ALASKA NATIVE MEDICAL CENTER

Covid-19 and Respiratory Distress in Pediatric Patients

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Outline

- A lot of different people on this call

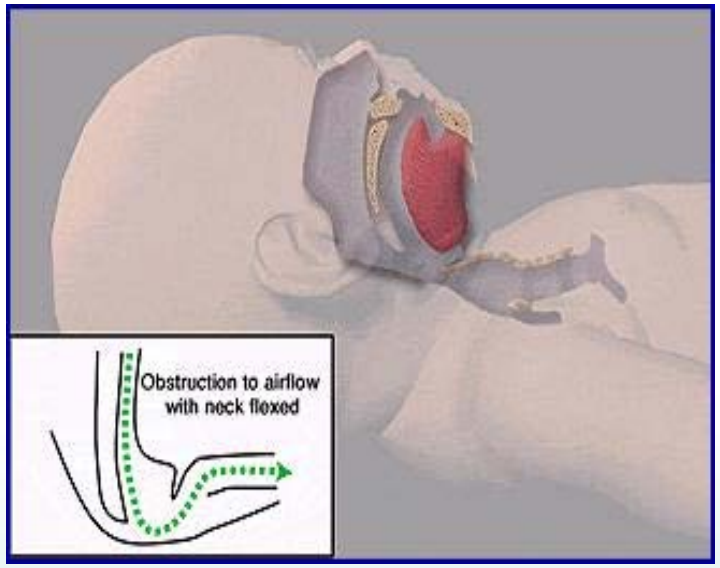
- Recognition
- Oxygen therapies
- Adjuncts and Medications
- Update on Covid-19 in Pediatrics
  - Clinical characteristics
  - Specific management recommendations

Recognition

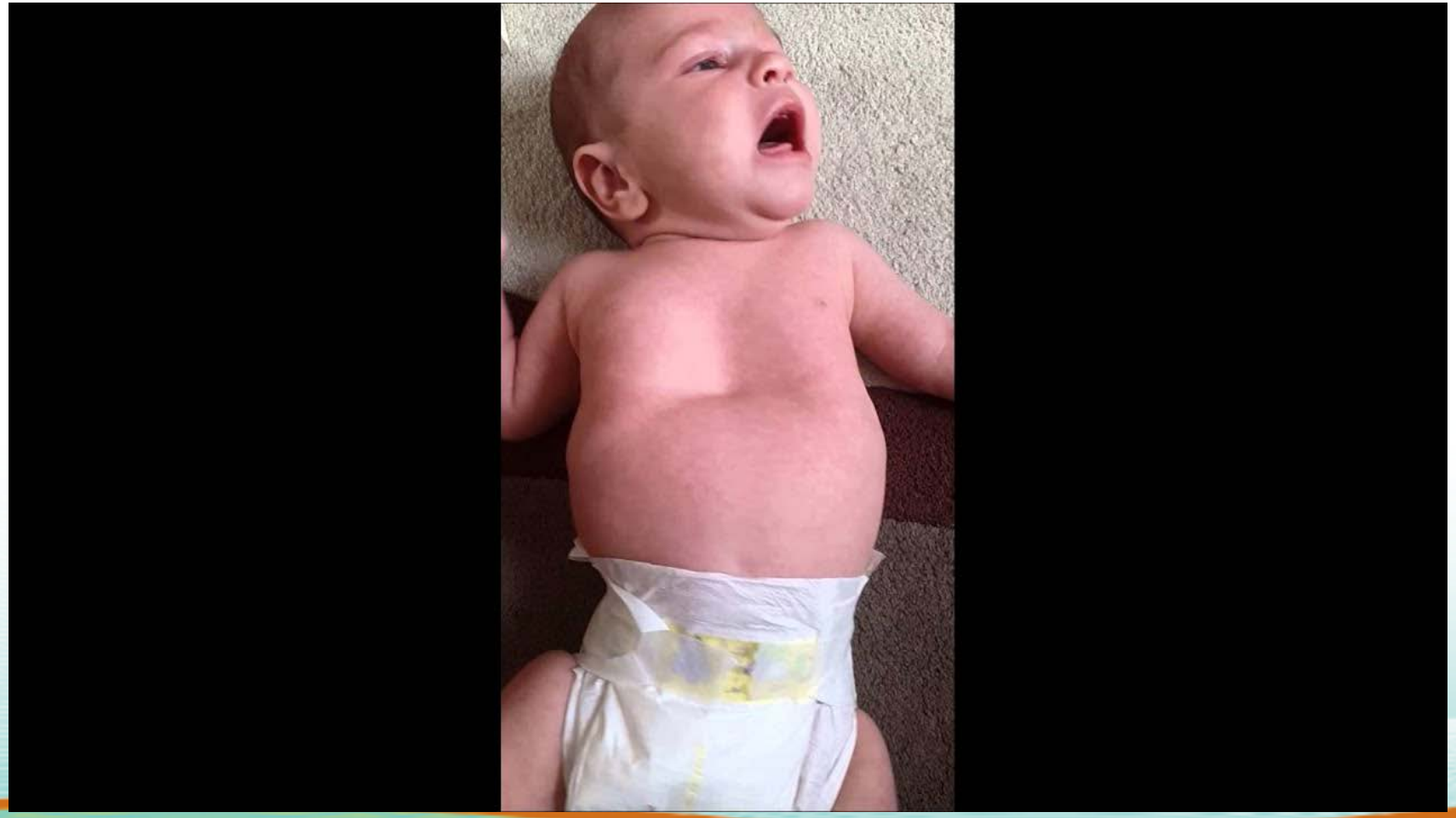
- 90% of pediatric cardiac arrests are from respiratory arrest
- Simple interventions can make incredible differences
- Anatomy and physiology of children different
- Pediatric Assessment Triangle

Anatomy and its Challenges

- Large occiput (relatively)
  - Neck flexion
  - Airway obstruction
- Large tongue (relatively) with small mouth
- Lower percentage of type- 1 (slow twitch) muscle fibers in diaphragm and intercostals
- Higher relative FRC (flat ribs and diaphragm)
  - Need to increase RR to increase minute ventilation
- Highly compliant chest wall

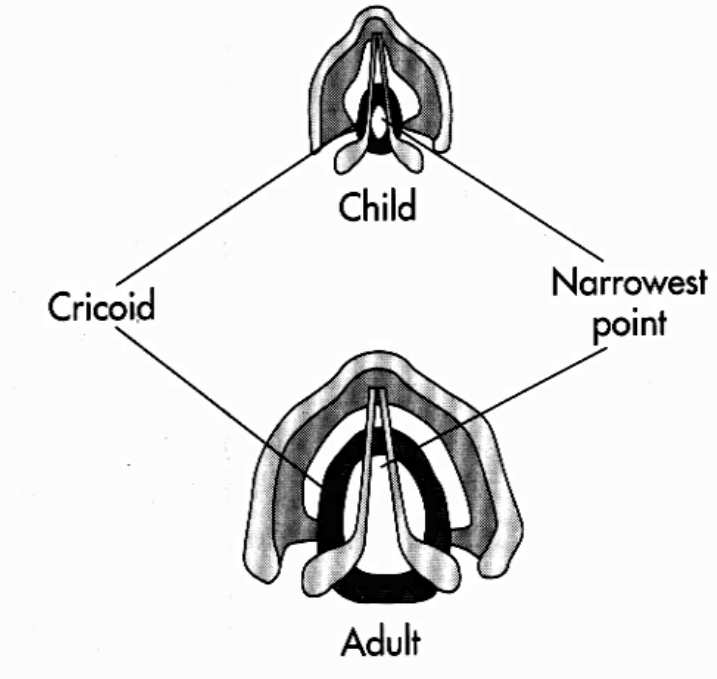


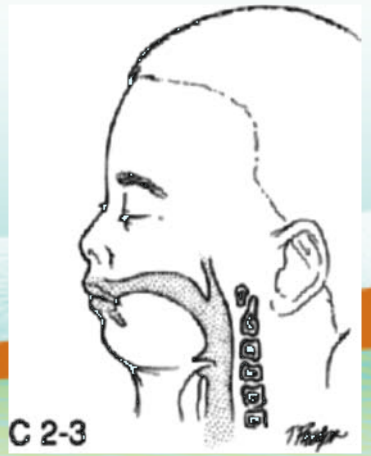
Compliant Chest Wall



Anatomy and its Challenges

- Relatively smaller airway = significantly increased airway resistance ($R \alpha 1/r^4$)
- High and anterior airway
- More acute angle between tracheal opening and epiglottis
- Narrowest diameter at cricoid ring…below vocal cords

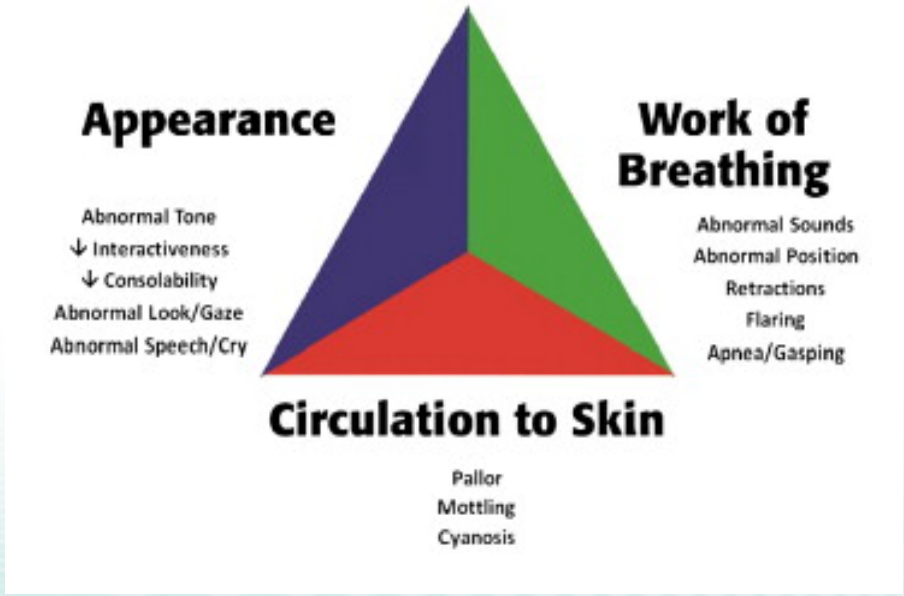




Warning signs

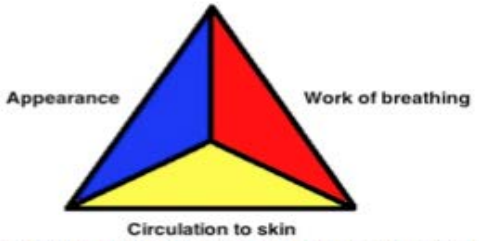
- Stridor
- Difficulty Swallowing / Drooling
- Retractions
- Agitation
- Cyanosis
- Preferred positioning
- Voice changes
- Apnea or “pauses”
- Bradypnea

Pediatric Assessment Triangle



Pediatric Assessment Triangle

Dieckmann R et al. *Pedriatr Emerg Care* 2010. PMID 20386420
ER CAST: http://blog.ercast.org/2010/05/the-toxic-neonate/
(Courtesy of Dr. Michelle Reina & Dr. Rob Bryant)



The PAT functions as a rapid, initial assessment to determine "sick" or "not sick," and should be immediately followed by/not delay the ABCDEs. It can be utilized for serial assessment of patients to track response to therapy.

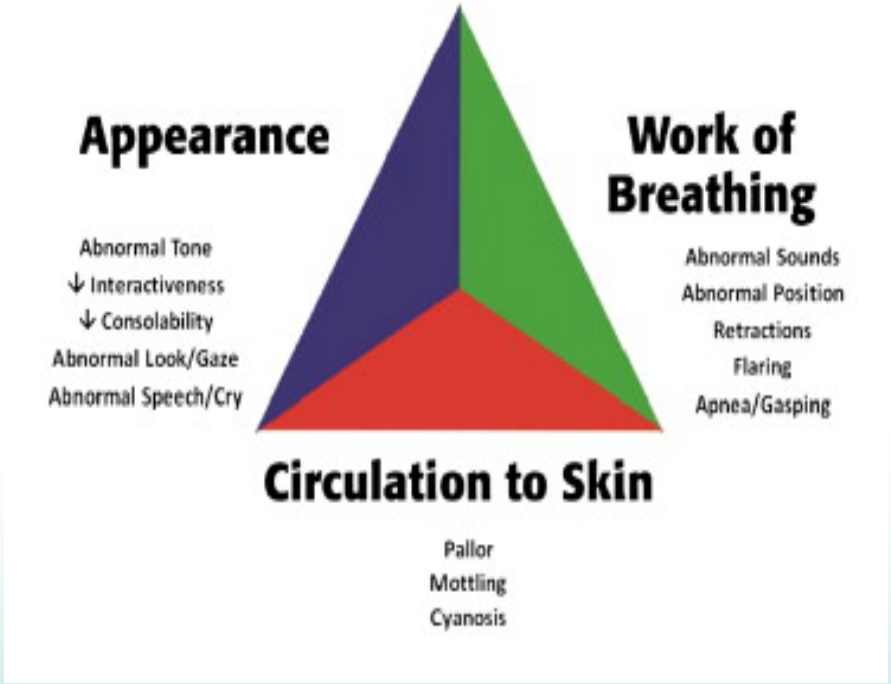
Appearance: The "Tickles" (TICLS) Mnemonic	
Characteristic	**Normal features**
T one	Move spontaneously, resists examination, sits or stands (age appropriate)
I nteractiveness	Appears alert/engaged with clinician or caregiver, interacts well with people/environment, reaches for objects
C onsolability	Stops crying with holding/comforting by caregiver, has differential response to caregiver vs. examiner
L ook/gaze	Makes eye contact with clinician, tracks visually
S peech/cry	Uses age-appropriate speech

Work of breathing	
Characteristic	**Abnormal features**
Abnormal airway sounds	Snoring, muffled/hoarse speech, stridor, grunting, wheezing
Abnormal positioning	Sniffing position, tripoding, prefers seated posture
Retractions	Supraclavicular, intercostal, or substernal, head bobbing (infants)
Flaring	Flaring of the nares on inspiration

Circulation to skin	
Characteristic	**Abnormal features**
Pallor	White/pale skin or mucous membranes
Mottling	Patchy skin discoloration due to variable vasoconstriction
Cyanosis	Bluish discoloration of skin/mucous membranes

Pediatric Assessment Triangle

- Respiratory Distress
- Respiratory Failure
- Shock
- *In Extremis*



Oxygen and Its Delivery

Hypoxia and Oxygen Delivery Outside of the Neonatal Period

- High oxygen content can be harmful to the newborn
- However HYPOXIA can be VERY harmful regardless of age
- Concept of “effective oxygen delivery” based upon delivery system

- Bottom line: If your patient is hypoxic or struggling and they’re not a newborn, give them as much oxygen as possible!!

What are we trying to do?

- Oxygen Content and Delivery Equation
  - $CaO_2 = (SaO_2 \times Hb \times 1.34) + .003(PaO_2)$
  - $DO_2 = CaO_2 \times C.O.$

Nasal Cannula

- 0.1 – 4 liters/min
- Beyond that very drying and painful
- Effective oxygen delivery max 30%

Simple Mask

- 6 liters/min (MINIMUM!!)
- Effective oxygen delivery 45%

Non- rebreather

- 10 liters/min (MINIMUM!!)
- Can approach 90% effective delivery in good fitting system

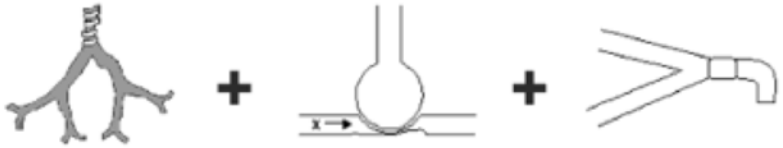
High Flow Nasal Cannula

So how does HFNC work???

Under normal breathing conditions,approximately 30% of an inspired tidal volume represents anatomical dead space. At the start of an inspiration, this dead space is filled with end-expiratory gas remaining from the previous expiration.

- Ventilated areas which do not participate in gas exchange

Total Deadspace = Anatomic + Alveolar + Mechanical

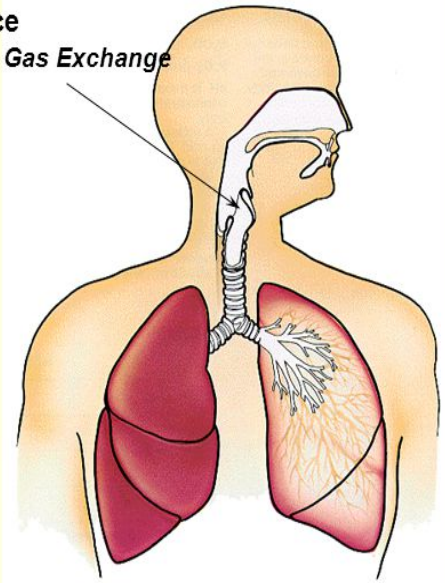


Anatomic Deadspace: airways leading to the alveoli	Alveolar Deadspace: ventilated areas in the lungs without blood flow	Mechanical Deadspace: artificial airways including ventilator circuits

Anatomical Dead Space

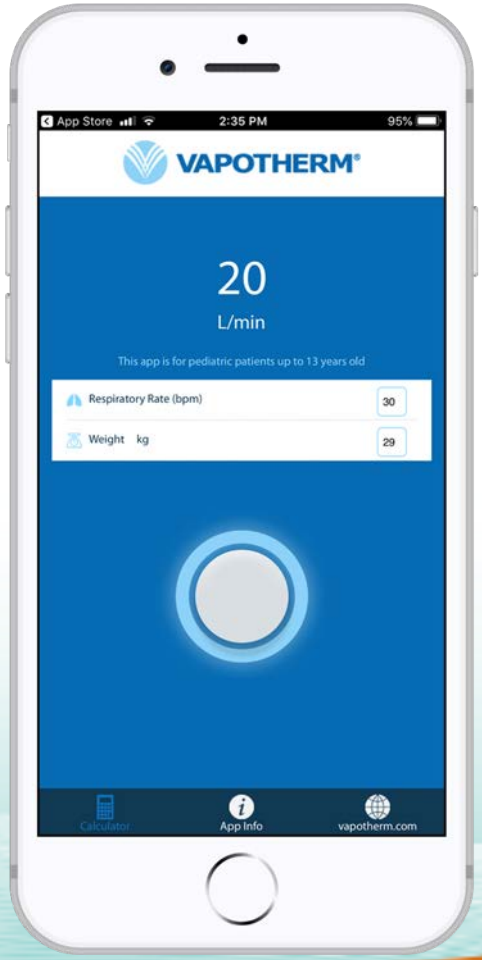
Anatomical Deadspace
Conducting Airway - No Gas Exchange

- Anatomical Dead Space
  - Internal volume of the upper airways
    - Nose
    - Pharynx
    - Trachea
    - Bronchi



How much flow????

- Not endorsing vapotherm, but a good app
- Estimates flow needed to overcome dead space volume based upon weight and respiratory rate
- Flows higher than you think
- Applicable to any true “high flow” system NOT simple nasal cannula



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Pressure vs. Flow

RAM cannula

Neotech RAM Cannula®

Nasal Oxygen Cannula

FEATURES AND BENEFITS

- For use with low/high flow oxygen
- Can be used with or without humidity
- Soft, curved prongs
- Color coded sizes
- 15 mm oxygen tubing adapter included
- Not made with natural rubber latex or plasticizer DEHP
- Individually packaged

Cat No.	Item	Qty/Unit
N4900	Micro Preemie	10/box
N4901	Preemie	10/box
N4902	Newborn	10/box
N4903	Infant	10/box
N4820	Oxygen Tubing Adapter	50/box

Made in USA

U.S. Patent #8,353,296; #D681,193

BiPAP/CPAP

Bag Valve Mask Ventilation

Endotracheal Intubation

Bag Valve Mask (BVM) Ventilation

- Pitfall – compressing soft tissue of neck
- “E – clamp” positioning
- Careful not to overventilate – choose appropriate bag size!!!
- Self inflating vs. Mapeleson – don’t suffocate your patient

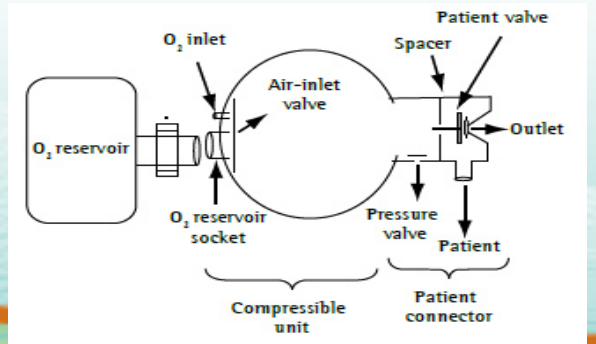


Figure 1 – Schematic representation of the components of a manually operated self-inflating resuscitation bag.

Bag Valve Mask (BVM) Ventilation

- Watch chest rise!!!
- SIZE MATTERS
- Typical tidal volume is 7 – 10 cc/kg
- Use a manometer
- Allow for adequate exhalation

GASTRIC DISTENTION!!

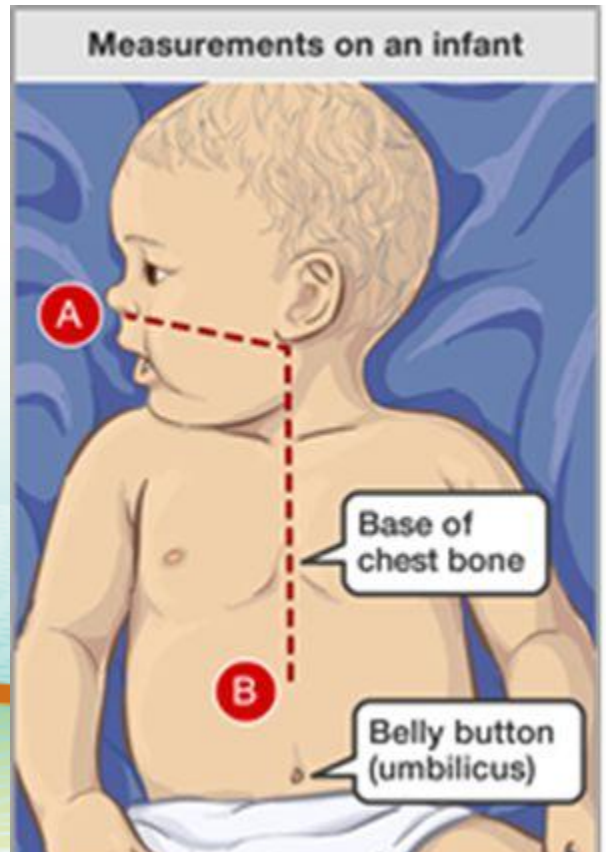
- May occur during BVM ventilation or BiPAP/CPAP
- Can occur just from child in respiratory distress
- Significantly competes with ability to oxygenate and ventilate

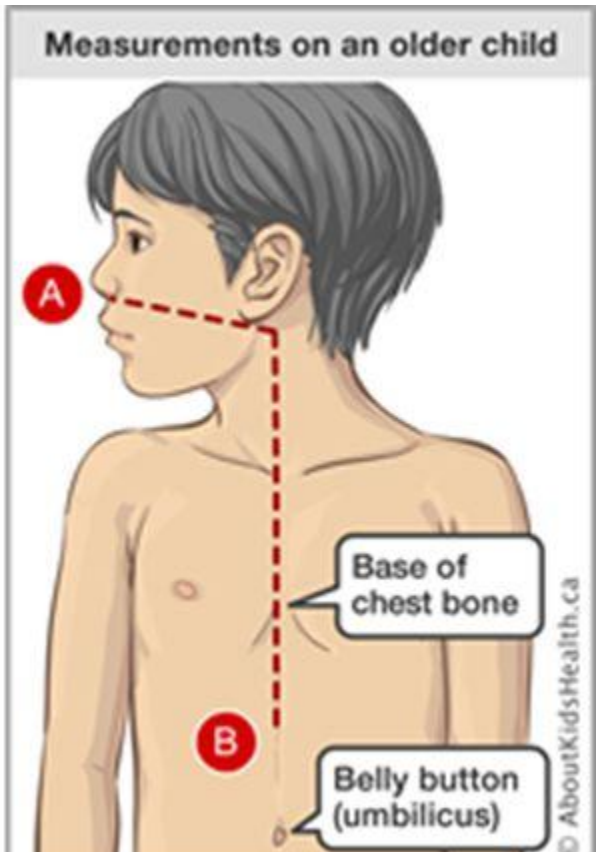
An Pediatr (Barc). 2015;82:106–7

Nasogastric Decompression

- Insert in advance of procedure if able
- Have ready if needed
- Will save you a lot of stress

size of NG tube		
	feeding	decompression
neonates	6fr	8fr
infants to 5 years	8fr	8-10fr
over 5 years	8-10fr	10-14fr





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Use PEEP!!

- PEEP – positive end expiratory pressure
- Prevents alveolar collapse and de-recruitment

Endotracheal Intubation

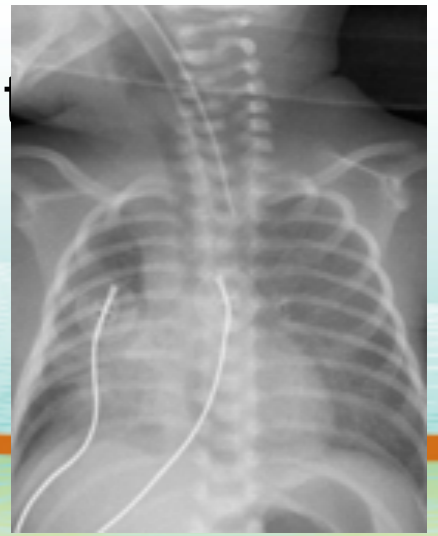
- Sizing
  - (age in years/4) + 4
- Depth
  - Approximately 3 times the ETT size
- Blade choice
  - Miller
  - Macintosh
  - Wis – Hipple
    - Wider tip
    - Size 1.5
- Cuffed vs Uncuffed
  - No difference in post extubation stridor/failure
  - Cuff helps when high pressures needed to ventilate
  - Decreased need to change out tube
  - More consistent ventilation

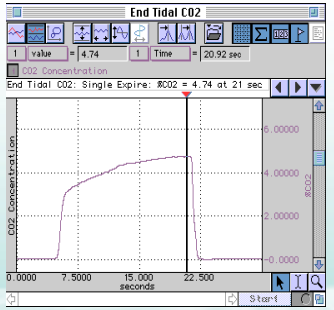
Endotracheal Intubation – Assistant Maneuvers

- Sellick
  - May collapse structures and obscure view
- BURP
  - Backward
  - Upward
  - Right
  - Pressure
- Mouth exposure
  - Gently pull right corner of mouth away to open mouth aperture

Endotracheal Intubation - Confir

- ETCO2 a must
  - Cuff may need to be inflated if large leak
  - A “blush” on the detector is likely ingested air in stomach
  - No cardiac output may have no ETCO2
- Auscultating breath sounds (and over stomach)
- “Mist” in tube just not sensit
- Xray to confirm depth





Apneic oxygenation reduces hypoxemia during endotracheal intubation in the pediatric emergency department

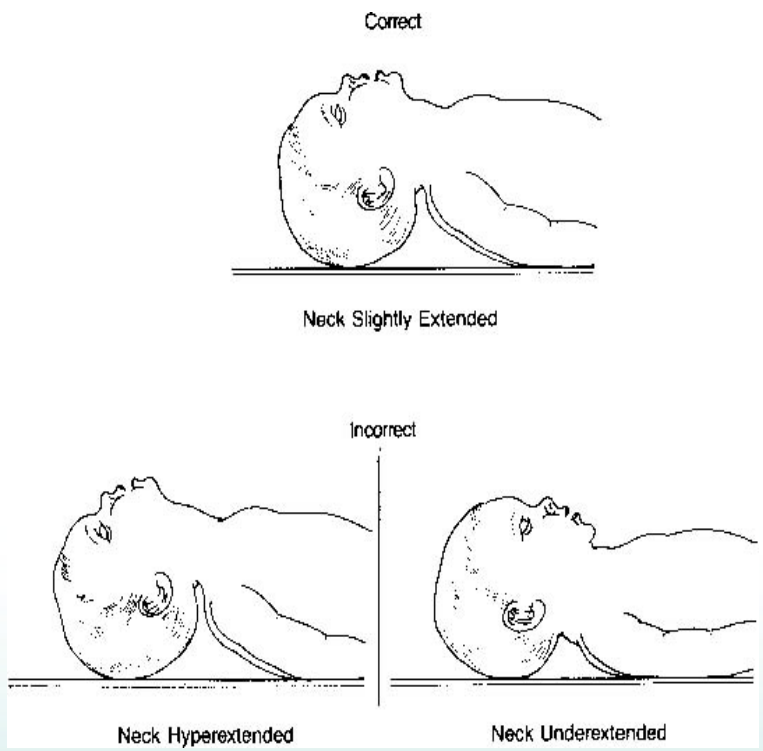
Adam A. Vukovic, MD, MEd a,*, Holly R. Hanson, MD, MSc a, et al.
American Journal of Emergency Medicine 37 (2019) 27–32

- Apneic oxygenation (AO), the application of high-flow oxygen by nasal cannula during the apneic period of intubation,
- 50 % reduction in hypoxemia during intubation attempt using AO

Adjuncts and Medications

Position

- Needed to facilitate intubation, but may fix problem necessitating intubation
- Head midline
- “sniffing” position
- Towel under shoulders to compensate for occiput



Suction!!!

- Infants near obligate nose breathers so suction may prevent intubation
- Excessive secretions pooling in the posterior pharynx (especially neurologically impaired)
- Necessary to assist in visualization during laryngoscopy (must have ready!!)

Suction Catheters

- Want the biggest reasonable size for your patient (Yankauer)
- Size also depends on what your suctioning
- Constant vs. occlusion suction
- 8 fr almost always too small for laryngoscopy

Airway Adjuncts

- Nasal Airway
- Oral Airway

Nasal Airway

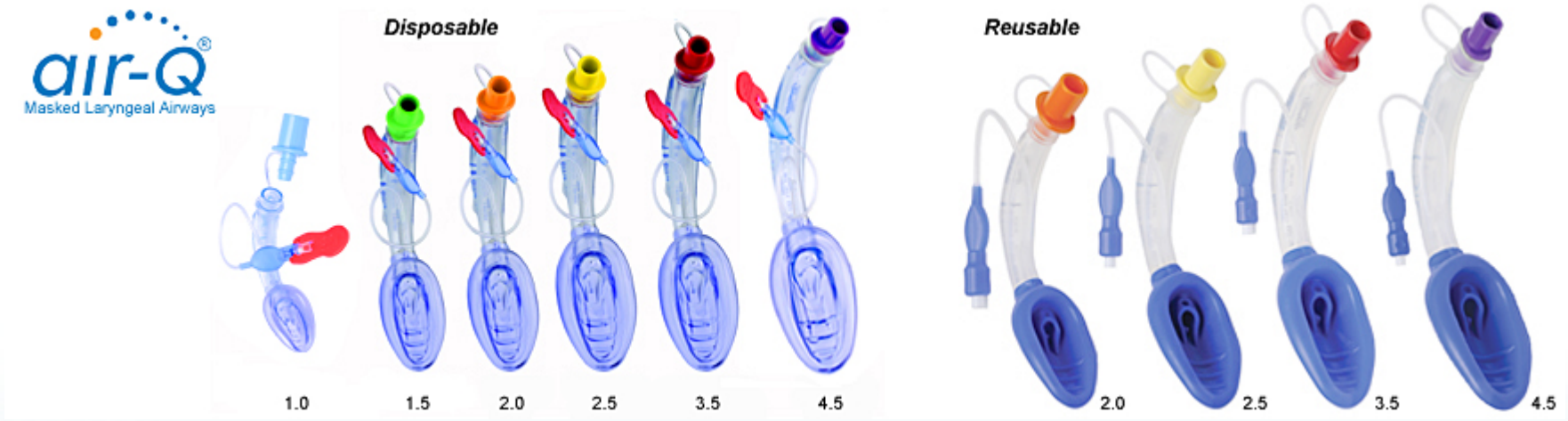
- Can be used in awake child
- Can reverse obstruction of upper airway from secretions, tonsilar hypertrophy, tongue
- Measure from nostril to tragus
- Sizes (24 fr, 26 Fr, 28 fr….)
- Soft, pliable
- Need lubrication
- Avoid if basilar skull fx, CSF leak, or coagulopathy
- Point bevel away from nasal septum to minimize trauma and bleeding

Oral Airway

- Used in comatose patients, too noxious in the conscious patient (gag reflex)
- Measure by holding flange at corner of mouth, tip should reach angle of mandible
- Very helpful if having difficult providing BVM ventilation

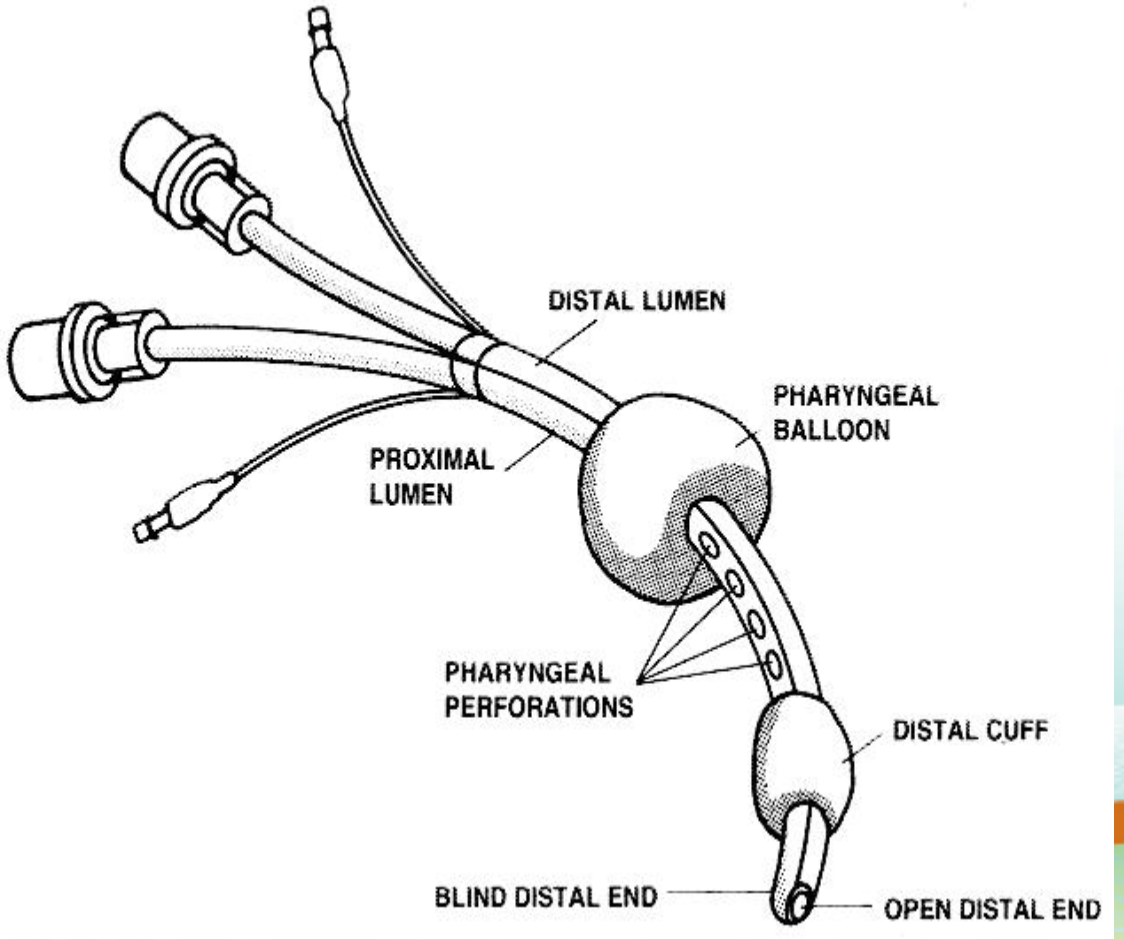
Laryngeal Mask Airways – LMA's

Air-Q


air-Q
Masked Laryngeal Airways
Disposable
1.0
1.5
2.0
2.5
3.5
4.5
Reusable
2.0
2.5
3.5
4.5

Bougies

Combitube


DISTAL LUMEN
PHARYNGEAL BALLOON
PROXIMAL LUMEN
PHARYNGEAL PERFORATIONS
DISTAL CUFF
BLIND DISTAL END
OPEN DISTAL END

Video Laryngoscope

- Variety of blade designs both miller and macintosh
- Design is the same as direct laryngoscope so can be used for direct laryngoscopy
- Can perform direct visualization with this device if you are unaware that airway may be difficult

Medications

Stridor vs Wheezing

Wheezing

- Albuterol
- Steroids
  - Solumedrol
  - Prednisolone
  - Decadron
- Duo-Nebs (Albuterol/Atrovent)
- Magnesium

Magnesium Sulfate

- Magnesium cause smooth muscle relaxation secondary to inhibition of calcium uptake.
- A single dose of IV magnesium sulfate has been shown to be safe and effective in those patients with acute severe asthma who have had a poor response to initial therapy.
- The response to magnesium appears to be best in patients who present with very severe illness.
- The recent GINA-guidelines suggest that iv magnesium may be considered in acute moderate and severe asthma with incomplete response to initial treatment during the first 1-2 hours
- The dose is 25 - 50 mg/kg/dose (maximum 2 g) by slow IV infusion.

Ciarallo L et al. J Pediatr 1996;129809-814

Global Strategy for Asthma Management and Prevention 2008 (update) [http://www.ginasthma.org]

Stridor

- Racemic epinephrine
- “NON-Racemic” epinephrine (0.5 ml racemic epinephrine = 5 ml of 1:1000 L-epinephrine)
- Steroids
  - Decadron
- Heliox
- Sedation???

Secretions

- Hypertonic saline nebulized
  - Bronchospasm?
- Saline nebulized
- Glycopyrrolate (0.004 – 0.01 mg/kg)

Intubation Meds (RSI)

- Sedatives
  - Fentanyl alone (2 – 4 micrograms/kg)
  - Fentanyl with versed (0.1 – 0.2 mg/kg)
  - Ketamine (0.5 – 1 mg/kg IV) (3 – 5 mg/kg IM)
  - Propofol (1 – 3 mg/kg)
- Paralytics
  - Rocuronium (0.6 – 1 mg/kg)
  - Vecuronium (0.1 mg/kg)
  - Succinylcholine (2 mg/kg)
- Adjuncts
  - Atropine (0.02mg/kg min 0.1 mg)
  - Glycopyrrolate (0.004 – 0.01 mg/kg)

ARDS

ARDS

- Acute, diffuse inflammatory lung injury that leads to increased pulmonary vascular permiability, increased alveolar/interstitial edema and a loss of aerated tissue

- Clinical hallmarks are hypoxia and bilateral infiltrates on CXR

- Pathologic hallmark is diffuse alveolar damage

ARDS

- In 1967, Ashbaugh and colleagues described a syndrome of tachypnea, hypoxia and decreased pulmonary compliance with pathologic features of interstitial and intra-alveolar edema and hemorrhage and hyaline membrane formation

- Syndrome was later defined as “Adult” Respiratory Distress Syndrome

Definition of ARDS

- 1994 American-European Consensus Conference
  - Changed the term from “Adult” to Acute

1. Acute onset
2. Bilateral pulmonary infiltrates on CXR
3. No evidence of left atrial hypertension or PAWP ≤ 18 mmHg
4. PaO2:FiO2 ratio ≤300=ALI
5. PaO2:FiO2 ratio ≤200=ARDS

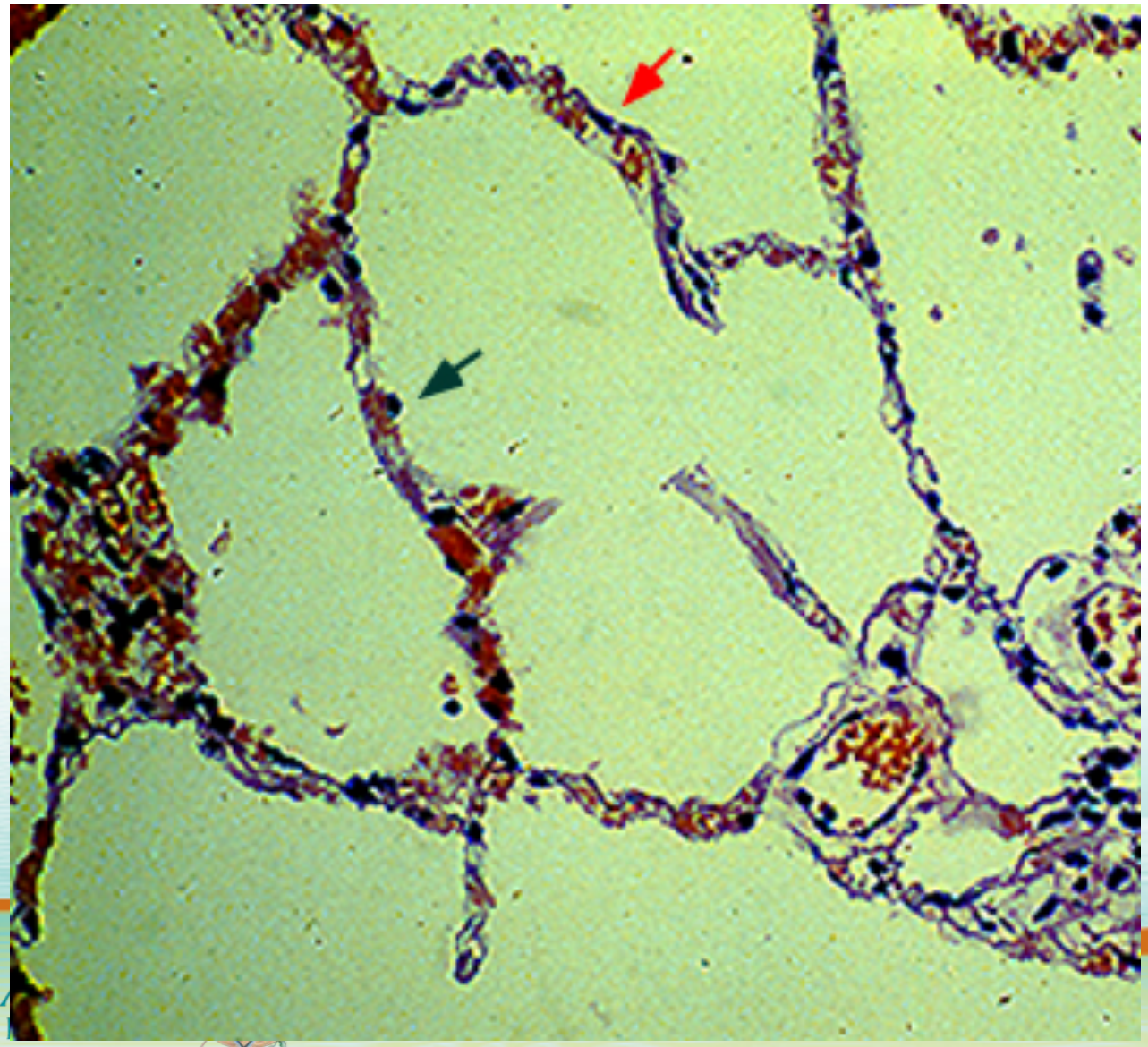
Berlin Definition of ARDS: 2012

1. Respiratory symptoms began within 1 week of known clinical insult (sepsis, trauma, aspiration or other accepted cause) OR patient must have new or worsening symptoms over past week
2. Bilateral infiltrates on imaging not fully explained by pleural effusions, lobar or lung collapse or pulmonary nodules
3. Pt's respiratory failure must not be fully explained by cardiac failure or fluid overload
4. Evidence of oxygenation impairment on PEEP ≥ 5 cmH2O
   - Mild: P/F = 201 to ≤ 300
   - Moderate: P/F = 101 – 200
   - Severe: P/F = ≤ 100

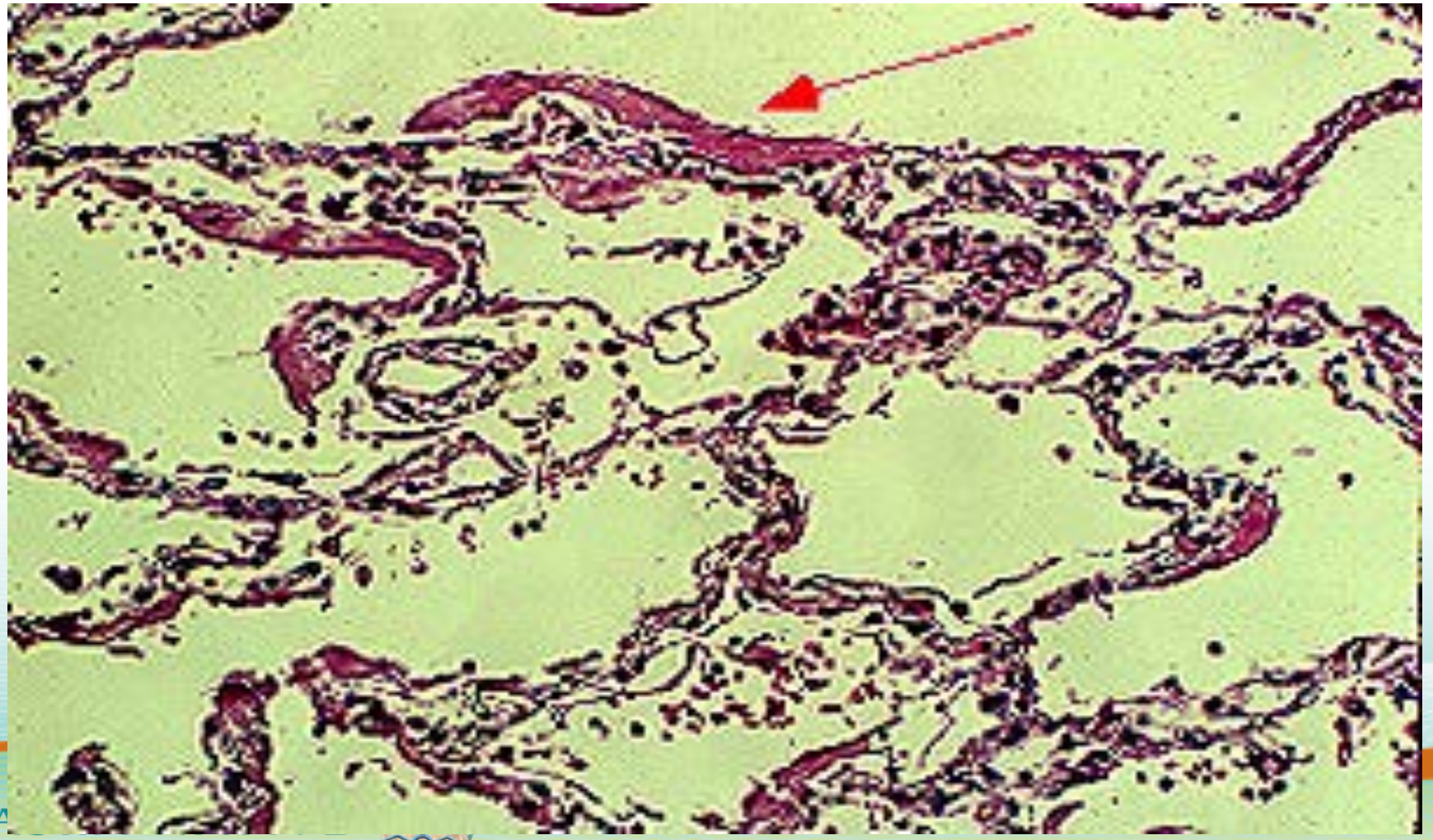
Major Changes:

- ALI term removed, PCWP criterion removed, minimal ventilator settings were added

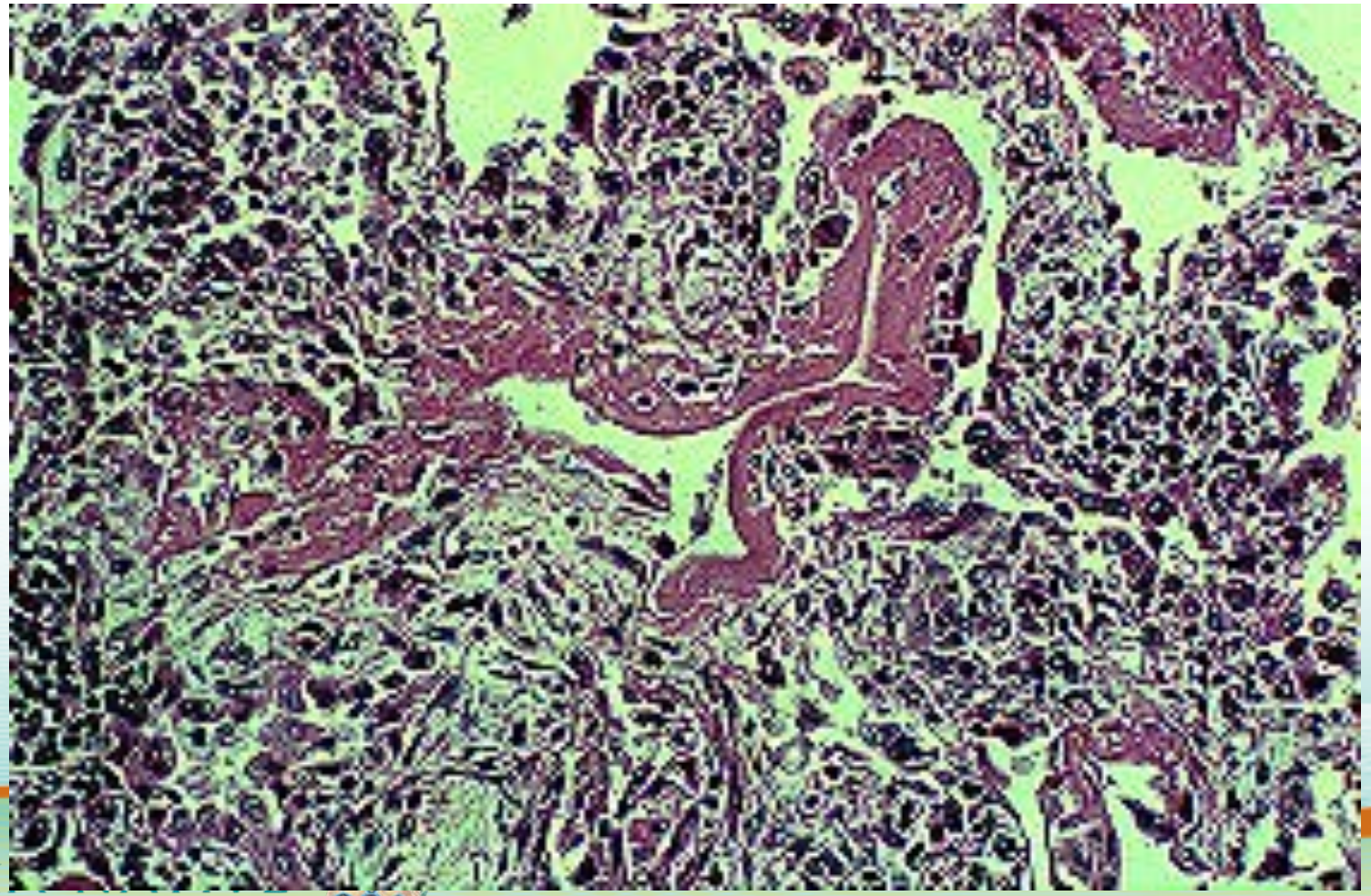
Normal Lung



Early Diffuse Alveolar Damage



Late Diffuse Alveolar Damage



Epidemiology of Covid-19 in Pediatrics

Epidemiological Characteristics of 2143 Pediatric Patients With 2019 Coronavirus Disease in China

Yuanyuan Dong, Xi Mo, Yabin Hu, Xin Qi, Fang Jiang, Zhongyi Jiang, Shilu Tong

DOI: 10.1542/peds.2020-0702

Journal: *Pediatrics*

Citation: Dong Y, Mo X, Hu Y, et al. Epidemiological characteristics of 2143 pediatric patients with 2019 coronavirus disease in China. *Pediatrics.* 2020; doi: 10.1542/peds.2020-0702

Table 1 Characteristics of Children' COVID-19 Cases in China

Characteristics	All cases	Different Category		
		Confirmed	Suspected	*P* Value
Median age (Interquartile range)	7.00 (11.0)	10.00(11.0)	6.00(10.0)	<0.001
Age group				
<1	379(17.7)	86(11.8)	293(20.8)	
1-5	493(23.0)	137(18.7)	356(25.2)	
6-10	523(24.4)	171(23.4)	352(24.9)	<0.001
11-15	413(19.3)	180(24.6)	233(16.5)	
>15	335(15.6)	157(21.5)	178(12.6)	
Gender				
Boy	1213(56.6)	420(57.5)	793(56.2)	0.567
Girl	930(43.4)	311(42.5)	619(43.8)	
Severity of illness				
Asymptomatic	94(4.4)	94(12.9)	0(0.0)	
Mild	1091(50.9)	315(43.1)	776(54.9)	
Moderate	831(38.8)	300(41.0)	531(37.6)	
Severe	112(5.2)	18(2.5)	94(6.7)	<0.001
Critical	13(0.6)	3(0.4)	10(0.7)	
Missing	2(0.1)	1(0.1)	1(0.1)	
Days from symptom onset to diagnosis				
Median days (Interquartile range)	2(4.0)	3(4.0)	2(4.0)	<0.001
Range	0-42	0-42	0-36	
Province				
Hubei	984(45.9)	229(31.3)	755(53.5)	
Surrounding areas*	397(18.5)	155(21.2)	242(17.1)	<0.001
Others	762(35.6)	347(47.5)	415(29.4)	
Total	2143	731(34.1)	1412(65.9)	

Data are presented with median (Interquartile range) and n (%).
*Surrounding areas are the provinces and Municipality bordering Hubei, they are Anhui, Henan, Huna
Jiangxi, Shaanxi and Chongqing.

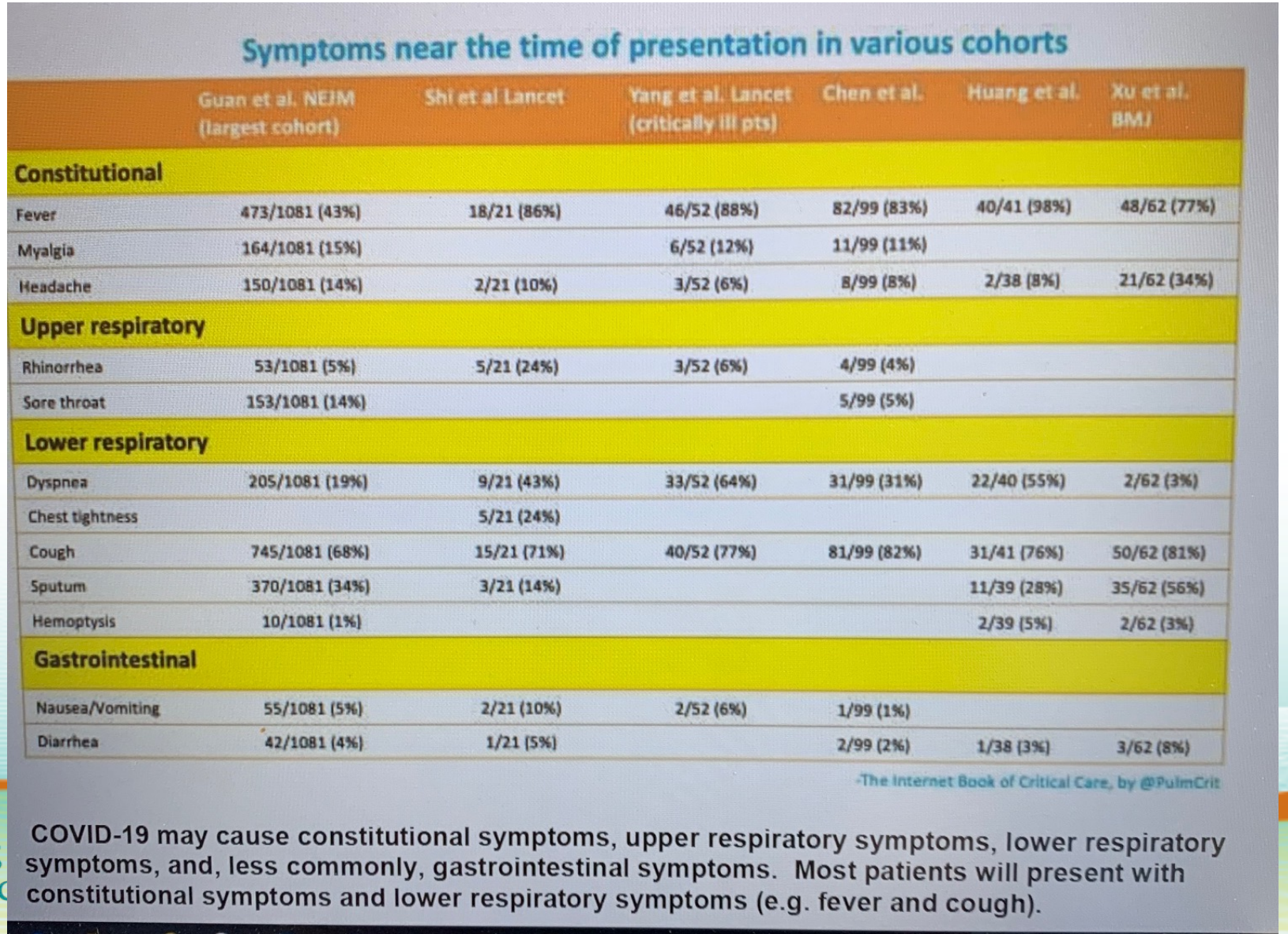
Table 2 Different Severity of Illness by Age Group

Age group*	Asymptomatic	Mild	Moderate	Severe	Critical	Total
<1	7(7.4)	205(18.8)	127(15.3)	33(29.5)	7(53.8)	379(17.7)
1-5	15(16.0)	245(22.5)	197(23.7)	34(30.4)	2(15.4)	493(23.0)
6-10	30(31.9)	278(25.5)	191(23.0)	22(19.6)	0(0)	521(24.3)
11-15	27(28.7)	199(18.2)	170(20.5)	14(12.5)	3(23.1)	413(19.3)
>15	15(16.0)	164(15.0)	146(17.5)	9(8.0)	1(7.7)	335(15.7)
Total	94	1091	831	112	13	2141(100)

Data were presented with number and percent (%);*Two cases had missing values.

- 1. **Asymptomatic infection**: without any clinical symptoms and signs and the chest imaging is normal, while the 2019-nCoV nucleic acid test is in a positive period.
- 2. **Mild:** symptoms of acute upper respiratory tract infection, including fever, fatigue, myalgia, cough, sore throat, runny nose, and sneezing. Physical examination shows congestion of the pharynx and no auscultory abnormalities. Some cases may have no fever, or have only digestive symptoms such as nausea, vomiting, abdominal pain and diarrhea.
- 3. **Moderate:** with pneumonia, frequent fever and cough, mostly dry cough, followed by productive cough , some may have wheezing, but no obvious hypoxemia such as shortness of breath, and lungs can hear sputum or dry snoring and / or wet snoring. Some cases may have no clinical signs and symptoms, but chest CT shows lung lesions, which are subclinical.
- 4. **Severe:** Early respiratory symptoms such as fever and cough, may be accompanied by gastrointestinal symptoms such as diarrhea. The disease usually progresses around 1 week, and dyspnea occurs, with central cyanosis. Oxygen saturation is less than 92%, with other hypoxia manifestations.
- 5. **Critical**: Children can quickly progress to acute respiratory distress syndrome (ARDS) or respiratory failure, and may also have shock, encephalopathy, myocardial injury or heart failure, coagulation dysfunction, and acute kidney injury. Organ dysfunction can be life threatening.

Clinical Presentation



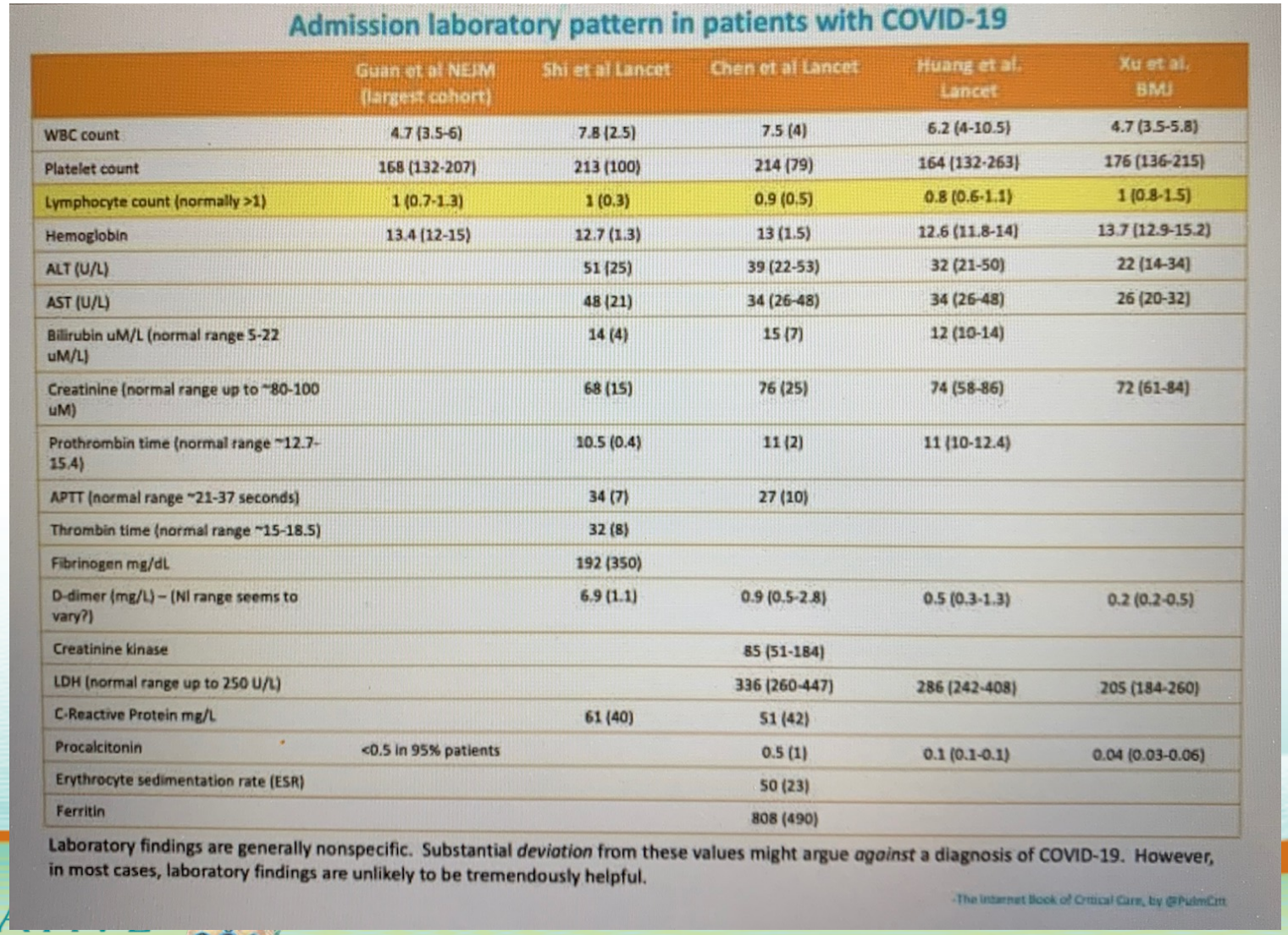
Symptoms near the time of presentation in various cohorts

	Guan et al. NEJM (largest cohort)	Shi et al Lancet	Yang et al. Lancet (critically ill pts)	Chen et al.	Huang et al.	Xu et al. BMJ
Constitutional						
Fever	473/1081 (43%)	18/21 (86%)	46/52 (88%)	82/99 (83%)	40/41 (98%)	48/62 (77%)
Myalgia	164/1081 (15%)		6/52 (12%)	11/99 (11%)		
Headache	150/1081 (14%)	2/21 (10%)	3/52 (6%)	8/99 (8%)	2/38 (8%)	21/62 (34%)
Upper respiratory						
Rhinorrhea	53/1081 (5%)	5/21 (24%)	3/52 (6%)	4/99 (4%)		
Sore throat	153/1081 (14%)			5/99 (5%)		
Lower respiratory						
Dyspnea	205/1081 (19%)	9/21 (43%)	33/52 (64%)	31/99 (31%)	22/40 (55%)	2/62 (3%)
Chest tightness		5/21 (24%)				
Cough	745/1081 (68%)	15/21 (71%)	40/52 (77%)	81/99 (82%)	31/41 (76%)	50/62 (81%)
Sputum	370/1081 (34%)	3/21 (14%)			11/39 (28%)	35/62 (56%)
Hemoptysis	10/1081 (1%)				2/39 (5%)	2/62 (3%)
Gastrointestinal						
Nausea/Vomiting	55/1081 (5%)	2/21 (10%)	2/52 (6%)	1/99 (1%)		
Diarrhea	42/1081 (4%)	1/21 (5%)		2/99 (2%)	1/38 (3%)	3/62 (8%)

-The Internet Book of Critical Care, by @PulmCrit

COVID-19 may cause constitutional symptoms, upper respiratory symptoms, lower respiratory symptoms, and, less commonly, gastrointestinal symptoms. Most patients will present with constitutional symptoms and lower respiratory symptoms (e.g. fever and cough).

Lab Data



Admission laboratory pattern in patients with COVID-19

	Guan et al NEJM (largest cohort)	Shi et al Lancet	Chen et al Lancet	Huang et al. Lancet	Xu et al. BMJ
WBC count	4.7 (3.5-6)	7.8 (2.5)	7.5 (4)	6.2 (4-10.5)	4.7 (3.5-5.8)
Platelet count	168 (132-207)	213 (100)	214 (79)	164 (132-263)	176 (136-215)
Lymphocyte count (normally >1)	1 (0.7-1.3)	1 (0.3)	0.9 (0.5)	0.8 (0.6-1.1)	1 (0.8-1.5)
Hemoglobin	13.4 (12-15)	12.7 (1.3)	13 (1.5)	12.6 (11.8-14)	13.7 (12.9-15.2)
ALT (U/L)		51 (25)	39 (22-53)	32 (21-50)	22 (14-34)
AST (U/L)		48 (21)	34 (26-48)	34 (26-48)	26 (20-32)
Bilirubin uM/L (normal range 5-22 uM/L)		14 (4)	15 (7)	12 (10-14)	
Creatinine (normal range up to ~80-100 uM)		68 (15)	76 (25)	74 (58-86)	72 (61-84)
Prothrombin time (normal range ~12.7-15.4)		10.5 (0.4)	11 (2)	11 (10-12.4)	
APTT (normal range ~21-37 seconds)		34 (7)	27 (10)		
Thrombin time (normal range ~15-18.5)		32 (8)			
Fibrinogen mg/dL		192 (350)			
D-dimer (mg/L) – (Nl range seems to vary?)		6.9 (1.1)	0.9 (0.5-2.8)	0.5 (0.3-1.3)	0.2 (0.2-0.5)
Creatinine kinase			85 (51-184)		
LDH (normal range up to 250 U/L)			336 (260-447)	286 (242-408)	205 (184-260)
C-Reactive Protein mg/L		61 (40)	51 (42)		
Procalcitonin	<0.5 in 95% patients		0.5 (1)	0.1 (0.1-0.1)	0.04 (0.03-0.06)
Erythrocyte sedimentation rate (ESR)			50 (23)		
Ferritin			808 (490)		

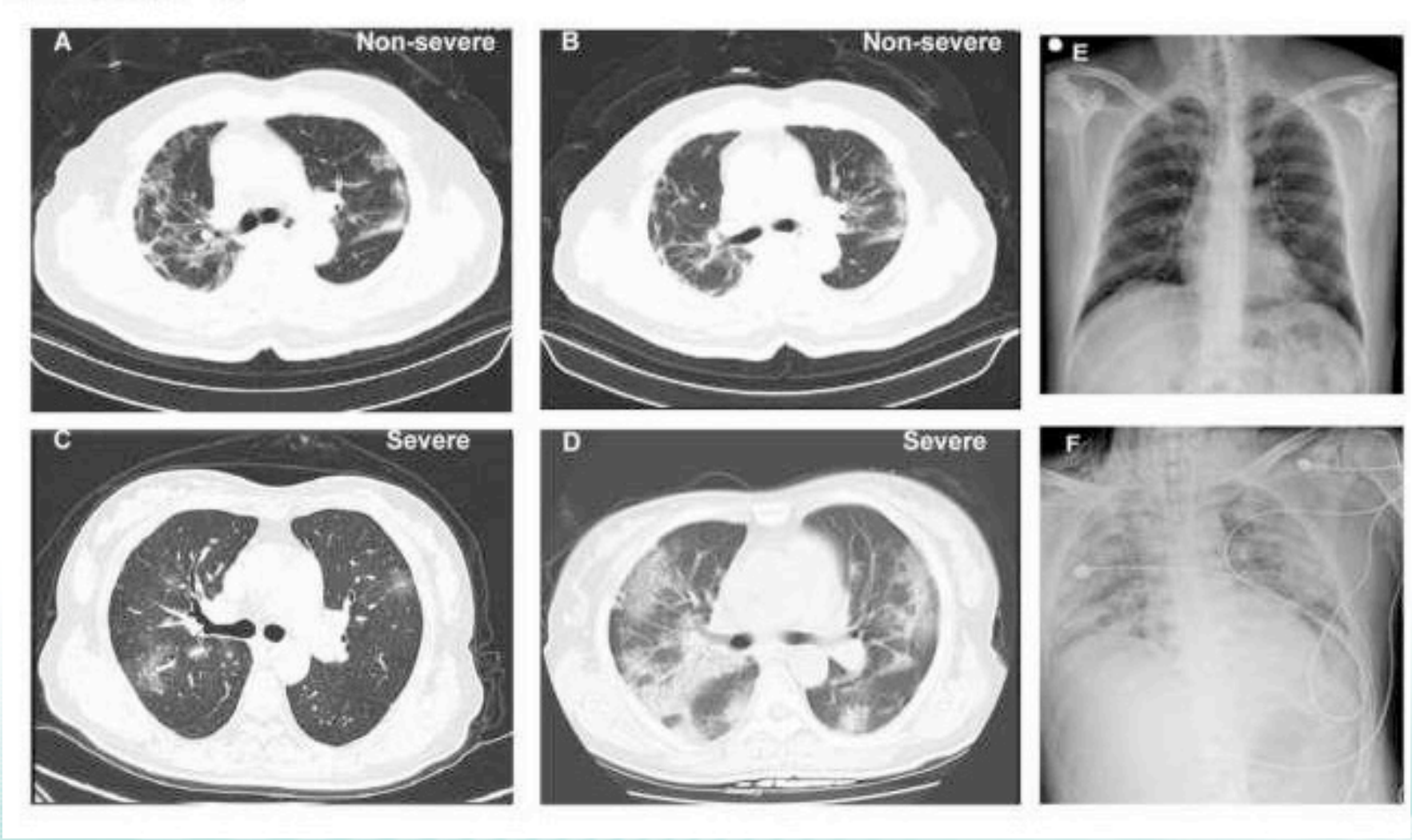
Laboratory findings are generally nonspecific. Substantial *deviation* from these values might argue *against* a diagnosis of COVID-19. However, in most cases, laboratory findings are unlikely to be tremendously helpful.

-The Internet Book of Critical Care, by @PulmCrit

Radiologic Findings - Xray

- The typical finding is patchy ground glass opacities, which tend to be predominantly peripheral and basal (Shi et al 2/24). The number of involved lung segments increases with more severe disease. Over time, patchy ground glass opacities may coalesce into more dense consolidation.
- • Infiltrates may be subtle on chest X-ray (example above from Silverstein et al).
- • Findings which *aren't* commonly seen, and might argue for an alternative or superimposed diagnosis: • Pleural effusion is uncommon (seen in only ~5%).
- • COVID-19 doesn't appear to cause masses, cavitation, or lymphadenopathy.

Figure: First case of 2019 novel coronavirus in Canada
Chest x-ray shows bilateral, peribronchovascular, ill-defined opacities in all lung zones.


A
Non-severe
B
Non-severe
E
C
Severe
D
Severe
F

Possible Therapies – Anti-Viral

- No anti-viral therapy has been proven to work for COVID-19 in humans. Multiple RCTs are ongoing; hopefully they will bring us further information soon.
- Another unknown is whether a *single* drug could work, or whether a combination of multiple anti-viral agents is needed.
- Remdesivir (protease inhibitor) is being used in one trial in the United States being sponsored by NIAID.
- Lopinavir/ritonavir (Kaletra) is currently under investigation within multiple RCTs in China (but none in the United States).

Chloroquine

- • Chloroquine is generally used for treatment of malaria and amebiasis. It has anti-viral activity in vitro, but no established track record in treatment of viral disease.
- • The toxicity profile seems to be acceptable (e.g. its widely used as malaria prophylaxis — albeit at a much lower dose than is currently being considered for COVID-19).

- • Chloroquine appears to work via multiple mechanisms, including: • Interference with with the cellular receptor ACE2 (potentially making it particularly effective against SARS and COVID-19).

- • Chloroquine also has immunosuppressive activities. It's unknown whether such immunosuppressive action could be *beneficial* or *harmful* (analogous to steroid therapy).

- In vitro data
- • *In vitro* data using cell lines shows that chloroquine can inhibit COVID-19 with an 50% inhibitory concentration of 1 uM, implying that therapeutic levels could be achieved in humans (Wang 2020).

Oseltamavir & other neuraminidase inhibitors

- • Neuraminidase inhibitors *don't* seem to work against COVID-19 (Tan et al 2004).
- • Initial empiric therapy with neuraminidase inhibitors could be reasonable during influenza season in critically ill

Specific Management Recommendations

- Steroids
- Nsaids
- BiPAP/CPAP
- HFNC
- Proning and PEEP

Proning and PEEP

- In ARDS in children proning has proven to be of some benefit
- If not meeting criteria for ARDS, no long term benefit to proning
- High PEEP strategies (PEEP 8-12 routine)

Steroids

- • Steroid should *not* generally be used. Steroid hasn't demonstrated benefit in prior SARS or MERS epidemics. Steroid may increase viral shedding (Lee 2004).

- • Nearly all articles recommend against the use of steroid.

NSAIDS

- The use of non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen, could worsen coronavirus disease (COVID-19). These news reports followed a March 11, 2020 letter in The Lancet medical journal, which hypothesized that the enzyme ACE-2 is increased by NSAIDs and could aggravate COVID-19 symptoms
- No specific recommendations on NSAID use

HFN and BiPAP/CPAP

- Risk of aerosolizing into room
- Allowing HFNC up to 30 L/min
- Prefer negative pressure rooms if possible
- Avoiding BiPAP and CPAP