Pediatric HIV: Opportunistic infections

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From

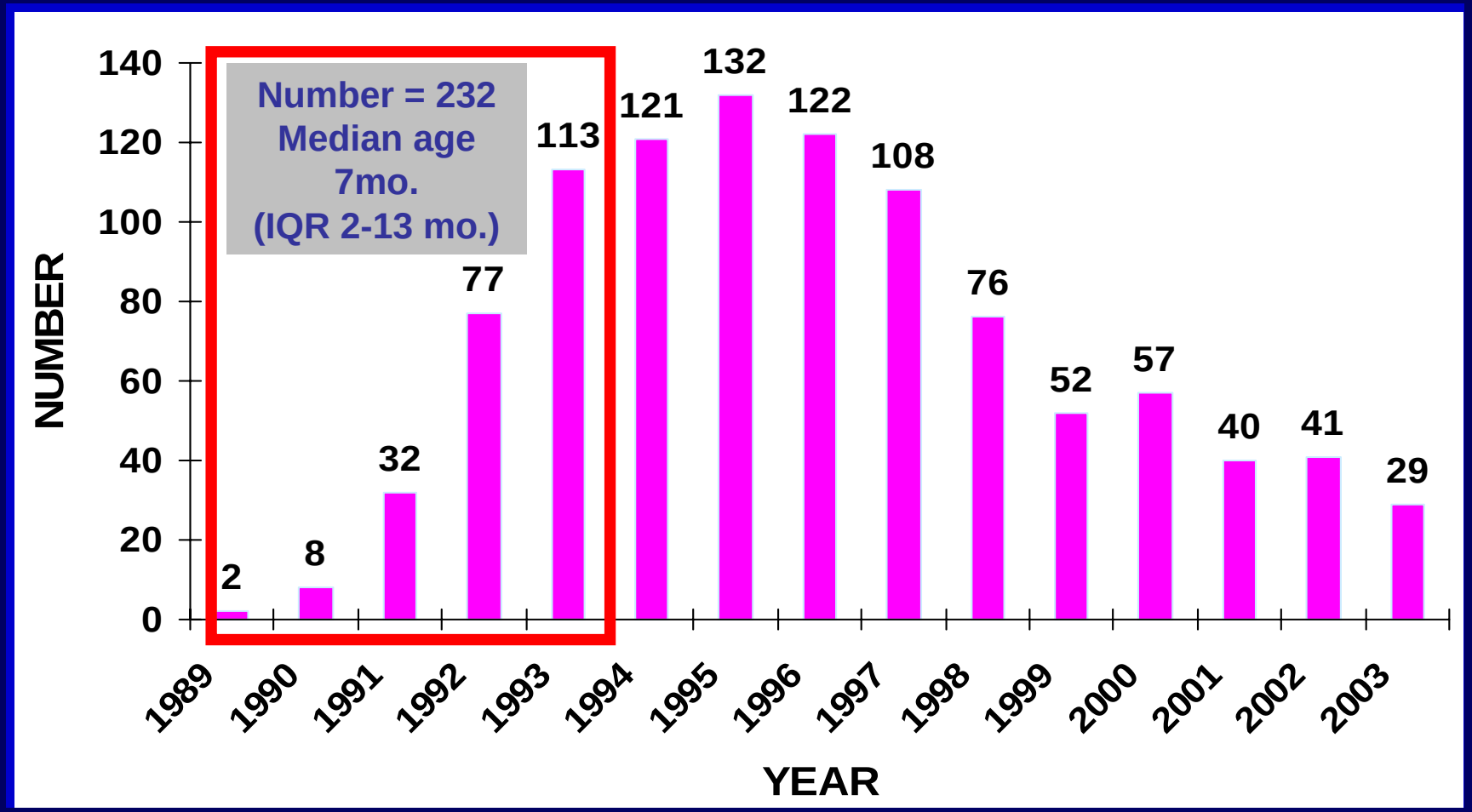
Topic

- Common opportunistic infection in HIV-infected children
- OI Treatment and prophylaxis
  - 6 case studies
- 2006 WHO guideline for the use of cotrimoxazole

Frequency of OI among HIV-Infected Children in US : Pre-HAART era

- OIs occurring at >1 events/100 child years
  - Serious bacterial infections (bacteremia and pneumonia), herpes zoster, *Pneumocystis jiroveci* pneumonia, candidiasis, *Mycobacterium avium* complex
- OIs occurring at <1 events/100 child years
  - Cytomegalovirus, toxoplasmosis, cryptosporidiosis, tuberculosis, systemic fungal infections

Cause of hospitalization among symptomatic HIV-infected children at CMU hospital 1989-93



Sirisanthana V. J Infect Dis Antimicrob Agents. 1995;12:59-62.

Medical problems of 232 symptomatic HIV-infected children (1989-1993)

Medical Problems	Cases	(%)
Infectious diseases	183	(78.9)
Non-ID		
Pulmonary infiltrates of unknown etiology	20	(8.6)
Chronic diarrhea of unknown etiology	14	(6.0)
Neurologic or hematologic problems	10	(4.3)
Lymphoid interstitial pneumonitis	5	(2.2)

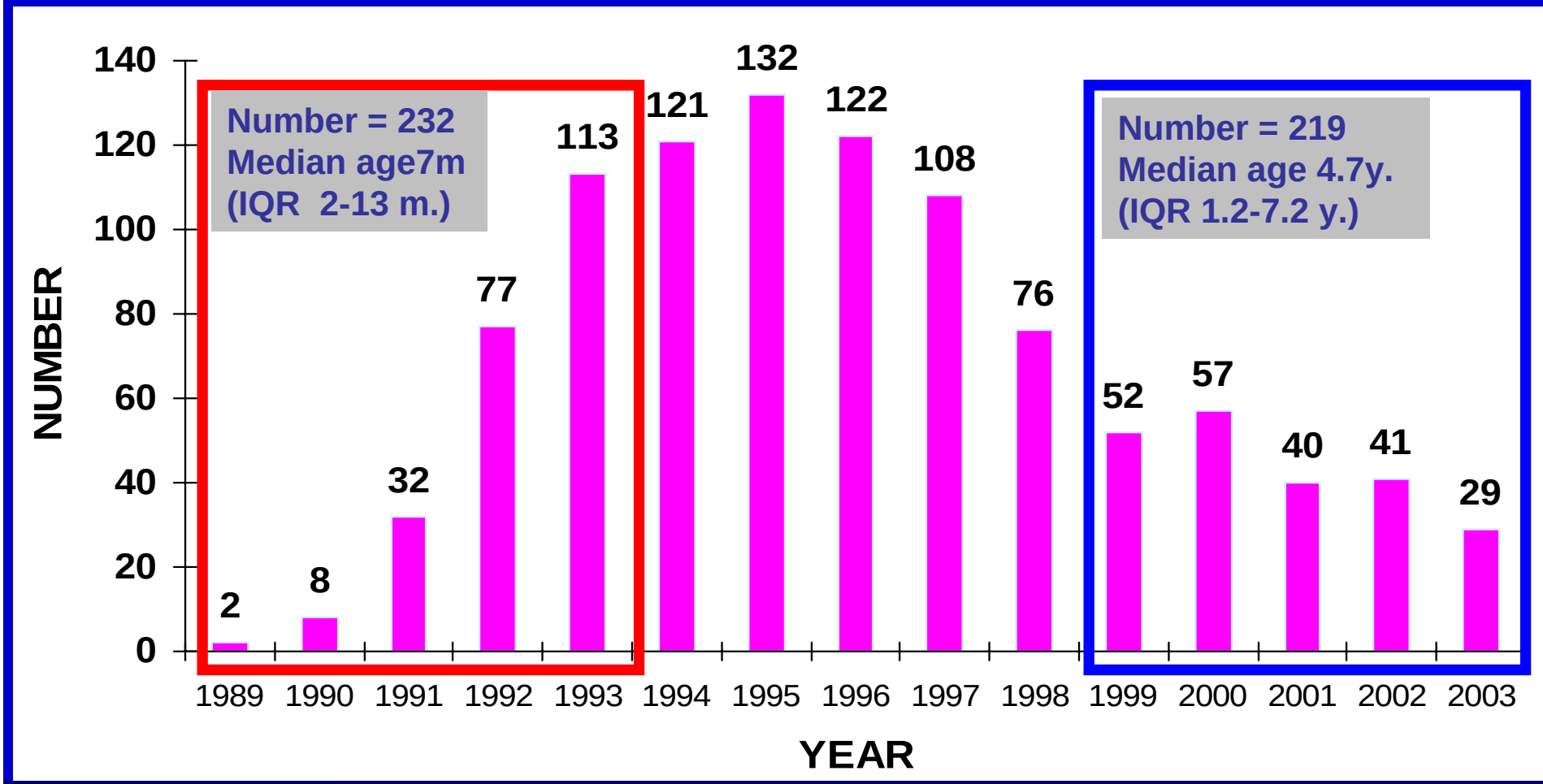
Sirisanthana V. J Infect Dis Antimicrob Agents. 1995;12:59-62.

Opportunistic infections of HIV-infected children between 1989-1993

Infectious diseases	183 cases (100%)	
Pneumocystis jirovecci pneumonia	59	(32%)
Salmonella septicemia	29	(16%)
Bacterial pneumonia	24	(13%)
Cytomegalovirus	18	(10%)
Septicemia (other than *Salmonella*)	13	(7%)
Cryptosporidium	9	(5%)
Penicilliosis	9	(5%)
Mycobacterium infection	5	(3%)
Other miscellaneous infections	16	(9%)

Sirisanthana V. J Infect Dis Antimicrob Agents. 1995;12:59-62.

Cause of hospitalization among symptomatic HIV-infected children at CMU hospital 1999-2003



Puthanakit T, Sirisanthana V. Presented at the 8th PIDST meeting, May 7, 2004

Medical problems of 219 symptomatic HIV-infected children (1999-2003)

Medical Problems	Case	(%)
Infectious diseases	172	(79)
Non-ID	47	(21)
Chronic diarrhea	17%	
Thrombocytopenia	15%	
Lymphoma/malignancy	13%	
Cardiomyopathy/Heart failure	13%	
HIV encephalopathy	11%	

Puthanakit T, Sirisanthana V. Presented at the 8th PIDST meeting, May 7, 2004

Opportunistic infections of HIV-infected children between 1999-2003

Infectious diseases	172 cases (100%)	
Bacterial pneumonia	44	(24%)
Penicillium marneffei infection	23	(13%)
Septicemia	21	(12%)
Pneumocytis jirovecii	21	(12%)
Mycobacterium infection	14	(8%)
Miscellaneous	49	(28%)

Sirisanthana V. J Infect Dis Antimicrob Agents. 1995;12:59-62.

การดูแลเด็กติดเชื้อเอชไอวี
ในประเทศไทย

http://pedaids.info

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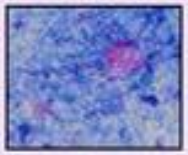


:: Case 15 Feb 05

An HIV-infected boy with abdominal pain

:: Prepared by

Nattiya Jareewit , M.D.
Aurmporn Oberdorfer, M.D., Ph.D.
Virat Sirisanthana, M.D.
Department of Pediatrics, Faculty of Medicine, Chiang Mai University

:: Case 14 Dec 04

An HIV-infected girl with an abscess at her left arm

:: Prepared by

Aurmporn Oberdorfer, M.D., Ph.D.
Virat Sirisanthana, M.D.
Department of Pediatrics, Faculty of Medicine, Chiang Mai University

:: Case 13 June 04

An HIV-infected child with prolonged fever and eye pain

:: Prepared by

Aurmporn Oberdorfer, M.D., Ph.D.
Virat Sirisanthana, M.D.
Department of Pediatrics, Faculty of Medicine, Chiang Mai University

:: Case 12 Apr 04

An HIV-infected boy with rash and abdominal pain

:: Prepared by

Virat Sirisanthana, M.D.
Department of Pediatrics, Faculty of Medicine, Chiang Mai University

:: Case 11 Dec 03

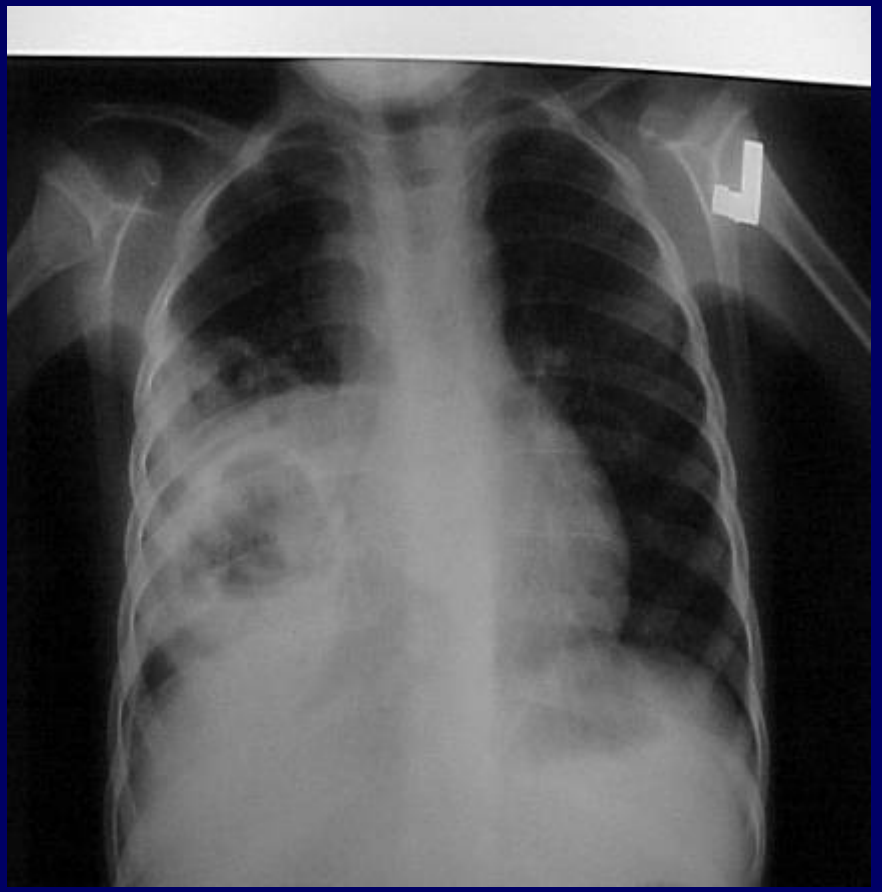
An HIV-infected boy with neck mass

:: Prepared by

Virat Sirisanthana, M.D.
Department of Pediatrics, Faculty of Medicine, Chiang Mai University

Case 1: Respiratory problem

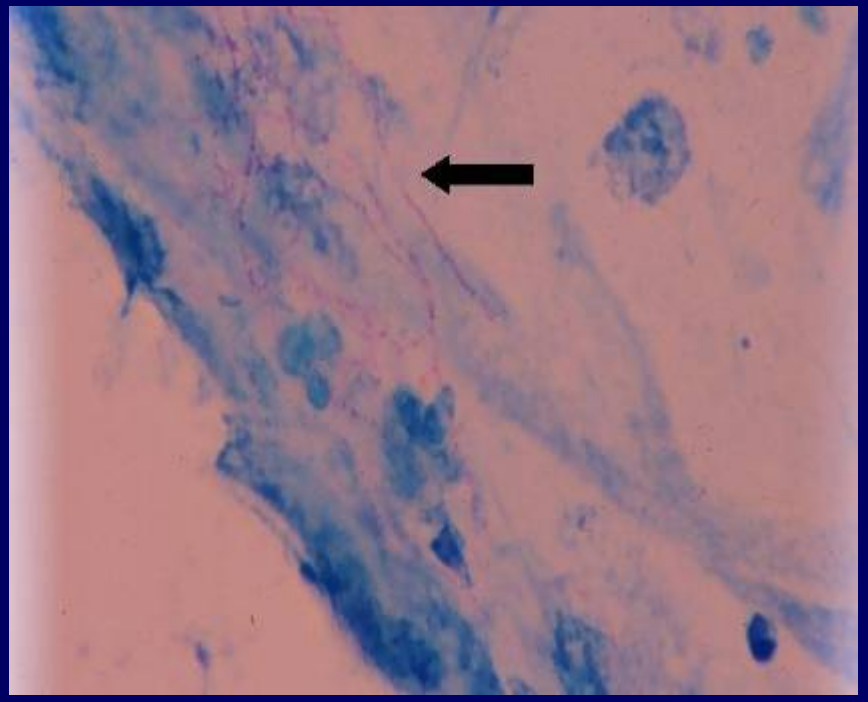
- A 6-year-old HIV-infected boy with clinical category C
- **CC:** Prolonged fever and cough for 2 months.
- Chest X-ray
- What is diagnosis?



Case I (cont.)

Gram stain: 1000x

beaded, branched, weakly Gram-positive rods



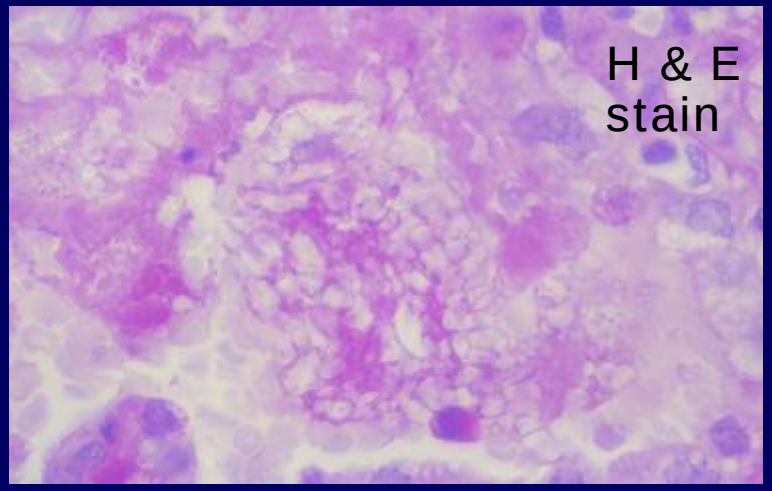
Modified AFB: 1000x

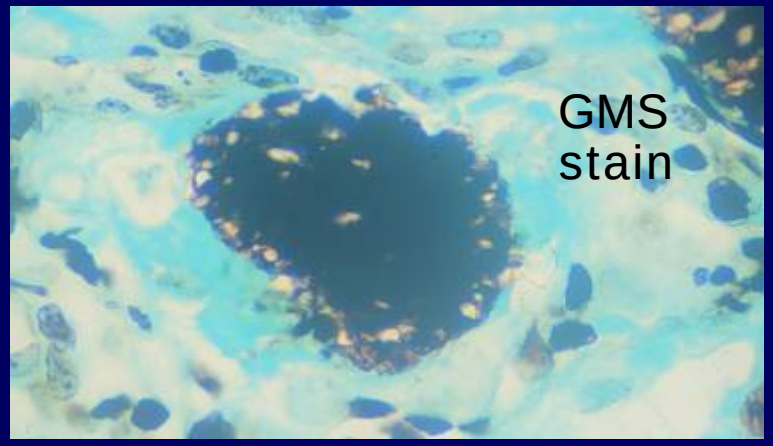
Positive acid fast bacilli

Case 2: Respiratory problem

- A 4-month-old infant
- 3 d history of difficulty of breathing, cyanosis
- Chest-x-ray
- PE: Lymphadenopathy
  Hepatosplenomegaly
  Crepitations

Case II (cont.)



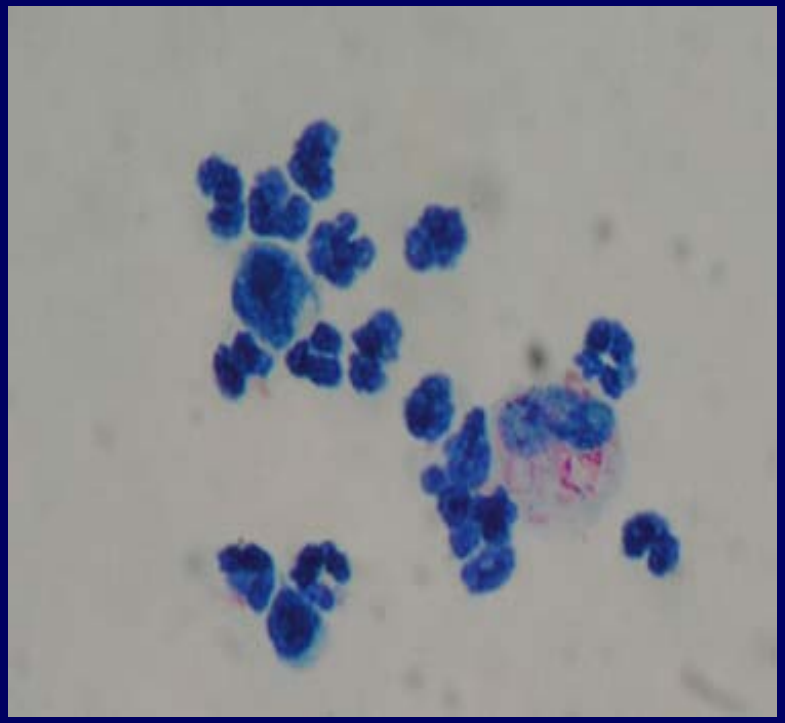


- Bronchoalveolar lavage findings
- Treatment
  - Cotrimoxazole for 21 days
  - Consider steriod in mod-severe cases within 72 hrs of Rx

Case 3 : Abscess

- An 8-year-old girl
- Abscess at Lt arm
  warm, tender,
  fluctuation not response
  to oral antibiotics
- CD4 prior to ART = 1%

Case III (cont.)



- Pus: acid fast bacilli
- Culture: M.bovis BCG strain
- Incidence: 2.7 per 100 persons
- Rx: aspiration, INH+Rifampin

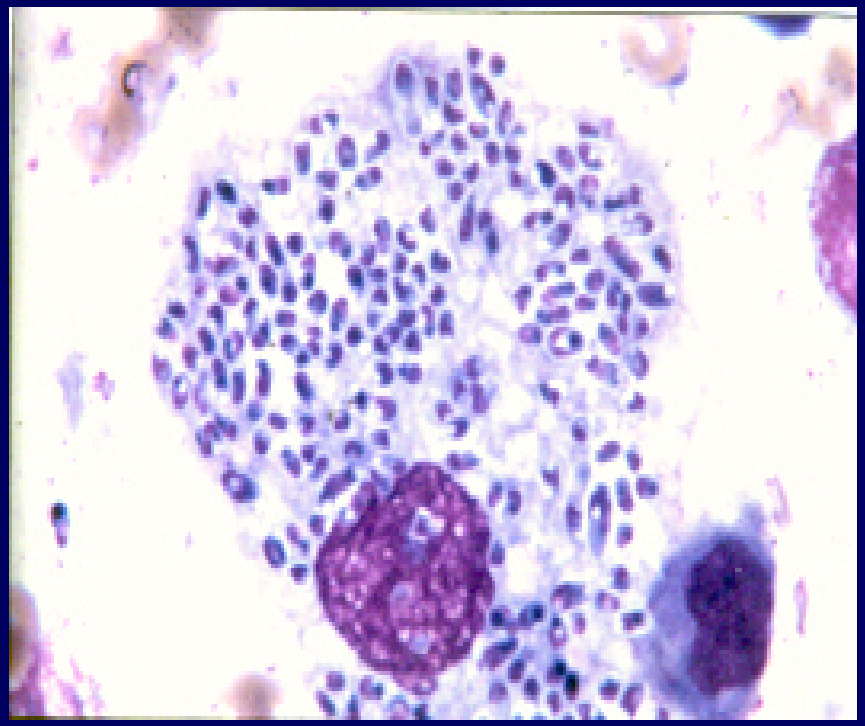
Sirisanthana V. Bacille Calmette-Guerin (BCG) vaccine complications in HIV-infected children. J Infect Dis Antimicrob Agents. 1995;12:63-67.

Puthanakit T, et al. Clin Infect Dis 2005; 41:1049-52.

Case IV: Skin papules with fever

- A 10-year old boy with 2-week of high grade fever, skin papules and pale
- PE: BT 40 C, marked pale, umbilicated papules hepatomegaly

Case IV (continue)



- Touch smears of a skin
- Basophilic, spherical or oval yeast-like organisms with clear central septation (diameter 3-8 uM)
- Sites: skin, LN, Bone marrow

Clinical manifestation of Pm in children (I)

- Apr 1989- Jan 1995: 21 cases of HIV children
- Sign and symptoms
  - 90% generalized lymphadenopathy
  - 90% hepatomegaly
  - 81% BT > 38.5 ° C
  - 67% papular skin lesions with central umbilication
  - 67% splenomegaly
  - 52% failure to thrive

Sirisanthana V, et al. Pediatr Infect Dis J. 1995;14:935-40.

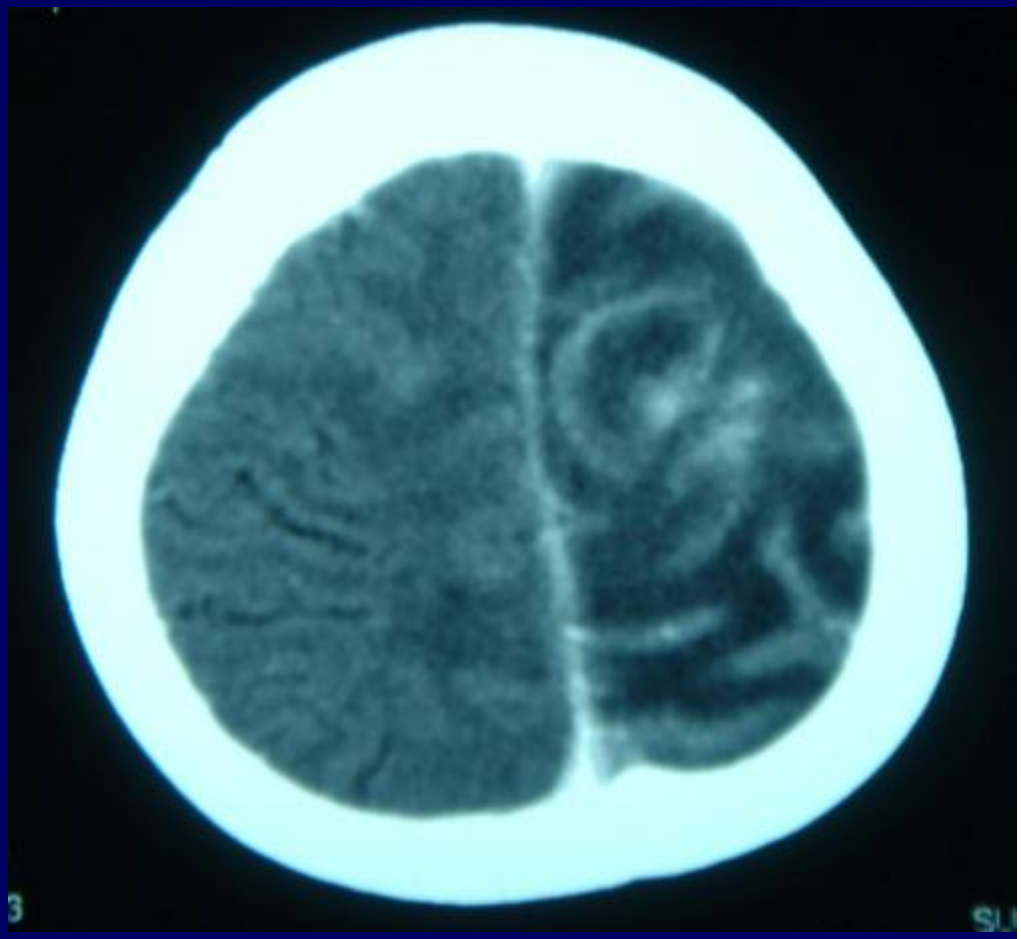
Clinical manifestation of Pm in children (II)

- Laboratory
  - 43% severe anemia (Hb < 6 g/dl)
  - 21% thrombocytopenia (plt < 50,000 / mm^3)
- Co-infection
  - 20% with bacterial septicemia
    (Salmonella, Pseudomonas)
- Treatment
  - Amphotericin B 0.6 MKD IV for 2 weeks
  - Itraconazole 10 mg/kg/day (max 400 mg) for 10 weeks then secondary prophylaxis

Sirisanthana V Pediatr Infect Dis J. 1995;14:935-40.

Case V: Seizure, weakness

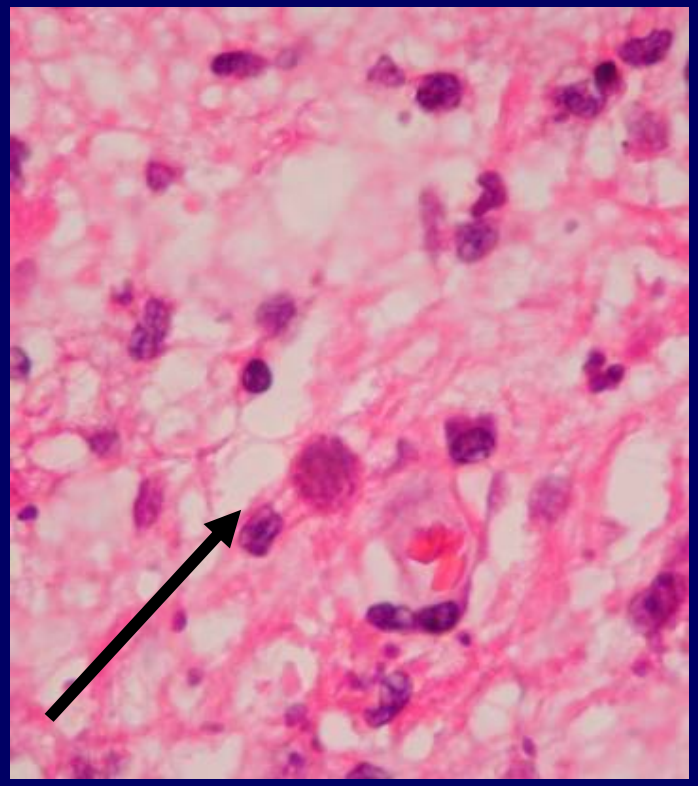
- **14-yr old boy**
- **Seizure, Rt hemiparesis, no fever for 1 week**
- **CT scan brain** abnormal brain swelling at left frontoparietal area with central enhanced lesion



Case V (continue)

- Pathology:

Multiple cyst contain toxoplasmosis bradyzoites



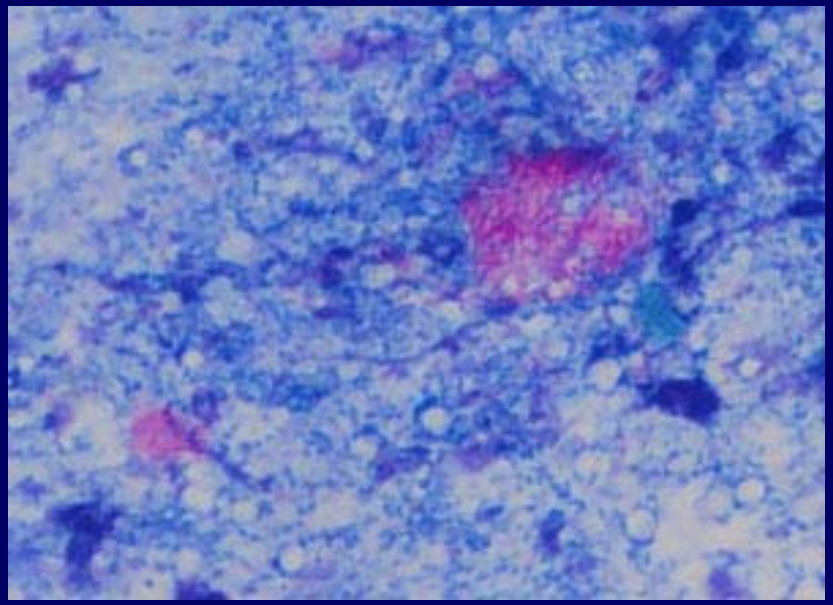
Toxoplasmosis Treatment

- Pyrimethamine: 2 mg/kg/day (max 50 mg/kg) orally for 3 days; then 1 mg/kg/day orally and leucovorin 10-25 mg/day plus sulfadiazine

  25-50 mg/kg/dose orally 4 times daily
- Alternative: Co-trimoxazole
- Continue acute therapy for 6 weeks
- Secondary prophylaxis required

Case VI: chronic abdominal pain

- A 7-yr old boy
- Low grade fever and chronic abdominal pain for 1 month with loose stool
- PE: distend abdomen with ill-defined mass
- Stool exam: mAFB



Mycobacterium Avium Complex

- Clarithromycin: 7.5-15 mg/kg BID (max 500 mg)
- Azithromycin: 10-12 mg/kg OD (max 500 mg)
- Ethambutol: 15-25 mg/kg OD (max 1 g)
- Rifabutin: 10-20 mg/kg OD (max 300 mg) Ciprofloxacin: 20-30 mg/kg OD(max 1.5 g)
- Amikacin: 15-30 mg/kg/day IV q 12-24 hours (max 1.5 g)

- Duration: 12 month in combination with ARV

Reference for OI in children

- Treating Opportunistic Infections Among HIV-Exposed and Infected Children - December 3, 2004 (aidsinfo.nih.gov)
- WHO case definitions of HIV for surveillance and revised clinical staging and immunological classification, August 2006
- bayloraids.org

Guidelines on co-trimoxazole prophylaxis for HIV related infections among children, adolescents and adults in resource-limited settings

WHO August 2006

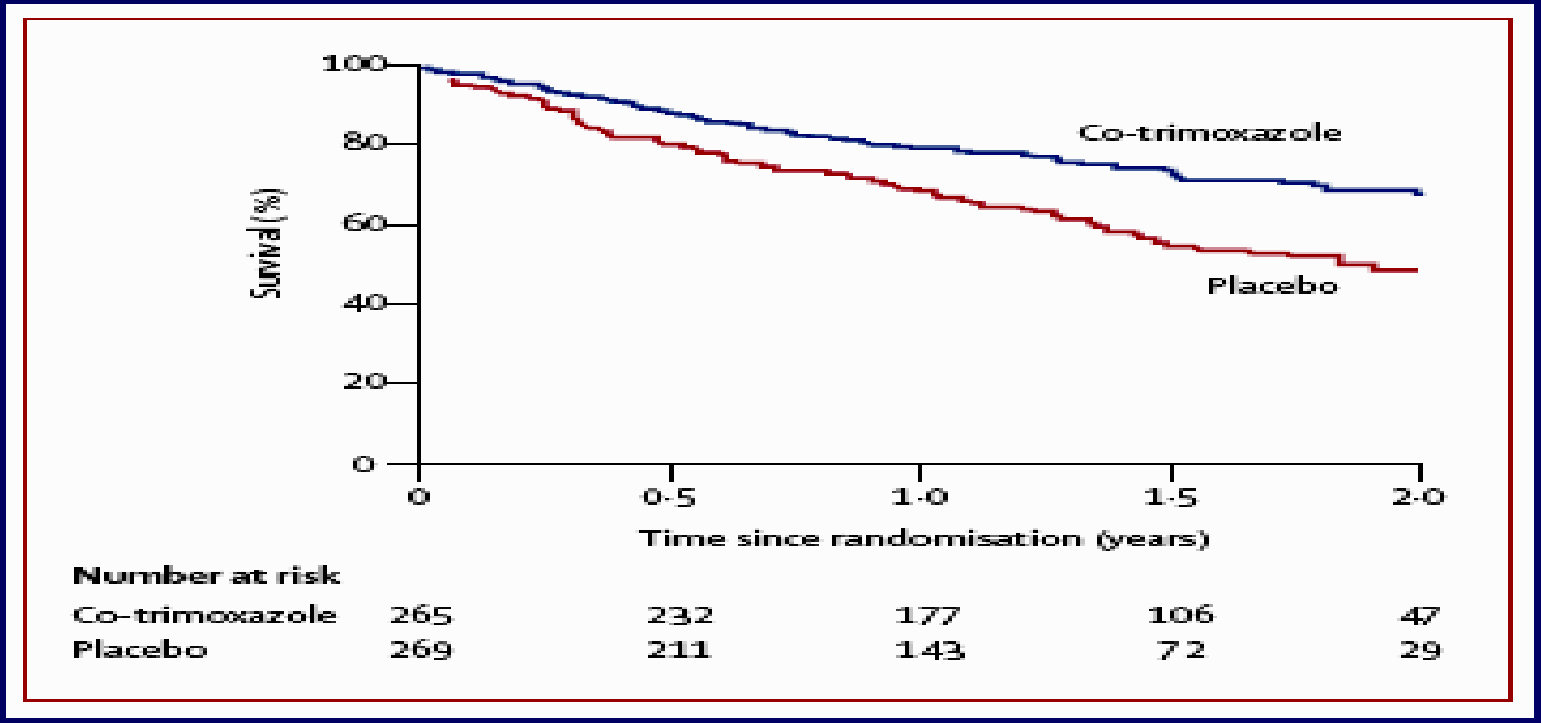
Cotrimoxazole

- Co-trimoxazole

  = sulfamethoxazole/trimethoprim
- Action: aerobic gram-positive and gram-negative bacteria, fungi,protozoa
- Prophylaxis; PCP, Toxoplasmosis, common bacterial infection

Cotrimoxazole-prophylaxis

- Cotrimoxazole OD (1-5 yr 240 mg, > 5 yr 480 mg)
- Reduce mortality by 43%
- Reduce hospital admission 23%



CHAP Trial –Lusaka, Zambia
Lancet 2004;364:1865-71

Criteria to initiate CTX

SITUATION			
HIV-EXPOSED INFANTS AND CHILDREN[a]	INFANTS AND CHILDREN CONFIRMED[b] TO BE LIVING WITH HIV		
	<1 YEAR	1–4 YEARS	≥5 YEARS
Co-trimoxazole prophylaxis is universally indicated, starting at four to six weeks after birth and maintained until cessation of risk of HIV transmission and exclusion of HIV infection **[A-III]**	Co-trimoxazole prophylaxis is indicated regardless of CD4 percentage or clinical status **[A-II]**[c]	WHO clinical stages 2, 3 and 4 regardless of CD4 percentage **OR** Any WHO stage and CD4 <25% **[A-I]**	Follow adult recommendations
Universal option: prophylaxis for all infants and children born to mothers confirmed or suspected of living with HIV. This strategy may be considered in settings with high prevalence of HIV, high infant mortality due to infectious diseases and limited health infrastructure **[C-IV]**.			

WHO stage 3, 4 or

CD4 < 350 cells

Dosage of CTX

Age	BW (kg)	Dose Sulfa	Dose Trimethoprim
< 6 mo	< 5 kg	100	20
6 mo-5 yr	5-15 kg	200	40
6-14 yr	15-30 kg	400	80
> 14 yr	> 30 kg	800	160

Alternative: Dapsone 2 mg/kg/day

Stop Prophylaxis

- Age < 1 year; not recommend

  (at risk of PCP irrespective of CD4)
- Age 1-5 year; recommend continue
- Age > 5 year
  - If CD4 > 15% for at least 6 months
- Adult
  - If CD4 $\geq$ 200 cells for 6 mo. for PCP, Tox
  - If CD4 $\geq$ 350 cells for 6 mo. for PCP, Toxo, bacterial infections

Nachman S, et al. (PACTG 1008) Pediatrics 2005; 115: 488-94
Urschela S et al. (PENTA group) AIDS 2005, 19: 2103-08.