there is no direct evidence for this interaction.1,2 Repeat testing may be considered in some circumstances, **see below**.

A TST or IGRA may take place at any time after a COVID-19 infection.

Rationale: There is limited evidence that severe COVID-19 infection impacts cell-mediated immunity and IGRA results.3,4,5 A COVID-19 infection theoretically has the potential to impact cell-mediated immunity similar to other major viral infections.6 Repeat testing may be considered in some circumstances, **see below**.

A repeat TST or IGRA, at least four weeks post-COVID-19 immunization or four weeks following resolution of severe COVID-19 infection, of individuals with negative TST or IGRA results for whom there is high suspicion of tuberculosis (TB) infection may be considered in order to avoid missing persons with TB infection.

BCCDC Website This communication is posted on the TB Clinical Resources and BCCDC TB Manual webpages.

- www.bccdc.ca/health-professionals/clinical-resources/tuberculosis-guidelines
- www.bccdc.ca/health-professionals/clinical-resources/communicable-disease-control manual/tuberculosis

CAMFiC
societat catalana de medicina familiar i comunitària

Moltes gràcies