Imaging HIV – and the problem of TB Co-infection in Children

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Why HIV is important for me

- 2/3 of all HIV infections = sub-Saharan Africa
- 91% of newly HIV infected children = born in Africa
- ..the result is …top 30 infant mortality rates = in Africa

- > 90% of children with TB live in developing world
- Incidence TB sub-Saharan Africa = 2X S-E Asia (350/100,000)
- Cape Town South Africa has the second highest rate of TB in the world (935/100,000)

- Of global 8, 6 million TB cases 13% are HIV +ve and of these 75% = in Africa (WHO 2013).

What I will show you today

HIV

CHEST

CNS

Co-infection with TB

HIV and imaging the Chest

CXR differential in HIV is wide

Infections

- Bacterial / TB / MAC
- Fungi / Pneumocystis
- Viral

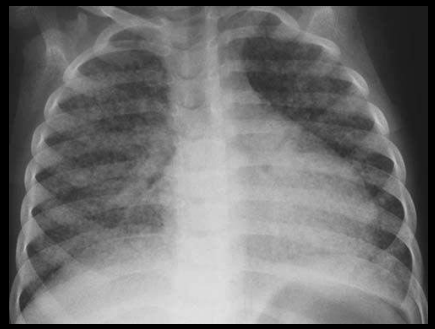
Neoplastic

- Lymhoma
- Kaposi

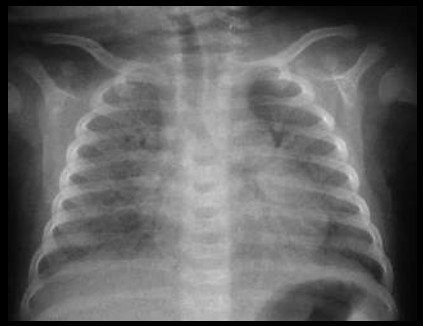
Other

- LIP
- IRIS
- Interstitial
- Bronchiectasis
- Aspiration
- Cardiac

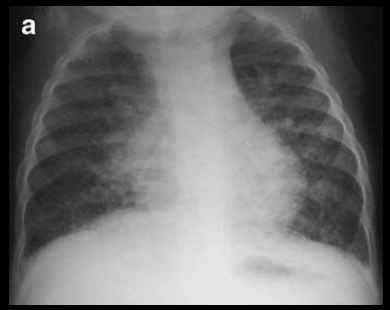
Please choose:



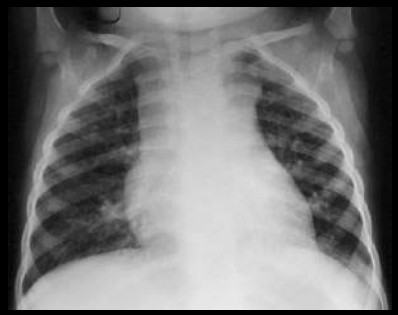
Milliary TB



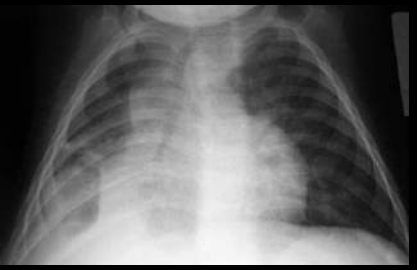
Pneumocystis



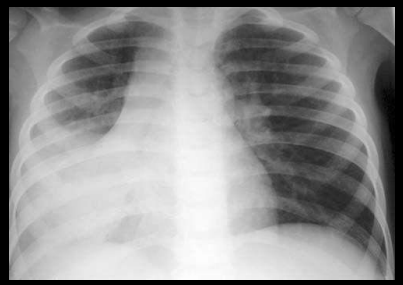
Kaposi



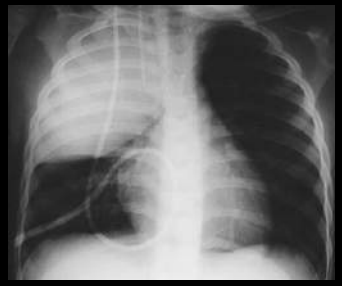
LIP



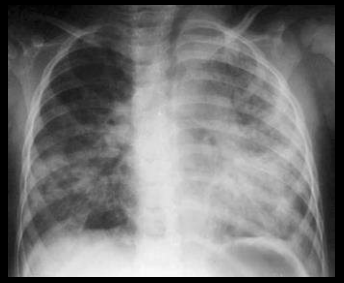
Strep



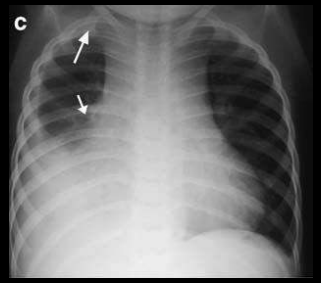
TB



Aspergilosis



Varicella



Kaposi




"Una Faccia Una Razza" (One Face, One Race)

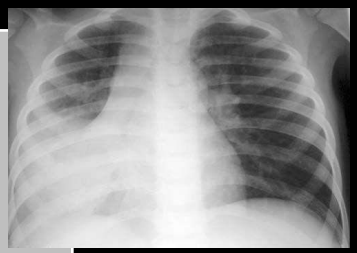
Sav’s three tricks in HIV:

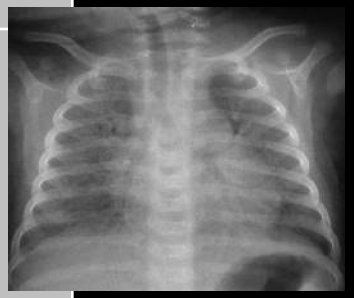
CD 4 Trick:
Fever + CD4 > 200 = bacteria or TB

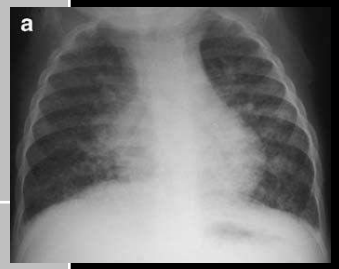
Any CD 4	Bacteria TB
CD4 < 200 c/mm^3	Pneumocystis Cryptococcus
CD4 < 50 c/mm^3	Coccidiodomycosis CMV MAI Aspergillus

CXR lung parenchyma trick

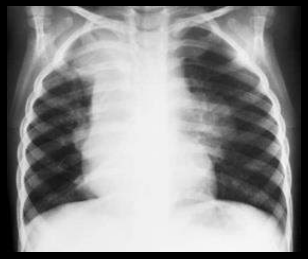
Bacteria **TB**	**Unilateral ---- (bilateral)** **Focal ----------(multifocal)** **Segmental-----(lobar)**
Pneumocystis **CMV** **LIP** **Kaposi** **Cardiac failure**	**Diffuse bilateral**
Aspiration	**Dependent**

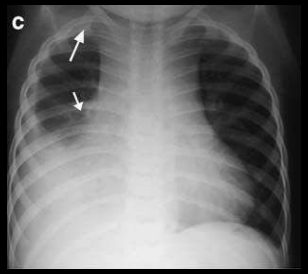


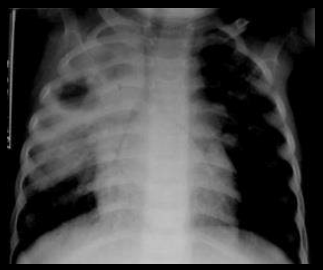




CXR Exclusion trick



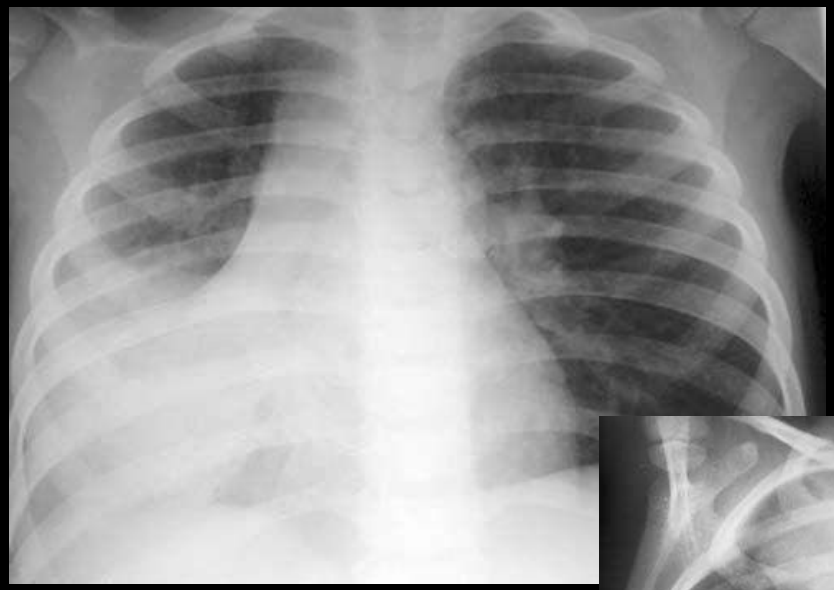




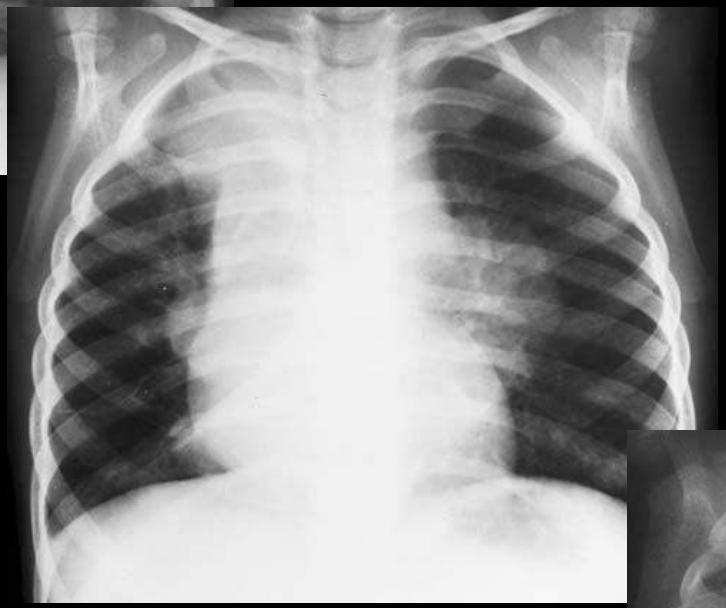
	NOT in
Lymph-adenopathy	bacteria and aspiration
Effusion	PJP / LIP
Cavities / cysts	lymphoma / Kaposi

However, clinicians usually want to know one thing:
before starting HAARTreatment, can we ‘exclude’ TB?

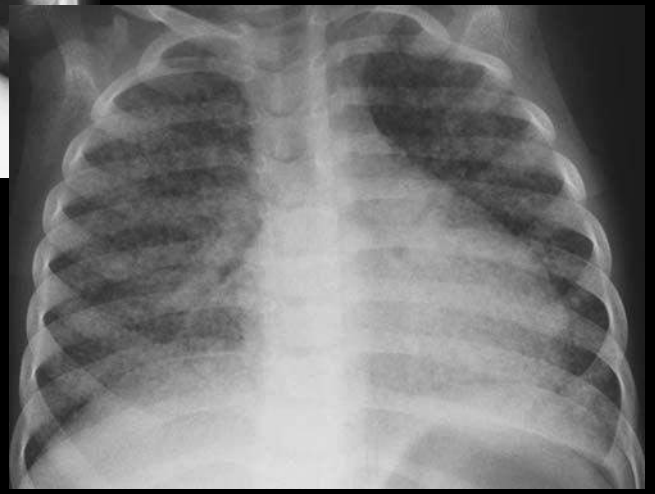
TB / HIV co-infection



Progressive primary



Lymphnode TB



Milliary

Diagnosis of TB in children

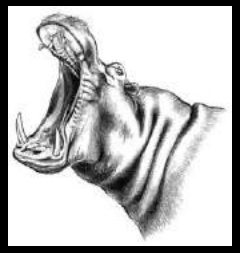
=

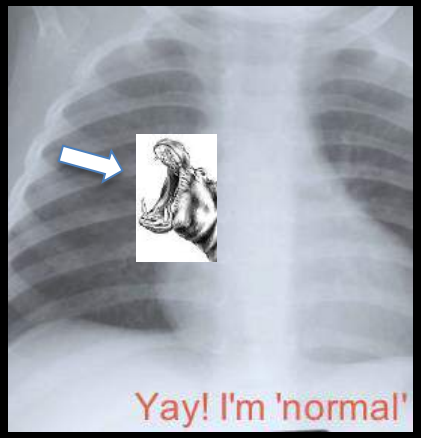
identify lymphadenopathy

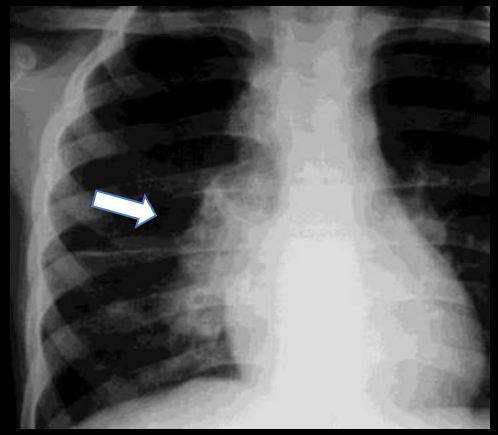
Lymphadenopathy on AP:

Hilum should be a hippo's open mouth

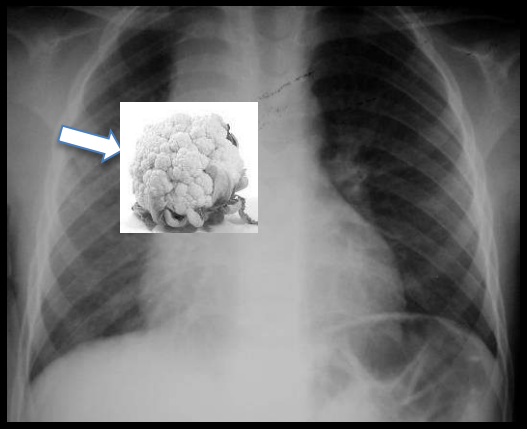
Nodes = a cauliflower in the mouth







Right hilar lymphadenopathy



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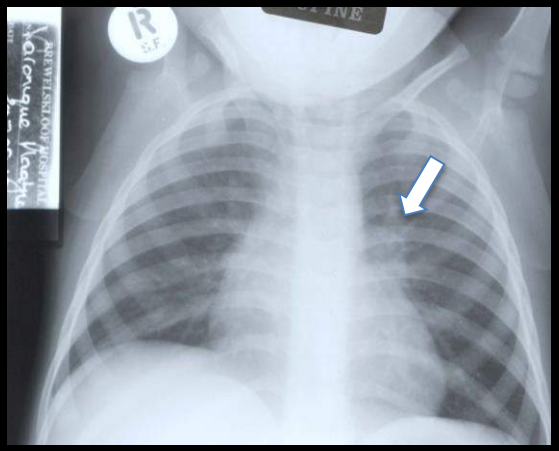
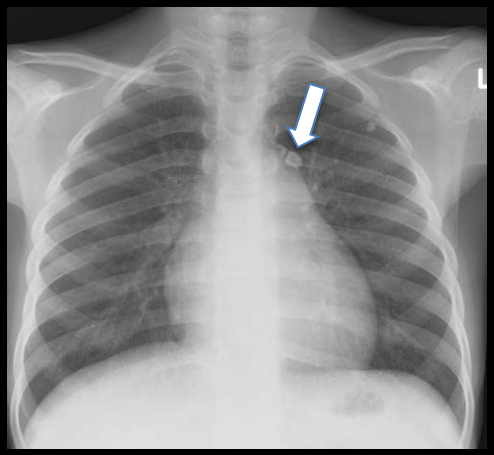
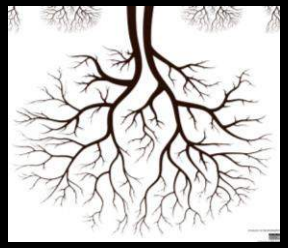


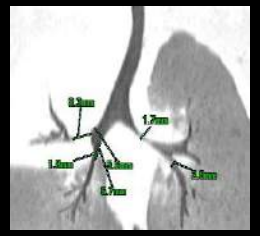
Left hilar lymphadenopathy

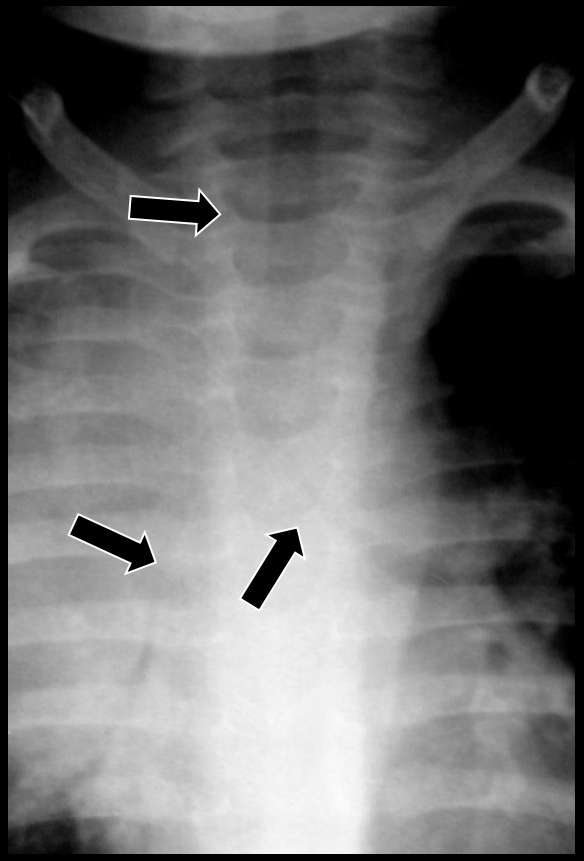


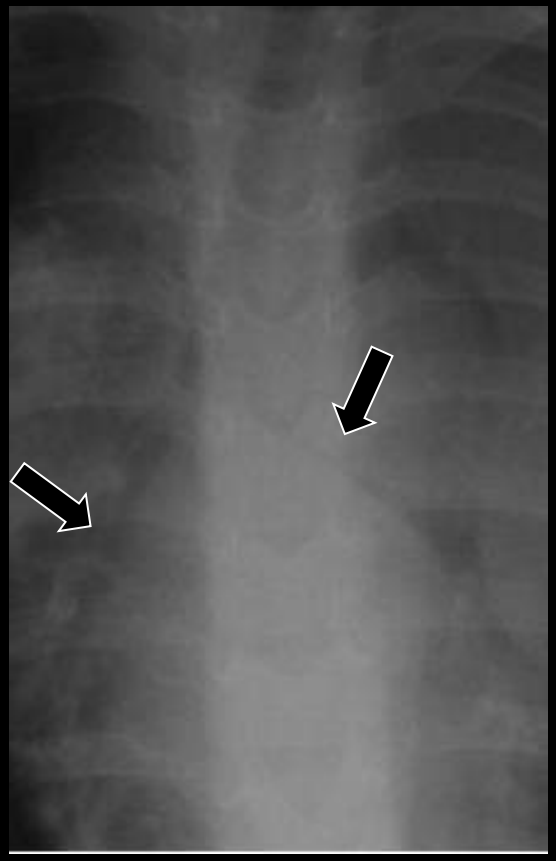
Calcified lymphadenopathy

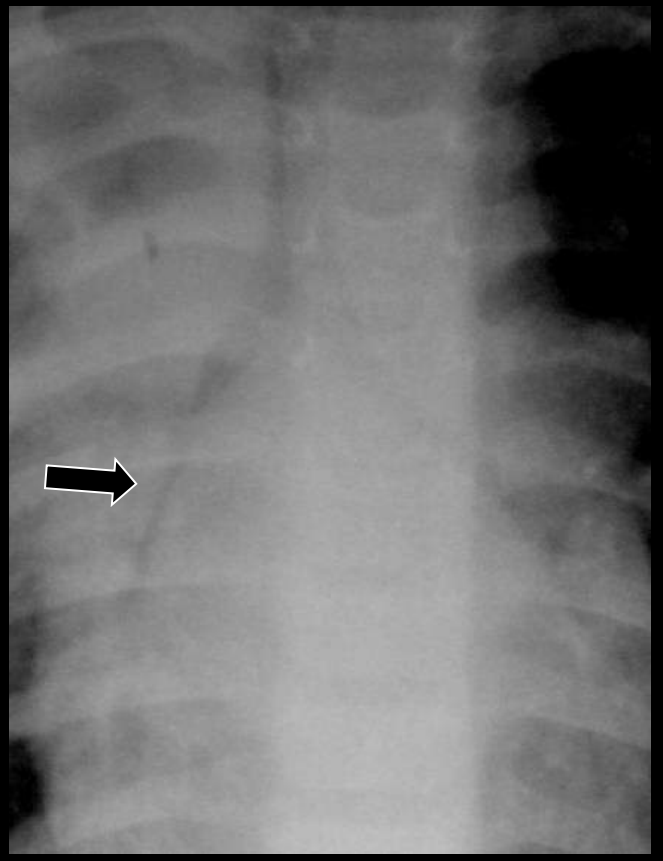
Airways are a up-side-down tree
Lymphadenopathy =
‘compressed air-way branches’



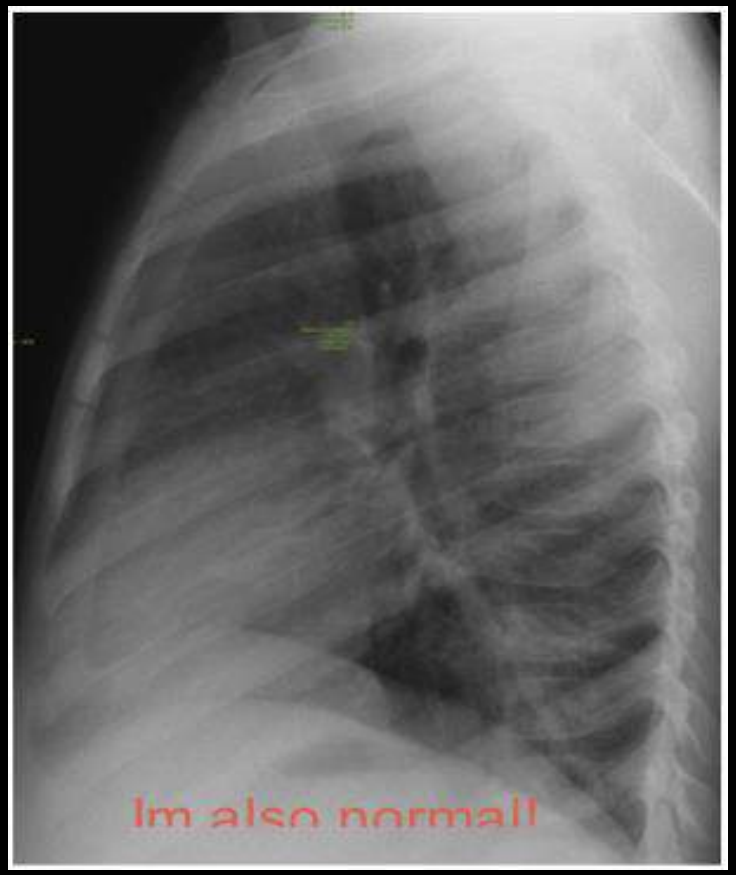




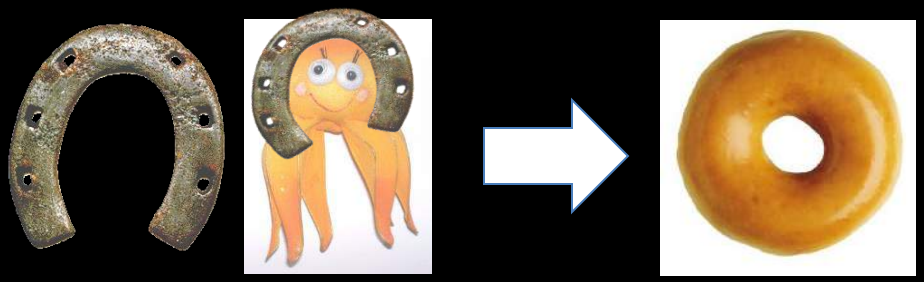




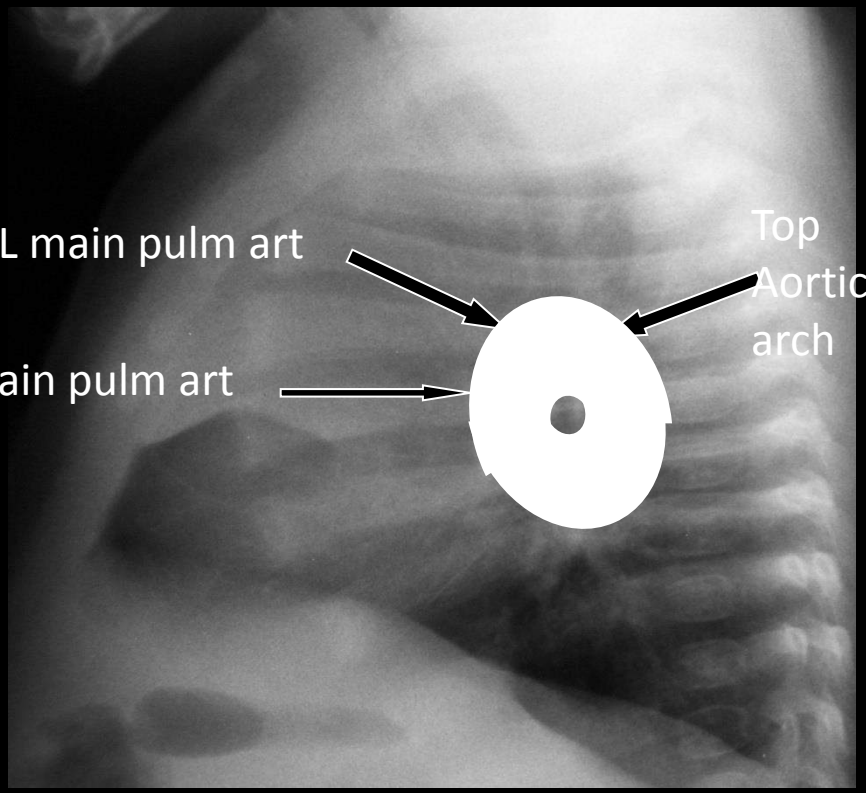
Lateral radiograph



Lymphadenopathy on Lateral



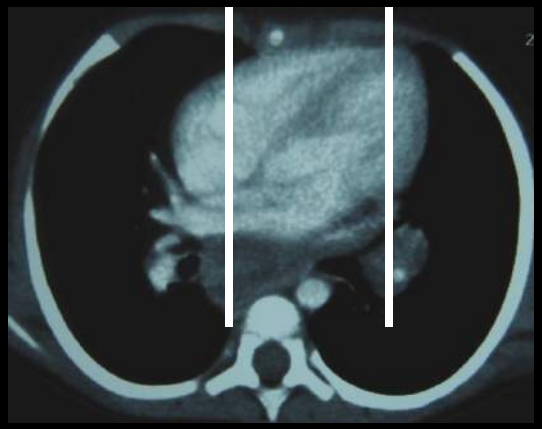
- Normal structures (=horseshoe)
- Diverging vessels (=tentacles)
- Lymphadenopathy (='doughnut')

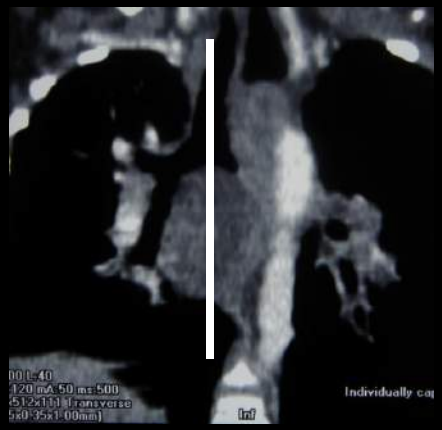


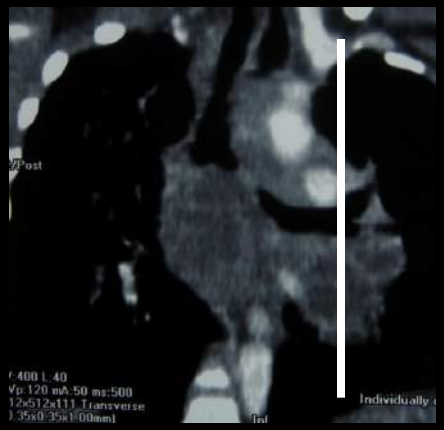
Lateral: doughnut replaces the horse-shoe and tentacles

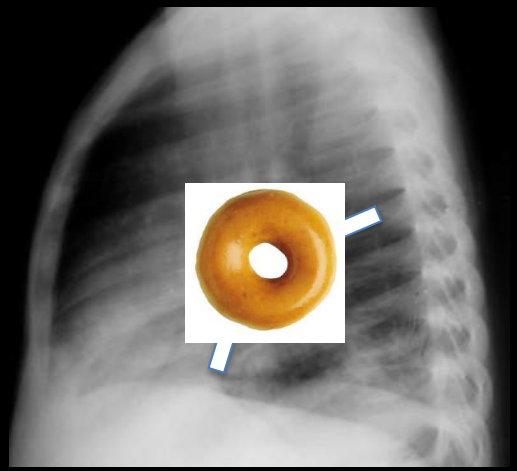
What makes the doughnut?

Subcarinal and left hilar lymphadenopathy

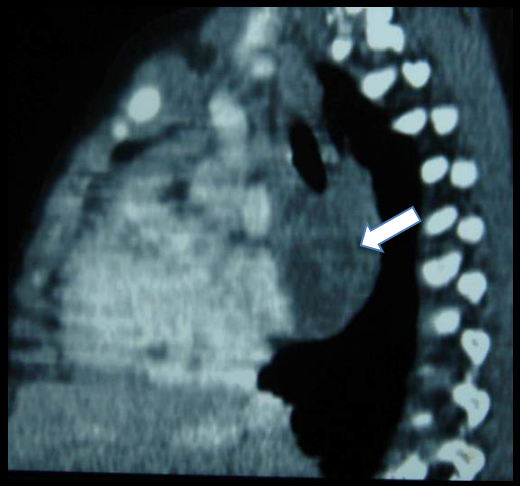




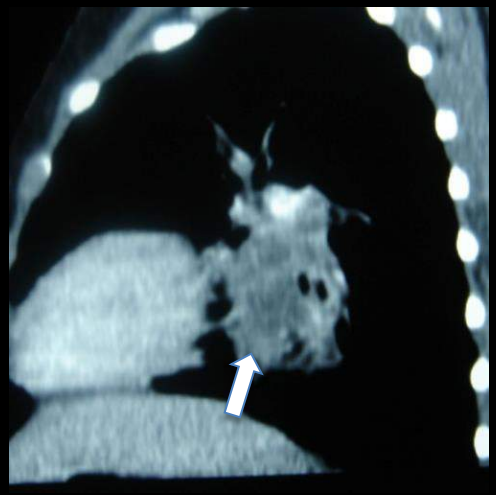




And there is the doughnut……

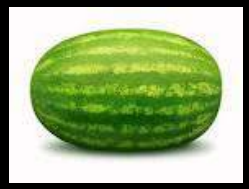


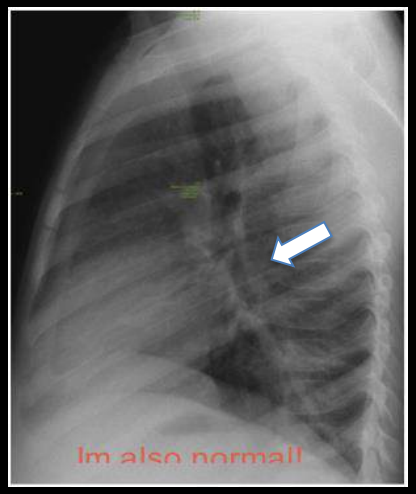
Midsagital:
subcarinal nodes

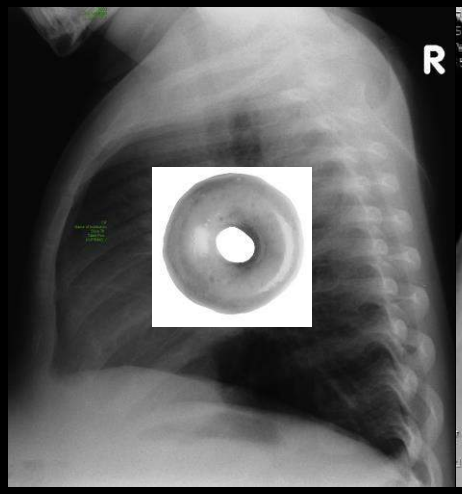


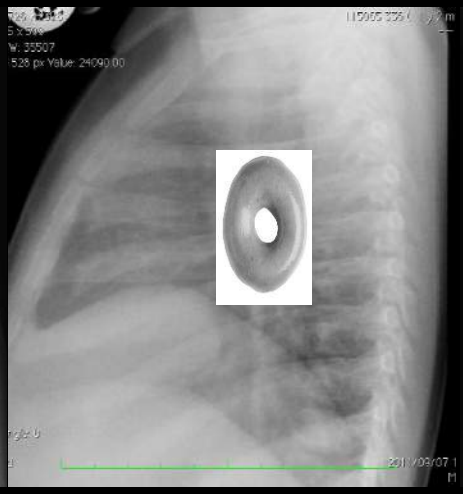
Far para-sagital:
Left hilar nodes

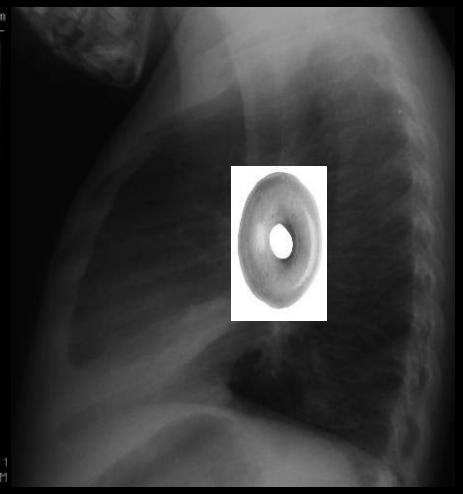
Doughnuts and other foods

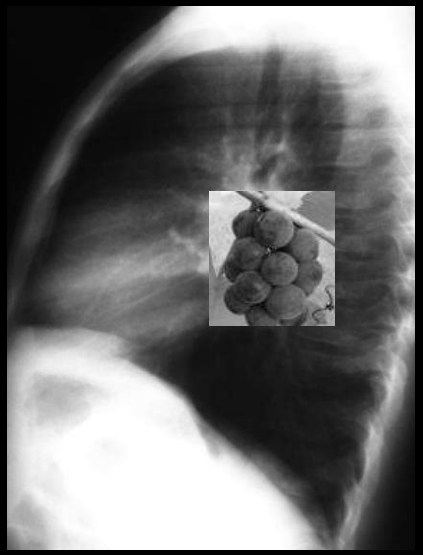



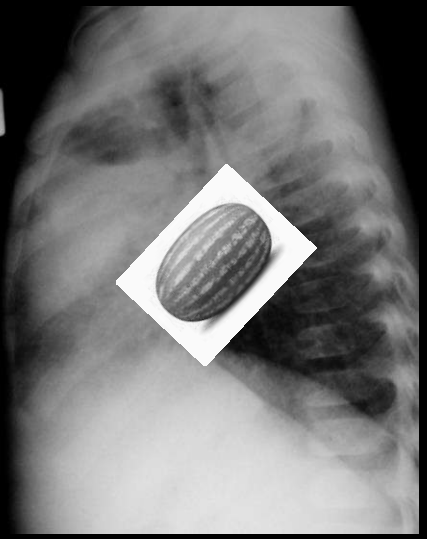


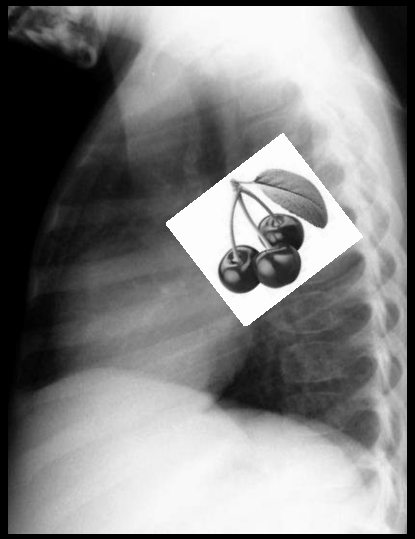




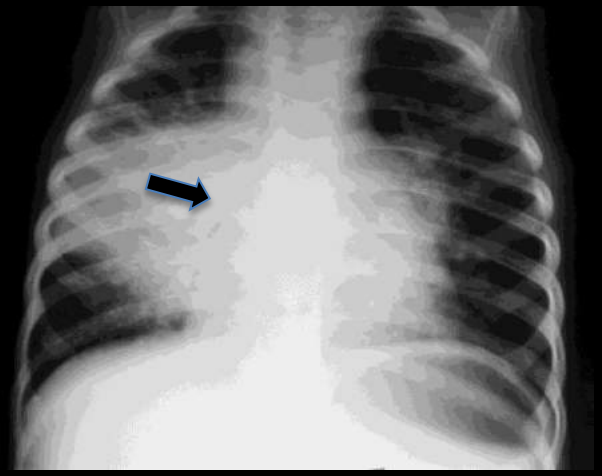
No mass behind bronchus intermedius



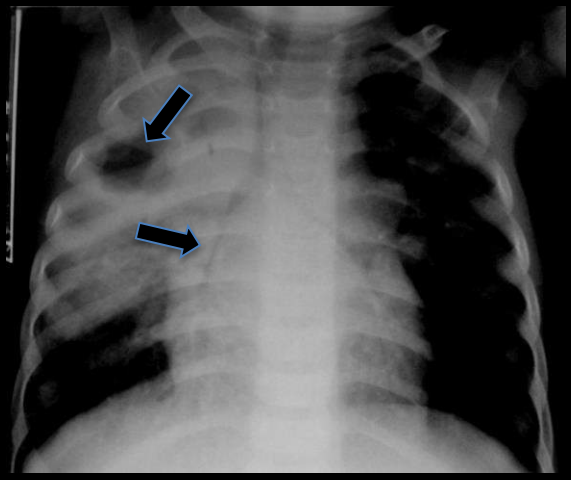




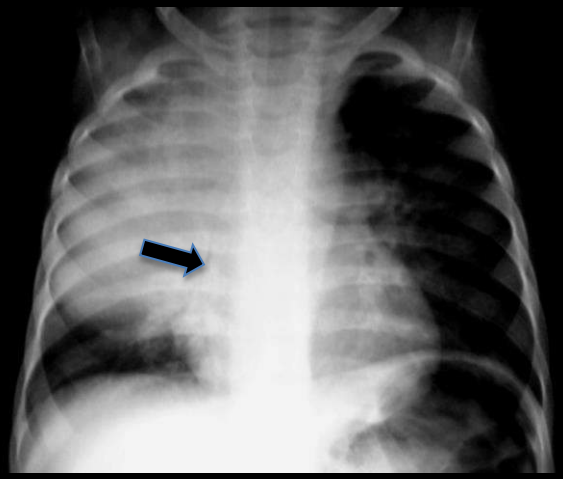
When child is HIV-infected: You've gottobe Sherlock Holmes and uncover TB



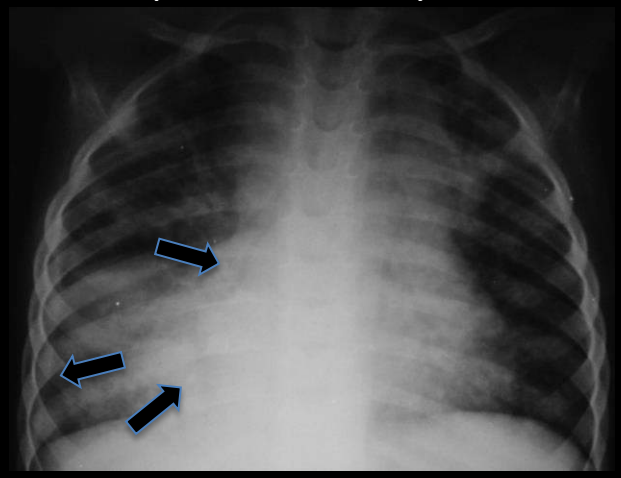
Air space and airway



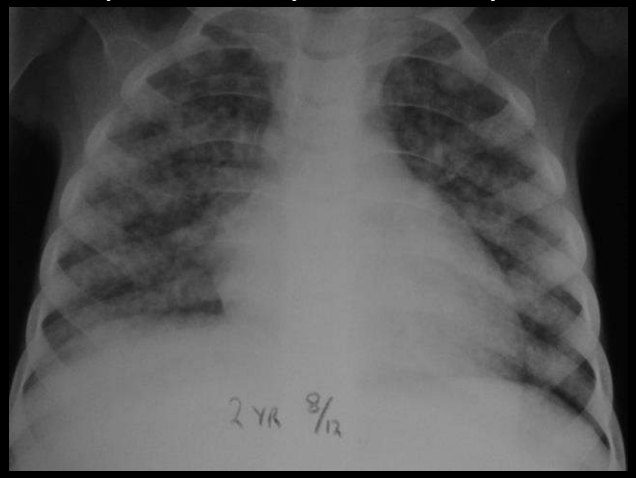
Air space, cavity and airway



Air space expansile and airway

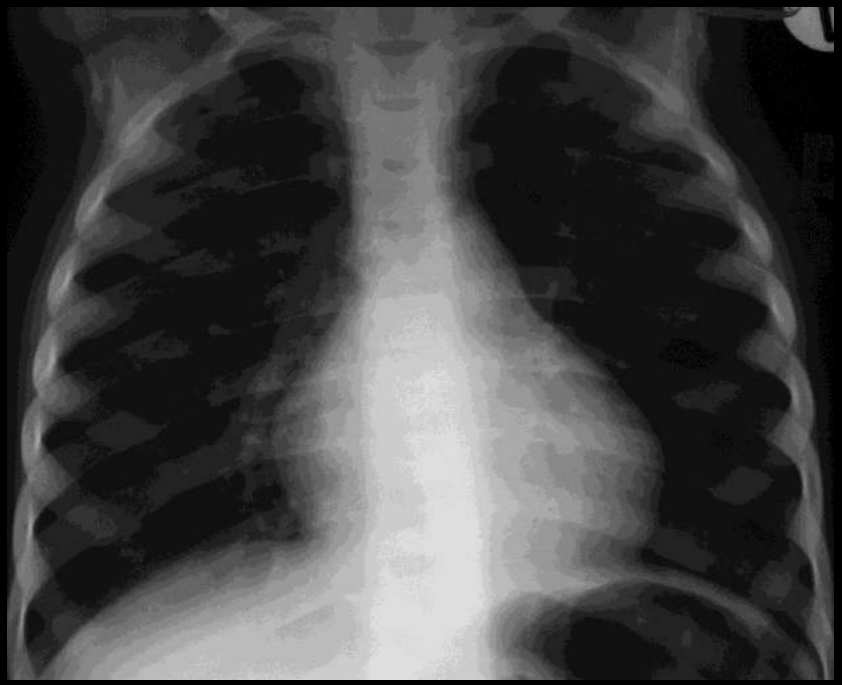


Air space, effusion and airway

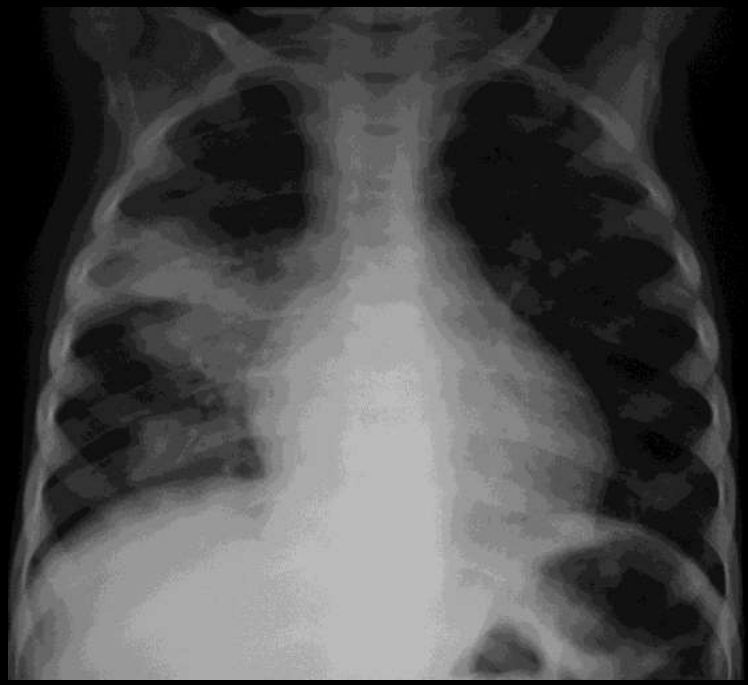


Milliary nodules

If you don’t see the TB you may get IRIS



Before HAART



After initiation of HAART

Is POC US the answer for Africa?

CHEST
Official publication of the American College of Chest Physicians

CHEST ONLINE

Relevance of Lung Ultrasound in the Diagnosis of Acute Respiratory Failure * : The BLUE Protocol

Daniel A. Lichtenstein and Gilbert A. Mezière

Chest 2008;134;117-125; Prepublished online April 10, 2008;
DOI 10.1378/chest.07-2800

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ARTICLE

JOURNAL CLUB

Prospective Evaluation of Point-of-Care Ultrasonography for the Diagnosis of Pneumonia in Children and Young Adults

Vaishali P. Shah, MD; Michael G. Tunik, MD; James W. Tsung, MD, MPH

Objective: To determine the accuracy of point-of-care ultrasonography for the diagnosis of pneumonia in children and young adults by a group of clinicians.

Design: Prospective observational cohort study.

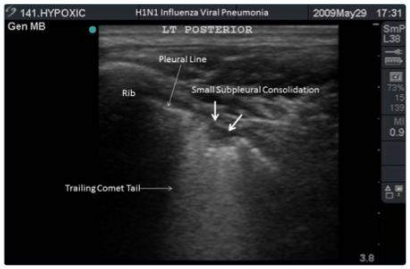
Setting: Two urban emergency departments.

Participants: Patients from birth to age 21 years undergoing chest radiography for suspected community-acquired pneumonia.

less with sonographic air bronchograms undetectable by chest radiography.

Results: Two hundred patients were studied (median age, 3 years; interquartile range, 1-8 years); 56.0% were male, and the prevalence of pneumonia by chest radiography was 18.0%. Ultrasonography had an overall sensitivity of 86% (95% CI, 71%-94%), specificity of 89% (95% CI, 83%-93%), positive LR of 7.8 (95% CI, 5.0-12.4), and negative LR of 0.2 (95% CI, 0.1-0.4) for diagnosing pneumonia by visualizing lung consolidation

Critical Ultrasound Journal
a SpringerOpen Journal



Prospective application of clinician-performed lung ultrasonography during the 2009 H1N1 influenza A pandemic: distinguishing viral from bacterial pneumonia

Tsung *et al.*

Springer
Tsung et al. Critical Ultrasound Journal 2012, 4:16
http://www.criticalultrasoundjournal.com/content/4/1/16

Pediatr Radiol (2013) 43:1427–1434
DOI 10.1007/s00247-013-2756-4

REVIEW

Chest ultrasound in children: critical appraisal

Paolo Tomà · Catherine M. Owens

Received: 25 February 2013 / Revised: 27 May 2013 / Accepted: 1 June 2013

Abstract We analyze the potential use of ultrasound in the study of the thorax in children. The physical limitations imposed on sonography by the ventilated lung and thoracic cage are well known. We want to discuss new US applications based on the clinical and methodological experience

chest radiography in the evaluation of areas of increased opacification of the peripheral lung, pleural abnormalities and mediastinal widening and in the study of chest wall lesions [1].

One essential prerequisite for using US is the presence of

Pediatr Radiol
DOI 10.1007/s00247-014-2930-3

LETTER TO THE EDITOR

Pediatric chest ultrasound versus conventional radiology: experimental evidence first

Francesco Raimondi · Luigi Cattarossi · Roberto Copetti

Received: 21 January 2014 / Accepted: 12 February 2014

Sir,
Reading the critical appraisal of chest ultrasound in children by Tomà and Owens [1], one has to fully endorse the authors' word of caution against an uncritical replacement of the standard radiograph by an ultrasound scan. Indeed, recent data

Unfortunately, in the critical appraisal by Tomà and Owens [1] the objective evaluation of these experimental data and of those increasingly produced worldwide is constantly neglected in the fear of "the misuse or the abuse of paediatric chest ultrasound." Under these circumstances, we would glad-

EDITORIAL

New imaging approaches for improving diagnosis of childhood tuberculosis

In South Africa (SA), childhood tuberculosis (TB) still accounts for considerable morbidity and mortality. The incidence of TB disease and risk of progression to severe or disseminated forms are especially high in young children or those with HIV infection. Childhood TB presents most commonly as primary TB, often with non specific signs and symptoms; TB may also present as acute pneumonia. The clinical diagnosis can therefore be challenging.[1] Furthermore, due to difficulty in obtaining good-quality specimens and the paucibacillary nature of childhood TB, microbiological confirmation is only achieved in a minority of children, especially in settings where there is limited capacity for microbiological confirmation.[2]

Imaging is a major part of the diagnostic work-up for childhood TB. Chest X-rays are relatively inexpensive and widely available. However, detection of mediastinal and hilar lymphadenopathy – cardinal signs of primary pulmonary TB – is often limited, there is wide inter-observer

Mediastinal ultrasound for intrathoracic lymphadenopathy

Mediastinal and hilar lymphadenopathy are the hallmarks of primary pulmonary TB. Sensitivity and specificity for identifying lymphadenopathy, using traditional anterior-posterior and lateral radiographs in children, is relatively poor. CT studies found lymphadenopathy in up to 60% of TB patients who had normal chest X-rays,[3] but because of the significant radiation burden, CT is not a standard imaging option in children. Mediastinal ultrasound is currently being investigated as an alternative imaging test despite the anatomically limited access. Windows for mediastinal ultrasound include the suprasternal notch and parasternal intercostal spaces, which allow detection of enlarged lymph nodes in the superior and anterior mediastinum. One paediatric imaging study showed that mediastinal ultrasound detected lymphadenopathy in 67% of children with TB who had a normal chest X-ray; the mediastinal ultrasound findings were confirmed on CT.[4] Current research,

ELSEVIER
Canadian Association of Radiologists Journal 65 (2014) 1
CANADIAN ASSOCIATION OF RADIOLOGISTS JOURNAL
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Editorial / Éditorial

The Changing Landscape of Radiology: Ultrasound Training for Nonradiologists

Education is the most powerful weapon which you can use to change the world.

Nelson R. Mandela (1918-2013), president of South Africa (1994-1999)

Be the change that you wish to see in the world.

Mohandas K. (Mahatma) Gandhi, Indian nationalist (1869-1948)

Confusion of goals and perfection of means seems, in my opinion, to characterize our age.

Albert Einstein, German-American physicist (1879-1955)

This past year, 2013, was the 65th anniversary of medical

established in doing many aspects of ultrasound imaging, and this will not change. The horse is out of the barn, and inflexibly in opposing having clinicians involved in this aspect of imaging is not only unrealistic at this point but impractical. Radiologists' main concern with respect to diagnostic ultrasound examinations by nonradiologists should be that they have appropriate training and assessment, and that they are aware of their limitations so to ensure quality studies and patient safety. Such studies, as with any radiology study, should be subject to audit and peer review. Inherent to this entire topic are the issues of setting up proper training, which would start with guidelines and standards. Logistics such as time and compensation for a radiologist to train nonradiologists would have to be sorted out, but, more importantly, which regulating body is responsible for

Current Practice

Remote Sonographic Interpretation: Comparison of Standardized Video Clips to Still Images

Arman Parsai, MD,[1] Imene Zerizer, MSc,[2] Joachim Hohmann, MD,[3] Georg Bongartz, MD,[3] Christoph Beglinger, MD,[4] Giuseppe Sperandeo, MD[5]

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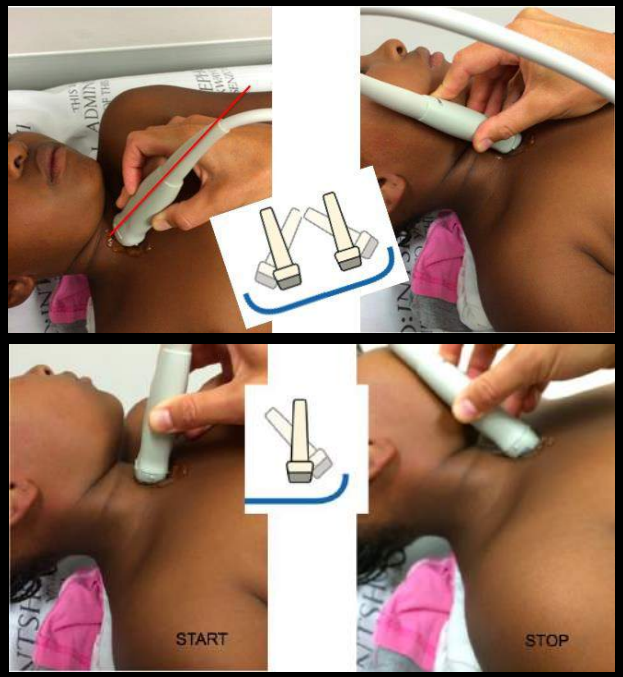
[5] Department of Radiology, Casa Sollievo della Sofferenza Hospital, Viale Cappuccini 1, 71013 San Giovanni Rotondo, Italy

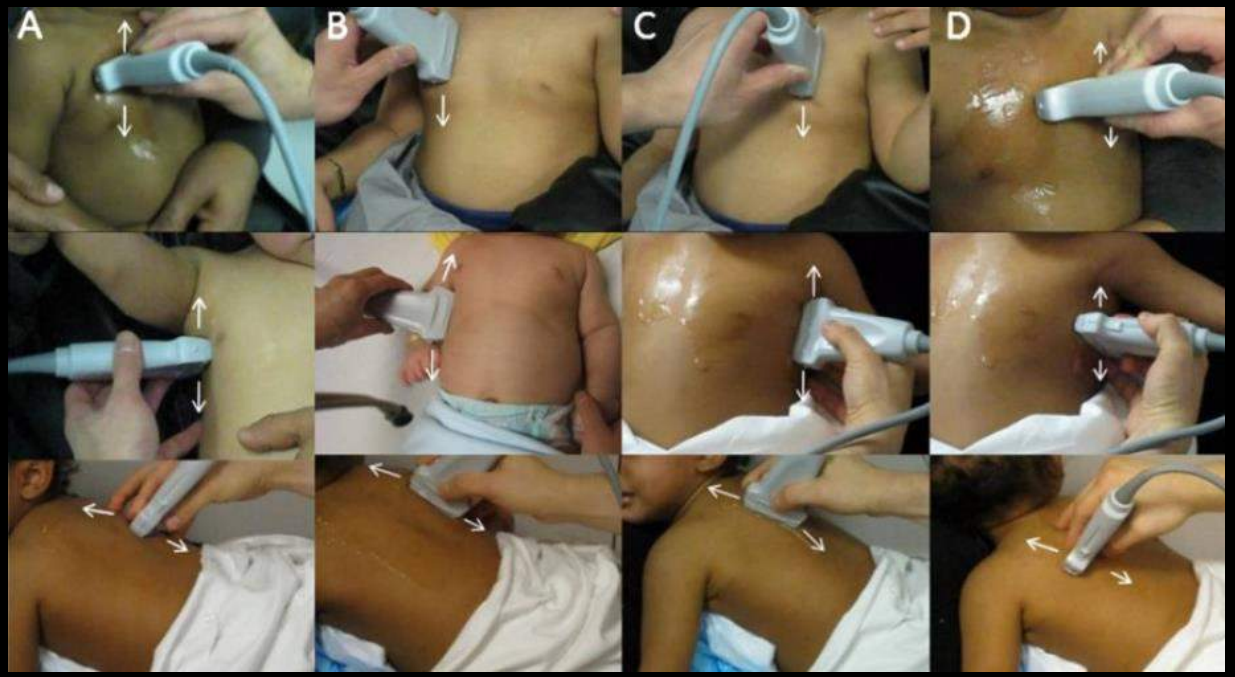
Received 15 August 2011; accepted 22 June 2012

ABSTRACT: *Objective.* The aim of our study was to evaluate the role of standardized video clips compared with still images in the diagnostic accuracy of remote sonographic interpretation

liver,[1,2] where it offers a great potential to diagnose focal pathologies such as hepatocellular carcinoma, hemangioma, metastasis, abscess, or dif-

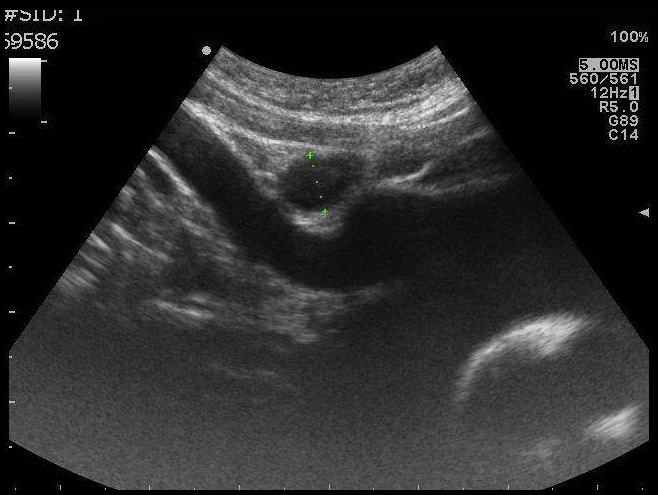
Point of Care US:
for TB and Pneumonia





Tsung 2012

Some research going on



- **Research projects** using US at the Red Cross Children's Hospital in Cape Town, South Africa for mediastinal TB lymphadenopathy and pneumonia
- Others are using TCD for TB and HIV

Childs Nerv Syst. 2014 May 15. [Epub ahead of print]

The value of transcranial Doppler imaging in children with tuberculous meningitis.

van Toorn R[1], Schaaf HS, Solomons R, Laubscher JA, Schoeman JF.

⊕ **Author information**

Abstract

PURPOSE: Transcranial Doppler imaging (TCDI) is potentially a valuable investigational tool in children with tuberculous meningitis (TBM), a condition often complicated by pathology relevant to Doppler imaging such as raised intracranial pressure (ICP) and cerebral vasculopathies.

METHODS: Serial TCDI was performed on 20 TBM children with the aim of investigating cerebrovascular haemodynamics and the relationship between pulsatility index (PI) and ICP.

RESULTS: We observed a poor correlation between ICP and PI in children with communicating hydrocephalus ($p = 0.72$). No decline in PI was noted following 7 days of medical therapy for communicating hydrocephalus ($p = 0.78$) despite a concomitant decline in ICP. Conversely, a decline in PI was noted in all four children with non-communicating hydrocephalus who underwent cerebrospinal fluid diversion. High blood flow velocities (BFV) in all the basal cerebral arteries were observed in 14 children (70 %). The high BFV persisted for 7 days suggesting stenosis due to vasculitis rather than functional vasospasm. Complete middle cerebral artery (MCA) occlusion, subnormal mean MCA velocities (<40 cm/s) and PIs (<0.4) correlated with radiologically proven large cerebral infarcts.

CONCLUSIONS: TCDI-derived PI is not a reliable indicator of raised ICP in children with tuberculous hydrocephalus. This may be attributed to individual variation of tuberculous vascular disease, possibly compromising cerebral vascular compliance and resistance. Basal artery stenosis secondary to vasculitis is observed during the acute stage of TBM in the majority of children.

PMID: 24828794 [PubMed - as supplied by publisher]

HIV and the CNS

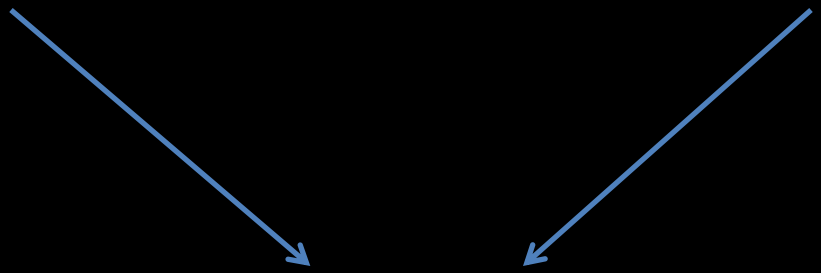
What can be seen with imaging?

‘HIV ENCEPHALOPATHY’
(HIVE)

- Atrophy
- White matter abnormality

‘CONSEQUENCES of HIV’

- Calcifications
- Infections
- Vascular events / lesions
- Maliganancy [uncommon]



Additional:
monitoring disease
progression and treatment response

What can I show you to look for?

- To look for atrophy as a marker of HIVE
- To identify HIVE and PML (progressive multifocal leukoencephalopathy) white matter signal patterns
- Understand that HIV is a major cause of BG calcification
- Look for vascular events
- Look for infections
- To understand the effects of HIV on TBM

HIV Encephalopathy (HIVE)

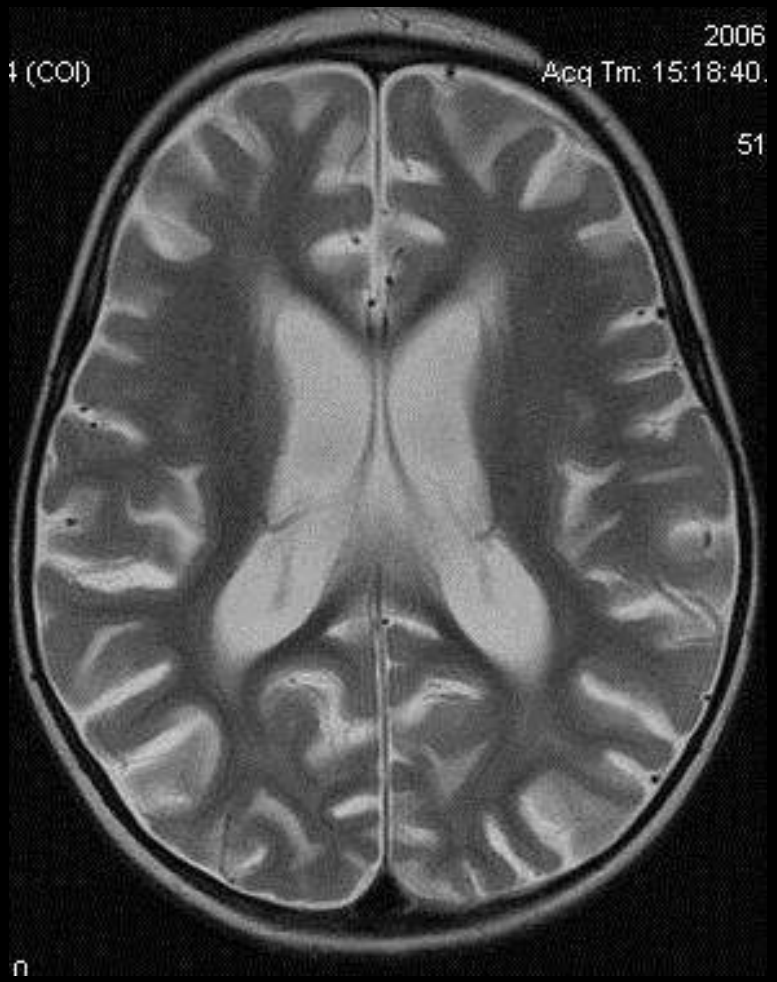
Atrophy and
White matter abnormality

What about atrophy?

- It is the most common finding (90%) in HIV imaging
  (Kauffman et al 1992, Safriel et al 2000, Kieck and Andronikou 2004)
- It's the imaging representation of HIV encephalopathy
- It correlates with severity and viral load
- It is reversible or can be halted on HAART (Di Carli et al 1991)
- It is measurable on imaging
- But it is a late finding - we need something earlier in the disease

Volume loss

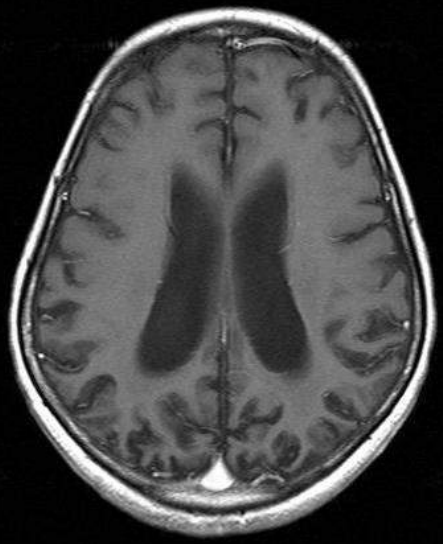
This patient is HIV-infected



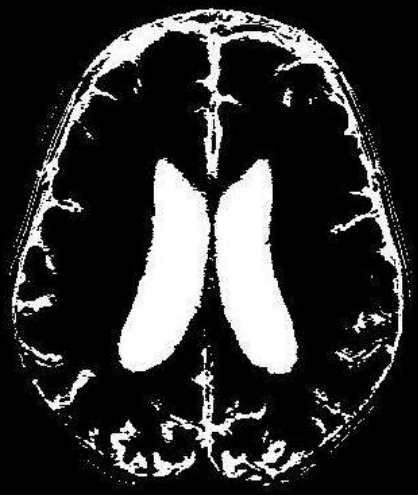
White matter:
- Expanded ventricles
(in presence of large SAS)
- deep sulci
(near ventricles)

Doesn’t it remind you of chronic evolution of HIE???

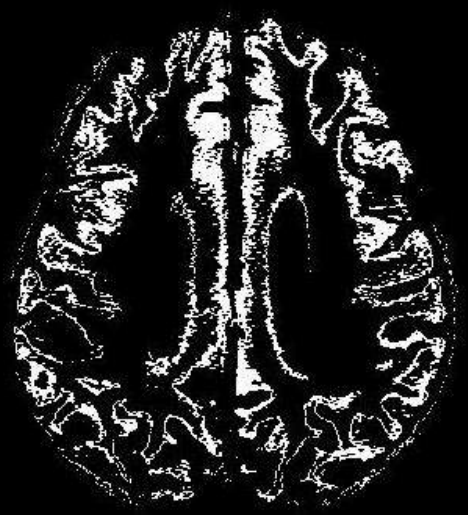
An objective, automated method of measuring volume loss: Matlab



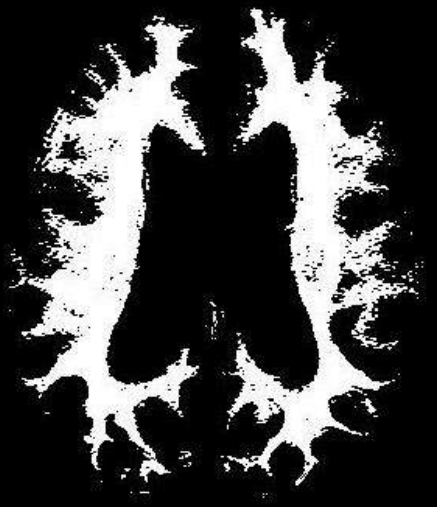
T1 image



CSF segmented

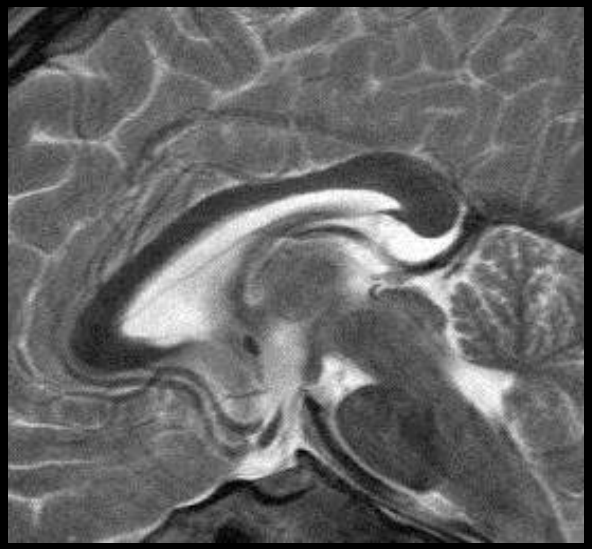


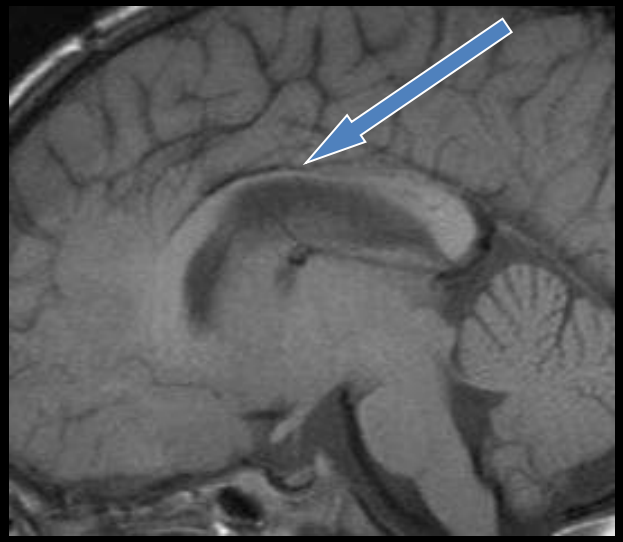
Cortex segmented

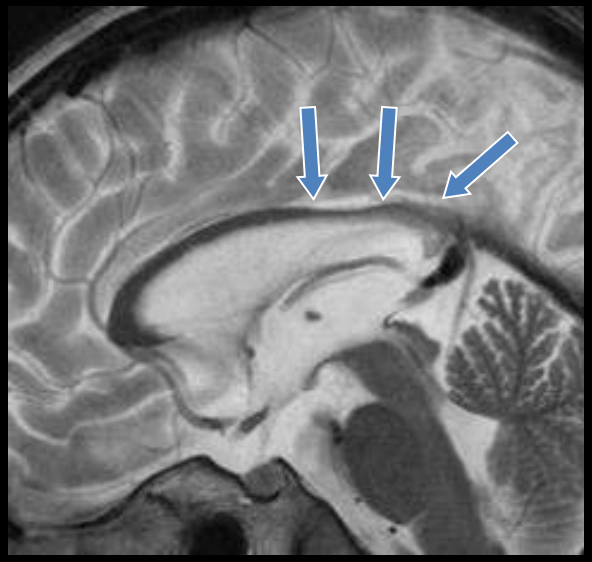


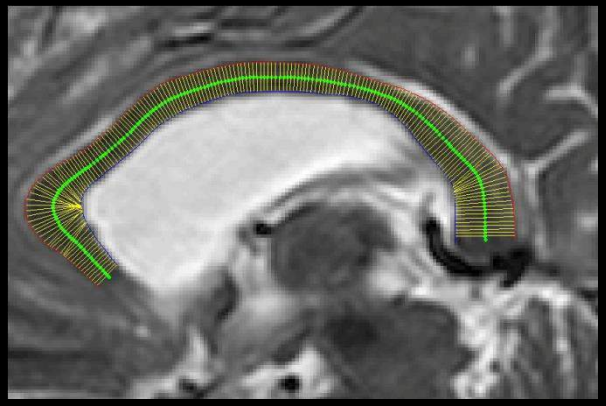
White matter segmented

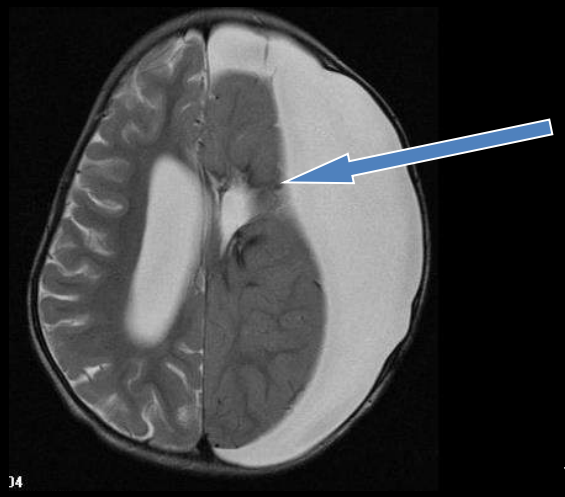
Corpus Callosum: a surrogate marker of WM volume?

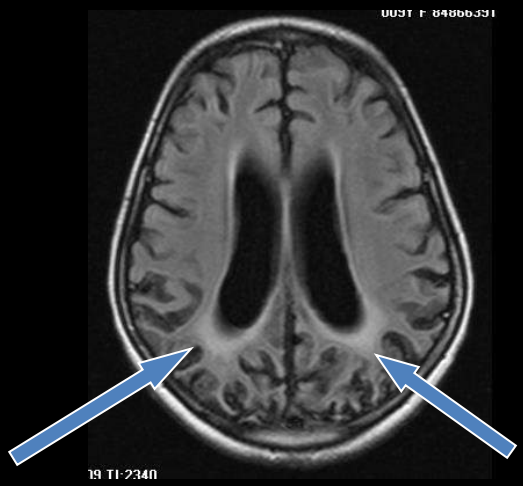












FOCAL LOSS

GLOBAL LOSS

Results:

Brain volume only showed a trend relationship with nadir CD4.

Correlation degree of mental development and motor segmental CC thickness

Correlation of the CC length with immunity and microcephaly

Childs Nerv Syst
DOI 10.1007/s00381-014-2434-3

ORIGINAL PAPER

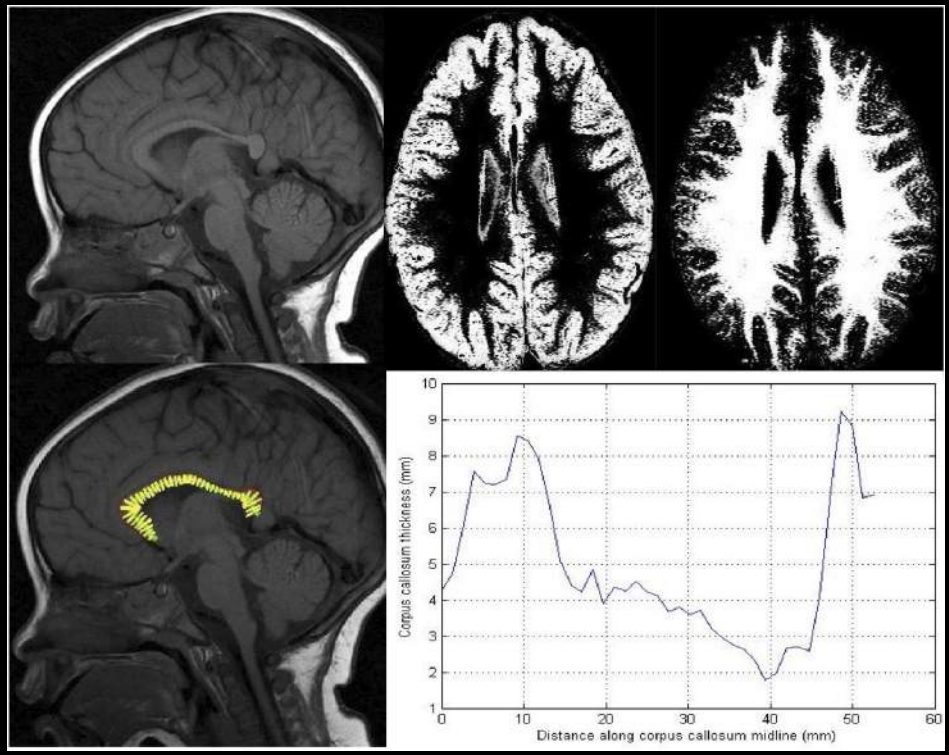
Correlating brain volume and callosal thickness with clinical and laboratory indicators of disease severity in children with HIV-related brain disease

Savvas Andronikou · Christelle Ackermann · Barbara Laughton · Mark Cotton · Nicollette Tomazos · Bruce Spottiswoode · Katya Mauff · John M. Pettifor

Received: 15 March 2014 / Accepted: 30 April 2014

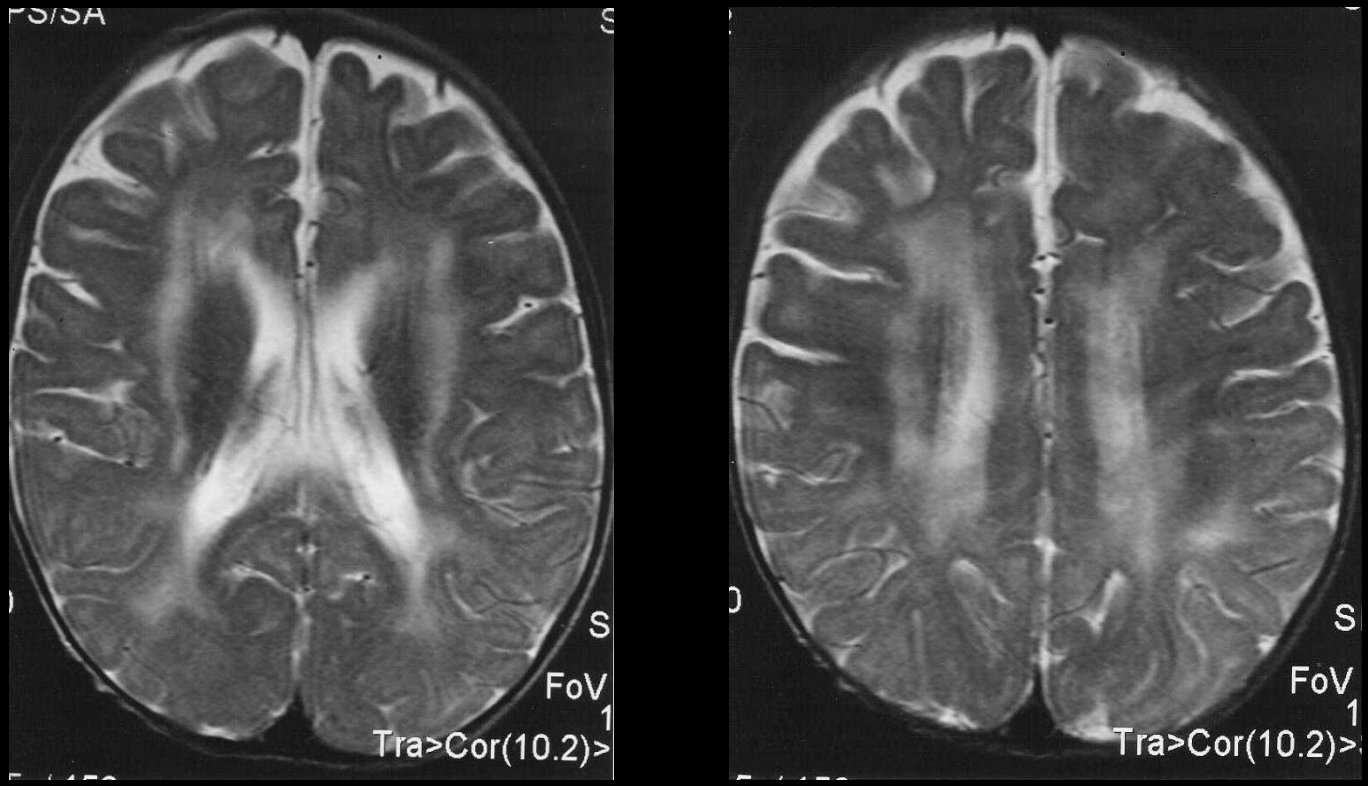
Abstract
Background Objective MRI markers of central nervous system disease severity may precede subjective features of HIV encephalopathy in children. Previous work in

associated with low CD4 and with neuropsychological impairment. Significant thinning of the corpus callosum (CC), predominantly anteriorly, was also found in HIV-infected adults and correlated with CD4 levels. These



What about the white matter signal?

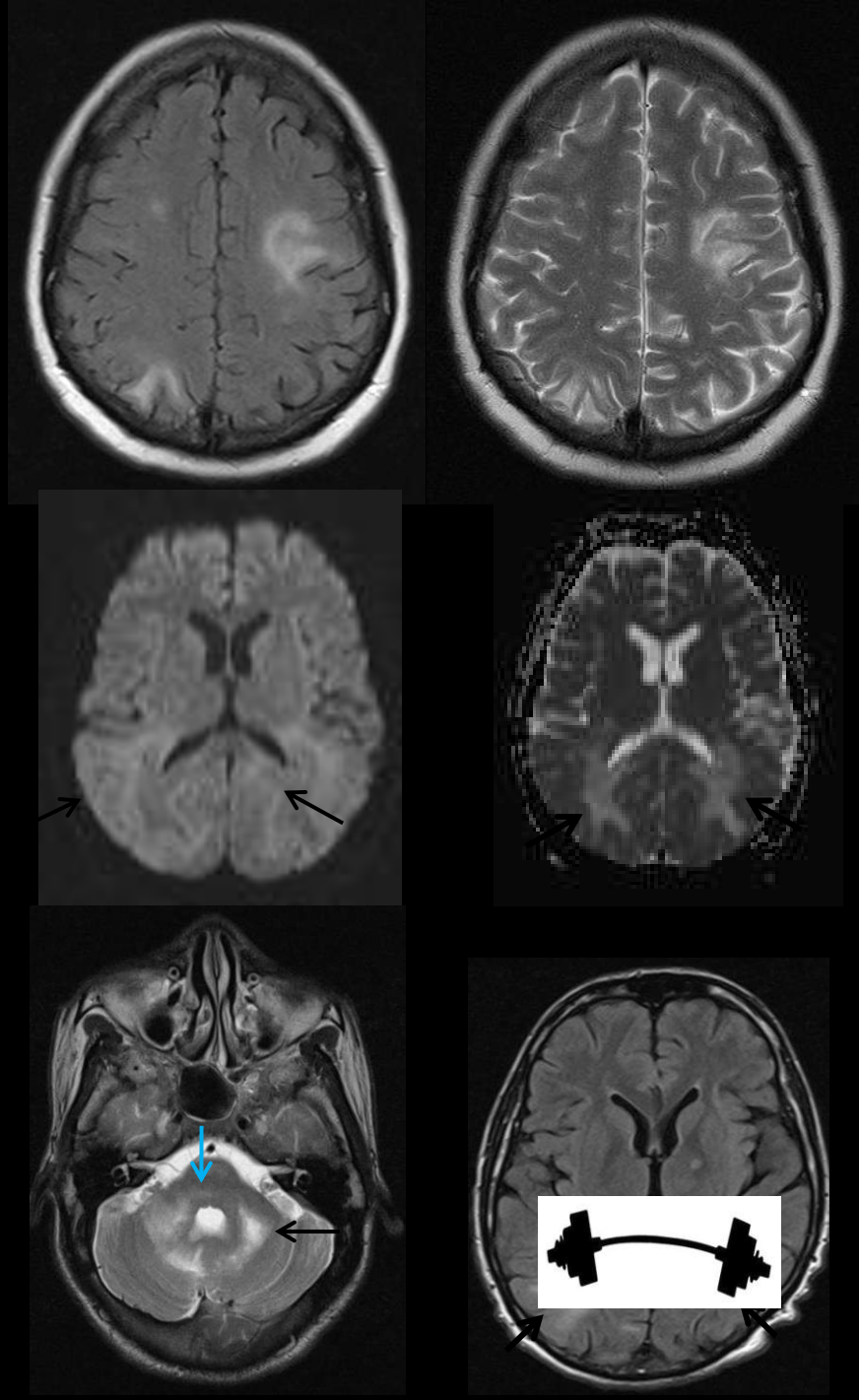
Encephalopathy (HIVE): T2 high signal



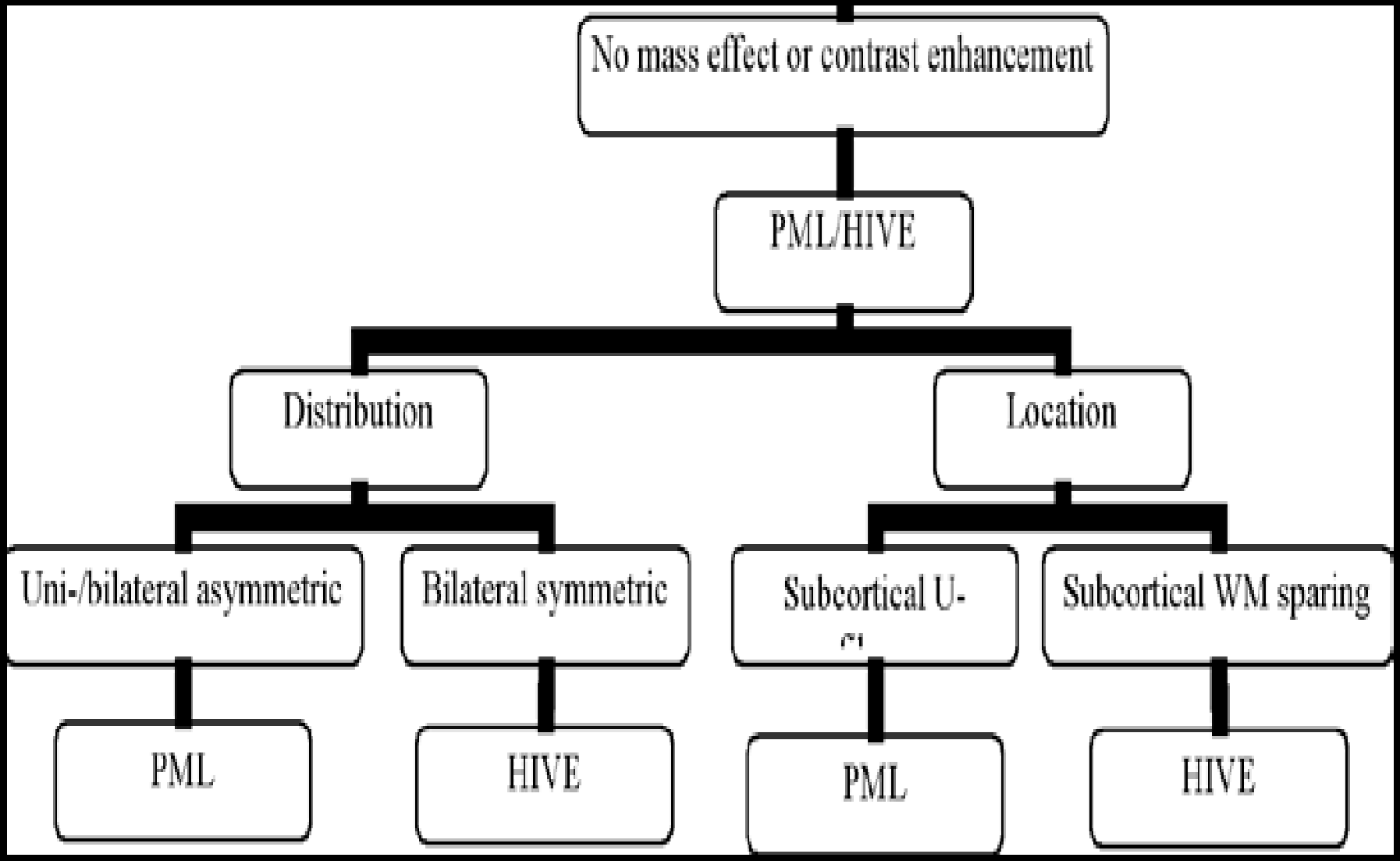
Bilateral ‘symmetric’
Spares sub-cortical U-fibres

Progressive multifocal leukoencephalopathy (PML)

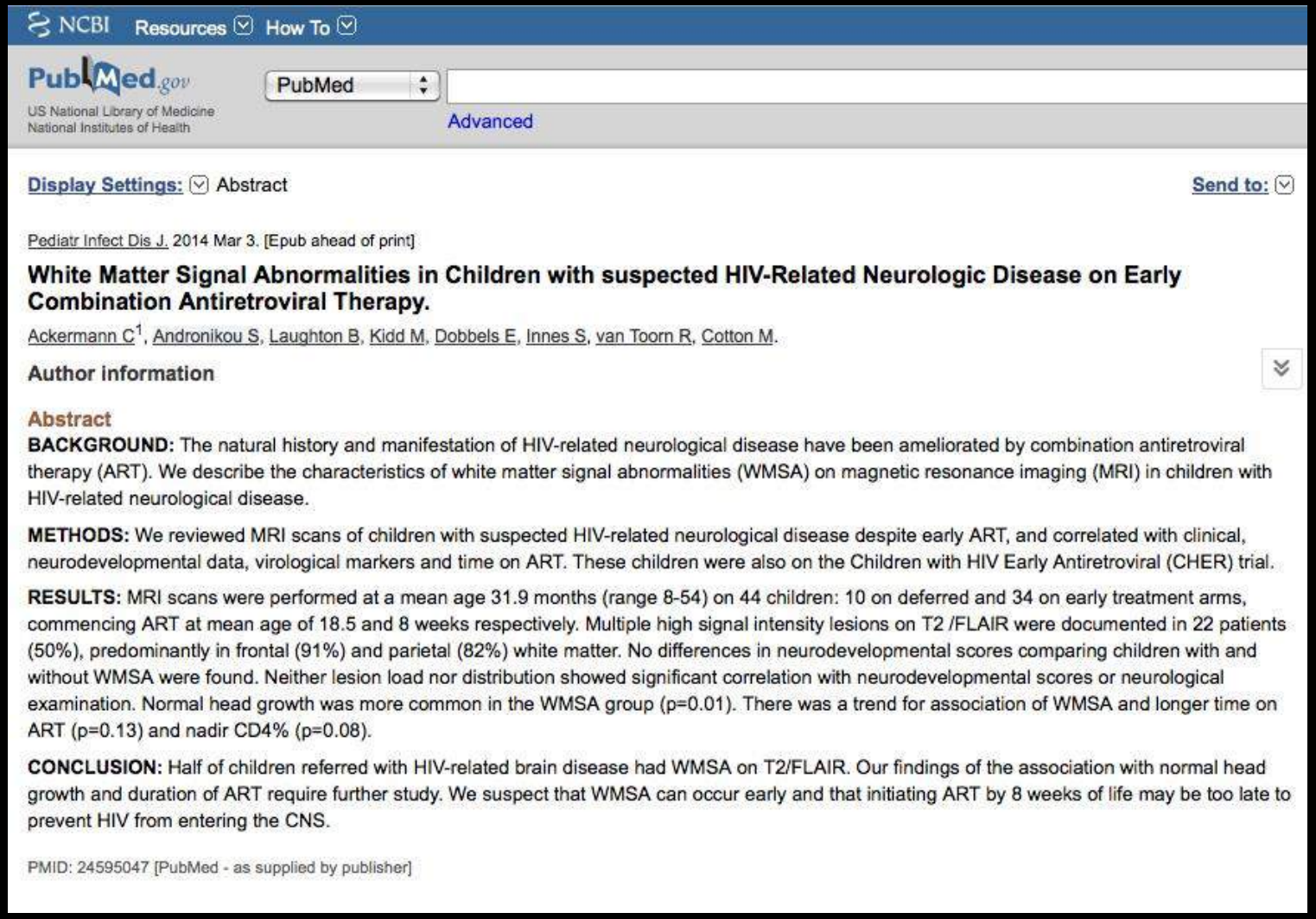
- Much less common
- Have the JC virus
- Confused with HIVE but…
- More focal
- Asymmetrical
- Common posterior parietal
- Involve U-fibres
- Advanced cases - ‘bar-bell’ sign



Summary HIVE vs. PML



More subtle WM abnormalities?



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Pediatr Infect Dis J. 2014 Mar 3. [Epub ahead of print]

White Matter Signal Abnormalities in Children with suspected HIV-Related Neurologic Disease on Early Combination Antiretroviral Therapy.

Ackermann C[1], Andronikou S, Laughton B, Kidd M, Dobbels E, Innes S, van Toorn R, Cotton M.

Author information

Abstract

BACKGROUND: The natural history and manifestation of HIV-related neurological disease have been ameliorated by combination antiretroviral therapy (ART). We describe the characteristics of white matter signal abnormalities (WMSA) on magnetic resonance imaging (MRI) in children with HIV-related neurological disease.

METHODS: We reviewed MRI scans of children with suspected HIV-related neurological disease despite early ART, and correlated with clinical, neurodevelopmental data, virological markers and time on ART. These children were also on the Children with HIV Early Antiretroviral (CHER) trial.

RESULTS: MRI scans were performed at a mean age 31.9 months (range 8-54) on 44 children: 10 on deferred and 34 on early treatment arms, commencing ART at mean age of 18.5 and 8 weeks respectively. Multiple high signal intensity lesions on T2 /FLAIR were documented in 22 patients (50%), predominantly in frontal (91%) and parietal (82%) white matter. No differences in neurodevelopmental scores comparing children with and without WMSA were found. Neither lesion load nor distribution showed significant correlation with neurodevelopmental scores or neurological examination. Normal head growth was more common in the WMSA group (p=0.01). There was a trend for association of WMSA and longer time on ART (p=0.13) and nadir CD4% (p=0.08).

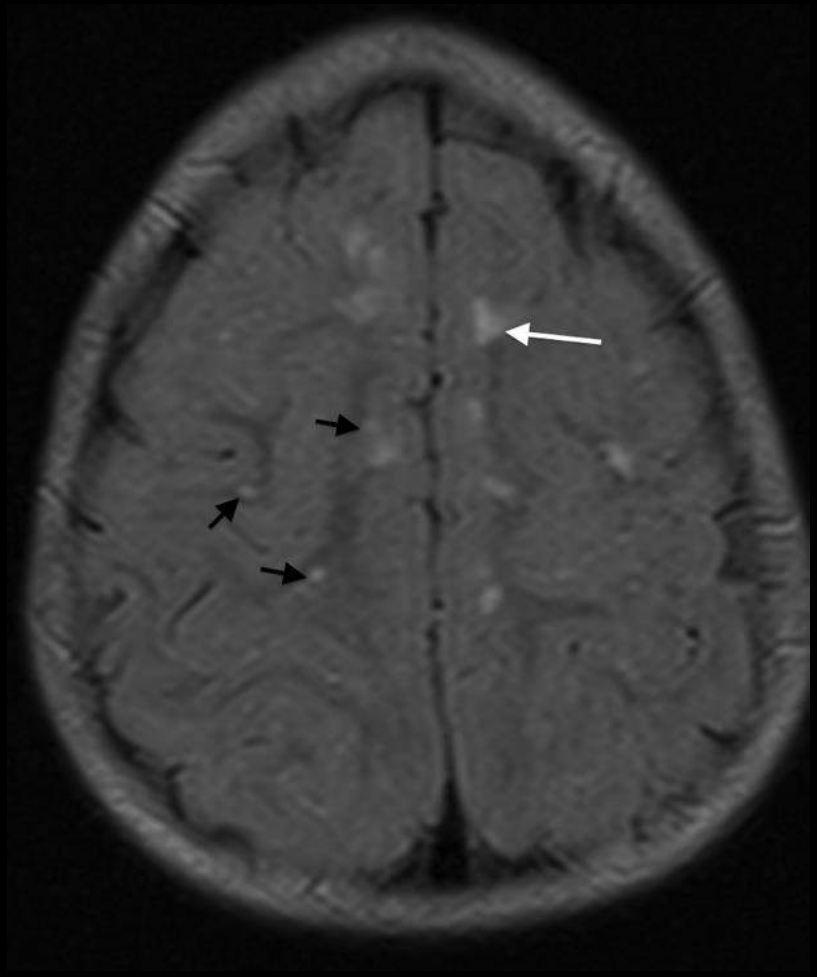
CONCLUSION: Half of children referred with HIV-related brain disease had WMSA on T2/FLAIR. Our findings of the association with normal head growth and duration of ART require further study. We suspect that WMSA can occur early and that initiating ART by 8 weeks of life may be too late to prevent HIV from entering the CNS.

PMID: 24595047 [PubMed - as supplied by publisher]

Prevalence of WMSA "HIV related brain disease" = 50%

Of the 22 patients with WMSA:

- 17 patients pinpoint lesions < 1cm
- 8 confluent lesions
- 2 patients lesions > 1cm
- Lesion size: 5 -12mm
  (mean 7.2mm)



WMSA

- Half of children referred for HIV-related brain disease had WMSA on T2MRI
- Involved mainly frontal and parietal lobes.
- **Positive correlation of ‘time on ART’ and presence of WMSA**
- Trend correlating nadir CD4% and presence of WMSA.

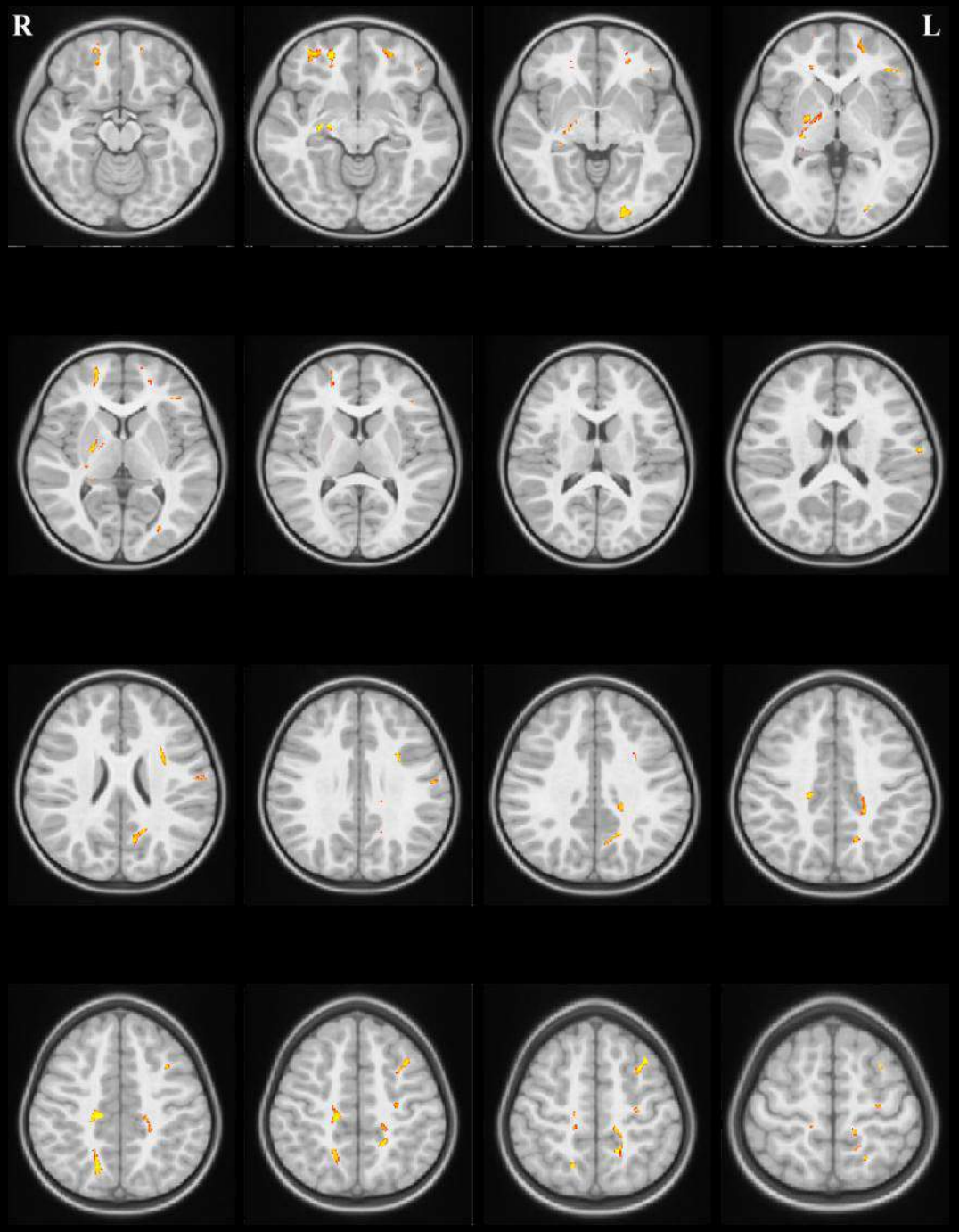
HIVE with a normal signal?

Work in HIV infected adults: DTI and FA

- Normal looking subcortical WM and CC
- BUT…areas where FA decreased
- Patients with lowest FA had most advanced HIV [Filippi CG et al 2001]

- Abnormalities corpus callosum in patients with HIV, associated with dementia severity and motor speed losses [Wu Y et al 2006]
- Reasons: trafficking of virus from ventricular CSF

DTI: FA group comparison of HIV infected vs. Controls



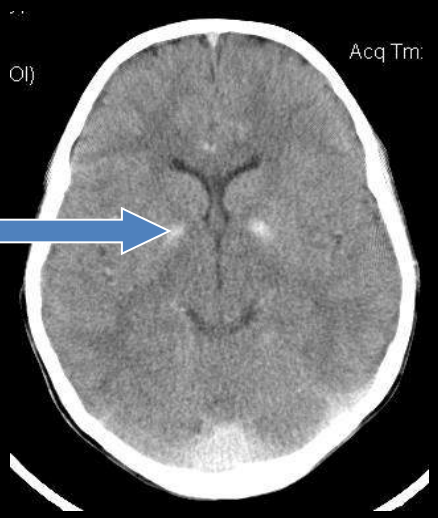
Consequences

Calcification

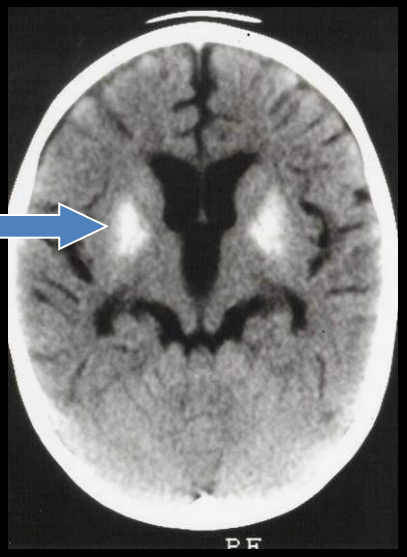
Basal ganglia calcification

- Commonest cause of BG calcification in children is HIV
- Up to 1/3 of children with HIV have calcification
- Usually affect palidus and putamen
- Less often frontal white matter / cerebellum
- Not seen before 10 months age

palidus

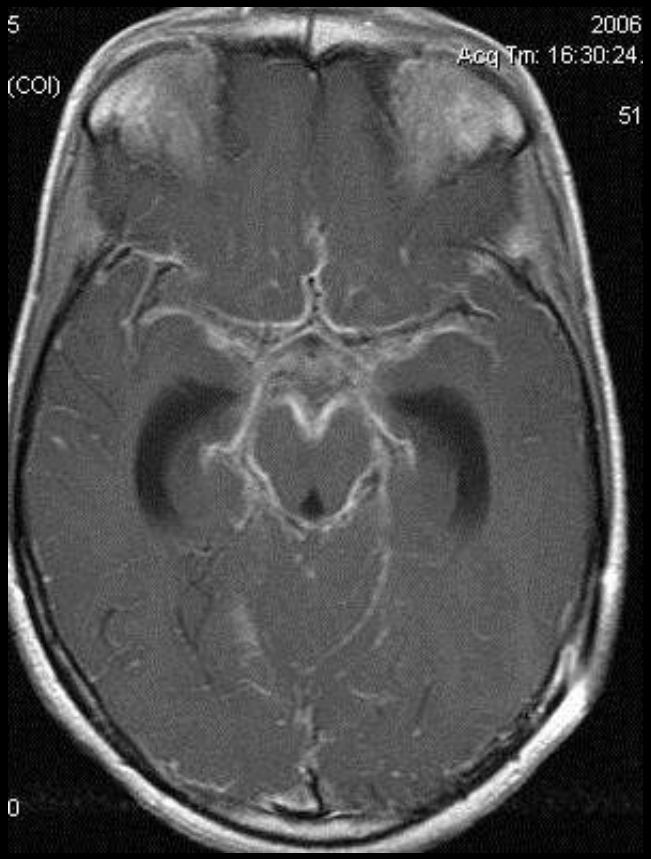


Palidus and Putamen

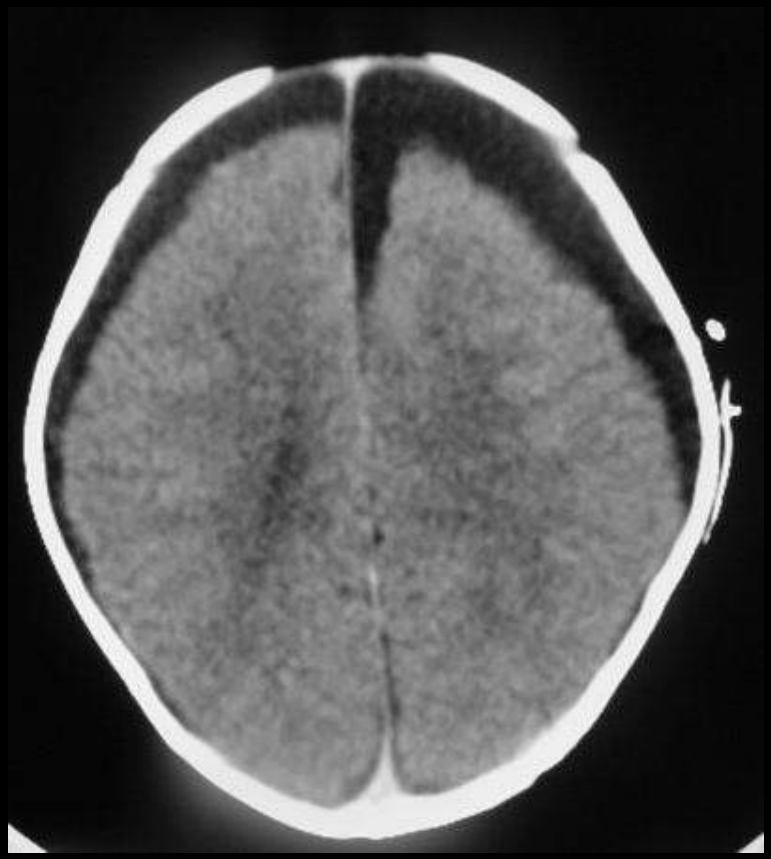


Infections:

Infection:



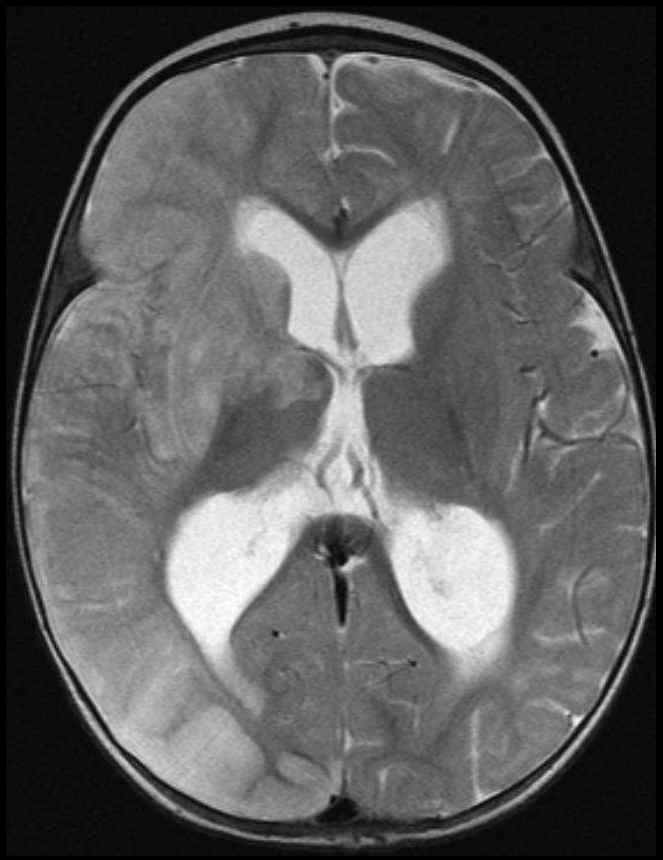
TBM: best feature is basal enhancement



Pyogenic meningitis:
Surface collections; Venous infarctions

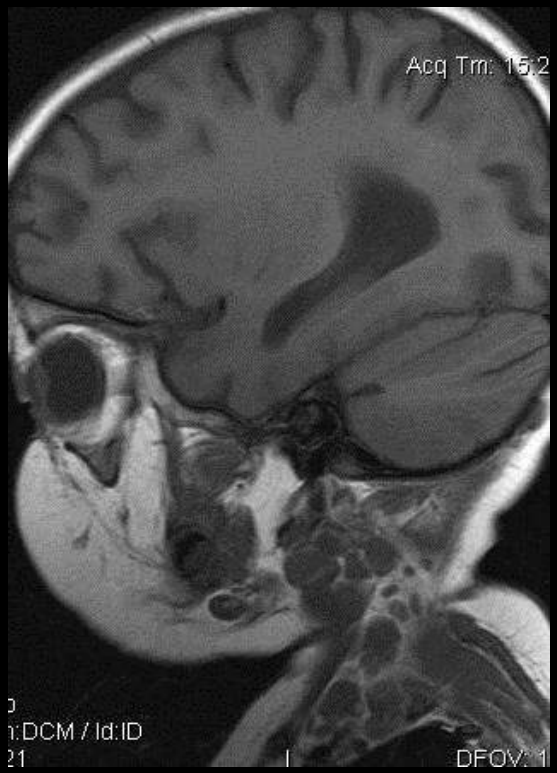
Vascular: Infarction / aneurysms

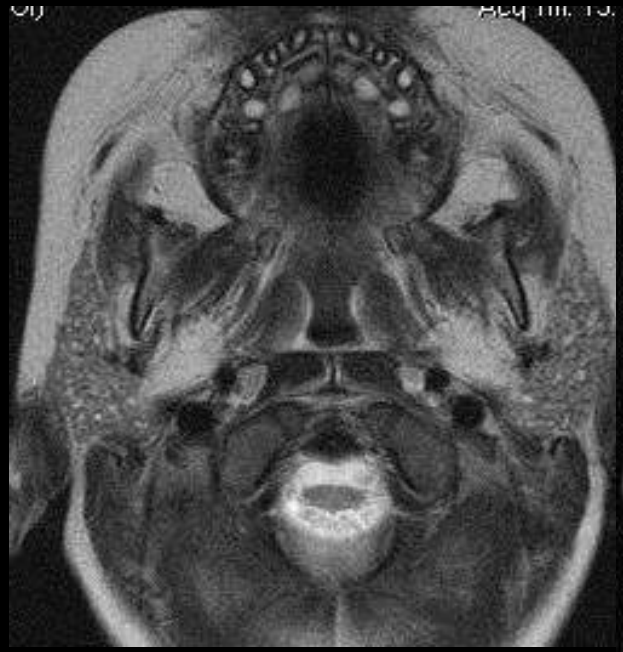
Infarction

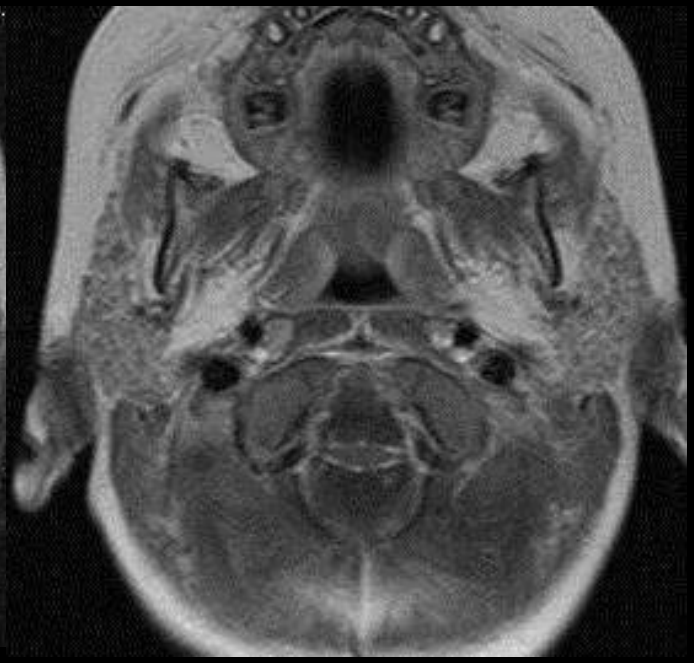


Other findings on the scan

Parotidomegally - painless bilateral
Lymphadenopathy - cervical







HIV and TB together:
Add petrol to the fire?

HIV and TB

- Because the body fails to contain TB in the lungs…..
- HIV predisposes to blood borne and extra-pulmonary TB……
- BUT
- HIV also affects imaging appearances of TB

TB and HIV co-infection: CNS

Childs Nerv Syst
DOI 10.1007/s00381-011-1451-8

ORIGINAL PAPER

MRI findings in children with tuberculous meningitis: a comparison of HIV-infected and non-infected patients

Gerrit Dekker · Savvas Andronikou · Ronald van Toorn · Shaun Scheepers · Andrew Brandt · Christelle Ackermann

PERSPECTIVE

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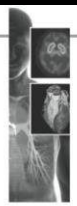

MRI appearances of tuberculous meningitis in HIV-infected children: a paradoxically protective mechanism?

Immune suppression predisposes HIV-infected children to opportunistic infections including *Mycobacterium tuberculosis*. HIV infection increases the risk of progression to active disease and also increases the risk for extrapulmonary involvement, including tuberculous meningitis (TBM). Brain injury in TBM is the consequence of an immune-mediated vasculopathy. HIV-related immune dysfunction prevents the production of thick exudates that cause parenchymal infarctions and cerebrospinal fluid flow obstruction. It could be postulated that HIV may be 'protective' from some of the common complications related to TBM. The aim of this paper is to highlight the 'protective' features of HIV-related immune suppression observed on MRI in children with TBM and promote the use of MRI for detecting subtle and atypical meningeal enhancement in HIV and TBM coinfected children.

KEYWORDS: atrophy basal ganglia basal meningeal enhancement HIV hydrocephalus immune suppression infarction milliary TB MRI tuberculous meningitis

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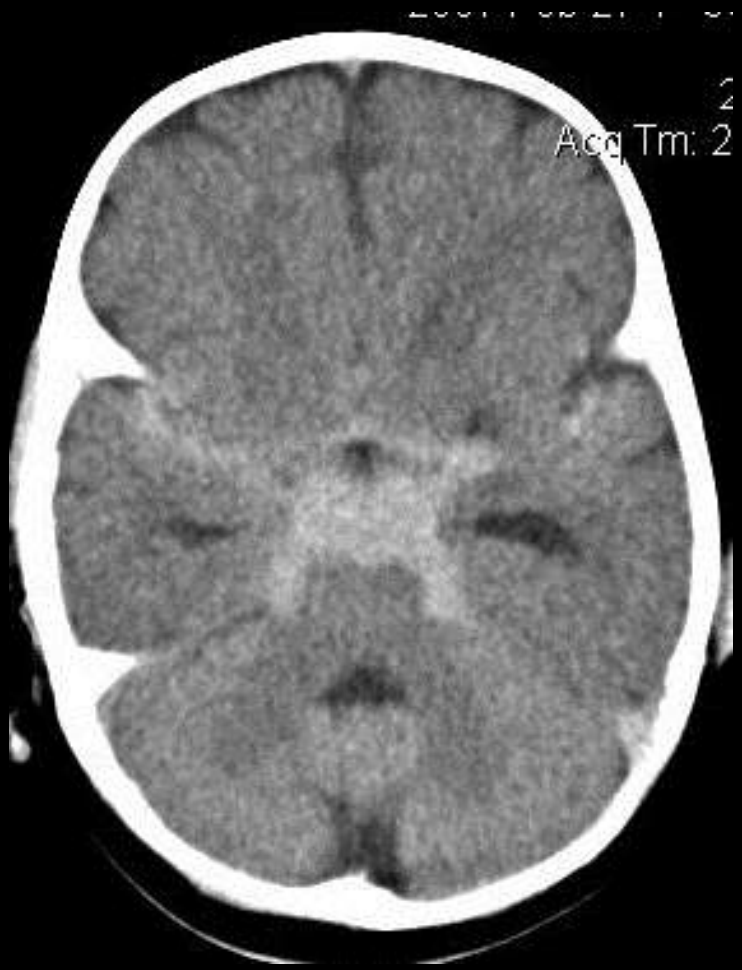
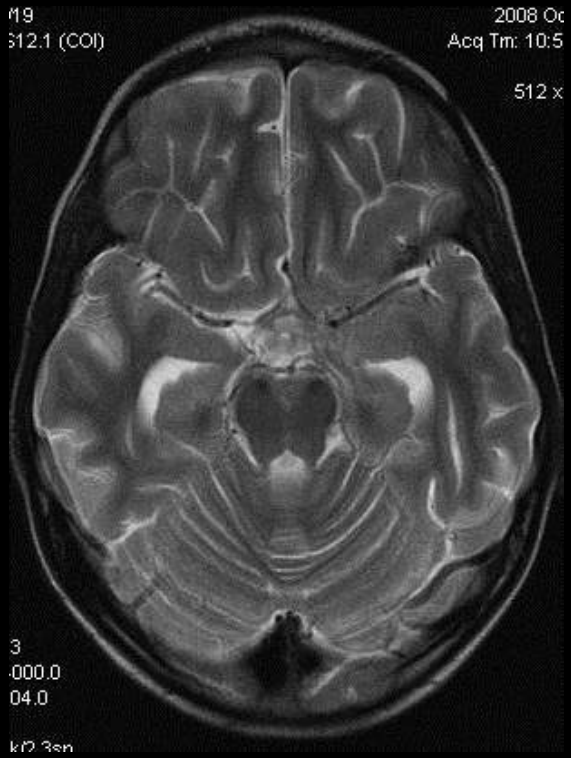
Concepts in imaging TBM

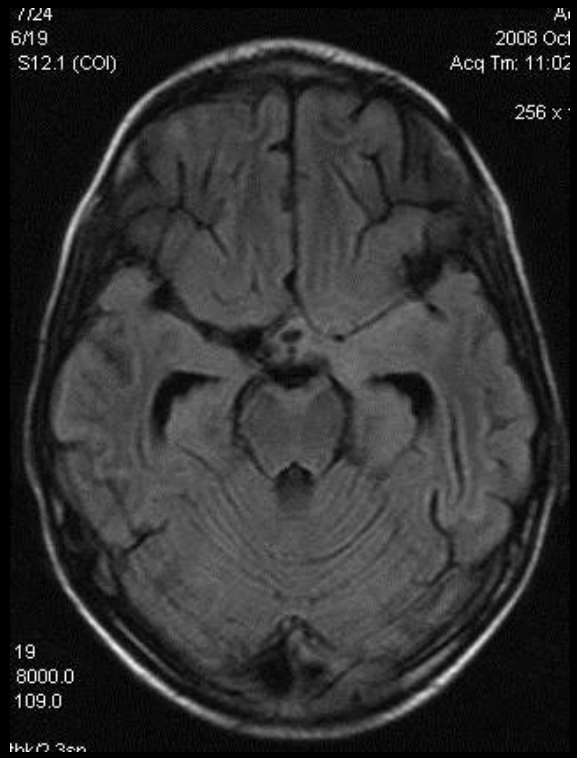


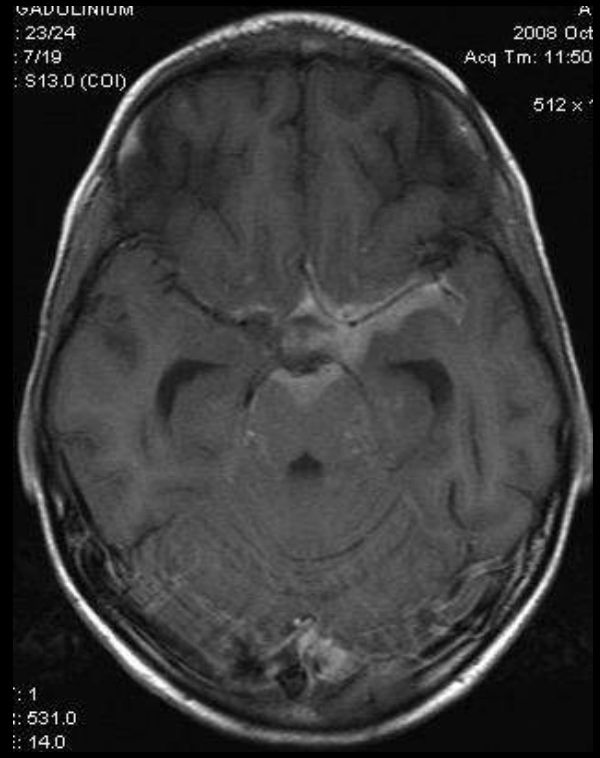
- It’s the immune response to bacilli in the meninges that results in pathological features of TBM…..

Diagnosis of TBM:

MRI diagnosis of pediatric TBM = basal enhancement (93%)

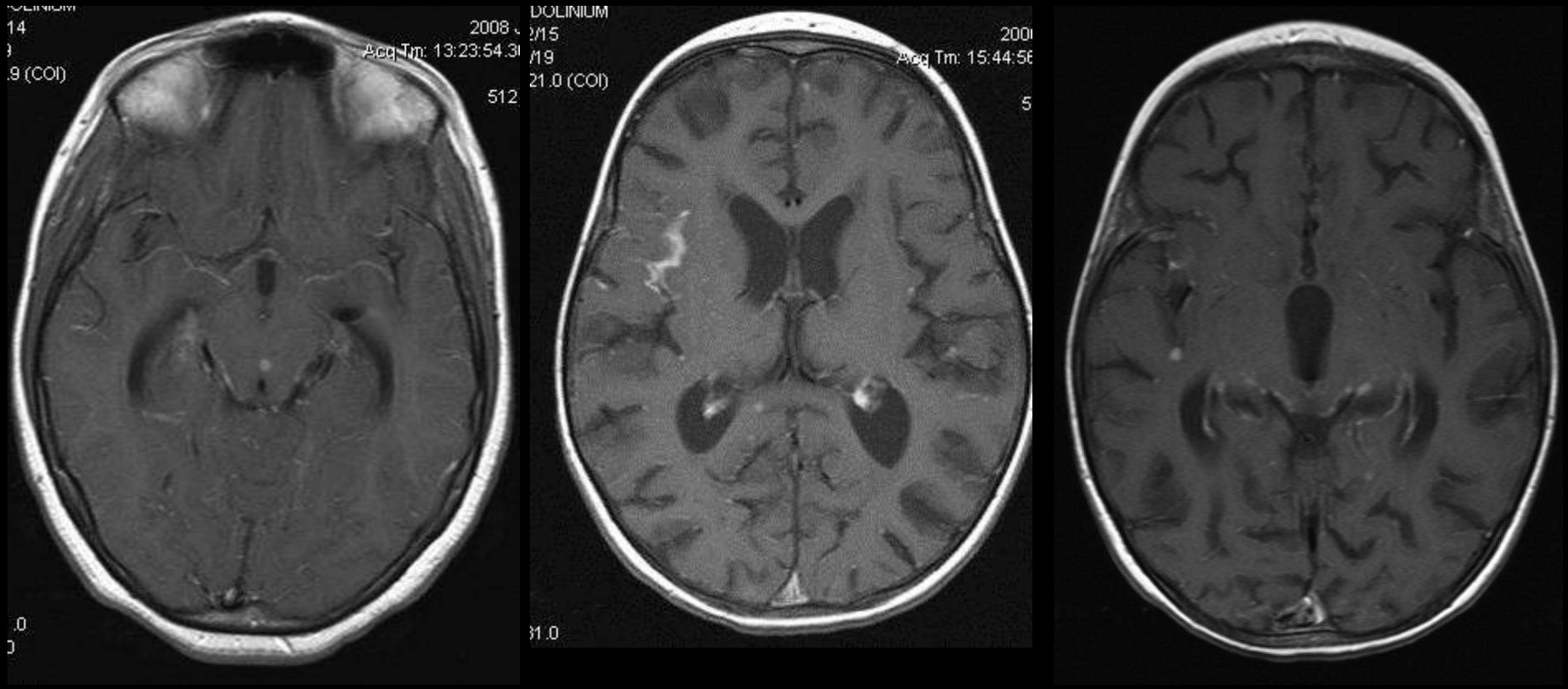






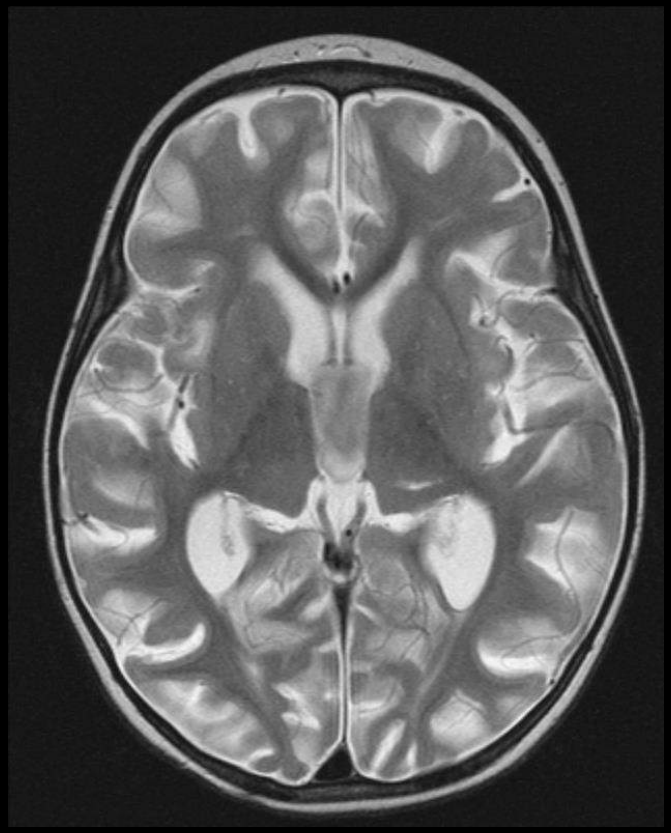
Basal Enhancement in HIV

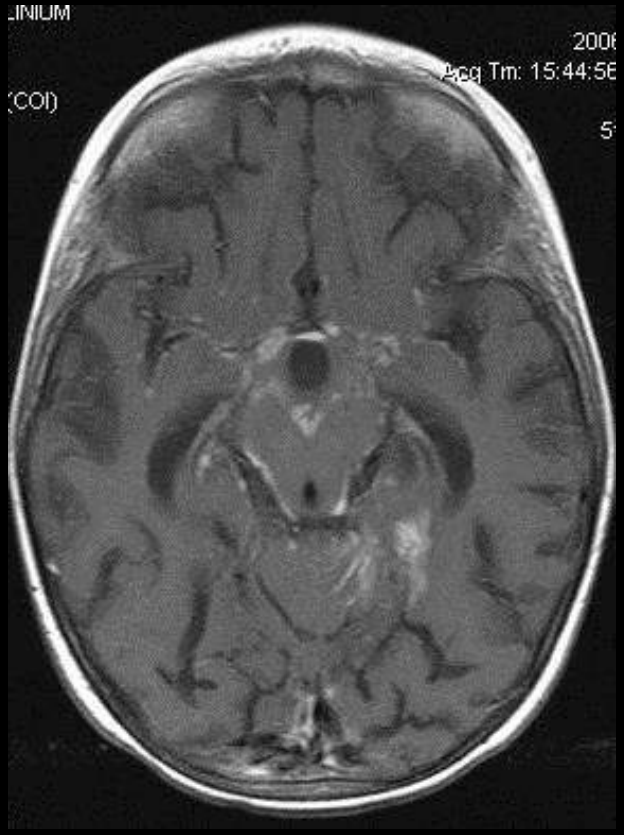
BE = infrequent, less prominent, atypically distributed, milliary nodules (100%)



Ventriculomegally in HIV

CSF space = result of atrophy; hydrocephalus less frequent and exclusively communicating





So now you know....

HIV

CHEST

CNS

Co-infection with TB