Somewhat short cases

Cross Canada Rounds

June 21, 2018

Connie Yang

CASE 1

- Male toddler
  - Pulmonary valve stenosis with only trivial gradient across the pulmonary valve, left ventricular outflow tract obstruction
  - Suspicion of Noonan syndrome
  - Presented with hypoxemia and increased work of breathing
  - Chest x-ray showing a pleural effusion

Details of case removed

Investigations

- Pleural fluid
  - Bloody in appearance
  - Bacterial, fungal, mycobacterial culture negative
  - Cell count: lymphocytes 98%, macrophages 2%
    - Lymphocytes not clonal, cytology negative
  - Glucose 4.2
  - Protein 42, LDH 1308 (blood protein 63, LDH 866)
  - Triglycerides 8.89mmol/L

- Pleural:Blood ratio Protein 0.67, LDH 1.5

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- **CHYLOTHORAX**
- **NON-BACTERIAL INFECTION (TB)**
- **MALIGNANCY**
- **CONNECTIVE TISSUE DISEASE**

OVER 1.24mmol/L

- Pleural:Blood ratio Protein 0.67, LDH 1.5

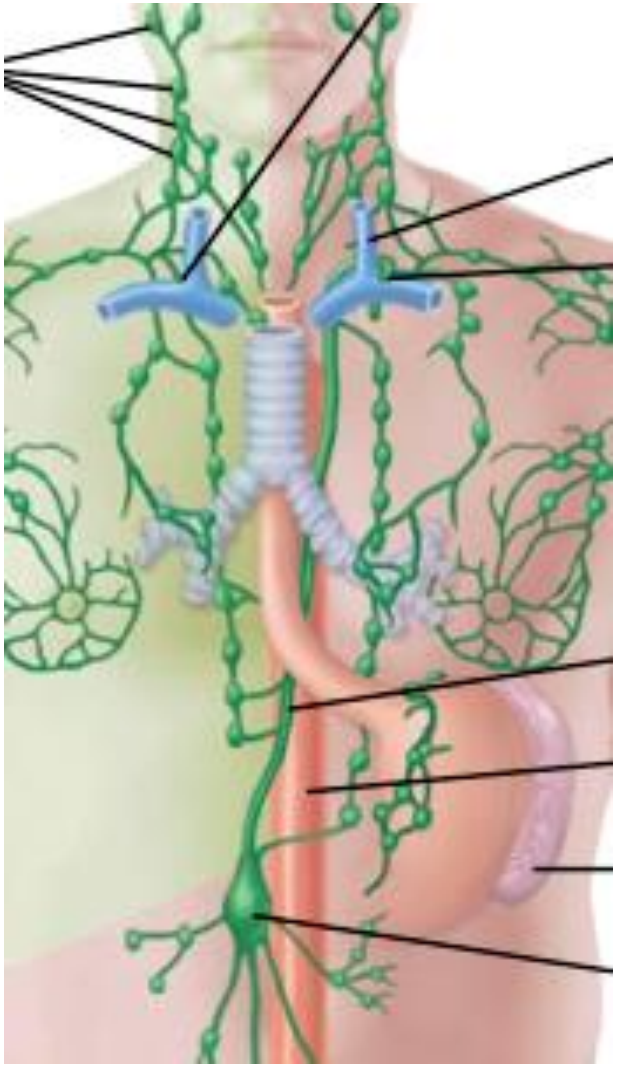
EXUDATE
- protein ratio>0.5
-LDH ratio> 0.6
- LDH >2/3 serum

CHYLOHEMOTHORAX

What is your differential diagnosis for a chylous effusion?

DDx: Chylothorax in Children

1. Thoracic Duct
2. High venous pressure
3. Congenital / Primary lymphatic

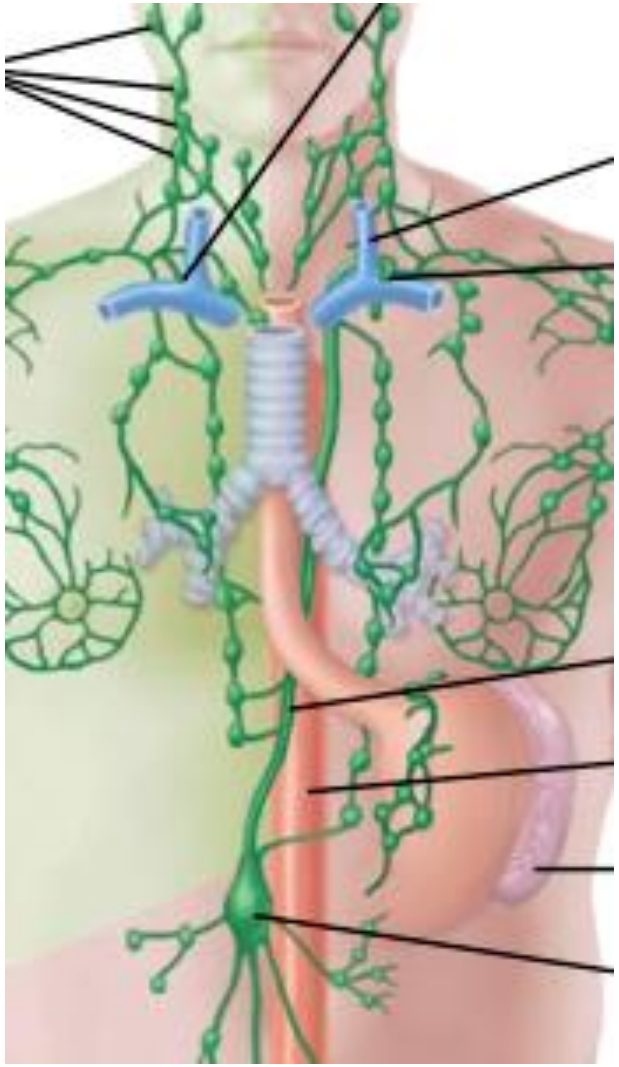


Adapted from JD Tutor Pediatrics. 2014, Wassel Pediatrics 2015, Faul AJRCCM 2000

DDx: Chylothorax in Children

1 **Thoracic Duct** damage, compression, erosion

- Post-operative
- Trauma
- Malignancy
  - Neurogenic
  - Lymphoma
  - Teratoma
  - Wilms
  - Sarcoma
- Nodes
  - TB (can also get pleural fibrosis)



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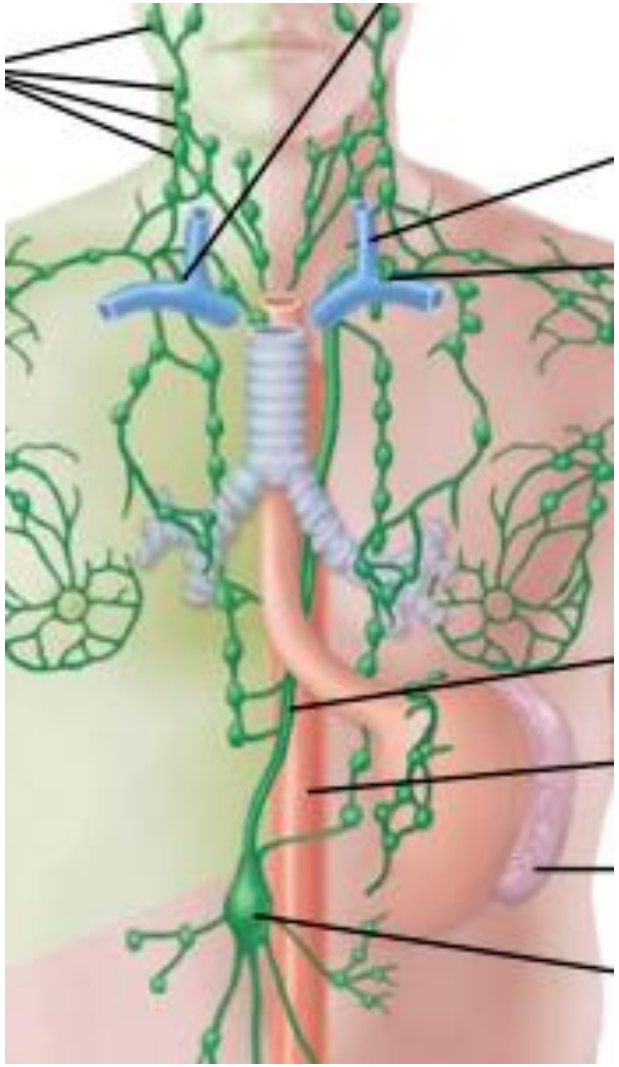


2 High venous pressure

- SVC thrombus
- Post-Fontan

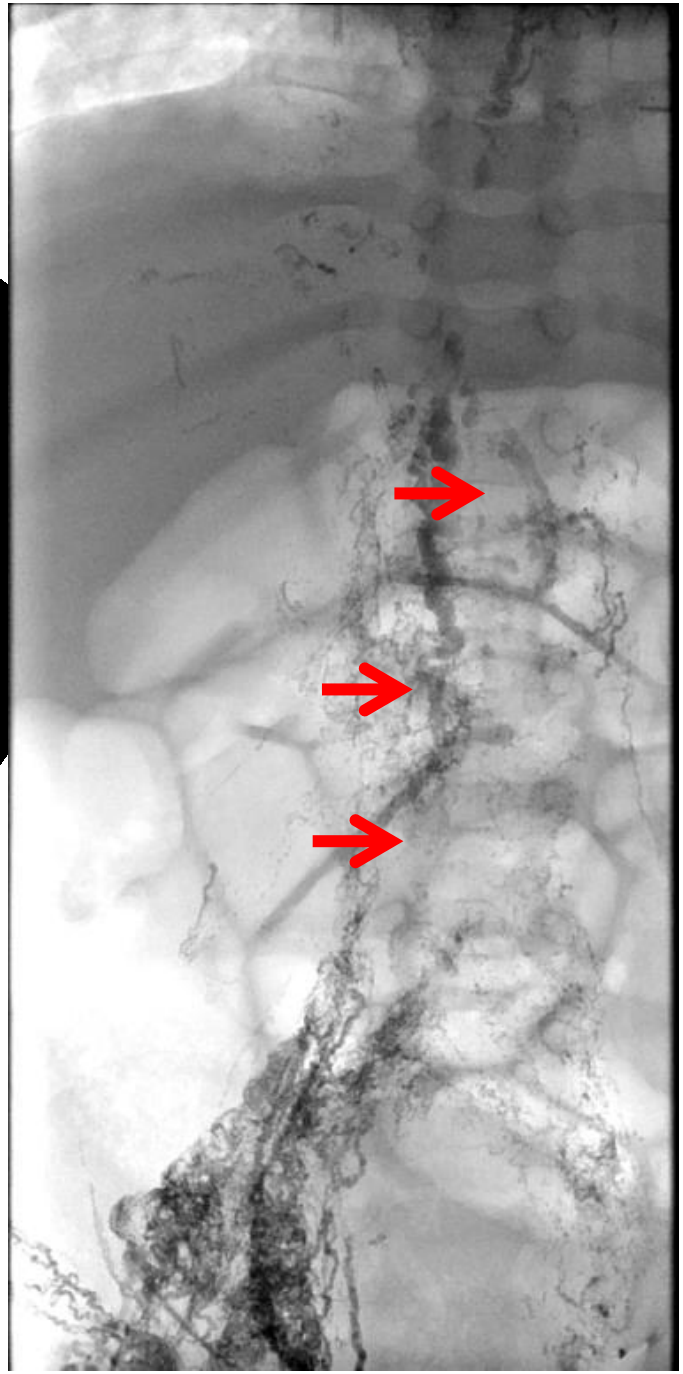
3 Congenital / Primary lymphatic

- Primary Lymphangiectasia
- Atresia/absence of thoracic duct
- Lymphatic Malformations
  - Common (Lymphangiomas)
  - Generalized lymphatic anomaly (Lymphangiomatosis)
- Syndromes (T21, XO, Noonan)

Barker ERJ 2004
Wassel Pediatrics 2015

Failed conservative treatment with diet and octreotide

Lymphangiogram done with clinical improvement



http://unitec.researchbank.ac.nz/handle/10652/3990

- Represented 6 months later with recurrent chylohemothorax and again failed conservative management with diet and octreotide
- The evening following his second lymphangiogram he had worsening work of breathing and hypoxemia with an x-ray showing diffuse bilateral infiltrates

Differential diagnosis?

- Water
  - pulmonary edema (post-obstructive pulmonary edema, pulmonary embolus with pulmonary edema, ARDS)
- Blood
  - diffuse alveolar hemorrhage due to reaction to lipiodol
- Pus
  - pneumonia

- CBC showing Hb 76 (previously 111), WBC 16.1, Plt 362
- CRP <5, INR/PTT normal

- Increasing hypoxemia requiring intubation
- Bronchoscopy confirmed blood in airways and on lavage
- Treated with methylprednisolone 4mg/kg/day
- Eventually extubated and weaned to room air with removal of chest tubes and discharged on a one month wean of prednisone

Risks of lymphangiogram

- Pulmonary hemorrhage
  - First reported in 1995 following bipedal lymphography in a 50 year old with Hodgkin's lymphoma
  - Presented 4 days after procedure with fever, cough and increasing dyspnea, alveolar hemorrhage confirmed on BAL, self-resolved in 2 days
- Extravasation of lipiodol into soft tissue
- Pulmonary embolism

Lee EW Korean J Rad 2014
Dupont Intensive Care Med 1995

Take home messages

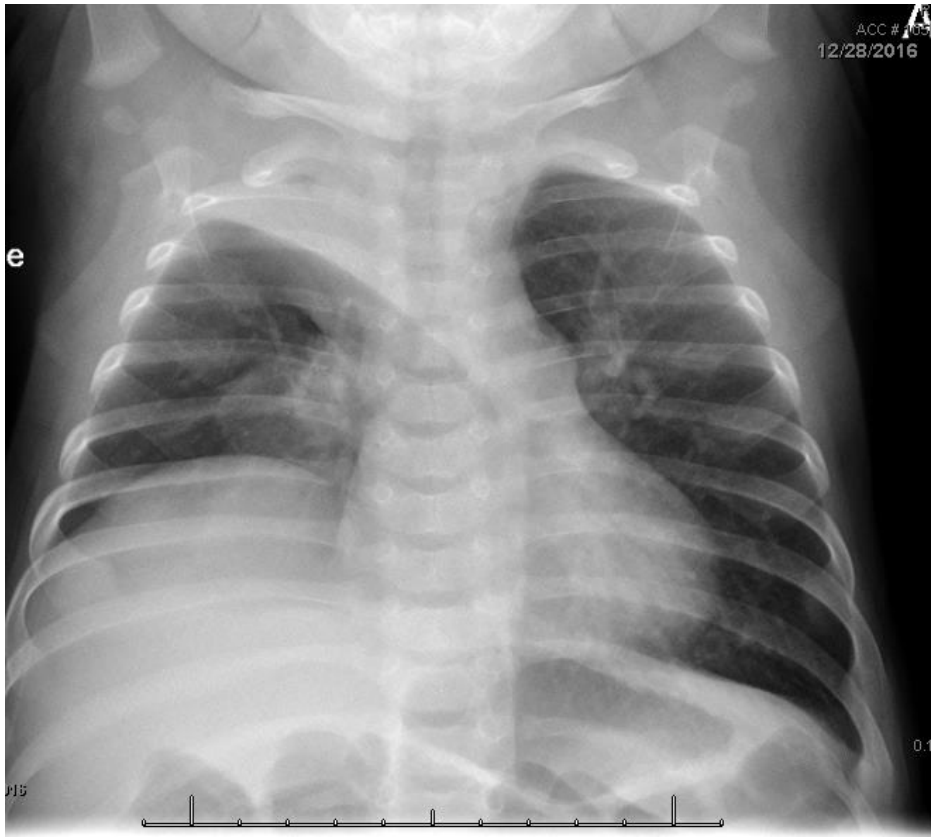
- Lymphangiectasia in Noonan's syndrome can present with later onset chylothorax
- Lymphangiogram seems to be useful in the treatment of chylothorax secondary to lymphangiectasia
- Pulmonary hemorrhage is a rare but life threatening complication of lymphangiogram

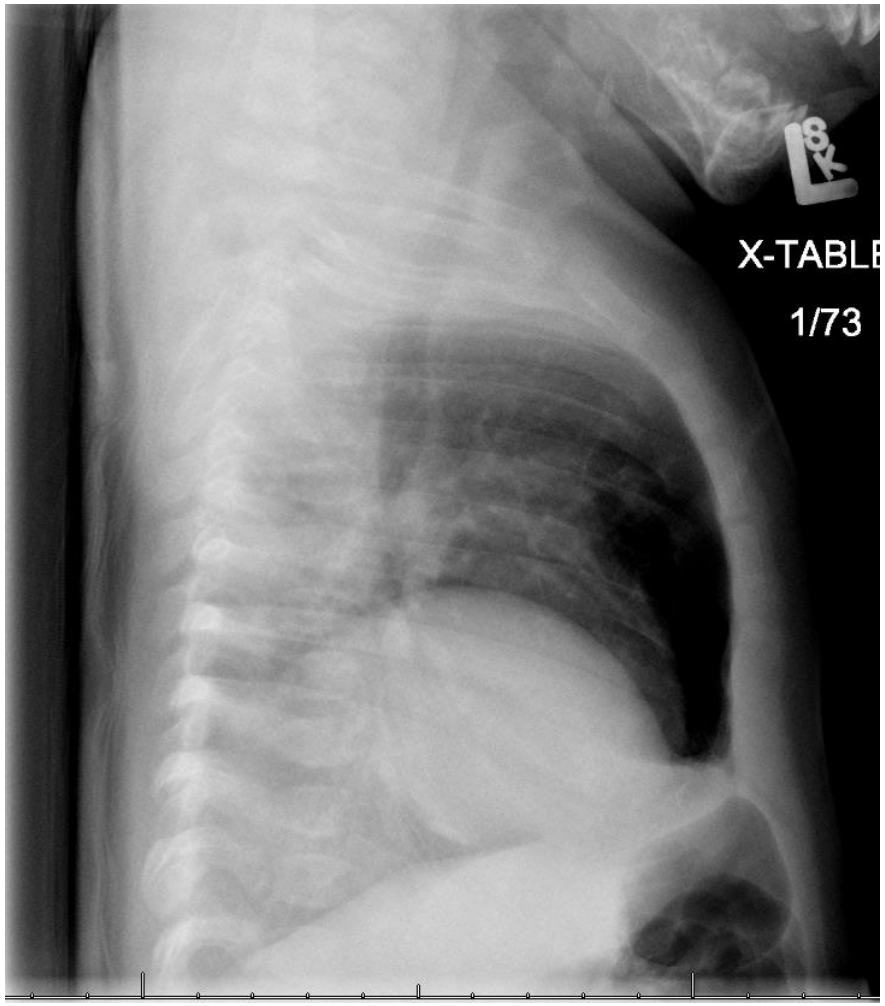
CASE 2: AN INTERESTING X-RAY

- 6 month old boy
  - Ex 36+5 week infant, uncomplicated pregnancy and delivery
  - Well until admitted at 5 months of age with RSV+ bronchiolitis for total of 6 days
  - Respirology consulted during his second admission at 6 months of age because of his chest x-ray

Clinical Presentation

- Increased work of breathing, wheezing, saturations in the mid-80s on room air
- Admitted to the PICU for bipap due to his increased work of breathing and hypoxemia
- Treated with Ventolin (no change in work of breathing), broad spectrum antibiotics, 1 dose of dexamethasone
- Positive for human metapneumonvirus and strep.pneumo on PCR


12/28/2016


X-TABLE
1/73

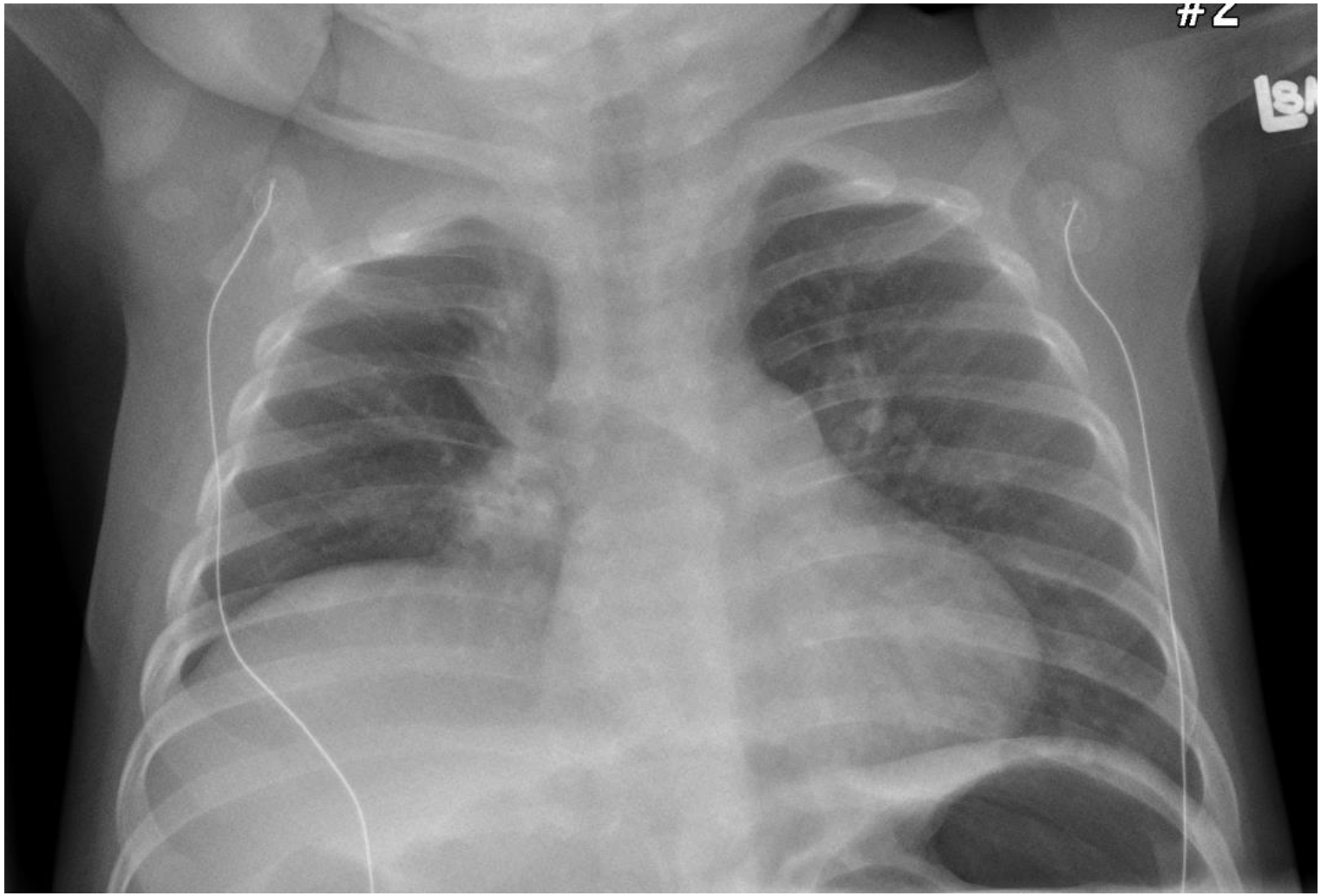
Differential diagnosis

- Right upper lobe collapse

AND

- Right diaphragm eventration
- Right diaphragm paralysis
- Right lung hypoplasia

- Clinically improved and on room air with no work of breathing 6 days after admission, although chest x-ray remained the same
- Fluoroscopy showed no paradoxical movement with some movement of the diaphragm, consistent with diaphragmatic eventration


#2

CASE 3: FIFTY SHADES OF GREY

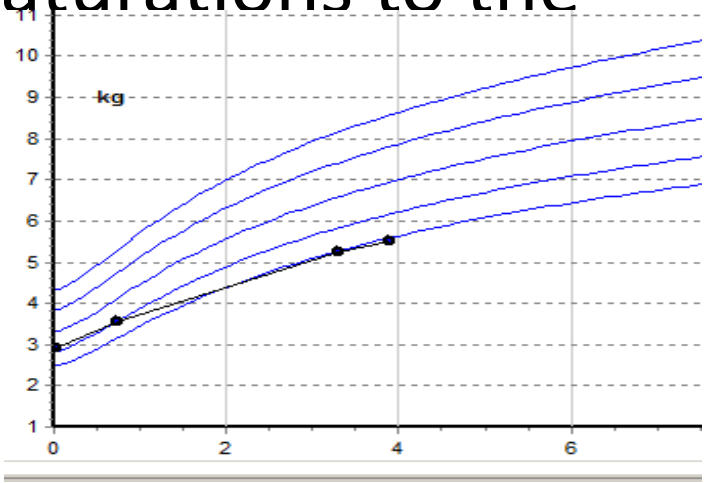
- 16 month old with chronic tachypnea

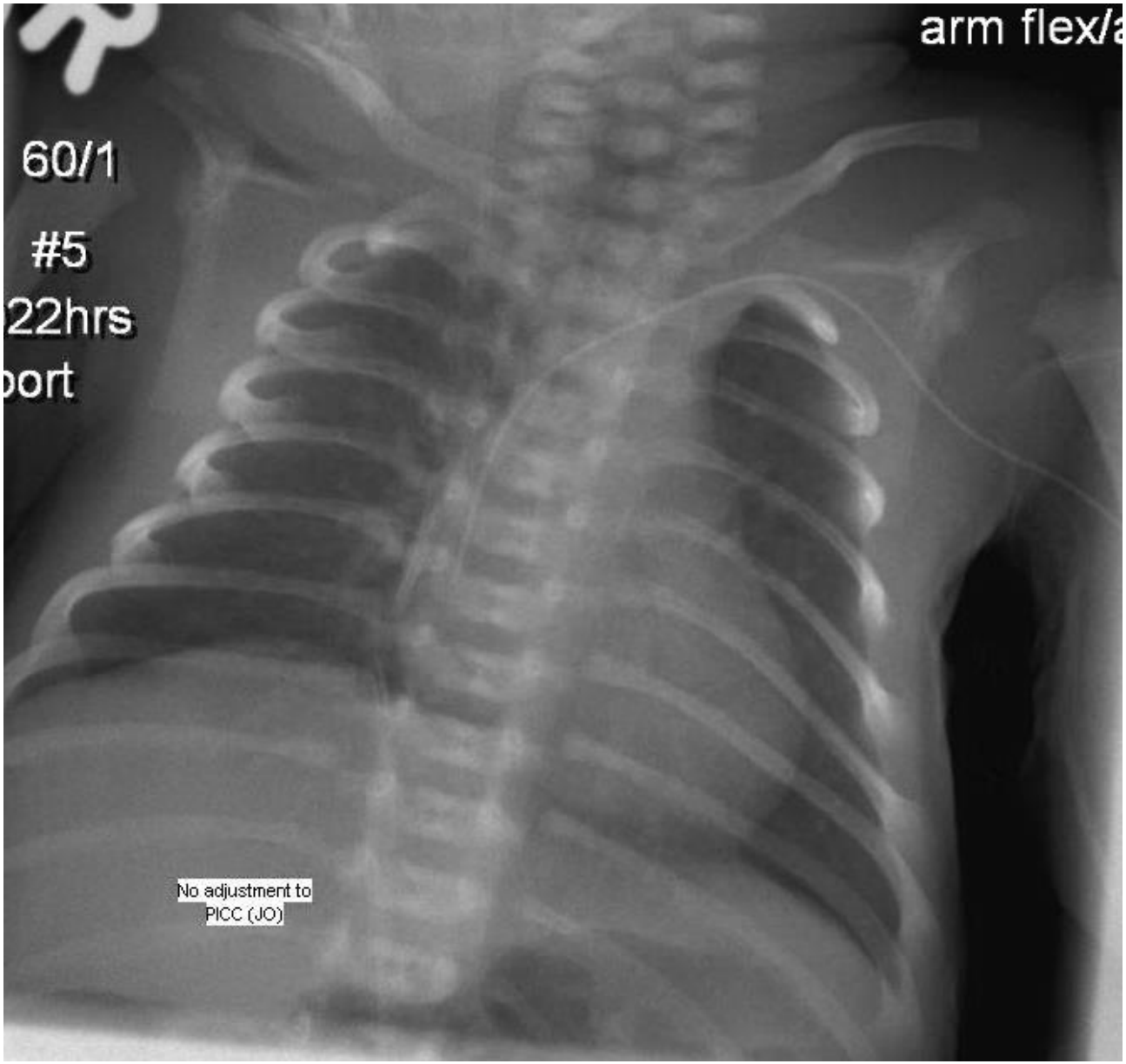
- Born at 39+4 days after uneventful pregnancy
  - GBS negative, ROM x 26 hours with maternal fever
  - APGAR 4^{1},6^{5} 9^{10}, BW 2940gm
  - Full septic workup negative
  - LP had blood, head ultrasound and MRI were done which showed multiple punctate parenchymal hemorrhages suggestive of intraventricular hemorrhage, treated for possible HSV encephalitis

- CPAP for <12 hours but otherwise well
- Noted to have significant pectus excavatum but not tachypneic and had good saturations at discharge

Initial presentation

- At 3 months of age, presented with a 2 week history of increased work of breathing and poor weight gain with history of poor feeding and reflux
- Saturation 98% on room air in the day but overnight oximetry showed baseline saturation of 94% with intermittent desaturations to the high 80s
- Gas 7.39/33/22

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22hrs
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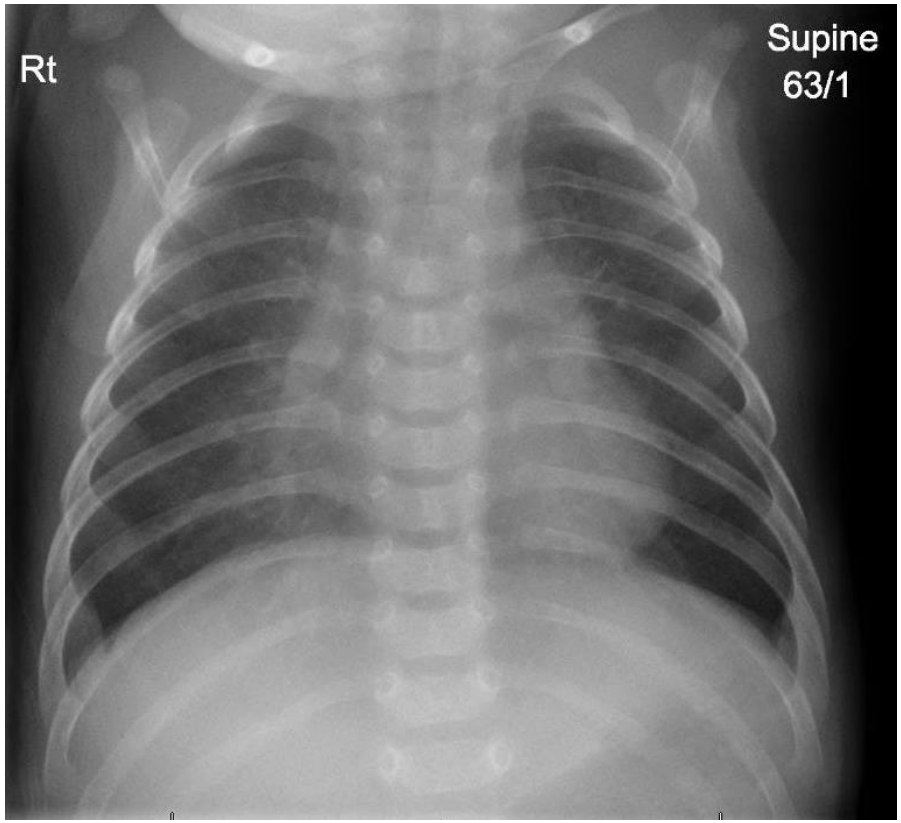
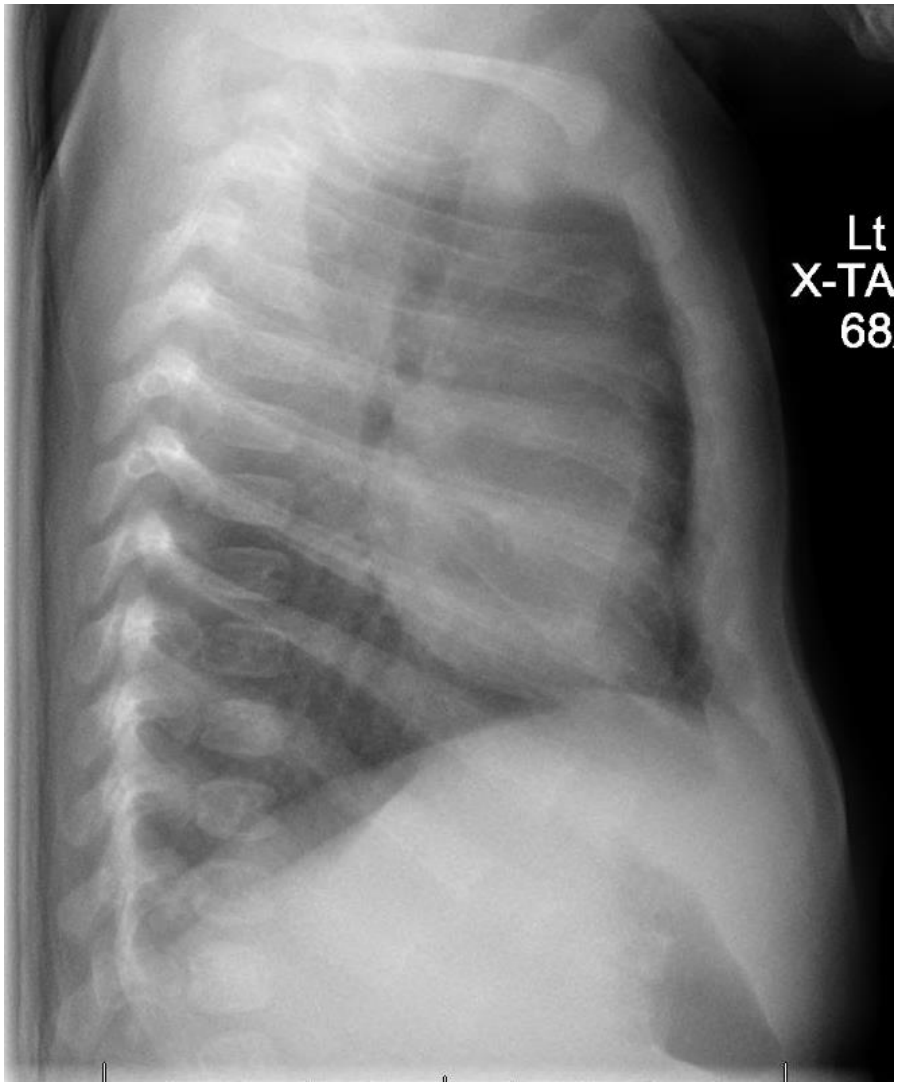
No adjustment to
PICC (JO)


Rt
Supine
63/1


Lt
X-TA
68

chILD Syndrome

Common causes of diffuse lung disease excluded

AND

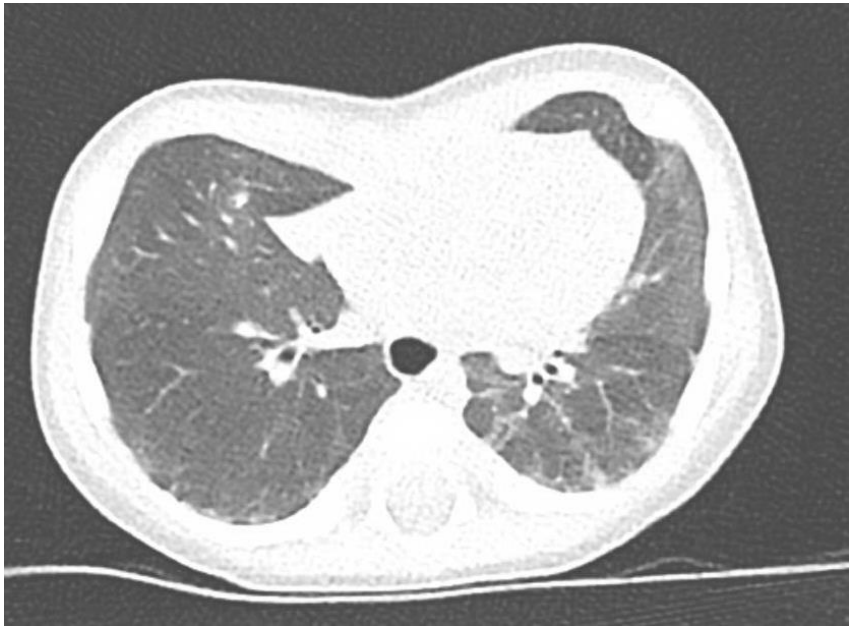
Three of the following:

1) Respiratory symptoms
2) Respiratory signs (including FTT)
3) Hypoxemia
4) Diffuse abnormalities on CXR or CT

Assess for common causes of DLD

- Infection (CRP 12, negative viral respiratory panel including ureaplasma, chlamydia trachomatis)
- Cardiac (trivial PFO, unable to estimate RVSP, pulmonary veins visualized and normal)
- Cystic fibrosis (sweat Cl=10mmol/L, fecal elastase 420)
- Primary Ciliary Dyskinesia (normal ciliary motility)
- Immunodeficiency (WBC 20.6, neutrophils 3.65, lymphocytes 14.93, flow cytometry normal, HIV negative, IgG 2.9, IgA 0.11, IgM 0.55, positive titres for diphtheria and tetanus)
- Aspiration (normal upper GI, feeding study)
- Alveolar Hemorrhage Syndrome (Hb 116)
- Metabolic workup negative

Inspiratory



Expiratory

- Sensitivity 78%
- Specificity 100%

Brody AJR 2010

Bronchoscopy

- Normal anatomy
- Cell count: Macrophages 40%, lymphocytes 51%, neutrophils 9%
- Bacterial, fungal, atypical mycobacterial cultures negative
- Respiratory viral panel negative
- No hemosiderin/lipid laden macrophages

DDx for lymphocytic BAL fluid

- Viral infection
- Sarcoidosis
- Pulmonary histiocytosis
- Hypersensitivity pneumonitis
- Drug-induced lung disease
- Collagen vascular disease
- Lymphocytic interstitial pneumonia
- Cryptogenic organizing pneumonia
- Lymphoma

ATS guideline Pediatric ILD 2005
ATS guideline BAL in ILD 2012

- PJP stains negative, PJP PCR positive
- CMV PCR positive (serum viral load 0)

Immunodeficiency!

- Flow cytometry, oxidative burst, CH50, CD40 ligand testing normal
- In vitro mitogen stimulation testing normal
- Whole exome sequencing normal, deletion/duplication testing normal

- Treated with gancyclovir and septra with possible improvement in tachypnea then worsening coinciding with discontinuation of valgancyclovir prophylaxis 2 months later

Repeat bronchoscopy

- Cell count: Macrophages 87%, Lymphocytes 10%, Neutrophils 3%
- Cultures negative
- CMV PCR positive (Serum viral load 0, cycle count 34)
- PJP stains and PCR negative

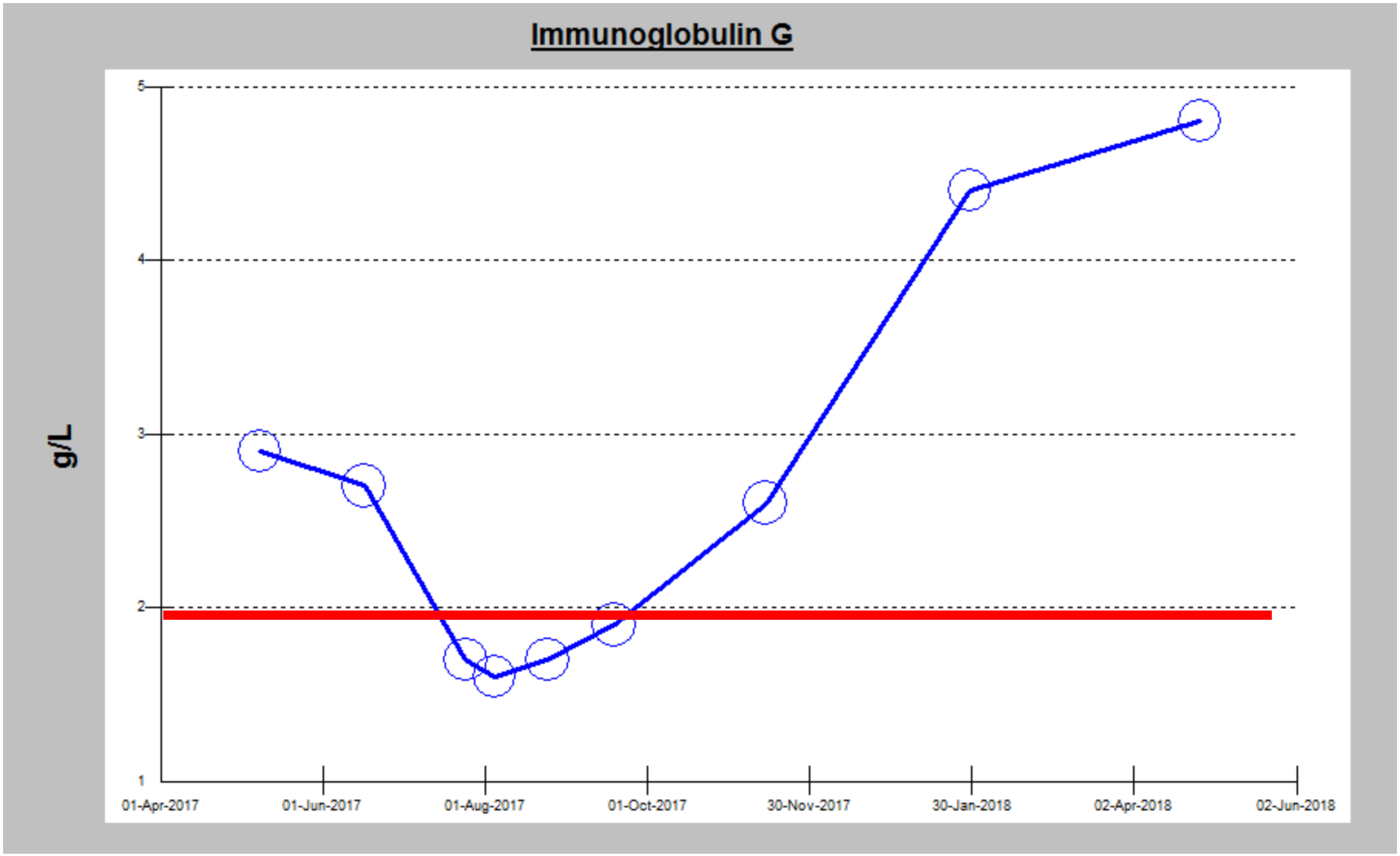
PJP colonization?

PJP detected in 9.4 to 100% of infants who were immunocompetent

Study	Subjects, no.	Diagnostic sample	Diagnostic method	Population	Colonized with *Pneumocystis*, %
Vargas et al. 1999 [11]	695	Autopsy lung	IHC stain	IC infants dying of SIDS and other causes	9.4
Vargas et al. 2001 [9]	74	NPA	Nested PCR	IC with respiratory infection	32.0
Morgan et al. 2001 [1]	79	Autopsy lung	IHC stain	Infants dying of SIDS	13.9
Nevez et al. 2001 [12]	178	NPA	Nested PCR	IC with bronchiolitis	24.3
Kasolo et al. 2002 [13]	75	Autopsy lung	PCR	Children with and without HIV and dying of non-PCP respiratory illness	17.3
Totet et al. 2003 [14]	240	NPA	Nested and real-time PCR	IC with bronchiolitis	24.6
Beard et al. 2005 [15]	58	Autopsy lung (4 samples)	Nested PCR	IC infants dying of various causes	100.0
Vargas et al. 2005 [16]	112	Autopsy lung (1 sample), tracheal aspirate	Nested PCR	IC infants dying in community/hospital	44.6
Vargas et al. 2007 [17]	130	Autopsy lung	GMS stain	IC infants dying in the community	32.3
Larsen et al. 2007 [18]	422	NPA	Real-time PCR	IC infants hospitalized with acute respiratory infection	15.9

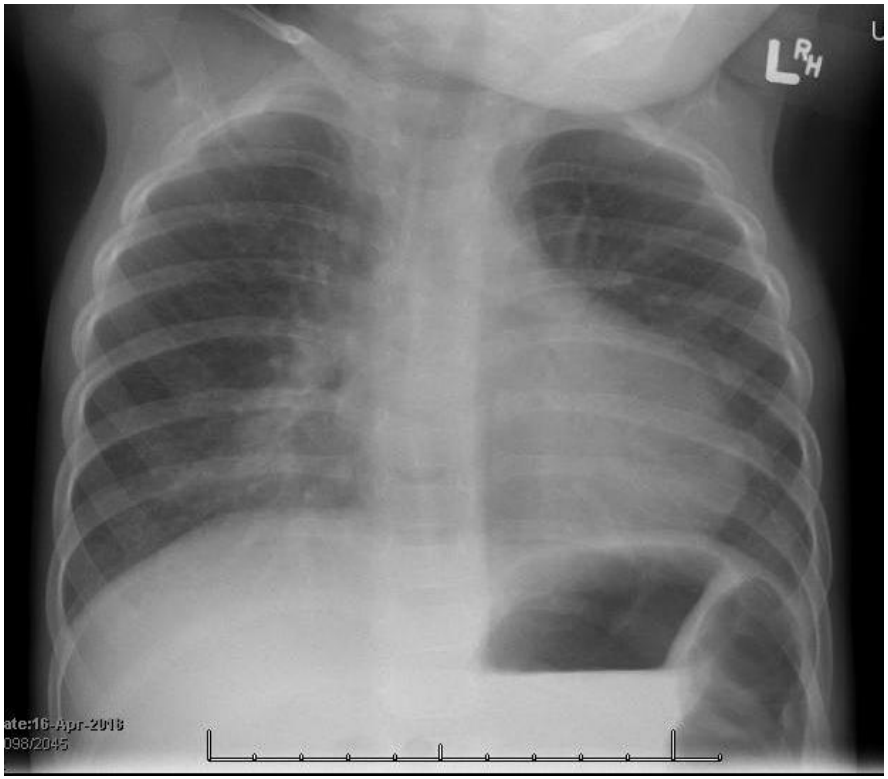
NOTE. GMS, Gomori methenamine silver; IC, immunocompetent; IHC, immunohistochemical; NPA, nasopharyngeal aspirate; PCR, polymerase chain reaction; SIDS, sudden infant death syndrome.

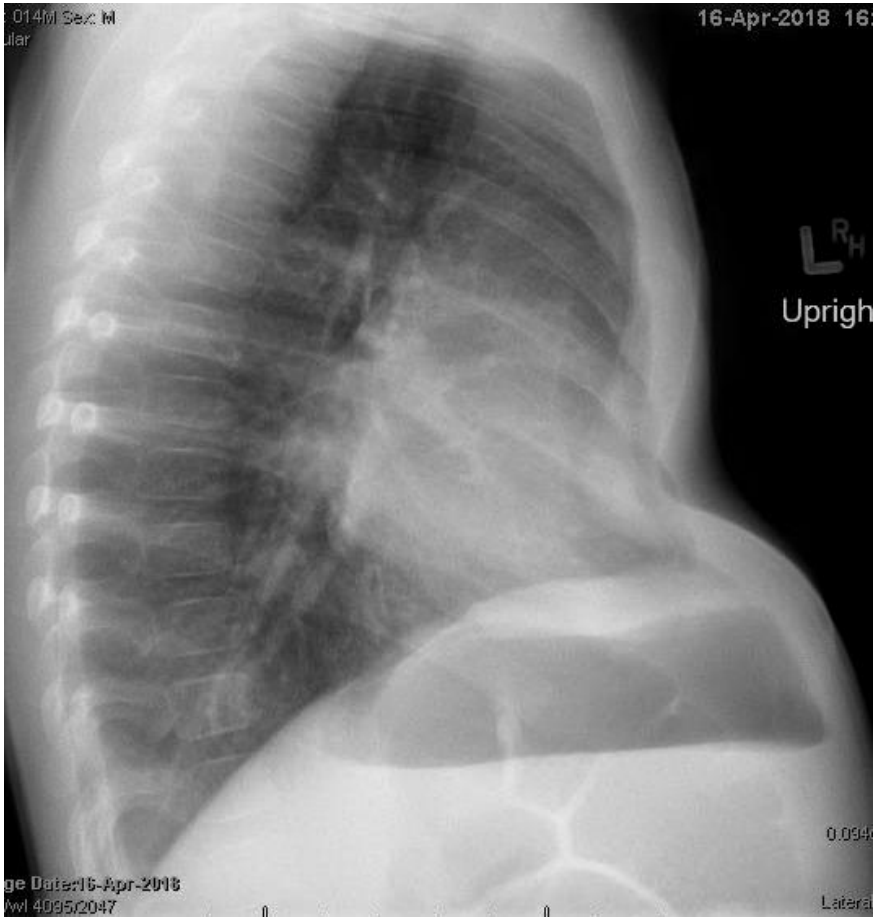
Morris J ID 2008


Immunoglobulin G
g/L
5
4
3
2
1
01-Apr-2017
01-Jun-2017
01-Aug-2017
01-Oct-2017
30-Nov-2017
30-Jan-2018
02-Apr-2018
02-Jun-2018

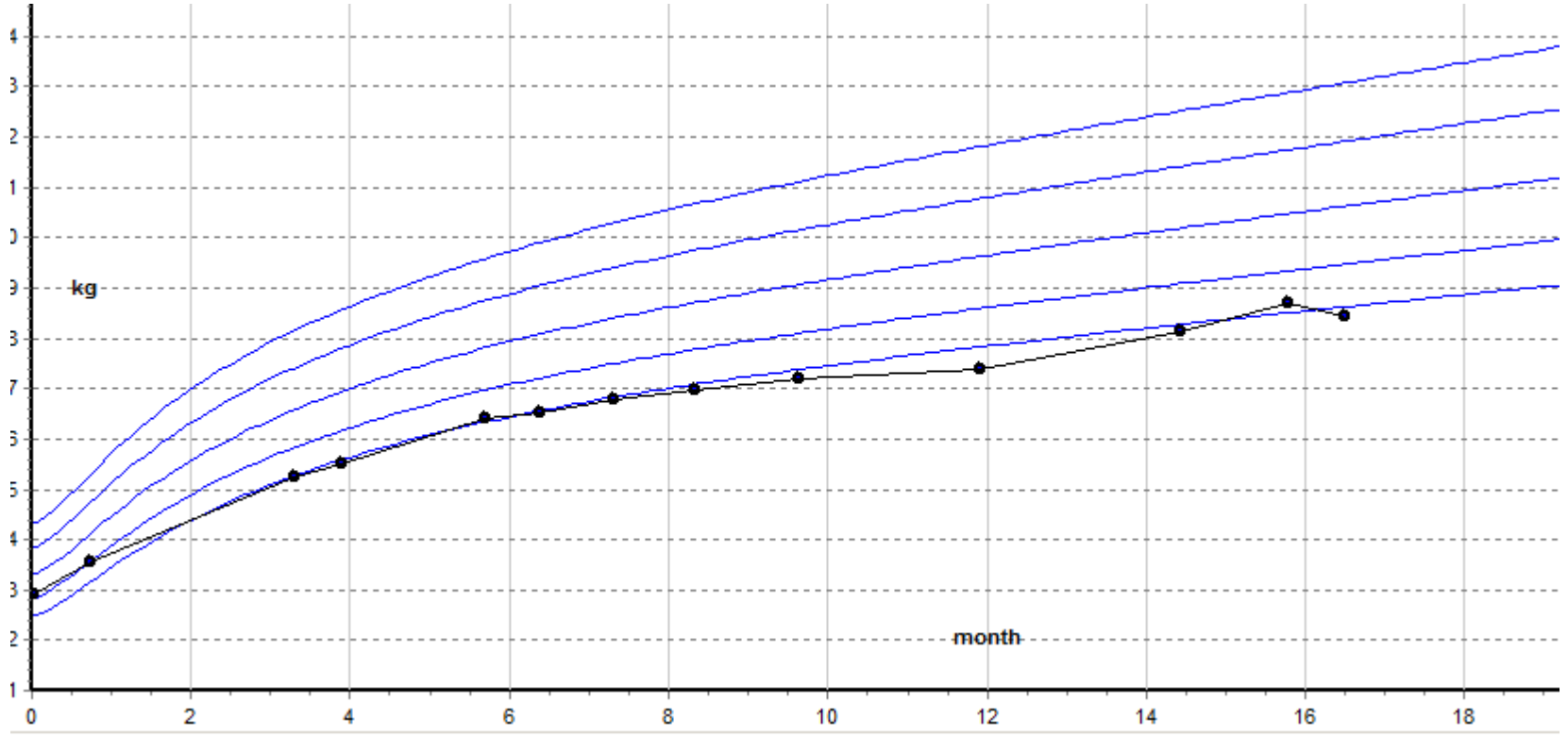
Current status

- Imaging unchanged





- Growth tracking along the 3rd %ile except for recent dip with teething
- Mild gross motor delay

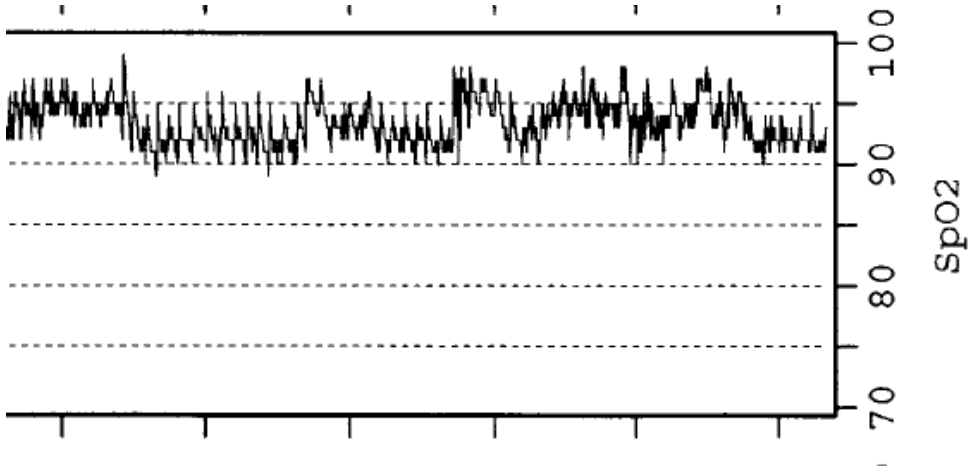


- Overnight Oximetry
  - Mean saturation 91.3-92.2% (June 2017: 95.4%)
  - Time with SpO2 <90% is 1.9-8.3% (June 2017: 3.4%)

Normal in children >1 year old:
Median baseline saturation 98% with a 5%ile of 96-97%

Healthy child 5-11yo: no more than 5% time with saturation below 94% while sleeping

Healthy infant <1 year old:
Only 5% of infants have saturation <90% for >4% of the time



BTS guidelines for home oxygen 2009

- Clinically same: tachypneic RR~60, intercostal indrawing, pectus

Picture removed

ILD more common in infancy

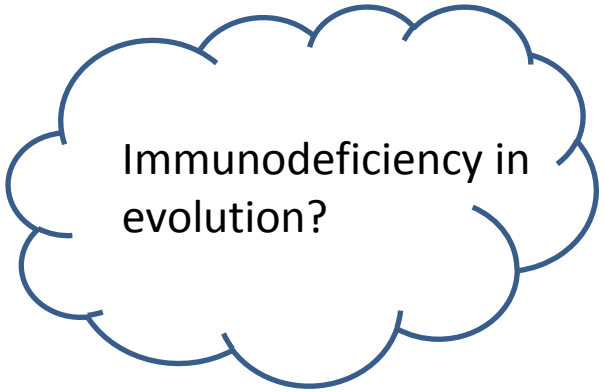
1) Diffuse developmental disorder

2) Surfactant dysfunction mutation
   - Surfactant protein C
   - ABCA3
   - Brain lung thyroid syndrome (NKX2.1)
   - GMCSF abnormalities (CSF2RA/B)

3) Growth abnormalities

4) Pulmonary interstitial glycogenosis (PIG)

5) Neuroendocrine Cell Hyperplasia (TTF1/NKX2.1 mutation)



What would you do next?

1) Repeat CT scan +/- bronchoscopy
2) Lung biopsy
3) Watchful waiting
4) Trial of steroids
5) Refer somewhere for lung function testing
6) Something else

Take home messages

- Systematic approach to children with chronic respiratory symptoms is useful
- Evolution over time directs management
- Personalized medicine is about applying algorithms to your specific patient