INT J TUBERC LUNG DIS 10(12):1331–1336

OFFICIAL STATEMENT

Guidance for National Tuberculosis Programmes on the management of tuberculosis in children
CHAPTER 3 IN THE SERIES

Chapter 3: Management of TB in the HIV-infected child

Stop TB Partnership Childhood TB Subgroup

World Health Organization, Geneva, Switzerland

SUMMARY

Human immunodeficiency virus (HIV) infected children are at risk of a range of lung diseases related to HIV infection, including tuberculosis (TB). As in non-HIV-infected children, the presence of three or more of the following four features strongly suggests the diagnosis of TB: 1) chronic symptoms suggestive of TB; 2) physical changes highly suggestive of TB; 3) a positive tuberculin skin test; 4) a chest radiograph suggestive of TB. Every effort must be made to expedite the process of making the diagnosis, as TB may be rapidly progressive in HIV-infected children. As many children who present with chronic symptoms suggestive of TB may not have been tested for HIV infection, in high HIV prevalence settings (and in all settings where HIV is suspected in a child) children and their families should be offered HIV counselling and testing as part of a full TB work-up. Most current international guidelines recommend that TB in HIV-infected children, as in non-HIV-infected children, should be treated with a 6-month regimen containing rifampicin throughout. All HIV-infected children with advanced immunosuppression, including many with TB, should receive cotrimoxazole prophylaxis. Although the optimal timing for the initiation of antiretroviral treatment (ART) during TB treatment is not known, the decision to initiate ART should take into consideration the degree of immune suppression and the child's progress during TB treatment.

KEY WORDS: tuberculosis; management; treatment; HIV; children

DIAGNOSIS

Human immunodeficiency virus (HIV) infected children are at risk of tuberculosis (TB). However, these children often have other lung disease related to their HIV infection, including *Pneumocystis jirovecii* (PCP, formerly *Pneumocystis carinii* pneumonia), lymphoid interstitial pneumonitis (LIP) and viral and bacterial pneumonias. Table 1 shows the differential diagnosis of respiratory illness in HIV-infected children. The final common pathway of multiple lung infections is bronchiectasis and chronic lung disease for many HIV-infected children. Most of these diagnoses must be made clinically, often resulting in confusion about which opportunistic infections are causing a child's illness. Children with HIV may also have multiple and concurrent opportunistic infections, so the presence of one diagnosis does not exclude other causes of illness. There is therefore a risk both that TB will be overdiagnosed in children (and they will be treated unnecessarily) and also that TB may be missed, and therefore an opportunity to treat an HIV-infected child for a curable disease will also be missed. LIP is the most difficult condition to distinguish from TB, due to radiological similarities. Bacteriologically confirmed TB can occur in children with an underlying diagnosis of LIP, bronchiectasis or any other lung infection.

The approach to diagnosing TB in HIV-infected children is essentially the same as for non-HIV-infected children, i.e., the presence of three or more of the following should strongly suggest the diagnosis of TB:

1 A positive tuberculin skin test (defined as ⩾5 mm if HIV-infected)
2 Chronic symptoms suggestive of TB
3 Physical changes highly suggestive of TB
4 Chest radiograph suggestive of TB.

Adapted from: World Health Organization. Guidance for national tuberculosis programmes on the management of tuberculosis in children. WHO/HTM/TB/2006.371. Geneva, Switzerland: WHO, 2006.
Previous chapters in this series **Editorial:** R. P. Gie. Childhood tuberculosis: mainstreamed into National Tuberculosis Programs. Int J Tuberc Lung Dis 2006; 10(10): 1067. **Chapter 1:** Introduction and diagnosis of tuberculosis in children. Int J Tuberc Lung Dis 2006; 10(10): 1091–1097. **Chapter 2:** Anti-tuberculosis treatment in children. Int J Tuberc Lung Dis 2006; 10(11): 1205–1211.

Correspondence to: Dermot Maher, Stop TB Department, World Health Organization, Geneva, Switzerland. Tel: (+41) 22 791 2655. Fax: (+41) 22 791 4268. e-mail: maherd@who.int

[A version in French of this article is available from the Editorial Office in Paris and from the Union website www.iuatld.org]

Table 1 Differential diagnosis of respiratory illness in HIV-infected children

Illness	Causative agent(s)	Clinical features	Age ranges	Radiological features	Diagnostic technique	Treatment*
Tuberculosis	*Mycobacterium tuberculosis*	Subacute onset,† persistent and unremitting cough, weight loss, fevers	All ages	Lymph node enlargement, infiltration, primary complex	Smear microscopy, chest radiograph, tuberculin skin test, history of contact (other tests where available)	TB medications
Bacterial pneumonia	*S. pneumoniae, H. influenzae, Salmonella spp., S. aureus, K. pneumoniae, E. coli*	Rapid onset, high fever, elevated leukocyte count on full blood count (FBC)	All ages	Bronchopneumonia	Sputum culture not useful in children; blood cultures	Broad spectrum antibiotics (including coverage of gram-negative organisms)
Viral pneumonia	Respiratory syncytial virus, adenovirus, influenza, cytomegalovirus, Epstein-Barr virus	Air trapping with wheezing	Infants >older children	Diffuse interstitial infiltrates, hyperinflation	Clinical	Supportive care
Lymphoid interstitial pneumonitis (LIP)	Immune response to Epstein-Barr virus	Slow onset, cough, mild hypoxia, associated with generalised lymphadenopathy, parotid enlargement, finger clubbing	Older children	Diffuse reticulonodular pattern, lymph node enlargement	Clinical	Antiretroviral therapy, corticosteroids in some cases
PCP	*Pneumocystis jirovecii*	Abrupt severe pneumonia, severe hypoxia	Infants	Diffuse interstitial infiltration, hyperinflation	Clinical	Cotrimoxazole, corticosteroids for moderate to severe cases
Bronchiectasis	Recurrent respiratory infections (usually complication of LIP or TB)	Slow onset, cough productive of copious sputum (purulent, occasionally blood-stained), halitosis, finger clubbing	Older children	Honeycombing, usually of lower lobes	Chest X-ray	Physiotherapy, treatment of superinfections, rarely lung resection (lobectomy)

* Note that in addition to the improvement in many of these conditions with the specific treatment indicated, their severity and frequency usually improve with antiretroviral therapy.
† Onset can occasionally be acute, especially in immunocompromised infants.
HIV = human immunodeficiency virus; TB = tuberculosis; LIP = lymphoid interstitial pneumonitis.

Many children who present with chronic symptoms suggestive of TB may not have been tested for HIV infection. In high HIV prevalence settings (and in all settings where HIV is suspected in a child), children and their families should be offered HIV counselling and testing as part of a full TB work-up.

MANAGEMENT

Treatment of tuberculosis

Most current international guidelines recommend that TB in HIV-infected children should be treated with a 6-month regimen, as in non-HIV-infected children.[1] However, some national guidelines recommend that HIV-infected children with pulmonary TB be treated for 9 months and those with extra-pulmonary TB be treated for 12 months.[2] Where possible, children should be treated with rifampicin for the entire treatment duration, as higher relapse rates among HIV-infected adults have been found when ethambutol is used in the continuation phase. Most children with TB, including those who are HIV-infected, have a good response to the 6-month regimen. Possible causes for failure, such as non-compliance with therapy, poor drug absorption, drug resistance and alternative diagnoses should be investigated in children who are not improving on TB treatment. A study is in progress to determine the effectiveness of a 9-month compared to a 6-month treatment course.

As in children not infected with HIV, a trial of TB treatment is not generally recommended in HIV-infected children. A decision to treat any child for TB should be carefully considered, and once this is done the child should receive a full course of treatment.

Cotrimoxazole prophylaxis

Daily cotrimoxazole prophylaxis (20 mg trimethoprim [TMP] + 100 mg sulfamethoxazole [SMX] if aged $<$6 months; 40 mg TMP + 200 mg SMX if $<$5 years; 80 mg TMP + 400 mg SMX if $\geqslant$5 years) prolongs survival in HIV-infected children and reduces the incidence of respiratory infections and hospitalisation. No studies have been done in HIV-infected children with TB, but a number of studies of cotrimoxazole prophylaxis in HIV-infected adults with TB have shown clear and consistent benefit. The World Health Organization (WHO) and the Joint United Nations Programme on HIV/AIDS (UNAIDS) have recently revised provisional recommendations for HIV-infected children.[3] All HIV-infected children with advanced immunosuppression should be started on cotrimoxazole. There is no consensus yet on whether children on antiretroviral therapy (ART) who have immune reconstitution can safely stop cotrimoxazole.

Antiretroviral therapy

The WHO has published standardised recommendations for managing TB in HIV-infected infants and children.[4] HIV-infected children benefit from treatment

Table 2 Recommendations for the timing of ART following the initiation of TB treatment with a rifampicin-containing regimen in HIV-infected infants and children[4]

Clinical stage of child with TB (as an event indicating need for ART)	Timing of ART following initiation of TB treatment (rifampicin-containing regimen)*	Recommended ARV regimen
WHO paediatric clinical stage 4†	Start ART soon after TB treatment (between 2 and 8 weeks following start of TB treatment)	In children <3 years • Preferred: triple NRTI first-line regimen (d4T or AZT + 3TC + ABC) • Alternative: standard first-line regimen of two NRTIs + NVP§
WHO paediatric clinical stage 3‡	With clinical management alone: • Start ART soon after TB treatment (between 2 and 8 weeks following start of TB treatment) • If excellent clinical response to TB treatment in first 2 to 8 weeks of TB treatment, and child is stable and on cotrimoxazole preventive therapy (CPT)* it may be reasonable to delay initiation of ART	In children >3 years:¶ • Preferred: triple NRTI first-line regimen (d4T or AZT + 3TC + ABC) • Alternative: standard first-line regimen of two NRTIs + EFV#
	Where CD4 is available: • Evaluate the possibility of delaying initiation of ART depending on assessment of clinical status and CD4, and clinical and immunological response to TB treatment: Severe and advanced immunodeficiency:** initiate ART soon after TB treatment (between 2 and 8 weeks following start of TB treatment) Mild or no immunodeficiency:†† initiation of ART may be delayed until after the completion of TB treatment; closely monitor response to TB treatment and reassess for ART after TB treatment; if no improvement, consider starting ART	Following completion of TB treatment it is preferable to remain on the ART regimen as outlined above. • Regimens as recommended above • Where ART can be delayed until after completion of TB treatment, initiation with a standard two NRTIs + NNRTI first-line regimen is recommended

* Administration of CPT is important in children with TB-HIV coinfection.
† All children with clinical stage 4 (that includes extra-pulmonary TB other than lymph node TB) should be initiated on ART regardless of CD4 criteria.
‡ Pulmonary TB and lymph node TB represent clinical stage 3.
§ Careful clinical monitoring with laboratory support, if available, is recommended where NVP is administered concurrently with rifampicin.
¶ Because of lack of data the ranking of preferred or alternative ARV regimens is not a consensus recommendation.
# EFV is not currently recommended for children <3 years of age or <10 kg, and should not be given to postpubertal adolescent girls who are either in the first trimester of pregnancy or are sexually active and not using adequate contraception.
** Severe immunodeficiency; advanced immunodeficiency is assumed to be up to 5% above the age-specific CD4 threshold for severe immunodeficiency or CD4 200–349 cells/mm^3 for children ⩾5 years of age.
†† Mild or nonsignificant immunodeficiency is assumed at CD4 levels above those defining advanced immunodeficiency.
ART = antiretroviral treatment; TB = tuberculosis; HIV = human immunodeficiency virus; WHO = World Health Organization; NRTI = nucleoside reverse transcriptase inhibitors; d4T = stavudine; AZT = zidovudine; 3TC = lamivudine; ABC = abacavir; EFV = efavirenz; NNRTI = non-nucleoside reverse transcriptase inhibitors; NVP = nevirapine.

of HIV with ART. In HIV-infected children with confirmed or presumptive TB, the initiation of TB treatment is the priority. Treatment of TB in HIV-infected children on ART or who are planned to start on ART needs careful consideration, as the rifamycins, especially rifampicin, and some of the non-nucleoside reverse transcriptase inhibitors (NNRTIs) and protease inhibitors (PIs) cause clinically significant drug interactions. Furthermore, the adverse events of anti-tuberculosis drugs and antiretroviral drugs are similar and can cause confusion as to which drugs need to be stopped. Rifampicin reduces the serum concentrations of most PIs by 80% or more, and NNRTIs by between 20% and 60%. Because recommendations on combinations of anti-tuberculosis drugs and antiretroviral drugs are frequently revised, obtaining the most recent information from the WHO website* is advised. The CDC website† also provides useful information.

Although the optimal timing for the initiation of ART during anti-tuberculosis treatment is not known, the decision to initiate ART should take into consideration the degree of immune suppression and the child's progress during anti-tuberculosis treatment. Table 2 shows the recommendations for the timing of

* http://www.who.int/hiv/mediacentre
† http://www.cdc.gov/nchstp/tb/

Table 3 Proposed classification of HIV-associated immunodeficiency in infants and children[4]

	Age-related CD4 values			
Classification of HIV-associated immunodeficiency	⩽11 months %	12–35 months %	36–59 months %	⩾5 years cells/mm^3
Not significant	>35	>30	>25	>500
Mild	30–35	25–30	20–25	350–499
Advanced	25–30	20–25	15–20	200–349
Severe	<25	<20	<15	<200 or <15%

HIV = human immunodeficiency virus.

ART following the initiation of anti-tuberculosis treatment in children who are coinfected with HIV. The clinical and immunological condition of the HIV-infected child should guide the decision as to whether to:

- start ART treatment soon (2–8 weeks) after the start of anti-tuberculosis treatment;
- delay ART until after completion of the initial phase of anti-tuberculosis treatment; or
- delay start of ART until anti-tuberculosis treatment is completed.

Where possible, the initiation of ART should be deferred for at least 2–8 weeks in children starting anti-tuberculosis treatment who have not yet started ART (i.e., antiretroviral 'naïve' patients). A careful review of any possible drug interactions between ART and anti-tuberculosis medications should be carried out, and any modifications should be determined with the guidance of an HIV treatment expert.

Immune reconstitution inflammatory syndrome

Immune reconstitution inflammatory syndrome (IRIS), characterised by clinical deterioration after initial improvement, has been observed in patients on anti-tuberculosis treatment who have started ART. The reaction may occur during the first 3–6 months of ART, is generally self-limiting and lasts 10–40 days.

Sometimes a child on ART may develop TB. Consideration of the timing of development of TB after starting ART is important in determining the likely cause of TB. TB occurring in the first 6 months of ART may be part of IRIS. TB occurring after 6 months of ART may be a sign of failure of the ART regimen. TB occurring at any time during ART may be attributable to a new TB infection, depending on exposure. Anti-tuberculosis treatment should be started without delay. The CD4 cell count or percentage is useful to guide clinical management (see Tables 2 and 3).

PREVENTION

General and specific strategies

Global efforts to control the co-epidemics of TB and HIV will benefit children.[5] This includes the expansion of prevention of maternal-to-child transmission (PMTCT) programmes that will reduce new HIV infections in young children, and expansion of the Stop TB strategy. However, additional specific strategies are needed. At a minimum, all HIV-infected children should be screened for TB and all children with TB should be offered HIV testing and counselling in high HIV prevalence settings. Irrespective of age, all HIV-infected children who are household contacts of infectious cases should be evaluated for TB disease and treated with prophylaxis (see Chapter 4 in this series 'Childhood contact screening and management'*). Innovative approaches are needed to ensure that co-infected children are identified, and that where possible, disease is prevented.

BCG vaccination

The HIV pandemic has implications for BCG vaccination (see section on BCG in Chapter 5 in this series 'Roles and responsibilities, recording and reporting, and BCG vaccination'†). Although there have been a few reports of disseminated BCG infection after BCG immunisation of HIV-infected children, prospective studies comparing BCG immunisation in HIV-infected and non-infected infants have showed no difference in risk of complications. It is recommended that BCG vaccination policy should depend on the prevalence of TB in a country. In countries with a high TB prevalence, the benefits of BCG vaccination outweigh the risks, and the WHO recommends a policy of routine BCG immunisation for all neonates.[6] A child who has not had routine neonatal BCG immunisation and has symptoms of HIV/AIDS should not be given BCG because of the risk of disseminated BCG disease. BCG should not be given to HIV-infected children in low TB prevalence countries.

Concerning the management of BCG disease in HIV-infected children (or children with other immunodeficiencies), the diagnosis is difficult and the treatment is specialized, as *Mycobacterium bovis* is resistant to pyrazinamide and requires higher doses of other first-line TB medications. Some experts recommend 15 mg/kg/dose of isoniazid and 15–20 mg/kg/dose of rifampicin. HIV-infected children suspected of having BCG disease should be referred to an expert for management.

References

1 World Health Organization. Treatment of tuberculosis: guidelines for national programmes. 3rd ed. WHO/CDS/TB/2003. 313. Geneva, Switzerland: WHO, 2003.

2 Centers for Disease Control and Prevention. Treating opportunistic infections among HIV-exposed and infected children. MMWR 2004; 53(RR-14): 1–63. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5314a1.htm Accessed August 2006.

* To appear in the January 2007 issue of the *Journal*.

† To appear in the February 2007 issue of the *Journal*.

3 World Health Organization. Guidelines for cotrimoxazole prophylaxis for HIV-related infections in children, adolescents and adults in resource-limited settings. Recommendations for a public health approach. Geneva, Switzerland: WHO, 2006. http://www.who.int/hiv/pub/guidelines/en/index.html Accessed August 2006.
4 World Health Organization. Antiretroviral therapy of HIV infection in infants and children in resource-limited settings: towards universal access. Recommendations for a public health approach. Geneva, Switzerland: WHO, 2006. http://www.who.int/hiv/paediatric/en/index.html Accessed August 2006.
5 World Health Organization. Strategic framework to decrease the burden of TB/HIV. WHO/CDS/TB/2002.296. Geneva, Switzerland: WHO, 2002.
6 World Health Organization. Issues related to the use of BCG in immunization programs: a discussion document. WHO/V&B/99.23. Geneva, Switzerland; WHO, 1999.

Suggested reading

Berggren Palme E, Gudeta B, Bruchfeld J, Muhe L, Giesecke H. Impact on human immunodeficiency virus 1 infection on clinical presentation, treatment outcome and survival in a cohort of Ethiopian children with tuberculosis. Pediatr Infect Dis J 2002; 21: 1053–1061.

Blusse van Oud-Alblas H J, van Vliet M E, Kimpen J L, de Villiers G S, Schaaf H S, Donald P R. Human immunodeficiency virus infection in children hospitalised with tuberculosis. Ann Trop Paediatr 2002; 22: 15–23.

Chintu C, Bhat G J, Walker A S, et al. Co-trimoxazole as prophylaxis against opportunistic infections in HIV-infected Zambian children (CHAP): a double-blind randomised placebo-controlled trial. Lancet 2004; 364: 1865–1871.

Chintu C, Mudenda V, Lucas S, et al. Lung diseases at necropsy in African children dying from respiratory illnesses: a descriptive necropsy study. Lancet 2002; 360: 985–990.

Coovadia H M, Jeena P, Wilkinson D. Childhood human immunodeficiency virus and tuberculosis co-infection: reconciling conflicting data. Int J Tuberc Lung Dis 1998; 2: 844–851.

Cotton M F, Schaaf H S, Hesseling A C, Madhi S A. HIV and childhood tuberculosis: the way forward. Int J Tuberc Lung Dis 2004; 8: 675–682.

Graham S M, Coulter J B, Gilks C F. Pulmonary disease in HIV-infected African children. Int J Tuberc Lung Dis 2001; 5: 12–23.

Graham S M, Gibb D M. HIV disease and respiratory infection in children. Br Med Bull 2002; 61: 133–150.

Jeena P M, Pillay P, Pillay T, Coovadia H M. Impact of HIV-1 co-infection on presentation and hospital-related mortality in children with culture proven pulmonary tuberculosis in Durban, South Africa. Int J Tuberc Lung Dis 2002; 6: 672–678.

Jeena P M, Mitha T, Bamber A, Wesley A, Coutsoudis A, Coovadia H M. Effect of human immunodeficiency virus on tuberculosis in children. Tubercle Lung Dis 1996; 77: 437–443.

Lucas S B, Peacock C S, Hounnou A, et al. Disease in children infected with HIV in Abidjan, Côte d'Ivoire. Br Med J 1996; 312: 335–338.

Luo C, Chintu C, Bhat G, et al. Human immunodeficiency virus type-1 infection in Zambian children with tuberculosis: changing seroprevalence and evaluation of a thioacetazone-free regimen. Tubercle Lung Dis 1994; 75: 110–115.

Kiwanuka J, Graham S M, Coulter J B, et al. Diagnosis of pulmonary tuberculosis in children in an HIV-1 endemic area, Malawi. Ann Trop Paediatr 2001; 21: 5–14.

Madhi S A, Huebner R E, Doedens L, Aduc T, Wesley D, Cooper P. HIV co-infection in children hospitalised with tuberculosis in South Africa. Int J Tuberc Lung Dis 2000; 4: 448–454.

Puthanakit T, Oberdorfer P, Akarathum N, Wannarit P, Sirisanthana T, Sirisanthana V. Immune reconstitution syndrome after highly active antiretroviral therapy in human immunodeficiency virus-infected Thai children. Pediatr Infect Dis J 2006; 25: 53–58.

Schaaf H S, Geldenhuys A, Gie R P, Cotton M F. Culture-positive tuberculosis in human immunodeficiency virus type 1-infected children. Pediatr Infect Dis J 1998; 17: 599–604.

Shelburne S A, Hamill R J, Rodriguez-Barradas M C, et al. Immune reconstitution inflammatory syndrome. Emergence of a unique syndrome during highly active antiretroviral therapy. Medicine 2002; 81: 213–227.

Thomas P, Bornschlegel K, Singh T P, et al. Tuberculosis in human immunodeficiency virus-infected and human immunodeficiency virus-exposed children in New York City. The New York City Pediatric Spectrum of HIV Disease Consortium. Pediatr Infect Dis J 2000; 19: 700–706.

World Health Organization. Issues related to the use of BCG in immunization programs: a discussion document. WHO/V&B/99.23. Geneva, Switzerland: WHO, 1999.

World Health Organization. TB/HIV—a clinical manual. 2nd ed. WHO/HTM/TB/2004.329. Geneva, Switzerland: WHO, 2004.

World Health Organization. Antiretroviral therapy of HIV infection in infants and children in resource-limited settings: towards universal access. Recommendations for a public health approach. Geneva, Switzerland: WHO, 2006.

World Health Organization. Guidelines for cotrimoxazole prophylaxis for HIV-related infections in children, adolescents and adults in resource-limited settings. Recommendations for a public health approach. Geneva, Switzerland: WHO, 2006.

RÉSUMÉ

Les enfants infectés par le virus de l'immunodéficience humaine (VIH) encourent le risque de toute une série de maladies pulmonaires liées à l'infection par le VIH, y compris la tuberculose (TB). Comme chez les enfants non-infectés par le VIH, la présence de trois ou davantage des quatre signes suivants suggère vigoureusement le diagnostic de TB : 1) un test cutané tuberculinique positif ; 2) des symptômes chroniques suggestifs de TB ; 3) des signes objectifs hautement suggestifs de TB ; 4) et un cliché thoracique suggestif de TB. Il faut faire des efforts maximaux pour accélérer le processus de diagnostic car la TB peut s'étendre rapidement chez les enfants infectés par le VIH. Puisque beaucoup d'enfants qui se présentent avec des symptômes chroniques suggestifs de TB peuvent ne pas avoir été testés pour l'infection VIH, dans les contextes à prévalence élevée du VIH (ainsi que dans tous les contextes où l'on suspecte le VIH chez un enfant), les enfants et leurs familles devraient se voir offrir l'accompagnement et le test VIH au sein d'une mise au point globale de la TB. La plupart des directives internationales actuelles recommandent que, chez les enfants infectés par le VIH comme chez ceux qui ne le sont pas, la TB devrait être soignée par un régime de 6 mois comportant la rifampicine de bout en bout. Tous les enfants infectés par le VIH et dont l'état d'immunodépression est avancé, y compris ceux atteints de TB, devraient bénéficier d'une prophylaxie au cotrimoxazole. Bien que le moment optimal de mise en œuvre du traitement anti-

rétroviral (ART) au cours du traitement de la TB ne soit pas connu, la décision de mettre en route l'ART devrait prendre en considération le degré d'immunodépression ainsi que l'amélioration de l'enfant au cours du traitement de la TB.

RÉSUMÉ

Los niños con infección por el virus de la inmunodeficiencia humana (VIH) son vulnerables a una variedad de enfermedades pulmonares asociadas con dicha infección, entre ellas la tuberculosis (TB). Al igual que en niños sin infección por el VIH, la presencia de tres o más de las siguientes cuatro características representa un alto grado de presunción diagnóstica de TB : 1) una prueba cutánea positiva a la tuberculina ; 2) síntomas crónicos compatibles con TB ; 3) cambios físicos indicativos de TB y 4) radiografía de tórax con signos de TB. Es preciso hacer todo lo posible por facilitar el diagnóstico, pues la TB puede progresar rápidamente en los niños infectados por el VIH. Puesto que muchos niños con signos crónicos indicativos de TB pueden no haber tenido la prueba serológica para el VIH, la orientación y la prueba para el VIH deben formar parte de todo estudio completo de TB en los entornos con alta prevalencia (y en cualquier medio cuando se sospecha la infección por el VIH en un niño). La mayor parte de las normas internacionales recomiendan el tratamiento de la TB en niños infectados o no por el VIH con una pauta de 6 meses que contenga rifampicina durante todo el tratamiento. Todos los niños infectados por el VIH con inmunodepresión avanzada, incluidos aquellos con TB, deben recibir profilaxis con la cotrimoxazol. Aunque se desconoce el momento óptimo para la iniciación del tratamiento antirretrovírico durante el régimen antituberculoso, la decisión de comenzar los medicamentos antirretrovíricos debe tomarse considerando el grado de depresión inmunitaria y el progreso del niño durante el tratamiento antituberculoso.