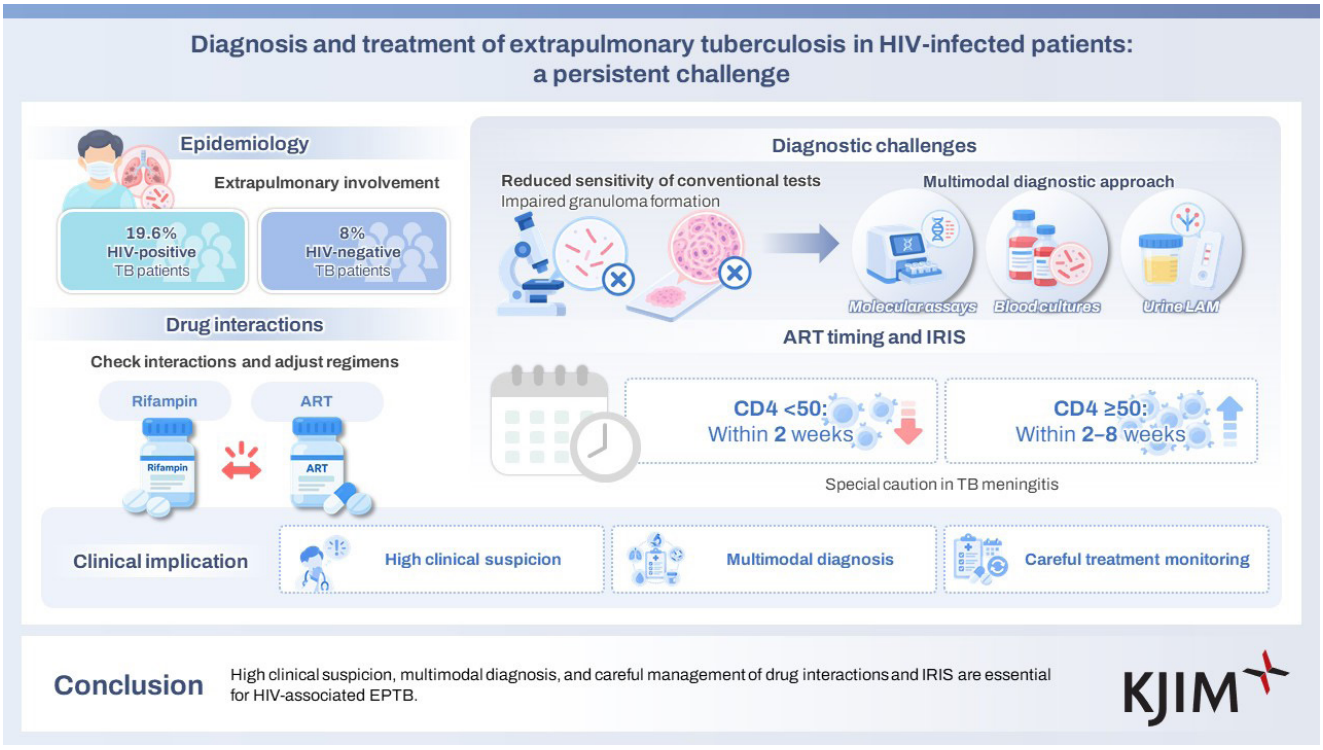
REVIEW

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Diagnosis and treatment of extrapulmonary tuberculosis in HIV-infected patients: a persistent challenge

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This review summarizes the current knowledge regarding the epidemiology, diagnostic challenges, and therapeutic considerations of extrapulmonary tuberculosis (EPTB) in HIV-infected patients. Individuals with advanced HIV infection are particularly vulnerable to EPTB and disseminated disease; extrapulmonary involvement is observed more frequently than in non-HIV-infected populations. Diagnostic evaluation is complicated by the reduced sensitivity of smear microscopy and histopathology due to impaired granuloma formation. Therefore, molecular assays, blood cultures, and urine lipoarabinomannan testing may serve as useful adjuncts. Therapeutic management requires careful attention to drug–drug interactions between rifamycins and antiretroviral agents, as well as the risk of immune reconstitution inflammatory syndrome and timing of initiating antiretroviral therapy. Although many uncertainties remain, maintaining a high index of suspicion and adopting a multifaceted diagnostic and therapeutic approach may improve outcomes in patients with HIV-associated EPTB.

Keywords: HIV/AIDS; Extrapulmonary tuberculosis; Drug-drug interactions; Immune reconstitution inflammatory syndrome

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INTRODUCTION

Extrapulmonary tuberculosis (EPTB) is an opportunistic infection that occurs in individuals with AIDS. This review provides practicing clinicians with a comprehensive understanding of EPTB in the context of HIV infection. Specifically, it addresses the epidemiological characteristics, diagnostic strategies, fundamental principles of treatment, and the critical considerations required during therapeutic management. By synthesizing the current evidence and clinical experience, this study aimed to enhance the capacity of healthcare professionals to recognize, diagnose, and effectively manage EPTB in HIV-infected patients.

EPIDEMIOLOGY

According to the Joint United Nations Programme on HIV/AIDS (UNAIDS), the global incidence of new HIV infections has declined since approximately 1996 [1]. In contrast, data from the Korea Disease Control and Prevention Agency (KDCA) indicate that a reduction in newly confirmed HIV cases in Korea has only been observed since 2020 [2]. However, it is essential to note that the HIV/AIDS statistics reported by the KDCA are based on the number of confirmed cases rather than the total number of infections; therefore, these statistics require cautious interpretation [3-6].

Globally, in 2024, approximately 5.8% of incident tuberculosis cases occurred in people living with HIV [7]. Moreover, tuberculosis is the most common AIDS-defining opportunistic infection worldwide, with approximately 30% of cases presenting with EPTB [8,9]. Patients with advanced immunosuppression frequently develop EPTB, including disseminated tuberculosis, as their CD4 cell counts decline [10-14]. Regarding the most common sites of EPTB, lymphatic involvement is common in both HIV-infected and HIV-uninfected individuals. However, disseminated disease and central nervous system or meningeal involvement occur relatively more frequently in HIV-infected patients, whereas pleural involvement is proportionally more common in patients without HIV infection [10,15,16].

In Korea, tuberculosis accounts for 10–25% of all opportunistic infections, and together with pneumocystis pneumonia and candidiasis, it represents one of the most frequent opportunistic diseases among individuals with HIV [17-20]. According to a study by Lee et al. [21], 19.0% of HIV-infected patients with tuberculosis in Korea had extrapulmonary involvement, a proportion notably higher than the 8.0% observed in non-HIV-infected individuals. However, the study by Lee et al. was relatively small-scale and was conducted among patients enrolled between 2001 and 2005, which limits its applicability in capturing more recent trends. According to nationwide data released by the KDCA, approximately 22% of tuberculosis cases identified between 2020 and 2024 were extrapulmonary [22]. However, this study did not provide separate statistics regarding the HIV infection status, thereby limiting its ability to assess the overall burden of HIV-associated EPTB. Given that the proportion of EPTB is higher among HIV-infected patients than among HIV-uninfected individuals [10,12-14], HIV-associated EPTB can be regarded as a clinical scenario commonly encountered in practice. It should also be noted that pulmonary tuberculosis and EPTB frequently occur simultaneously in HIV-infected patients [23-25].

Nevertheless, with the widespread implementation of antiretroviral therapy (ART), the incidence of opportunistic infections, including tuberculosis, has markedly declined compared to that in previous decades [8,9,26,27].

Opportunistic infections, including tuberculosis, are also associated with failure of ART and therefore warrant careful attention [28,29].

DIAGNOSIS

The diagnostic principles of EPTB in HIV-infected individuals are largely similar to those in non-HIV-infected populations. However, several important points must be considered.

First, the sensitivity of smear microscopy can be reduced in HIV-infected patients (Table 1). Even in non-HIV-infected individuals, EPTB often exhibits a paucibacillary nature; this inherently lowers the sensitivity of smear testing [30]. Additionally, the HIV-associated impairment of cell-mediated immunity leads to the formation of incomplete granulomas. As a result, localized bacillary containment within specific lesions may be limited, particularly in advanced immunosuppression, whereas the risk of systemic dissemination of *Mycobacterium tuberculosis* is increased. Importantly, immunosuppression may lead to an overall increase in the bacillary burden in HIV-infected patients. However, due to impaired granuloma formation associated with immune deficiency, the bacillary burden within specific lesions may paradoxically

be lower. In pulmonary tuberculosis, HIV-infected patients frequently demonstrate a lower bacillary burden than their non-HIV-infected counterparts [31]. Collectively, these observations underscore the need for clinicians to recognize that the sensitivity of smear microscopy in diagnosing EPTB may be further diminished in patients with HIV. Diagnostic strategies should therefore be designed to address these limitations. When acid-fast bacilli are observed on smears, the possibility of a nontuberculous mycobacterial infection should also be considered.

Second, the sensitivity of histopathological diagnosis may be reduced. As noted earlier, in patients with HIV, decreased CD4 T-cell counts and immune dysregulation impair the formation and maintenance of tuberculous granulomas. Consequently, histological specimens often show incomplete or atypical patterns instead of well-structured granulomas. Indeed, lower CD4 counts have been associated with diminished structural integrity of granulomas [32,33]. Therefore, clinicians should be mindful of these limitations when attempting histopathological diagnoses in patients with advanced HIV infection. The absence of the classic granulomatous architecture or caseous necrosis should not be considered sufficient evidence to exclude the possibility of tuberculosis.

Third, molecular diagnostic techniques such as polymerase chain reaction (PCR), Xpert® MTB/RIF (Cepheid, Sunnyvale, CA, USA), Xpert® MTB/RIF Ultra (Cepheid, Sunnyvale, CA, USA), and loop-mediated isothermal amplification should be actively considered. These diagnostic assays can be particularly valuable for assessing specimens such as lymph node aspirates, cerebrospinal fluid (CSF), pleural fluid, ascitic fluid, and tissue biopsies, where the sensitivity of conven-

Table 1. Advantages and disadvantages of diagnostic tests for EPTB

Diagnostic modality	Advantages	Limitations	Clinical implications in HIV infection
AFB smear	Rapid and inexpensive	Low sensitivity in paucibacillary EPTB	Sensitivity may be further reduced due to impaired granuloma formation
Histopathology	Supports diagnosis and helps identify alternative conditions	Granulomas and caseous necrosis may be absent in advanced HIV	Negative histology does not exclude tuberculosis
Xpert® MTB/RIF	Rapid diagnosis and rifampin resistance detection	Sensitivity varies according to specimen type	Particularly useful when smear microscopy and histopathology are inconclusive
PCR	Rapid turnaround	Variable sensitivity	A useful adjunctive test, particularly for tissue specimens
LAMP	A simple and rapid molecular assay	Lower sensitivity than Xpert in some settings	Potential option in resource-limited environments
Mycobacterial culture	Considered the gold standard and allows comprehensive DST	Long turnaround time	Remains essential despite delayed results
Blood culture	Can detect disseminated tuberculosis	Low sensitivity	Particularly useful in advanced HIV infection, especially when disseminated disease is suspected
Urine LAM assay	Rapid, non-invasive point-of-care test	Limited sensitivity in general TB population	Especially useful in patients with advanced HIV infection
ADA measurement	A helpful adjunctive marker in serosal fluids and CSF	Limited specificity	Results should be interpreted with caution in HIV patients
IGRA	Useful for detecting TB infection and widely available	Cannot distinguish active TB from latent TB infection; false-negative and indeterminate results may occur in advanced HIV infection	Should be interpreted as an adjunctive test; positive results do not confirm active EPTB and negative results do not exclude disease

EPTB, extrapulmonary tuberculosis; PCR, polymerase chain reaction; LAMP, loop-mediated isothermal amplification; DST, drug susceptibility test; LAM, lipoarabinomannan; ADA, adenosine deaminase; CSF, cerebrospinal fluid; TB, tuberculosis; IGRA, interferon gamma release assay.

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tional AFB smears is relatively low. However, it is important to note that these tests also have limitations in sensitivity. For example, the sensitivity of Xpert MTB/RIF, which is widely used in Korea, has been reported to be approximately 90% in lymph node aspirates, 70% in CSF, 50% in pleural fluid, and 60% in ascitic fluid. Similarly, PCR assays demonstrate variable sensitivity depending on the specimen type: approximately 40% in lymph node aspirates, 50–100% in CSF, 80–95% in pleural fluid, and 35–75% in ascitic fluid [34-40].

Fourth, drug susceptibility testing should be performed. Although current evidence remains inconclusive, HIV infection may increase the risk of drug-resistant tuberculosis [41,42], and among patients with advanced HIV infection, the likelihood of multidrug-resistant tuberculosis is particularly elevated [43]. Therefore, when managing tuberculosis in HIV-infected individuals, clinicians should proactively employ molecular-based drug susceptibility assays such as Xpert® MTB/RIF (Cepheid, Sunnyvale, CA, USA), Xpert® MTB/RIF Ultra (Cepheid, Sunnyvale, CA, USA), BD MAX™ MDR-TB (Becton, Dickinson and Company, Franklin Lakes, NJ, USA), and Anyplex™ II (Seegene Inc., Seoul, Republic of Korea), in addition to conventional culture-based susceptibility testing.

Fifth, blood cultures can be particularly useful in patients with advanced immunosuppression (e.g., CD4 < 100 cells/μL) and suspected disseminated diseases. Due to HIV-associated immunosuppression, the likelihood of isolating *M. tuberculosis* from the blood of HIV-infected patients with tuberculosis is relatively high. In some cases, the organism may be identified exclusively in blood cultures while remaining undetected in specimens from other sites [44,45]. Moreover, repeated blood cultures have been reported to increase diagnostic yield [46].

Recently, a method was developed to detect the lipoarabinomannan (LAM) antigen in *M. tuberculosis* urine for the rapid diagnosis of tuberculosis. Although urinary LAM assay demonstrates high specificity, its sensitivity remains limited [47,48]. However, in patients with advanced HIV infection (CD4 ≤ 100 cells/mm³), the sensitivity of the assay is relatively higher, particularly for next-generation tests, allowing it to serve as a useful adjunct for rapid diagnosis [49,50]. Nevertheless, although some data suggest potential diagnostic utility for HIV-associated EPTB, direct evidence supporting this application remains limited.

As an adjunct to the diagnosis of EPTB, measurement of adenosine deaminase (ADA) levels in the CSF, pleural fluid, ascitic fluid, synovial fluid, or pericardial fluid may provide supportive information [51-56]. However, ADA levels can also be elevated in certain rheumatological diseases, malignancies such as lymphoma, and some cases of empyema. Moreover, ADA elevation may be less pronounced in HIV-infected patients; therefore, clinicians should interpret these results with caution [57-59].

Although the interferon gamma release assay (IGRA) test may serve as an adjunctive tool in the evaluation of EPTB, its limited sensitivity and specificity, particularly in immunocompromised patients, precludes its use as a standalone diagnostic test. Thus, IGRA results must always be interpreted in conjunction with clinical findings [60-62].

TREATMENT

The principles and treatment regimens for EPTB in HIV-infected patients are generally similar to those for HIV-negative individuals and HIV-positive patients with pulmonary tuberculosis. In patients with HIV-TB co-infection, two critical issues require special attention: (1) potential drug–drug interactions (DDIs) between antiretroviral agents and anti-tuberculosis medications, and (2) complications related to immune reconstitution inflammatory syndrome (IRIS).

DDIs are particularly problematic with rifampin. Although rifampin is an essential component of tuberculosis treatment, it is a potent inducer of several drug-metabolizing enzymes, including CYP3A4, CYP2C9, CYP2C19, and UGT. Additionally, rifampin affects drug transporters such as organic anion transporting polypeptides and P-glycoprotein (P-gp). These properties confer high potential for clinically significant drug interactions.

Rifampin does not exhibit clinically significant interactions with nucleoside reverse transcriptase inhibitors (NRTIs). However, rifampin induces P-gp, which reduces the efficacy of tenofovir alafenamide (TAF). However, co-administration of TAF with rifampin has been shown to maintain adequate intracellular concentrations of the active metabolite, tenofovir diphosphate [63]. Therefore, although TAF may be used concomitantly with rifampin when clinically necessary, careful monitoring is required. For similar reasons, TAF may also be administered to patients receiving rifabutin when clinically necessary, albeit with close monitoring [64].

Other agents, including bictegravir, cobicistat-boosted

elvitegravir, cabotegravir (both oral and injectable formulations), rilpivirine (both oral and injectable formulations), doravirine, etravirine, protease inhibitors, and lenacapavir, should not be coadministered with rifampin. When rifampin

Table 2. Interactions between rifamycins and antiretroviral agents — referencing the 2021 Korean Society for AIDS guidelines and the current US Panel on Antiretroviral Guidelines for Adults and Adolescents [58,59]

Rifamycin	Antiretroviral agents	Effect on antiretroviral agents and/or concomitant antimycobacterial medication	Dosing recommendations and clinical comments
Rifampin	All PIs	↓ PI concentration by > 75%	Contraindicated. Consider rifabutin if a rifamycin is indicated.
	BIC	BIC AUC ↓ 75%	Contraindicated
	CAB PO	CAB PO AUC ↓ 59% and C_{min} ↓ 50%	Contraindicated
	CAB IM	CAB IM ↓ expected	Contraindicated
	DTG	Rifampin with DTG 50 mg twice daily (Compared to DTG 50 mg twice daily alone): DTG AUC ↓ 54% and C_{min} ↓ 72% Rifampin with DTG 50 mg twice daily (Compared to DTG 50 mg once daily alone): DTG AUC ↑ 33% and C_{min} ↑ 22%	Patients without suspected or documented INSTI resistance mutations: use DTG 50 mg twice daily. In patients with suspected or documented INSTI resistance mutations: consider an alternative to rifampin, such as rifabutin.
	EVG/c	Significant ↓ EVG and cobicistat expected	Contraindicated
	RAL	RAL 400 mg: RAL AUC ↓ 40% and C_{min} ↓ 61% Rifampin with RAL 800 mg twice daily (Compared to RAL 400 mg twice daily alone): RAL AUC ↑ 27% and C_{min} ↓ 53%	Use RAL 800 mg twice daily instead of 400 mg twice daily.
	TAF	TAF is a P-glycoprotein substrate, its plasma concentrations may be reduced by rifamycin. TAF with rifampin (Compared with TAF alone): TAF AUC ↓ 55% TFV-DP AUC ↓ 36%	Use with caution Intracellular TFV-DP levels are higher when TAF is co-administered with rifampin compared to when TDF is administered alone, but clinical outcomes have not been studied.
	DOR	DOR AUC ↓ 88%	Contraindicated
	EFV	EFV AUC ↓ 26%	Maintain EFV dose at 600 mg daily and monitor for virologic response.
	ETR	Significant ↓ ETR possible	Do not co-administer
	RPV PO	RPV AUC ↓ 80%	Contraindicated
	RPV IM	↓ RPV possible	Contraindicated
	LEN	LEN AUC ↓ 84%	Contraindicated
Rifabutin	ATV/r	Compared with Rifabutin (300 mg once daily) Alone, Rifabutin (150 mg once daily) Plus ATV/r: Rifabutin AUC ↑ 110% and metabolite AUC ↑ 2,101%	Recommended dose is rifabutin 150 mg once daily.
	DRV/r	Compared with Rifabutin (300 mg once daily) Alone, Rifabutin (150 mg every other day) Plus DRV/r: ↔ rifabutin AUC and metabolite AUC ↑ 881%	Recommended dose is rifabutin 150 mg once daily.
	ATV/c	↑ rifabutin expected ↓ COBI expected	Do not co-administer
	DRV/c	↑ rifabutin expected ↓ COBI expected	Do not co-administer
	BIC	Rifabutin 300 mg once daily: BIC AUC ↓ 38% and C_{min} ↓ 56%	Do not co-administer

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Table 2. Continued

Rifamycin	Antiretroviral agents	Effect on antiretroviral agents and/or concomitant antimycobacterial medication	Dosing recommendations and clinical comments
	EVG/c	Rifabutin 150 mg every other day with EVG/c once daily (Compared to Rifabutin 300 mg once daily alone): ↔ rifabutin AUC 25-O-desacetyl-rifabutin AUC ↑ 625% EVG AUC ↓ 21% and C_{min} ↓ 67%	Do not co-administer
	TAF	↓ TAF possible	Use with caution
	DOR	DOR AUC ↓ 50%	Increase DOR dose to 100 mg twice daily.
	EFV	Rifabutin ↓ 38%	Increase rifabutin dose to 450–600 mg per day.
	ETR	↔ rifabutin and metabolite AUC ETR AUC ↓ 37%	Do not co-administer ETR plus PI/r with rifabutin Use rifabutin 300 mg once daily if ETR is administered without PI/r.
	RPV PO	Rifabutin Plus RPV 50 mg PO Once Daily Compared to RPV 25 mg Once Daily Alone: ↔ RPV AUC and C_{min}	Increase RPV dose to 50 mg PO once daily during coadministration.
	RPV IM	↓ RPV expected	Contraindicated
	LEN	↓ LEN expected	Do not co-administer

PI, protease inhibitor; BIC, bictegravir; AUC, area under the curve; CAB, cabotegravir; C_{min}, minimum concentration; DTG, dolutegravir; INSTI, integrase strand transfer inhibitor; EVG/c, elvitegravir/cobicistat; RAL, raltegravir; TAF, tenofovir alafenamide; TFV-DP, tenofovir-diphosphate; DOR, doravirine; EFV, efavirenz; ETR, etravirine; RPV, rilpivirine; LEN, lenacapavir; ATV/r, ritonavir-boosted atazanavir; DRV/r, ritonavir-boosted darunavir; ATV/c, cobicistat-boosted atazanavir; COBI, cobicistat; DRV/c, cobicistat-boosted darunavir.

is used, dose adjustments are required; dolutegravir should be increased to 50 mg twice daily and raltegravir to 800 mg twice daily (Table 2) [65,66].

Information on DDIs involving antiretroviral agents continues to evolve as new agents are introduced and additional data become available. For the most up-to-date guidance, clinicians can refer to the "HIV Drug Interactions" website maintained by the University of Liverpool, as well as the corresponding smartphone application (HIV iChart) [67].

In patients not receiving ART at the time of tuberculosis diagnosis, initiating ART concurrently with anti-tuberculosis therapy or within the first few weeks of treatment for tuberculosis increases the risk of IRIS [68]. Conversely, deferring ART until tuberculosis therapy is completed is not recommended as this approach has been associated with increased mortality [69].

Patients with EPTB or disseminated tuberculosis are known to be at relatively high risk of developing paradoxical tuberculosis-associated IRIS or paradoxical reactions following the initiation of ART [70-72]. This phenomenon is presumed to result from the combination of a high mycobacterial antigen burden before treatment and the widespread distribution of lesions, which together trigger excessive inflammatory responses during immune recovery. Lymph node tuberculosis may present with worsening lymphadenopathy, abscess formation, or fistula development, whereas central nervous system tuberculosis can lead to increased intracranial pressure, tuberculoma enlargement, and neurological deterioration, necessitating special caution.

When the peripheral blood CD4 T-cell count is < 50 cells/mm³, initiation of ART within 2 weeks after starting tuberculosis treatment is recommended. For patients with CD4 T-cell counts ≥ 50 cells/mm³, definitive data regarding the optimal timing of ART initiation are lacking. Nevertheless, given the overall benefit of early ART initiation in individuals with HIV infection, current guidelines recommend starting ART within 2–8 weeks of commencing anti-tuberculosis therapy in such patients [65].

Tuberculous meningitis is a condition in which IRIS poses a serious concern and requires careful management. Initiating ART concurrently with anti-tuberculosis therapy in patients with tuberculous meningitis has been associated with increased mortality [73]. Therefore, to mitigate the risk of life-threatening IRIS, ART should be initiated only after

clinical improvement of meningitis has been achieved with anti-tuberculosis therapy, and after at least 2 weeks of anti-tuberculosis treatment [65]. If profound immunosuppression necessitates earlier initiation of ART, close monitoring is essential [74].

IRIS typically develops within the first 3 months of ART initiation. The risk is particularly high in patients with low CD4 T-cell counts, a high mycobacterial burden, or when ART is started shortly after the initiation of anti-tuberculosis therapy [70,71,75,76]. Mild IRIS is often managed symptomatically with nonsteroidal anti-inflammatory drugs and careful observation. In contrast, severe IRIS may require treatment with corticosteroids (such as prednisolone, 1 mg/kg daily) with gradual tapering as clinical improvement occurs [72,77].

In patients with advanced HIV infection, opportunistic infections may present with absent or mild symptoms, owing to profound immunosuppression. Following the initiation of ART, restoration of immune function can lead to the emergence of clinical manifestations of previously unrecognized opportunistic infections, a phenomenon referred to as unmasking IRIS. Therefore, when new signs suggestive of infection appear within the first few months of ART, the possibility of unmasking IRIS should be considered.

Another important consideration is the possibility of drug-resistant tuberculosis. IRIS is characterized by clinical deterioration despite the administration of appropriate therapy; however, a lack of improvement may also occur when first-line anti-tuberculosis agents are ineffective owing to drug resistance. In practice, distinguishing between these two scenarios is challenging. Therefore, in HIV-infected patients with tuberculosis co-infection, drug susceptibility testing using both molecular and conventional methods should be performed proactively.

CONCLUSIONS

EPTB is a major complication in HIV-infected patients. In this population, establishing a diagnosis of EPTB can be challenging because the histopathological findings or smear results for *M. tuberculosis* may be inconclusive. Therefore, clinicians should maintain a high index of suspicion for EPTB, even in the absence of definitive diagnostic findings. When managing these patients, careful attention must be directed toward potential DDIs, the risk of IRIS, and the possibility of drug-resistant tuberculosis.

REFERENCES

1. UNAIDS. Global AIDS Update 2025 [Internet]. Geneva: UNAIDS, c2026 [cited 2025 July 10]. Available from: https://www.unaids.org/en/UNAIDS-global-AIDS-update-2025.
2. Korea Disease Control and Prevention Agency. Annual Report on the Notified HIV/AIDS in Korea, 2024. Cheongju: Korea Disease Control and Prevention Agency, 2025.
3. Lee E, Kim J, Lee JY, Bang JH. Estimation of the number of HIV infections and time to diagnosis in the Korea. J Korean Med Sci 2020;35:e41.
4. Lee M, Park WB, Kim ES, et al. Possibility of decreasing incidence of human immunodeficiency virus infection in Korea. Infect Chemother 2023;55:451-459.
5. Bhattacharya S. Response to possibility of decreasing incidence of human immunodeficiency virus infection in Korea. Infect Chemother 2024;56:92-93.
6. Bang J. Reply: Response to possibility of decreasing incidence of human immunodeficiency virus infection in Korea. Infect Chemother 2024;56:94-95.
7. World Health Organization. Global tuberculosis report 2025 [Internet]. Geneva: World Health Organization, c2025 [cited 2025 November 12]. Available from: https://www.who.int/teams/global-programme-on-tuberculosis-and-lung-health/tb-reports/global-tuberculosis-report-2025.
8. Low A, Gavriilidis G, Larke N, et al. Incidence of opportunistic infections and the impact of antiretroviral therapy among HIV-infected adults in low- and middle-income countries: a systematic review and meta-analysis. Clin Infect Dis 2016;62:1595-1603.
9. Buchacz K, Lau B, Jing Y, et al. Incidence of AIDS-defining opportunistic infections in a multicohort analysis of HIV-infected persons in the United States and Canada, 2000-2010. J Infect Dis 2016;214:862-872.
10. Aceves-Sánchez B, Rajme-López S, Martínez-Guerra BA, et al. Distinct clinical features of extrapulmonary and disseminated tuberculosis in HIV- and non-HIV-associated immunosuppression: a retrospective cohort study. Open Forum Infect Dis 2025;12:ofaf239.
11. Rugină S, Dumitru IM, Resul G, Cernat RC, Petcu AE. Disseminated tuberculosis in HIV-infected patients from the Regional HIV/AIDS Center Constanţa, Romania. Germs 2014;4:16-21.
12. Kruijshaar ME, Abubakar I. Increase in extrapulmonary

https://doi.org/10.3904/kjim.2026.196

tuberculosis in England and Wales 1999-2006. Thorax 2009;64:1090-1095.
13. Harshana A, Goyal M, Chako A, Mahajan R. Prevalence of extrapulmonary tuberculosis among people living with HIV/AIDS in Southeast Asia: a systematic review and meta-analysis. Monaldi Arch Chest Dis 2025;95.
14. Shivakoti R, Sharma D, Mamoon G, Pham K. Association of HIV infection with extrapulmonary tuberculosis: a systematic review. Infection 2017;45:11-21.
15. Leeds IL, Magee MJ, Kurbatova EV, et al. Site of extrapulmonary tuberculosis is associated with HIV infection. Clin Infect Dis 2012;55:75-81.
16. Naing C, Mak JW, Maung M, Wong SF, Kassim AI. Meta-analysis: the association between HIV infection and extrapulmonary tuberculosis. Lung 2013;191:27-34.
17. Kim YJ, Woo JH, Kim MJ, et al. Opportunistic diseases among HIV-infected patients: a multicenter-nationwide Korean HIV/AIDS cohort study, 2006 to 2013. Korean J Intern Med 2016;31:953-960.
18. Choi Y, Choi BY, Kim SM, et al. Epidemiological characteristics of HIV infected Korean: Korea HIV/AIDS Cohort Study. Epidemiol Health 2019;41:e2019037.
19. Oh MD, Park SW, Kim HB, et al. Spectrum of opportunistic infections and malignancies in patients with human immunodeficiency virus infection in South Korea. Clin Infect Dis 1999;29:1524-1528.
20. Kim JM, Cho GJ, Hong SK, et al. Epidemiology and clinical features of HIV infection/AIDS in Korea. Yonsei Med J 2003;44:363-370.
21. Lee CH, Hwang JY, Oh DK, et al. The burden and characteristics of tuberculosis/human immunodeficiency virus (TB/HIV) in South Korea: a study from a population database and a survey. BMC Infect Dis 2010;10:66.
22. Lee H, Kim J, Kim J, et al. Tuberculosis notification status in the Republic of Korea, 2024. Public Health Wkly Rep 2025;18(Suppl 11):S6-S22.
23. Barnes PF, Bloch AB, Davidson PT, Snider DE Jr. Tuberculosis in patients with human immunodeficiency virus infection. N Engl J Med 1991;324:1644-1650.
24. Peto HM, Pratt RH, Harrington TA, LoBue PA, Armstrong LR. Epidemiology of extrapulmonary tuberculosis in the United States, 1993-2006. Clin Infect Dis 2009;49:1350-1357.
25. Shafer RW, Kim DS, Weiss JP, Quale JM. Extrapulmonary tuberculosis in patients with human immunodeficiency virus infection. Medicine (Baltimore) 1991;70:384-397.
26. Buchacz K, Baker RK, Palella FJ Jr, et al. AIDS-defining opportunistic illnesses in US patients, 1994-2007: a cohort study. AIDS 2010;24:1549-1559.
27. Schwarcz L, Chen MJ, Vittinghoff E, Hsu L, Schwarcz S. Declining incidence of AIDS-defining opportunistic illnesses: results from 16 years of population-based AIDS surveillance. AIDS 2013;27:597-605.
28. Tilman EES, Damas E, Choi JY. Factors associated with viral load non-suppression among people living with HIV on antiretroviral therapy in Dili, Timor-Leste. Infect Chemother 2025;57:230-237.
29. Gupta-Wright A, Wood R, Bekker LG, Lawn SD. Temporal association between incident tuberculosis and poor virological outcomes in a South African antiretroviral treatment service. J Acquir Immune Defic Syndr 2013;64:261-270.
30. Chakravorty S, Sen MK, Tyagi JS. Diagnosis of extrapulmonary tuberculosis by smear, culture, and PCR using universal sample processing technology. J Clin Microbiol 2005;43:4357-4362.
31. Mugusi F, Villamor E, Urassa W, Saathoff E, Bosch RJ, Fawzi WW. HIV co-infection, CD4 cell counts and clinical correlates of bacillary density in pulmonary tuberculosis. Int J Tuberc Lung Dis 2006;10:663-669.
32. Diedrich CR, O'Hern J, Wilkinson RJ. HIV-1 and the *Mycobacterium tuberculosis* granuloma: a systematic review and meta-analysis. Tuberculosis (Edinb) 2016;98:62-76.
33. Luo G, Yan B, Shen Y. The impact and mechanism of HIV infection on tuberculous granuloma formation. AIDS 2025;39:1095-1105.
34. Suthar C, Rana T, Singh UB, et al. MRNA and DNA PCR tests in cutaneous tuberculosis. Indian J Dermatol Venereol Leprol 2013;79:65-69.
35. Cegielski JP, Devlin BH, Morris AJ, et al. Comparison of PCR, culture, and histopathology for diagnosis of tuberculous pericarditis. J Clin Microbiol 1997;35:3254-3257.
36. Hallur V, Sharma M, Sethi S, et al. Development and evaluation of multiplex PCR in rapid diagnosis of abdominal tuberculosis. Diagn Microbiol Infect Dis 2013;76:51-55.
37. Derese Y, Hailu E, Assefa T, et al. Comparison of PCR with standard culture of fine needle aspiration samples in the diagnosis of tuberculosis lymphadenitis. J Infect Dev Ctries 2012;6:53-57.
38. Rock RB, Olin M, Baker CA, Molitor TW, Peterson PK. Central nervous system tuberculosis: pathogenesis and clinical aspects. Clin Microbiol Rev 2008;21:243-261.
39. Berwal A, Chawla K, Vishwanath S, Shenoy VP. Role of multiplex polymerase chain reaction in diagnosing tubercular meningitis. J Lab Physicians 2017;9:145-147.

40. Yu G, Shen Y, Zhong F, Ye B, Yang J, Chen G. Diagnostic accuracy of the loop-mediated isothermal amplification assay for extrapulmonary tuberculosis: a meta-analysis. PLoS One 2018;13:e0199290.
41. Song Y, Jin Q, Qiu J, Ye D. A systematic review and meta-analysis on the correlation between HIV infection and multidrug-resistance tuberculosis. Heliyon 2023;9:e21956.
42. Lee CM, Lee E, Bang JH, et al. Prevalence of multidrug-resistant tuberculosis in HIV/tuberculosis co-infected patients. Infect Chemother 2021;53:792-795.
43. Joh JS, Hong HC, Jeong IA, et al. Proportion of multidrug-resistant tuberculosis in human immunodeficiency virus/*Mycobacterium tuberculosis* co-infected patients in Korea. J Korean Med Sci 2012;27:1143-1146.
44. Archibald LK, McDonald LC, Rheanpumikankit S, et al. Fever and human immunodeficiency virus infection as sentinels for emerging mycobacterial and fungal bloodstream infections in hospitalized patients >/=15 years old, Bangkok. J Infect Dis 1999;180:87-92.
45. Nguyen DN, Nguyen TV, Dao TT, et al. One year experience using mycobacterial blood cultures to diagnose tuberculosis in patients with prolonged fever in Vietnam. J Infect Dev Ctries 2014;8:1620-1624.
46. Barr DA, Kerkhoff AD, Schutz C, et al. HIV-associated *Mycobacterium tuberculosis* bloodstream infection is underdiagnosed by single blood culture. J Clin Microbiol 2018;56:e01914-17.
47. Drain PK, Losina E, Coleman SM, et al. Diagnostic accuracy of a point-of-care urine test for tuberculosis screening among newly-diagnosed HIV-infected adults: a prospective, clinic-based study. BMC Infect Dis 2014;14:110.
48. Broger T, Nicol MP, Sigal GB, et al. Diagnostic accuracy of 3 urine lipoarabinomannan tuberculosis assays in HIV-negative outpatients. J Clin Invest 2020;130:5756-5764.
49. Nakiyingi L, Moodley VM, Manabe YC, et al. Diagnostic accuracy of a rapid urine lipoarabinomannan test for tuberculosis in HIV-infected adults. J Acquir Immune Defic Syndr 2014;66:270-279.
50. World Health Organization. Lateral flow urine lipoarabinomannan assay (LF-LAM) for the diagnosis of active tuberculosis in people living with HIV, 2019 Update [Internet]. Geneva: World Health Organization, c2019 [cited 2019 October 28]. Available from: https://www.who.int/publications/i/item/9789241550604.
51. Ye Q, Yan W. Adenosine deaminase from the cerebrospinal fluid for the diagnosis of tuberculous meningitis: a meta-analysis. Trop Med Int Health 2023;28:175-185.
52. Liang QL, Shi HZ, Wang K, Qin SM, Qin XJ. Diagnostic accuracy of adenosine deaminase in tuberculous pleurisy: a meta-analysis. Respir Med 2008;102:744-754.
53. Foocharoen C, Sarntipipattana C, Foocharoen T, et al. Synovial fluid adenosine deaminase activity to diagnose tuberculous septic arthritis. Southeast Asian J Trop Med Public Health 2011;42:331-337.
54. Mahajan M, Prasad ML, Kumar P, et al. An updated systematic review and meta-analysis for the diagnostic test accuracy of ascitic fluid adenosine deaminase in tuberculous peritonitis. Infect Chemother 2023;55:264-277.
55. Carlos Cortés-Quiroz J, Ena J, Antonio Bernal J, Rosas J. Performance of adenosine deaminase activity in sinovial fluid for the early diagnosis of tuberculous arthritis: a meta analysis. Proceedings of the ACR Convergence 2022; 2022 Nov 10-14; Philadelphia, PA. Wiley, 2022:1598-1600.
56. Chau E, Sarkarati M, Spellberg B. Adenosine deaminase diagnostic testing in pericardial fluid. JAMA 2019;322:163-164.
57. Riantawan P, Chaowalit P, Wongsangiem M, Rojanaraweewong P. Diagnostic value of pleural fluid adenosine deaminase in tuberculous pleuritis with reference to HIV coinfection and a Bayesian analysis. Chest 1999;116:97-103.
58. Corral I, Quereda C, Navas E, et al. Adenosine deaminase activity in cerebrospinal fluid of HIV-infected patients: limited value for diagnosis of tuberculous meningitis. Eur J Clin Microbiol Infect Dis 2004;23:471-476.
59. Ghosh GC, Sharma B, Gupta BB. CSF ADA determination in early diagnosis of Tuberculous meningitis in HIV-infected patients. Scientifica (Cairo) 2016;2016:5820823.
60. Santin M, Muñoz L, Rigau D. Interferon-γ release assays for the diagnosis of tuberculosis and tuberculosis infection in HIV-infected adults: a systematic review and meta-analysis. PLoS One 2012;7:e32482.
61. Ma Y, Xu Y, Cao X, Chen X, Zhong Y. Diagnostic value of interferon-γ release assay in HIV-infected individuals complicated with active tuberculosis: a systematic review and meta-analysis. Epidemiol Infect 2021;149:e204.
62. Ling DI, Pai M, Davids V, et al. Are interferon-γ release assays useful for diagnosing active tuberculosis in a high-burden setting? Eur Respir J 2011;38:649-656.
63. Cerrone M, Alfarisi O, Neary M, et al. Rifampicin effect on intracellular and plasma pharmacokinetics of tenofovir alafenamide. J Antimicrob Chemother 2019;74:1670-1678.
64. Martin TCS, Hill LA, Tang ME, Balcombe SM. Tenofovir alafenamide and rifabutin co-administration does not lead to loss of HIV-1 suppression: a retrospective observational study.

https://doi.org/10.3904/kjim.2026.196

Int J Infect Dis 2020;100:470-472.
65. Ambrosioni J, Levi LI, Alagaratnam J, et al. Major revision version 13.0 of the European AIDS Clinical Society guidelines 2025. HIV Med 2026;27:18-32.
66. Korean Society for AIDS. Summary of 2021 Clinical Guidelines for the Diagnosis and Treatment of HIV/AIDS in HIV-infected Koreans. Infect Chemother 2021;53:592-616.
67. University of Liverpool. HIV drug interactions [Internet]. Liverpool: University of Liverpool, c2026 [visited 2026 April 13]. Available from: https://www.hiv-druginteractions.org/checker.
68. French MA. Disorders of immune reconstitution in patients with HIV infection responding to antiretroviral therapy. Curr HIV/AIDS Rep 2007;4:16-21.
69. Abdool Karim SS, Naidoo K, Grobler A, et al. Timing of initiation of antiretroviral drugs during tuberculosis therapy. N Engl J Med 2010;362:697-706.
70. Manosuthi W, Kiertiburanakul S, Phoorisri T, Sungkanuparph S. Immune reconstitution inflammatory syndrome of tuberculosis among HIV-infected patients receiving antituberculous and antiretroviral therapy. J Infect 2006;53:357-363.
71. Colebunders R, John L, Huyst V, Kambugu A, Scano F, Lynen L. Tuberculosis immune reconstitution inflammatory syndrome in countries with limited resources. Int J Tuberc Lung Dis 2006;10:946-953.
72. Lawn SD, Myer L, Bekker LG, Wood R. Tuberculosis-associated immune reconstitution disease: incidence, risk factors and impact in an antiretroviral treatment service in South Africa. AIDS 2007;21:335-341.
73. Török ME, Yen NT, Chau TT, et al. Timing of initiation of antiretroviral therapy in human immunodeficiency virus (HIV)--associated tuberculous meningitis. Clin Infect Dis 2011;52:1374-1383.
74. European AIDS Clinical Society. OI overview & when to start ART [Internet]. Brussels: European AIDS Clinical Society, c2025 [cited 2025 October 6]. Available from: https://eacs.sanfordguide.com/en/eacs-hiv/eacs-section4/ois/opportunistic-infections.
75. Shriner KA, Mathisen GE, Goetz MB. Comparison of mycobacterial lymphadenitis among persons infected with human immunodeficiency virus and seronegative controls. Clin Infect Dis 1992;15:601-605.
76. Michailidis C, Pozniak AL, Mandalia S, Basnayake S, Nelson MR, Gazzard BG. Clinical characteristics of IRIS syndrome in patients with HIV and tuberculosis. Antivir Ther 2005;10:417-422.
77. Navas E, Martín-Dávila P, Moreno L, et al. Paradoxical reactions of tuberculosis in patients with the acquired immunodeficiency syndrome who are treated with highly active antiretroviral therapy. Arch Intern Med 2002;162:97-99.

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