# Special Article

# Immune Reconstitution Inflammatory Syndrome in HIV-Infected Patients with Tuberculosis

Sasisopin Kiertiburanakul MD, MHS*

** Department of Medicine, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand*

*Tuberculosis (TB) remains an important problem in patients with human immunodeficiency virus (HIV) infection and acquired immune deficiency syndrome (AIDS). Concomitant administration therapy of both TB and HIV is fraught with difficulties. Despite the fact that the use of highly active antiretroviral therapy (HAART) led to significant improve quality of life and decrease morbidity including mortality-associated to HIV/AIDS, adverse drug effects lead to interruptions in both HIV and TB therapy. In addition, an important problem when HAART is initiated in patients with TB is the possibility of developing immune reconstitution inflammatory syndrome (IRIS). A six-month regimen consisting of isoniazid, rifampicin, pyrazinamide, and ethambutal for two months followed by isoniazid and rifampicin for four months is a standard regimen for the treatment of known or presumed drug-susceptible TB disease. The following strategy may minimize the risk of IRIS. Patients with CD4 cell counts < 100 cells/mm$^3$, efavirenz-based HAART regimen is recommended and should be initiated as soon as the patients can tolerate TB treatment. Patients with CD4 cell counts 100-350 cells/mm$^3$, HAART should be started at two months after TB treatment initiation. HAART should be deferred with closed follow-up of CD4 cell counts if patients have CD4 cell counts > 350 cells/mm$^3$.*

***Keyword:*** *AIDS, HIV, Tuberculosis, Immune reconstitution inflammatory syndrome, Immune reconstitution syndrome, Acquired immunodeficiency syndrome*

***J Med Assoc Thai 2010; 93 (2): 257-64***
***Full text. e-Journal:*** *http://www.mat.or.th/journal*

Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (*M. tuberculosis*) infection, remains an important problem in patients with human immunodeficiency virus (HIV) infection and acquired immune deficiency syndrome (AIDS). It is one of the most common opportunistic diseases among HIV/AIDS patients particularly in developing countries.

HIV and *M. tuberculosis* are two intracellular pathogens that interact at the population, clinical, and cellular levels[1]. The association between HIV infection and TB is complex and bi-directional. HIV-infected patients are at a markedly increased risk for primary or reactivation TB and for the second episode of TB from exogenous re-infection. Selective depletion of CD4 cells and reduced T lymphocytes response in advanced HIV-infected patients contribute to their susceptibility to develop TB[2]. TB itself may cause reversible CD4 cell depletion, possibly by the sequestration of CD4 cells in sites of active disease[3]. In addition, *M. tuberculosis* infection produces pro-inflammatory cytokines that up-regulate intracellular retroviral replication[4].

*Correspondence to: Kiertiburanakul S, Department of Medicine, Faculty of Medicine, Ramathibodi Hospital, 270 Rama VI Rd, Bangkok 10400, Thailand. Phone: 0-2201-1922, Fax: 0-2201-2107. E-mail: rasal@mahidol.ac.th*

**Clinical manifestation and diagnosis of tuberculosis**

The clinical presentation of TB varies widely. Even in HIV-infected patients, pulmonary TB is still the most common presentation. Typical symptoms and signs of pulmonary TB include cough with or without fever, night sweats, weight loss, and pulmonary infiltrate on chest radiography. However, unusual manifestations of pulmonary TB in patients with advanced stages of HIV infection had been reported and are attributed to difference in alterations of cell-mediated immunity[5]. Patients who are co-infected with HIV/TB and have CD4 cell counts $\geq$ 200 cells/mm$^3$, chest radiographic abnormalities include upper lobe infiltrate and cavitation, similar to classical reactivation-type disease in HIV-uninfected patients. Whereas

AIDS patients who have CD4 cell counts < 200 cells/$mm^3$ sometimes present with atypical radiographic patterns such as hilar lymphadenopathy or lower lung zone infiltrates which were secondary to depressed cellular immunity[5-7]. As the level of immunosuppression increases in HIV-infected patients, extrapulmonary involvement and disseminated disease were more common[7].

Timely diagnosis of TB is importance because of the patient's benefit and the moderate respiratory contagiousness of *M. tuberculosis*. Pulmonary TB is diagnosed clinically, by chest radiograph together with sputum smear for acid fast bacilli and is subsequently confirmed by the positive culture for *M. tuberculosis*. However, diagnosis of TB in some HIV-infected patients is quite difficult because of atypical signs and symptoms and a paucity of findings in chest radiography. When TB develops in HIV-infected patients, the prognosis is often poor. The degree of immunosuppression is the most important predictor of survival in HIV-infected patients with TB. Early mortality may be related to advanced TB, but deaths during the continuation phase of therapy are usually due to other AIDS-related conditions[8]. History of prior opportunistic infections and low CD4 cell counts are also found to be associated with increased mortality[9].

**Treatment of tuberculosis in HIV/AIDS patients**

Comprehensive treatment of TB requires a complex interaction between clinical care and public health. Recommendations for the treatment of TB in individuals with HIV infection are, with a few exceptions, the same as those for patients without HIV infection[8,10]. A six-month regimen consisting of isoniazid, rifampicin, pyrazinamide, and ethambutal for two months followed by isoniazid and rifampicin for four months is a standard regimen for the disease caused by organisms that are known or presumed to be susceptible to the first-line agents. This standard short-course regimens have shown similar early response rates in both HIV-positive and HIV-negative patients and long-term TB relapse rates in both groups are the same[11,12]. However, patients with slow or suboptimal response, miliary infection, skeletal TB, prolongation of the continuation phase to seven months should be strongly considered[8,13]. The longer regimens may have provided more effective treatment, reduced relapse rate, or may prevent re-infection, but this strategy does not improve the survival[14].

Rifabutin can be used as an alternative to rifampicin and can be administered with protease inhibitors (PIs) or non-nucleoside reverse transcriptase inhibitors (NNRTIs) with appropriate dose adjustments. Because variations in the degree of enzyme induction or inhibition can occur among patients, the use of therapeutic drug monitoring for levels of rifabutin, PIs, or NNRTIs might help to adjust dosing for individual patients[15].

**Antiretroviral therapy in HIV/AIDS patients with tuberculosis**

Most patients with TB have relatively advanced HIV disease and, thus, antiretroviral therapy is indicated. Since the introduction of HAART, the incidence of AIDS-defining events sustains decreased, and the quality of life of the patients are improved by appropriate diagnosis and treatment[16,17]. However, adverse drug effects in HIV/TB co-infected patients can lead to interruptions in both therapy[18]. Concomitant administration therapy of both HIV and TB is fraught with difficulties. Many issues should be considered before initiating HAART in HIV/TB co-infected patients such as drug toxicities (both anti-retroviral and anti-tuberculosis agents), drug-drug interaction, high pill burden, and immune reconstitution inflammatory syndrome (IRIS). Efavirenz-based HAART regimen is recommended for Thai patients with HIV/TB co-infection[19]. NVP at a normal dose of 400 mg/day can be used effectively with rifampicin[19]. If a patient cannot tolerate either EFV- or NVP-containing HAART and has very low CD4 cell counts, one should consider using non-rifampicin containing anti-TB treatment and PI-containing HAART[19].

**Immune reconstitution inflammatory syndrome (IRIS)**

An important problem when HAART is initiated in patients with TB is the possibility of developing IRIS. Other terms are paradoxical reactions, immune restoration disease, or immune restoration inflammatory syndrome. Nevertheless, the term IRIS is mostly used in HIV-infected patients who initiated HAART[20]. The condition has been described more frequently in patients receiving HAART (35-36%) than in others who have not received HAART (0-2%)[21].

Studies reported that the incidence of TB IRIS varies between 7.6% and 43.2%[21-28]. Scaling up of HAART in many developing countries where are endemic areas of TB diseases might increase the incidence of IRIS. The following risk factors for TB IRIS have been identified such as starting HAART within the first two months of TB treatment[21,22] and

extrapulmonary TB or disseminated disease[23-25]. Other potential risk factors include low CD4 cell counts at the initiation of HAART[24], good immunological response[21,24,26], and virological response after HAART initiation[21,27]. Selected studies of IRIS after antiretroviral therapy initiation among antiretroviral naive HIV-infected patients who had TB are summarized in Table 1.

The pathogenesis of IRIS in general and TB IRIS in particular remains poorly understood. It is generally thought to be the restoration of the immune responses to antigens (viable or not) producing exuberant inflammatory reactions. The increased immunological response is enhanced not only by TB treatment, but potentially also by the reduction in HIV RNA due to HAART, leading to a partial immune reconstitution. On the basis of current knowledge, it is tempting to hypothesize that the immunological basis of IRIS is a HAART-induced rapid clonal expansion and redistribution of *M. tuberculosis*-specific memory T cells[29], which drives a deregulated immune activation[30] and a cytokine storm[31]. The load of antigen could be responsible for the over-vigorous inflammatory response of a recovering immune system. The risk of IRIS may be related to the bacillary burden and it may therefore be observed more often in patients with very low CD4 cell counts because such patients may have a higher bacillary burden[32].

The interval between the start of HAART and develop IRIS varies across the studies and range from < 1 week to 15 months[22-28]. However, IRIS usually develops within first 4-8 weeks after HAART initiation. Clinical presentations of IRIS characterize by the transient worsening or appearance of new symptoms and signs such as fever, increasing chest radiographic infiltrate, peripheral and mediastinal lymphadenopathy, or changes of radiographic manifestations, either at a pre-existing site or the development of a new lesion. The recognition of IRIS is sometimes impaired and under recognized because of the wide spectrum of the clinical presentations, clinical manifestations depend on the site of TB, and no diagnostic test to confirm the diagnosis. Thus, diagnostic criteria of IRIS have been proposed[27].

IRIS is self-limited and generally last for 10-40 days. If not severe, these reactions should be managed with continuation of drugs for TB and HIV and with non-steroidal anti-inflammatory agents. However, some reactions are severe and may require a short course of glucocorticoids[21,33]. Differential diagnosis includes TB treatment failure, anti-tuberculosis drug resistance, nonadherence with therapy, drug fever, and development of conditions that do not related to neither TB nor HIV.

**Timing of HAART initiation**

Few studies have addressed either the practical difficulties of prescribing these complex regimens simultaneously. To reduce the incidence of TB IRIS, it has been suggested to reduce the organism load sufficiently prior to the start of HAART by respecting a lengthy enough interval between the start of anti-TB treatment and HAART. However, the ideal interval between the start of anti-tuberculosis treatment and the introduction of HAART has not yet known. Physicians try and balance the risk of HIV progression and HIV-related mortality against the risk of having to discontinue therapies because of toxicities or drug-drug interactions including risk of IRIS occurrence. Furthermore, overlapping toxicity profiles and IRIS may result in the interruption or alteration of TB and HIV regimens with potential subsequent virological failure.

The indication to start antiretroviral therapy in patients with HIV/TB co-infection depends on several factors but the most important ones are clinical status and CD4 cell counts. Of practical importance, timing of initiation of HAART is a predictive factor of the development of IRIS. The simultaneous initiation of treatment of both conditions has been associated with a high rate of side effects and IRIS. However, the main reasons of starting HAART within a few weeks of initiating of TB treatment are reduce the risk of the development of opportunistic infections including other HIV-related complications[34] and may improve survival[10,35]. Some authors recommend starting HAART early for patients with CD4 cell counts < 100 cells/mm$^3$[18]. The WHO guidelines also recommend for HAART initiation during two weeks and two months in patients with CD4 cell count < 200 cells/mm$^3$ or have extrapulmonary TB[36]. Most of IRIS events occur within the first two months after initiating HAART. The strategy of initiate HAART after two months of TB therapy, until the continuation phase of TB therapy, might be appropriate. This strategy may increase adherence, minimize overlap toxicities, and minimize risk of IRIS including morbidity and mortality related to IRIS. Some physicians delay HAART for $\geq$ 2 months to minimize the risk of IRIS, drug adverse effects, as after two months the TB pill burden and number of TB drugs will be reduced. Other reasons for delay HAART are drug-drug interactions, toxicities, non-

**Table 1.** Studies of IRIS (≥ 10 cases) after antiretroviral therapy initiation among adult naive HIV patients who co-infected with TB (listed by number of patients)

| Author | Country | Type of study | Prevalence or incidence | Risk factors | Timing of IRIS after start HAART | Mortality rate |
|---|---|---|---|---|---|---|
| Manosuthi W, et al[22] | Thailand | Retrospective cohort | 21/167 (12.6%) | Extrapulmonary TB | Median (IQR) 32 (14-115) days; 71.4% within first 2 months | 9.5% |
| Kumarasamy N, et al[38] | India | Retrospective cohort | 11/144 (7.6%) or 15.2 cases per 100 patient-years | No associated factors were found | Median (range) 42 (10–89) days | 0% |
| Serra FC, et al[24] | Brazil | Retrospective cohort | 10/84 (12%) or 25.93 per 100 person-years | HIV-naive patients with lymph node enlargement | Mean (SD) | 0% |
| Michailidis C, et al[23] | United Kingdom | Retrospective cohort | 14/55 (25.5%) | Lower baseline CD4 cell count, disseminated TB, and increased CD4 cell count after HAART | Median (range) 2.53 (0.53-14.97) month | 0% |
| Breen RAM, et al[21] | United Kingdom | Retrospective cohort | 14/50 (28%) | Started HAART within 6 weeks and disseminated TB | Median 11 days | 0% |
| Breton G, et al[25] | France | Retrospective cohort | 16/37 (43.2%) | Increased CD4 cell percentage, increased CD4/CD8 cells ratio, and disseminated TB | Median (range) 12 (2–114) days | 0% |
| Narita M, et al[26] | United States | Prospective | 12/33 (36%) | Larger drop in HIV RNA after start HAART | Mean (SD) 15 (11)days | 0% |

ART, antiretroviral therapy; HAART, highly active antiretroviral therapy; IQR, interquatile range, IRIS, immune resonstitution inflammatory syndrome; OIs, opportunistic infections; TB, tuberculosis; SD; standard deviation

adherence to complicated treatment regimens, and drug malabsorption[37]. Patients with CD4 cell counts < 100 cells/mm$^3$, efavirenz-based HAART should be started as soon patients can tolerate TB treatment, usually after 2 weeks of TB treatment[10]. Patients with CD4 cell counts 100-350 cells mm$^3$, HAART should be started at two months after TB treatment. However, patients with CD4 cell counts > 350 cells/mm$^3$, HAART should be deferred with closed CD4 cell counts monitoring. Practical approach to HAART initiation in antiretroviral naive HIV/TB co-infection is shown in Fig. 1.

In summary, timing of HAART initiation in these patients depends on several factors, especially patients' clinical status and CD4 cell counts, with regard to treatment naive patients with TB/HIV co-infection. Appropriate timing of HAART initiation with suitable regimens of both HIV and TB treatment can minimize the risk of IRIS. However, the further researches are needed such as the development of a case definition, studies to determine risk factors for IRIS, and studies of strategies to prevent IRIS including the optimal timing to initiate HAART.

**Acknowledgement**

The author would like to thank Associate Professor Somnuek Sungkanuparph and Joshua

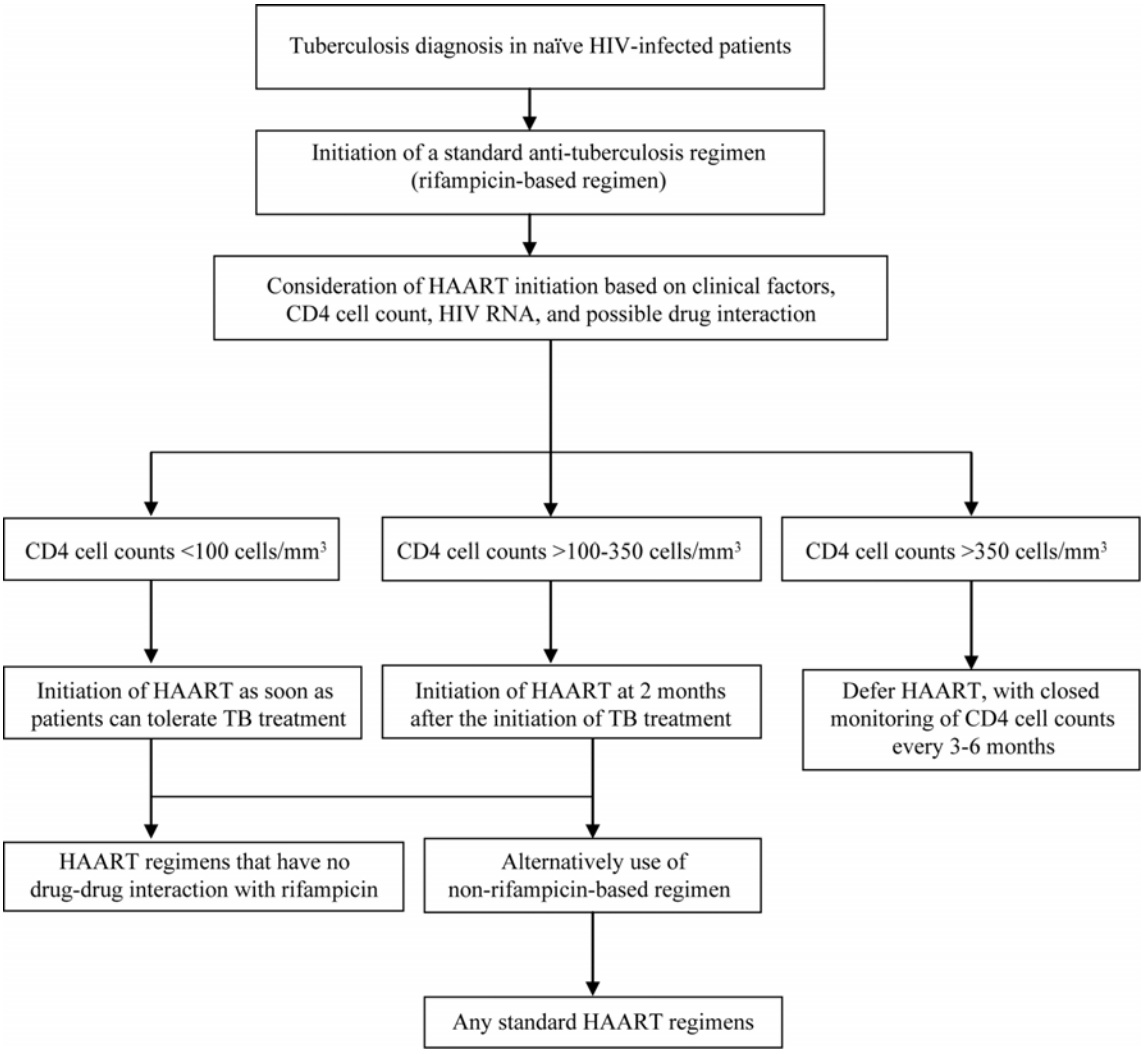


**Fig. 1** Practical approach to initiate antiretroviral therapy in naive HIV-infected patients receiving the treatment of tuberculosis (modified from reference 10, 19 and 36)

Josephs for comment and review the manuscript, and treatment of IRIS.

**References**


1. Centers for Disease Control and Prevention. Prevention and treatment of tuberculosis among patients infected with human immunodeficiency virus: principles of therapy and revised recommendations. MMWR Recomm Rep 1998; 47: 1-58.
2. Havlir DV, Barnes PF. Tuberculosis in patients with human immunodeficiency virus infection. N Engl J Med 1999; 340: 367-73.
3. Turett GS, Telzak EE. Normalization of CD4+ T-lymphocyte depletion in patients without HIV infection treated for tuberculosis. Chest 1994; 105: 1335-7.
4. Del Amo J, Malin AS, Pozniak A, De Cock KM. Does tuberculosis accelerate the progression of HIV disease? Evidence from basic science and epidemiology. AIDS 1999; 13: 1151-8.
5. Keiper MD, Beumont M, Elshami A, Langlotz CP, Miller WT, Jr. CD4 T lymphocyte count and the radiographic presentation of pulmonary tuberculosis. A study of the relationship between these factors in patients with human immunodeficiency virus infection. Chest 1995; 107: 74-80.
6. Diagnostic Standards and Classification of Tuberculosis in Adults and Children. Am J Respir Crit Care Med 2000; 161: 1376-95.
7. Lee MP, Chan JW, Ng KK, Li PC. Clinical manifestations of tuberculosis in HIV-infected patients. Respirology 2000; 5: 423-6.
8. Treatment of tuberculosis. MMWR Recomm Rep 2003; 52: 1-77.
9. Whalen C, Horsburgh CR Jr, Hom D, Lahart C, Simberkoff M, Ellner J. Site of disease and opportunistic infection predict survival in HIV-associated tuberculosis. AIDS 1997; 11: 455-60.
10. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents [database on the Internet]. November 3, 2008 [cited 2009 Jun 6]. Available from: http://aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf
11. Kassim S, Sassan-Morokro M, Ackah A, Abouya LY, Digbeu H, Yesso G, et al. Two-year follow-up of persons with HIV-1- and HIV-2-associated pulmonary tuberculosis treated with short-course chemotherapy in West Africa. AIDS 1995; 9: 1185-91.
12. Sterling TR, Alwood K, Gachuhi R, Coggin W, Blazes D, Bishai WR, et al. Relapse rates after short-course (6-month) treatment of tuberculosis in HIV-infected and uninfected persons. AIDS 1999; 13: 1899-904.
13. Horsburgh CR Jr, Feldman S, Ridzon R. Practice guidelines for the treatment of tuberculosis. Clin Infect Dis 2000; 31: 633-9.
14. Perriens JH, St Louis ME, Mukadi YB, Brown C, Prignot J, Pouthier F, et al. Pulmonary tuberculosis in HIV-infected patients in Zaire. A controlled trial of treatment for either 6 or 12 months. N Engl J Med 1995; 332: 779-84.
15. Kaplan JE, Benson C, Holmes KH, Brooks JT, Pau A, Masur H. Guidelines for prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from CDC, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. MMWR Recomm Rep 2009; 58: 1-207.
16. Kirk O, Gatell JM, Mocroft A, Pedersen C, Proenca R, Brettle RP, et al. Infections with Mycobacterium tuberculosis and Mycobacterium avium among HIV-infected patients after the introduction of highly active antiretroviral therapy. EuroSIDA Study Group JD. Am J Respir Crit Care Med 2000; 162: 865-72.
17. Palella FJ Jr, Delaney KM, Moorman AC, Loveless MO, Fuhrer J, Satten GA, et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV Outpatient Study Investigators. N Engl J Med 1998; 338: 853-60.
18. Dean GL, Edwards SG, Ives NJ, Matthews G, Fox EF, Navaratne L, et al. Treatment of tuberculosis in HIV-infected persons in the era of highly active antiretroviral therapy. AIDS 2002; 16: 75-83.
19. Sungkanuparph S, Anekthananon T, Hiransuthikul N, Bowonwatanuwong C, Supparatpinyo K, Mootsikapun P, et al. Guidelines for antiretroviral therapy in HIV-1 infected adults and adolescents: the recommendations of the Thai AIDS Society (TAS) 2008. J Med Assoc Thai 2008; 91: 1925-35.
20. 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: 946-53.
21. Navas E, Martin-Davila P, Moreno L, Pintado V, Casado JL, Fortun J, 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: 97-9.
22. Breen RA, Smith CJ, Bettinson H, Dart S, Bannister B, Johnson MA, et al. Paradoxical reactions during tuberculosis treatment in patients with and without HIV co-infection. Thorax 2004; 59: 704-7.
23. 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: 357-63.
24. 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: 417-22.
25. Serra FC, Hadad D, Orofino RL, Marinho F, Lourenco C, Morgado M, et al.Immune reconstitution syndrome in patients treated for HIV and tuberculosis in Rio de Janeiro. Braz J Infect Dis 2007; 11: 462-5.
26. Breton G, Duval X, Estellat C, Poaletti X, Bonnet D, Mvondo MD, et al. Determinants of immune reconstitution inflammatory syndrome in HIV type 1-infected patients with tuberculosis after initiation of antiretroviral therapy. Clin Infect Dis 2004; 39: 1709-12.
27. Narita M, Ashkin D, Hollender ES, Pitchenik AE. Paradoxical worsening of tuberculosis following antiretroviral therapy in patients with AIDS. Am J Respir Crit Care Med 1998; 158: 157-61.
28. Kumarasamy N, Chaguturu S, Mayer KH, Solomon S, Yepthomi HT, Balakrishnan P, et al. Incidence of immune reconstitution syndrome in HIV/tuberculosis-coinfected patients after initiation of generic antiretroviral therapy in India. J Acquir Immune Defic Syndr 2004; 37: 1574-6.
29. Autran B, Carcelain G, Li TS, Blanc C, Mathez D, Tubiana R, et al. Positive effects of combined antiretroviral therapy on CD4+ T cell homeostasis and function in advanced HIV disease. Science 1997; 277: 112-6.
30. Lawn SD, Bekker LG, Miller RF. Immune reconstitution disease associated with mycobacterial infections in HIV-infected individuals receiving antiretrovirals. Lancet Infect Dis 2005; 5: 361-73.
31. Bourgarit A, Carcelain G, Martinez V, Lascoux C, Delcey V, Gicquel B, et al. Explosion of tuberculin-specific Th1-responses induces immune restoration syndrome in tuberculosis and HIV co-infected patients. AIDS 2006; 20: F1-7.
32. Jones BE, Young SM, Antoniskis D, Davidson PT, Kramer F, Barnes PF. Relationship of the manifestations of tuberculosis to CD4 cell counts in patients with human immunodeficiency virus infection. Am Rev Respir Dis 1993; 148: 1292-7.
33. Wendel KA, Alwood KS, Gachuhi R, Chaisson RE, Bishai WR, Sterling TR. Paradoxical worsening of tuberculosis in HIV-infected persons. Chest 2001; 120: 193-7.
34. Pozniak A. Mycobacterial diseases and HIV. J HIV Ther 2002; 7: 13-6.
35. Schiffer JT, Sterling TR. Timing of antiretroviral therapy initiation in tuberculosis patients with AIDS: a decision analysis. J Acquir Immune Defic Syndr 2007; 44: 229-34.
36. Management of Tuberculosis and HIV Co-infection. Clinical protocol for the WHO European Region [database on the Internet]. Update July 18, 2008 [cited 2007 Dec 4]. Available From: http://www.euro.who.int/Document/SHA/Chap_4_TB_4_web.pdf.
37. Burman WJ, Jones BE. Treatment of HIV-related tuberculosis in the era of effective antiretroviral therapy. Am J Respir Crit Care Med 2001; 164: 7-12.

## *กลุ่มอาการปฏิกิริยาการฟื้นตัวของภูมิคุ้มกันในผู้ติดเชื้อเอชไอวีผู้ใหญ่ที่กำลังได้รับการรักษาวัณโรค*

***ศศิโสภิณ เกียรติบูรณกุล***

*วัณโรคยังเป็นปัญหาสำคัญของผู้ติดเชื้อเอชไอวีและผู้ป่วยเอดส์ การรักษาทั้งสองภาวะนี้พร้อมกันมีความยากลำบากทั้ง ๆ ที่ในความเป็นจริงแล้วการรักษาด้วยยาต้านไวรัสอย่างน้อยสามชนิดร่วมกันที่เรียกว่า ฮาร์ท นำไปสู่การมีคุณภาพชีวิตดีขึ้น และการลดลงของอัตราทุพพลภาพ รวมไปถึงการลดลงของอัตราการเสียชีวิตที่เกี่ยวข้องกับการติดเชื้อเอชไอวีหรือเอดส์ อย่างไรก็ตามอาจจะพบผลข้างเคียงจากยา ซึ่งนำไปสู่การหยุดการรักษาทั้งการติดเชื้อเอชไอวีและวัณโรค นอกจากนี้ปัญหาที่สำคัญของการเริ่มยาต้านไวรัส ในผู้ติดเชื้อเอชไอวีที่มีการติดเชื้อวัณโรคร่วมด้วยคือ ภาวะกลุ่มอาการอักเสบ และภูมิกลับ สูตรยาต้านวัณโรคมาตรฐานประกอบด้วย ไอโซไนอะซิด ไรแฟมพิซิน ไพราซินามายด์ และอีแธมบูทอล นาน 2 เดือน ต่อด้วยไอโซไนอะซิดและไรแฟมพิซินนาน 4 เดือน ในกรณีที่ไม่มีการดื้อยาต้านวัณโรค มาตรการดังต่อไปนี้อาจช่วยลดความเสี่ยง ต่อการเกิดภาวะกลุ่มอาการอักเสบ และภูมิกลับ ผู้ติดเชื้อที่มีซีดีสี่น้อยกว่า 100 เซลล์/ลบ.มม. ควรเริ่มสูตรยาต้านไวรัสที่ประกอบด้วยเอฟาไวเรนเร็วที่สุด เมื่อผู้ติดเชื้อทนต่อการรักษาด้วยยาต้านวัณโรคได้ ผู้ติดเชื้อที่มีซีดีสี่ 100-350 เซลล์/ลบ.มม. ควรเริ่มยาต้านไวรัสที่ 2 เดือนหลังจากเริ่มการรักษาวัณโรค ควรชะลอการเริ่มยาต้านไวรัส ในผู้ติดเชื้อที่มีซีดีสี่ มากกว่า 350 เซลล์/ลบ.มม. ร่วมกับมีการติดตามระดับซีดีสี่อย่างใกล้ชิด*