

Simplified COVID 19 management in adults and pediatrician themselves



Home to Hospital



Total slides 117 – 20 (hidden) = 97
Time – 40 – 50 min

Aim in covid 19 management

Classify patients – high risk vs low risk

Target of catching patients before

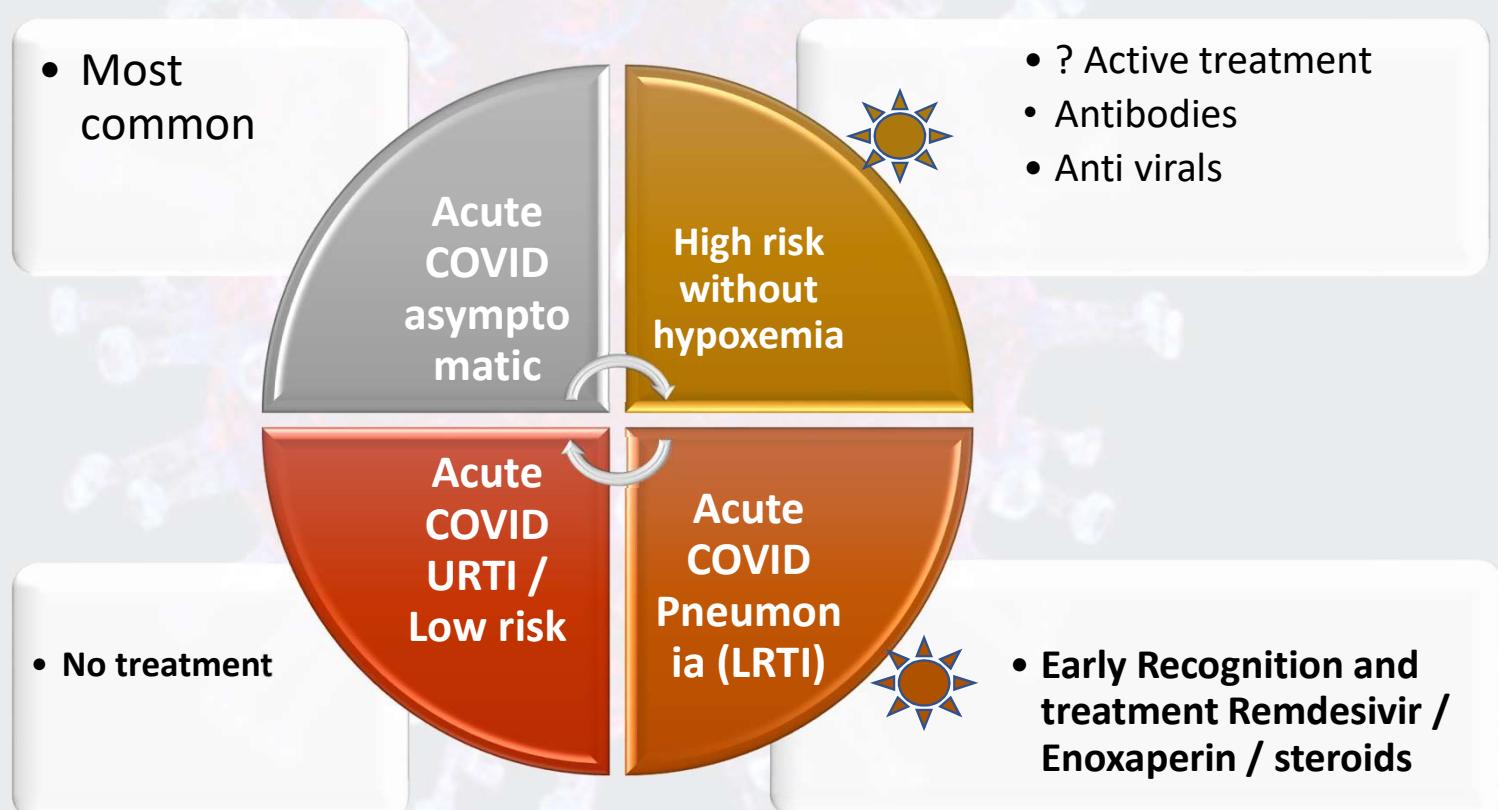
Essentials of home and ward care

Use of antiviral drugs

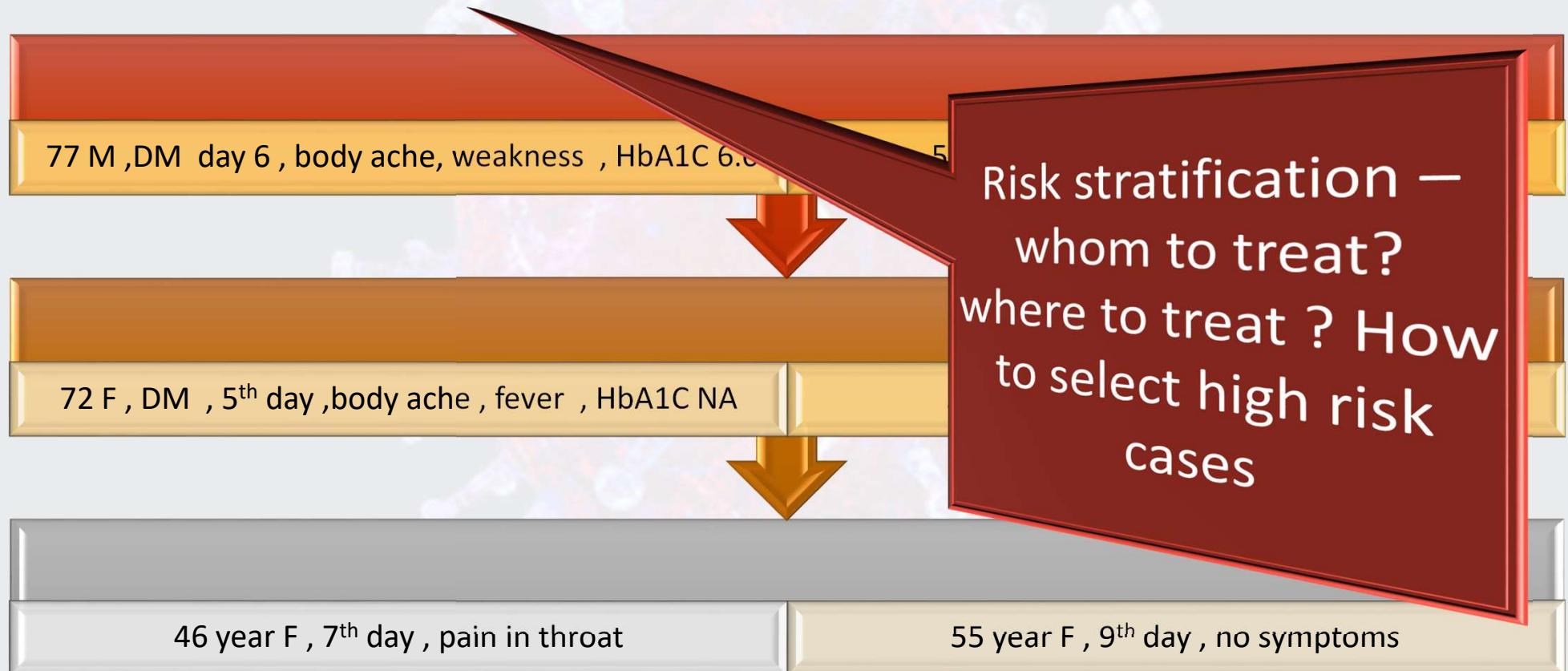
Use of steroids

Disclaimer
All cases are real
scenarios

COVID 19 SPECTRUM – TREATMENT OPTIONS



Case – Family of 6 (Family of Ashi)– all obese



Where to treat ?

Low risk – Home monitoring

High risk – Asymptomatic – Home / COVID care center

High risk symptomatic – hospital

High risk symptomatic with saturation less than 95 percent – Hospital with ICU backup



High risk situations

High risk – Age > 50 , Comorbidity (Obesity , diabetes) , family history of death due to acute covid , male

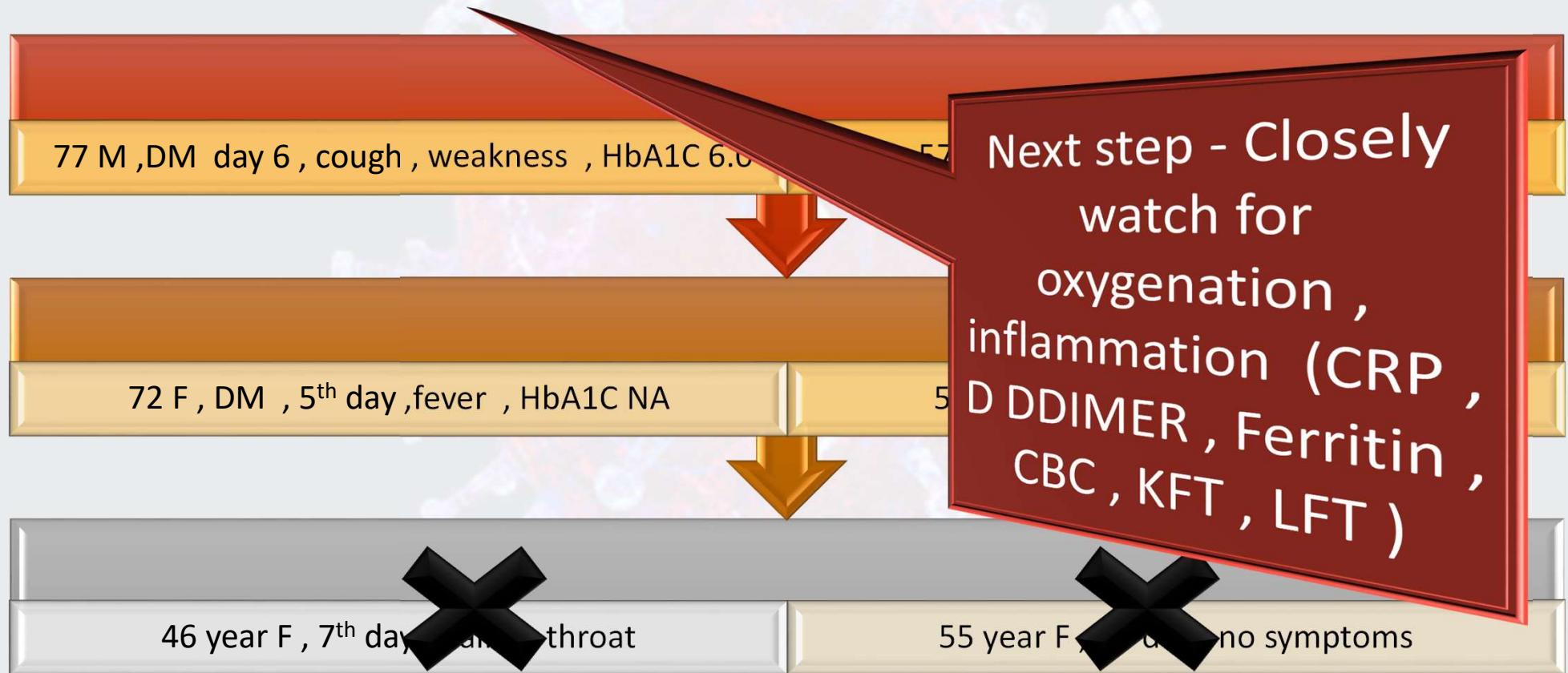


High risk symptoms – Persistent fever > 5 days , high grade fever >102 degree F beyond 2 days , chills and rigor , breathlessness , biphasic fever (return of fever after 5 days)

Investigations – Rising inflammatory markers , Significant Chest infiltrates in radiology

Hypoxemia – drop from baseline

Case continued – SpO₂ more than 97



Options available for care

High risk home care

Hospital care

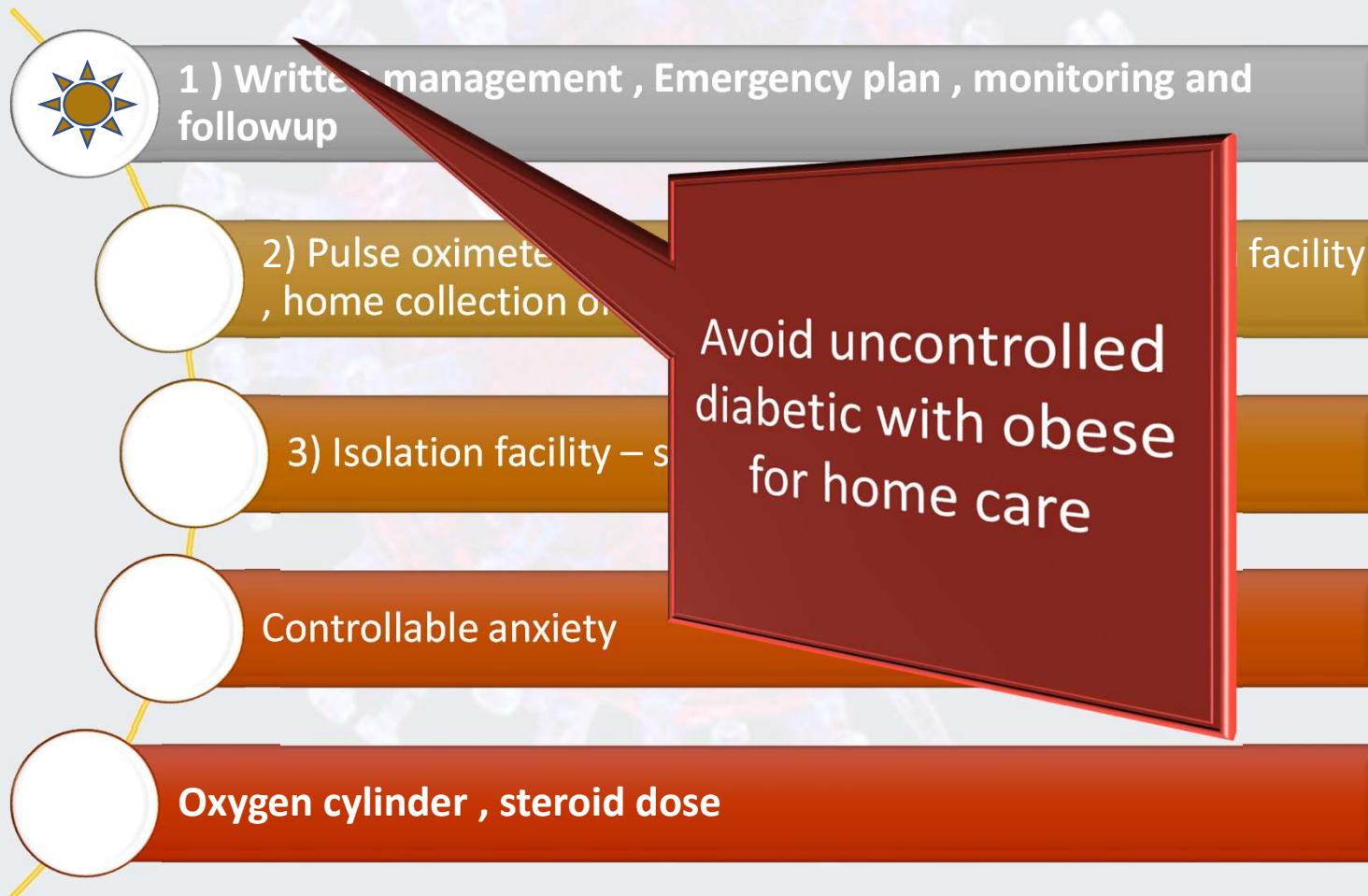
Hospital with ICU

In house helper / health facilities available

Avoid uncontrolled diabetic with obese for home care

Oxygenation priority

Home care – Prerequisites



Details required for management plan , monitoring (Make monitoring chart)

Age , sex , comorbidity

SpO2 rest , after walk

**Symptoms – Fever ,
breathlessness**

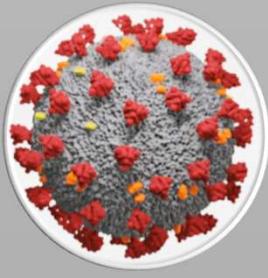
**Investigations – serial
wise**

Treatment – steroid dose

Monitoring at home (high risk patients) – Make monitoring chart

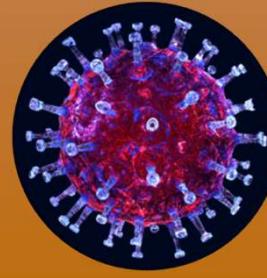


Steps of telephonic video consultations

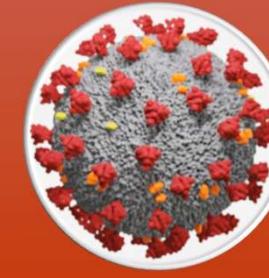


Make a group of family members

Introduction – your self , family members – whatsapp video chat



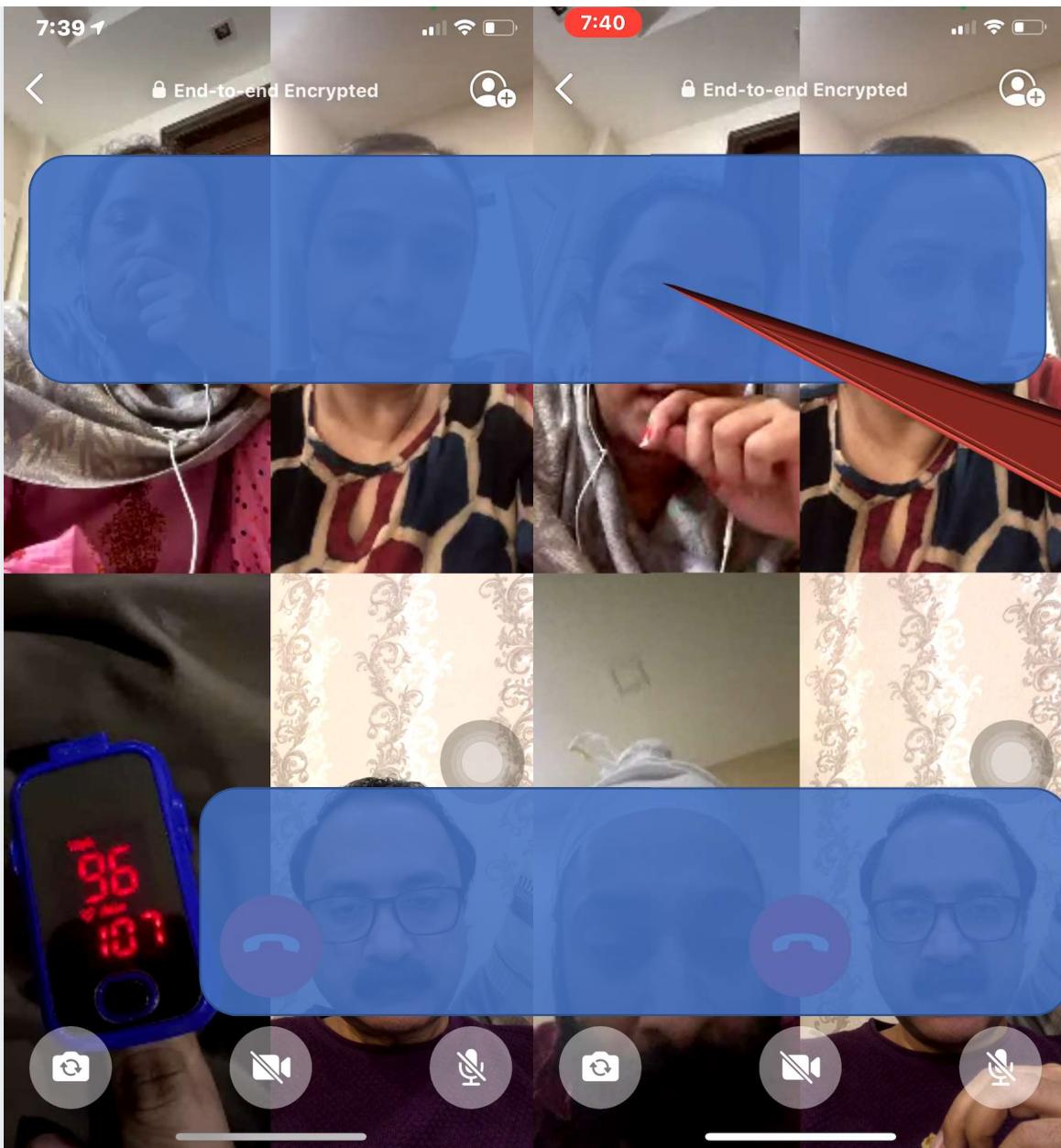
Explain the disease – Risk involved – high risk features



Written treatment plan

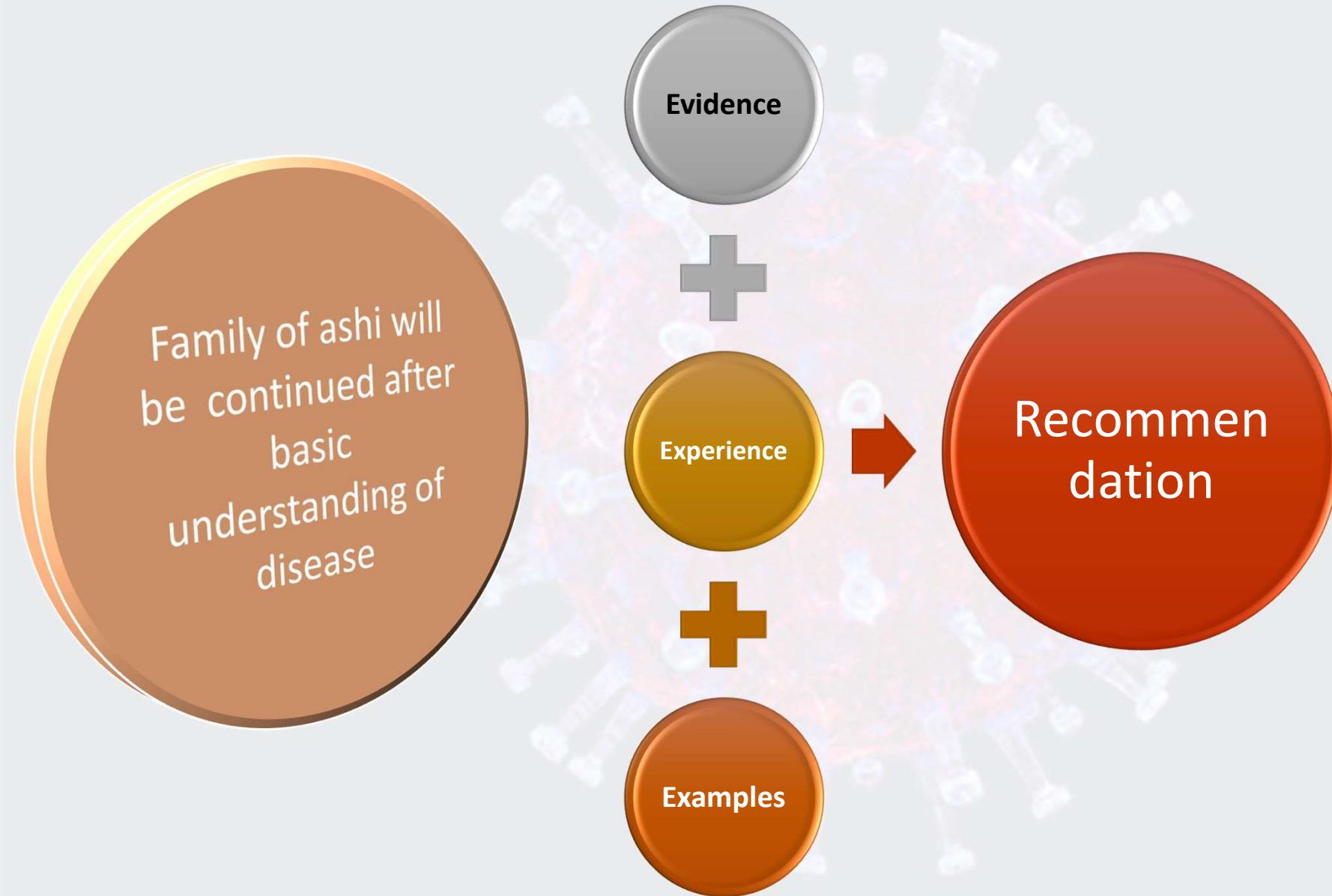
Don't emphasise on efficacy of drugs but monitoring



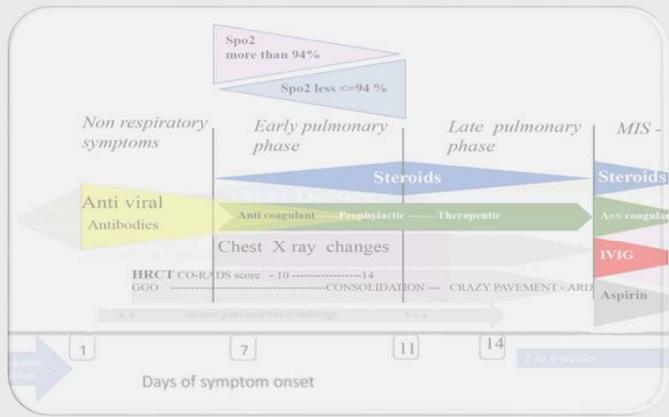
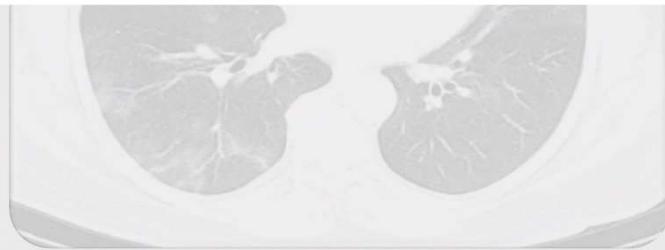


Example of counselling - 42 year old
non diabetic , non obese ,
persistence of cough x 8 days , low
grade fever x 8 days

Young patient with high risk
clinical features shouldn't be
taken lightly
Any patient found hypoxic
immediately one dose of
steroid to be given before
initiating admission process
(Hit hard and fast)



MANAGEMENT

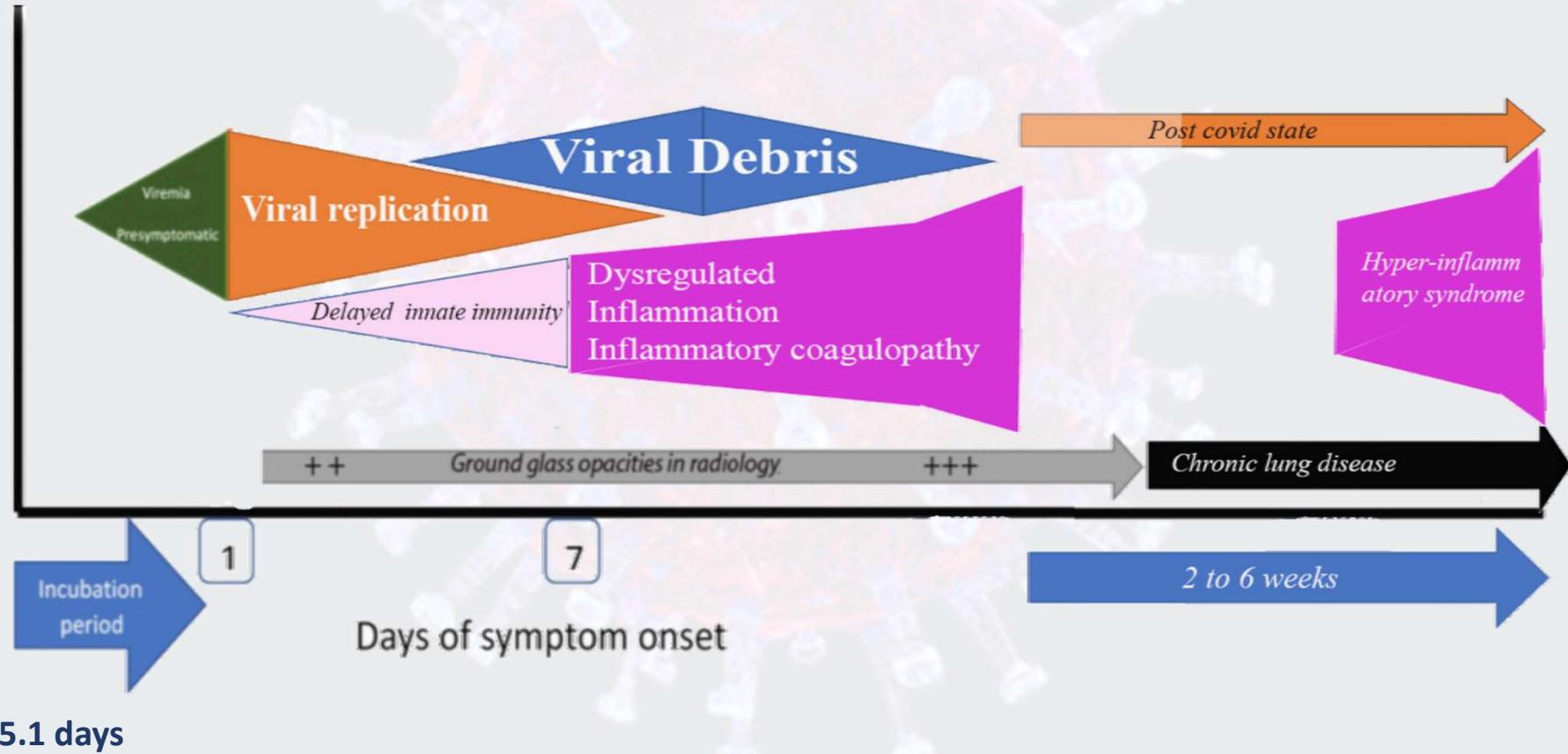


Pathogenesis

Diagnosis /Monitoring

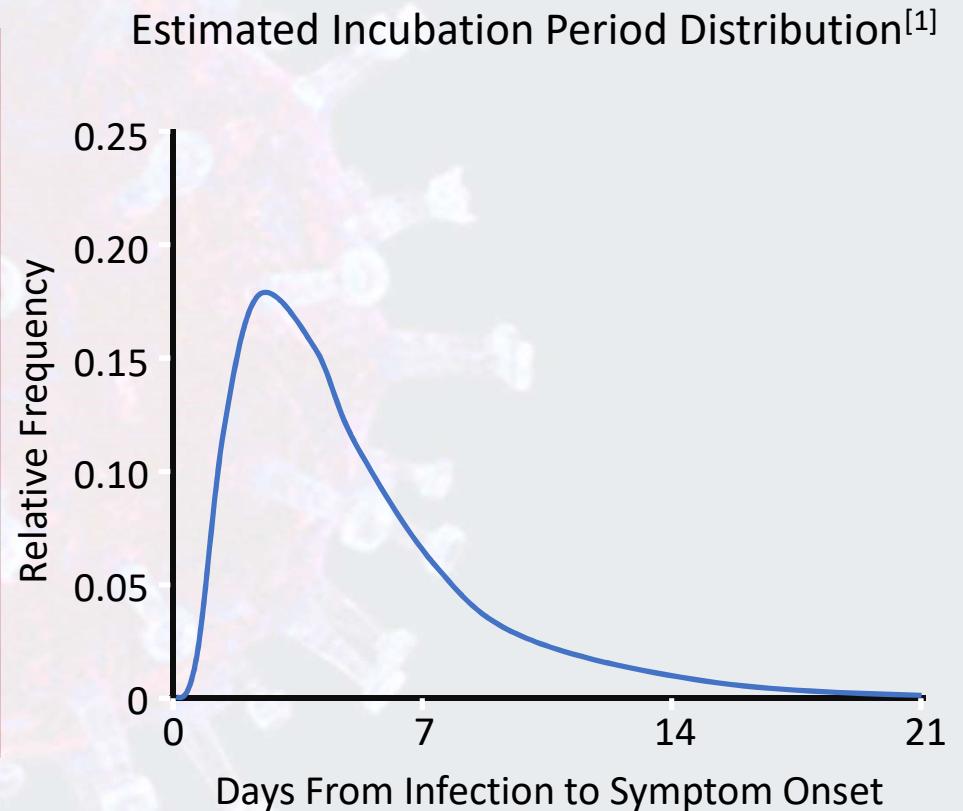
Treatment

What we understand about pathogenesis ?



COVID-19 – Infection to Contagion

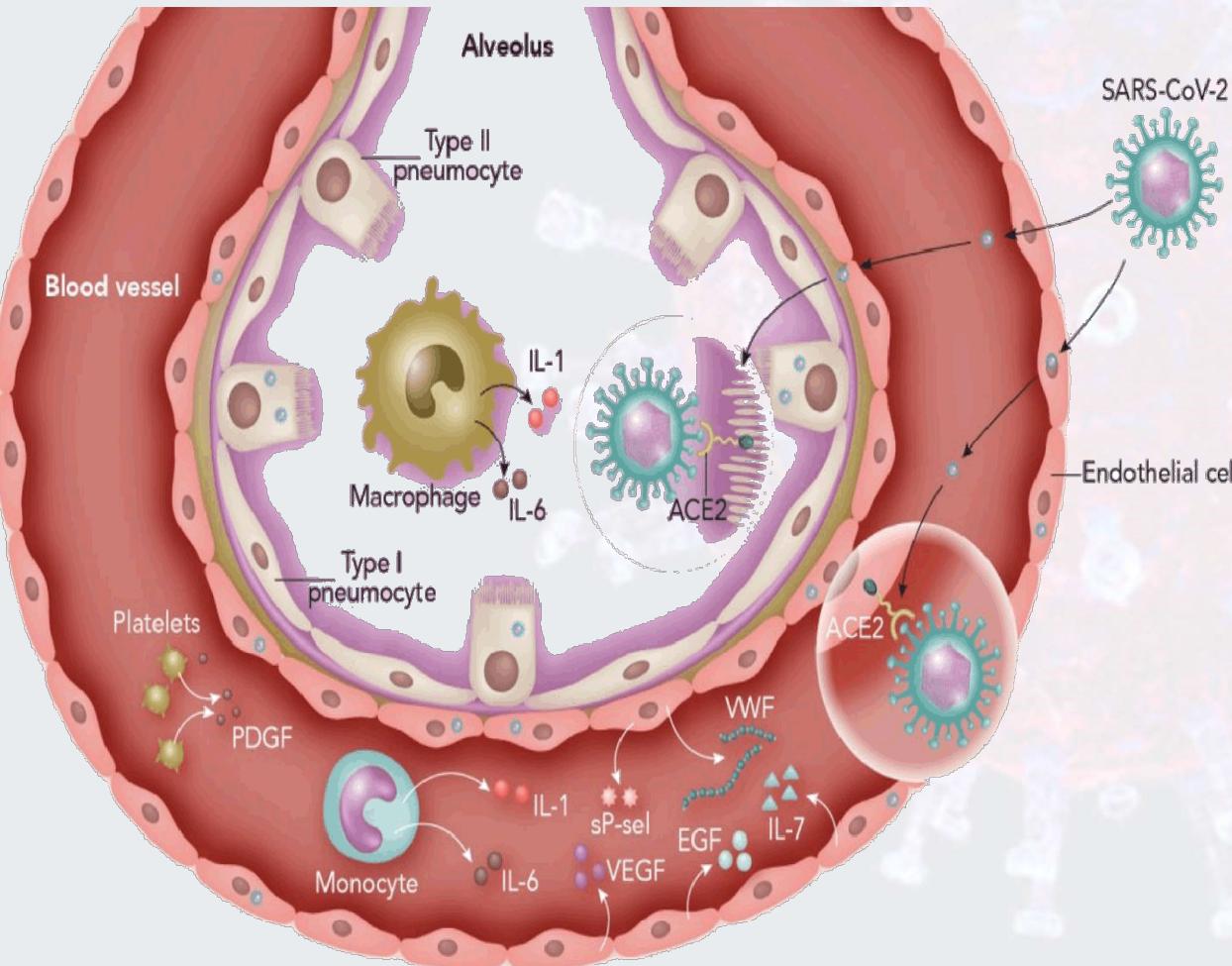
2.3 days before symptoms or 3 days
after contact (Maximum infectious)
0.7 days before onset of symptoms)



1. Li. NEJM. 2020;382:1199. 2. Lauer. Ann Intern Med. 2020;172:577.

Why some gets mild disease ?

Confronting the controversy: Interleukin-6 and the COVID-19 cytokine storm syndrome. Eur Respir J 2020

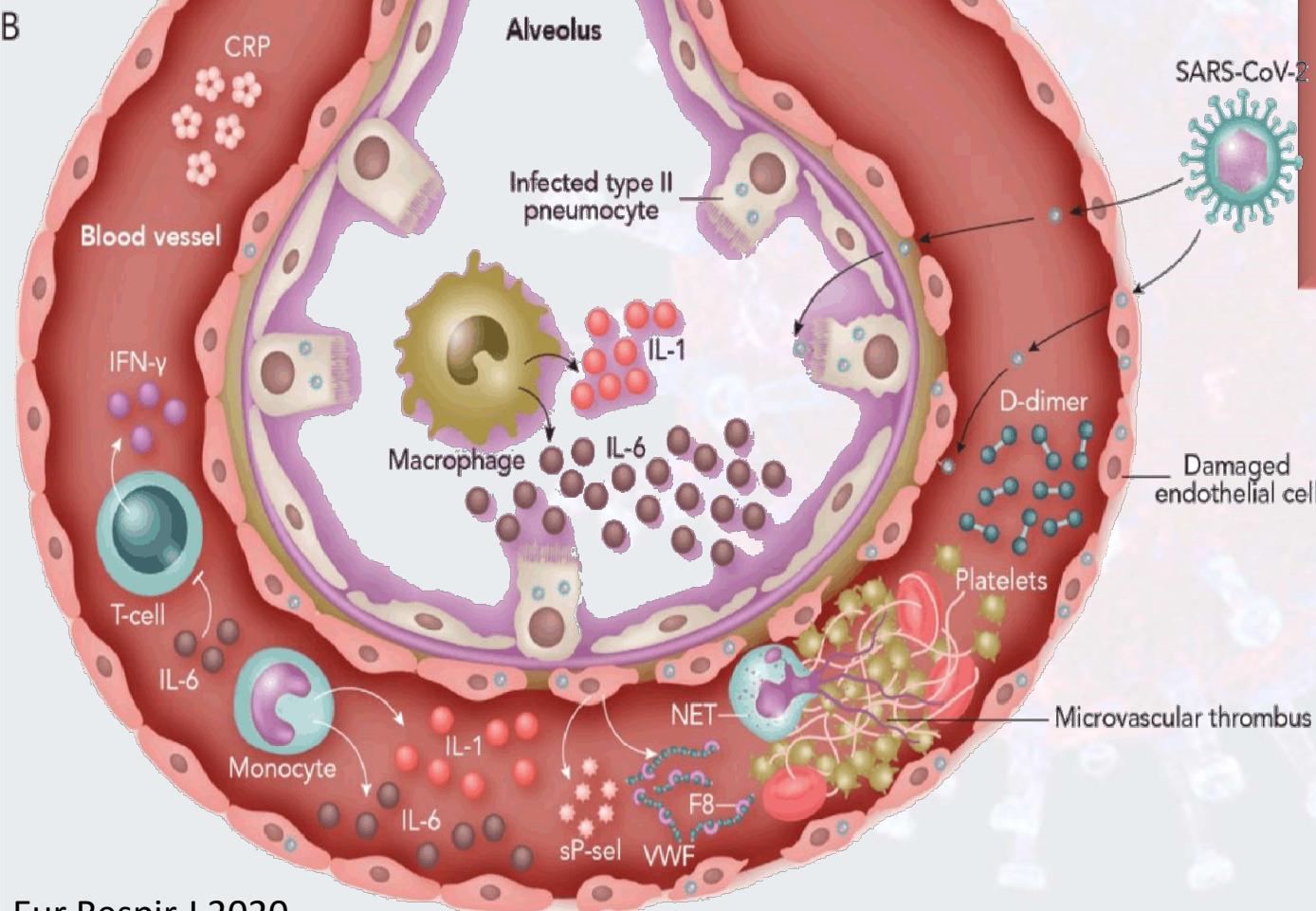


Low serum inflammatory cytokines and high tissue reparative growth factors such as platelet derived growth factor (PDGF), and interleukin(IL)-7



Low incidence of coagulopathy and thrombosis

Why some gets severe disease ?

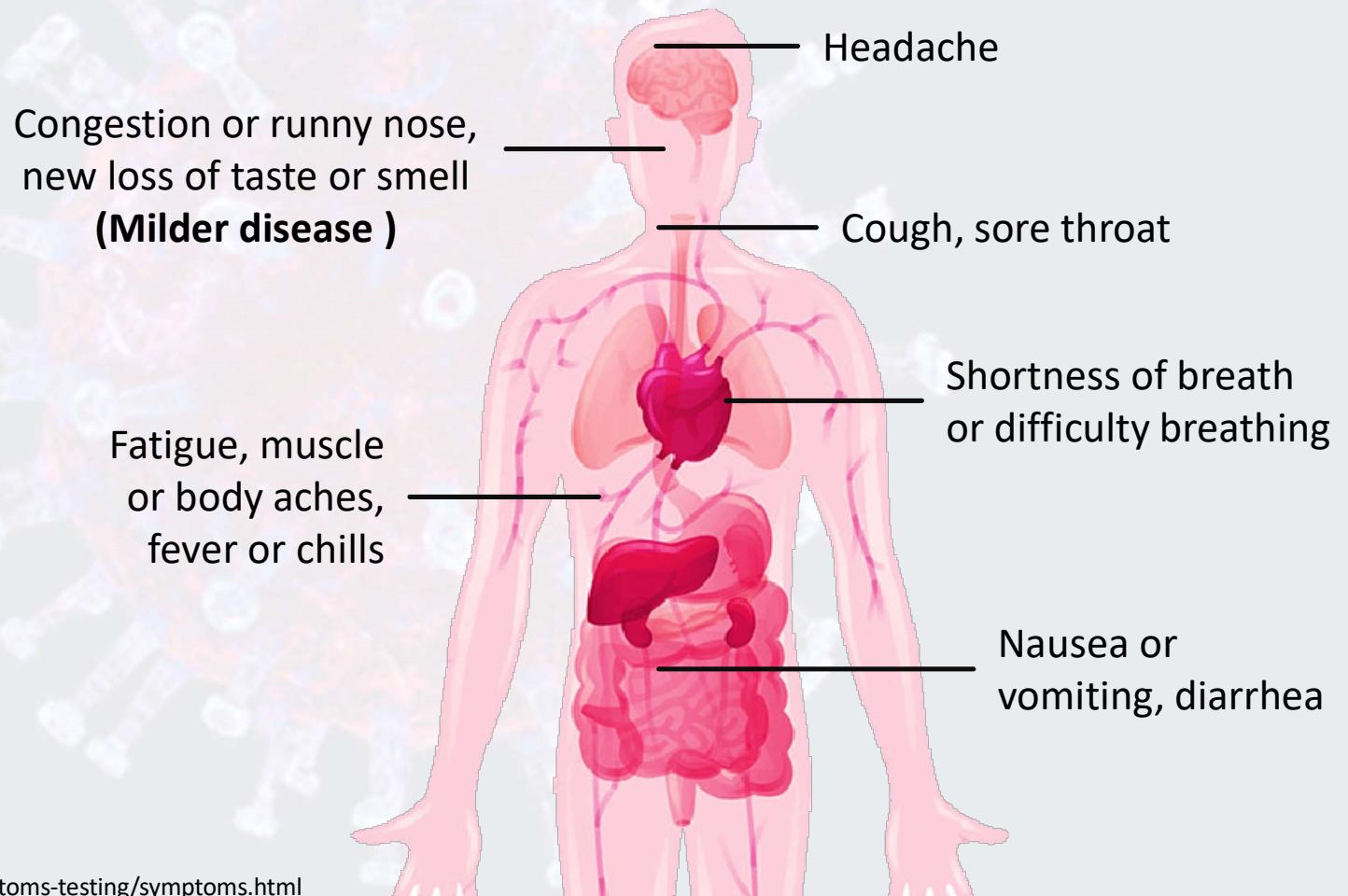


cytokine storm, with high serum inflammatory cytokines (such as IL-6, IL-1, IFN- γ) and markers of endothelial activation such as von Willebrand factor (vWF). Netosis

High incidence of coagulopathy and thrombosis

Severe disease

Common Symptoms of COVID-19



Case - 48 year old male , poorly controlled diabetic

- Fever x 7 days
- Loss of taste , smell x 2 days
- Afbrile x 2 days
- Day 9 – breathless , oxygen saturation 93%
- Inflammatory markers – IL 6 22 , CRP 18
- CT SS – 12 /25

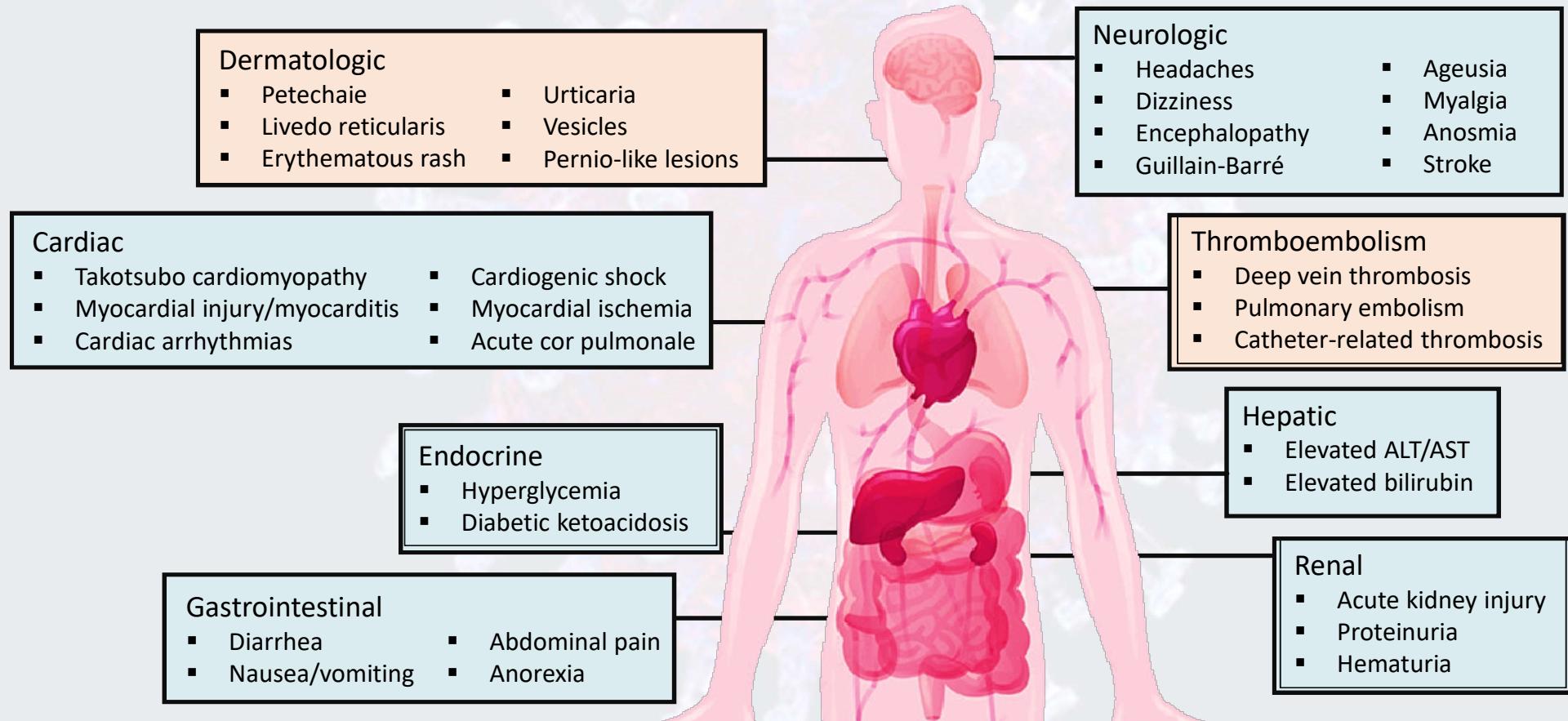
Loss of taste and smell doesn't give guarantee in high risk patients



COVID-19 Clinical Presentation – Facts

- **Mean duration of symptoms** : 11.5 ± 5.7 days
 - Ear, nose, throat complaints more common in **young patients**; fever, fatigue, loss of appetite, diarrhea in **elderly patients**
 - Loss of smell, headache, nasal obstruction, throat pain, fatigue more common in **women**; cough, fever in **men**
- **Median time from first symptom to death:**
 - 14 days (range: 6-41)
 - Numerically faster in **older patients**: 11.5 days if ≥ 70 yrs vs 20 days if < 70 yrs

Extrapulmonary Manifestations of COVID-19





Classification of disease - severity



Government of India
Ministry of Health & Family Welfare
Directorate General of Health Services
(EMR Division)

Revised Guidelines on Clinical Management of COVID – 19



- **Mild**
- **Asymptomatic**
- **Fever /URTI**

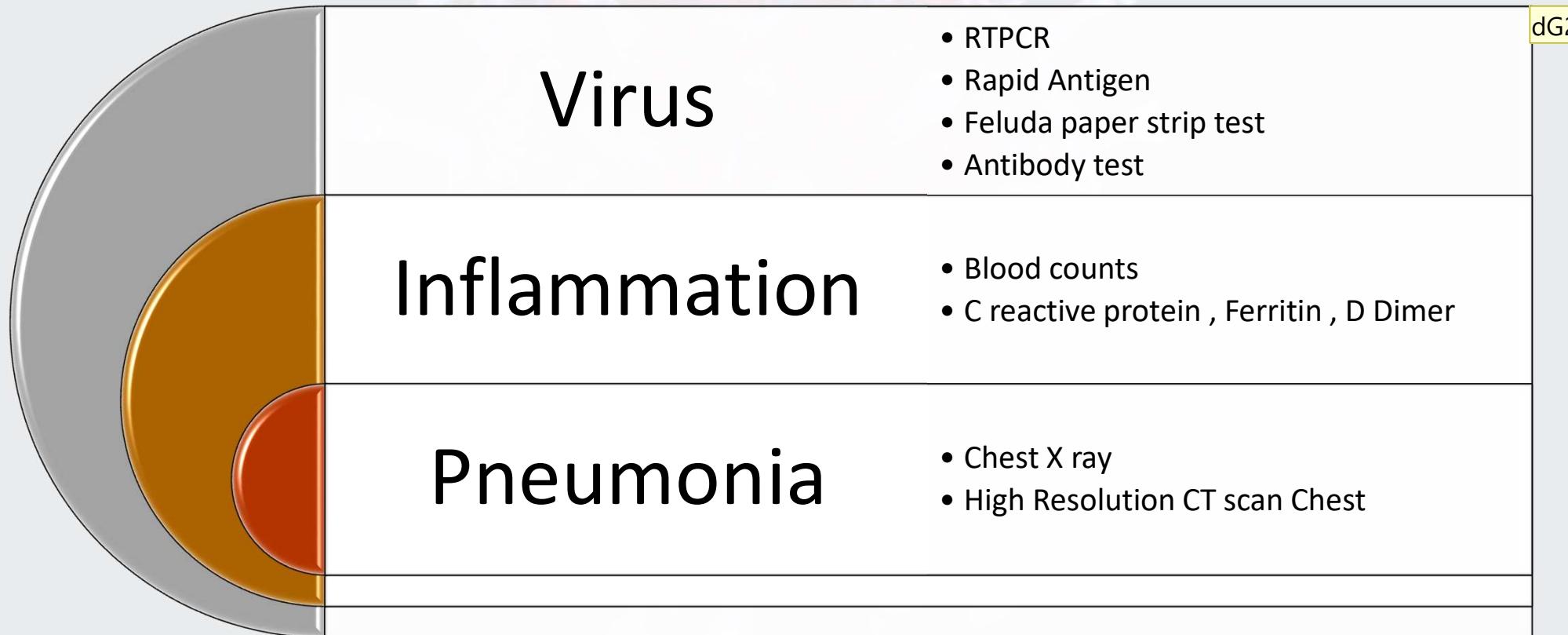


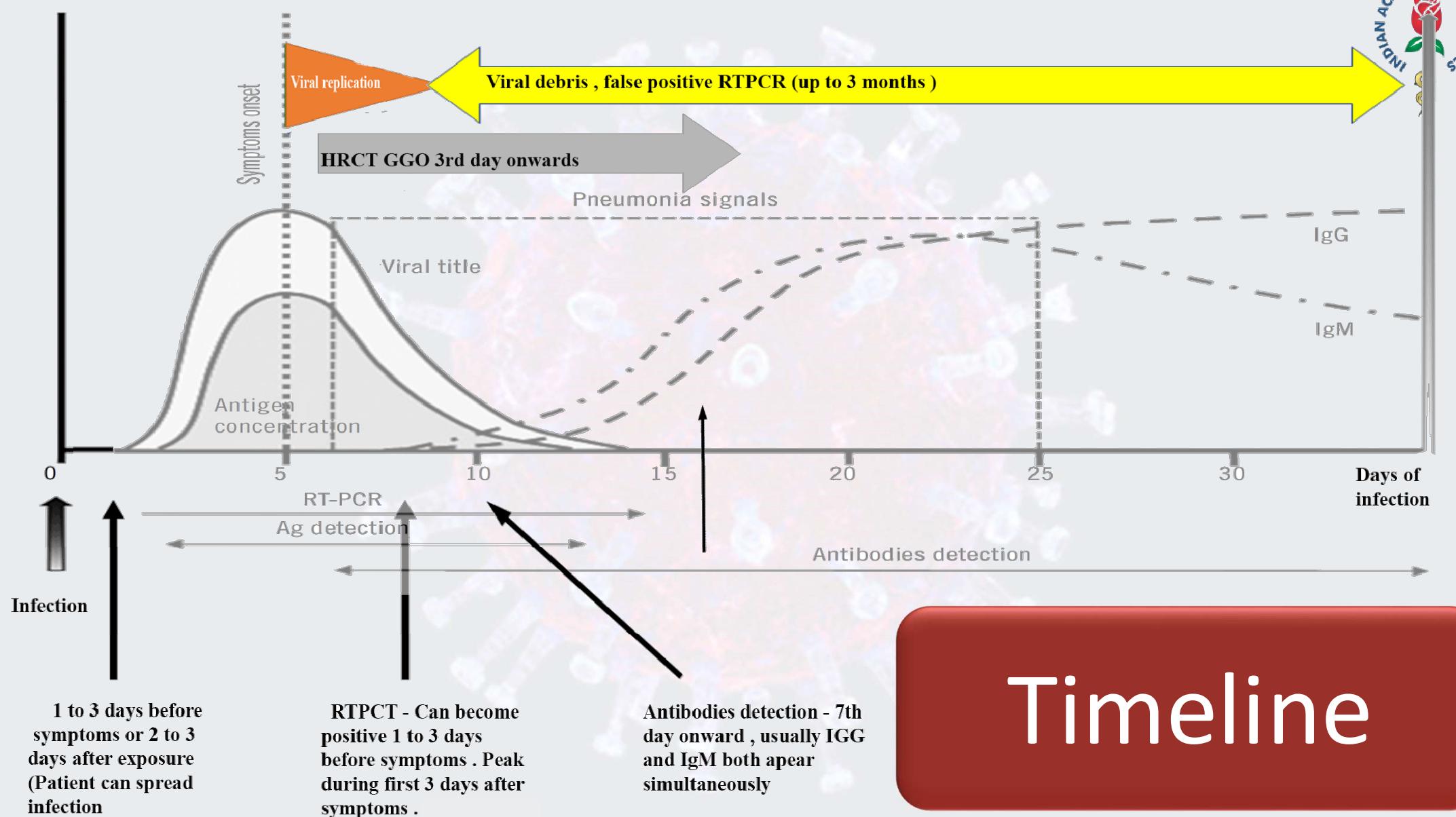
- **Moderate**
- Pneumonia with SpO_2 94 to 90 percent
- RR 15 TO 30 /min



- **Severe**
- SpO_2 less than 90 percent
- $\text{RR} > 30 / \text{MIN}$

Investigations





Timeline

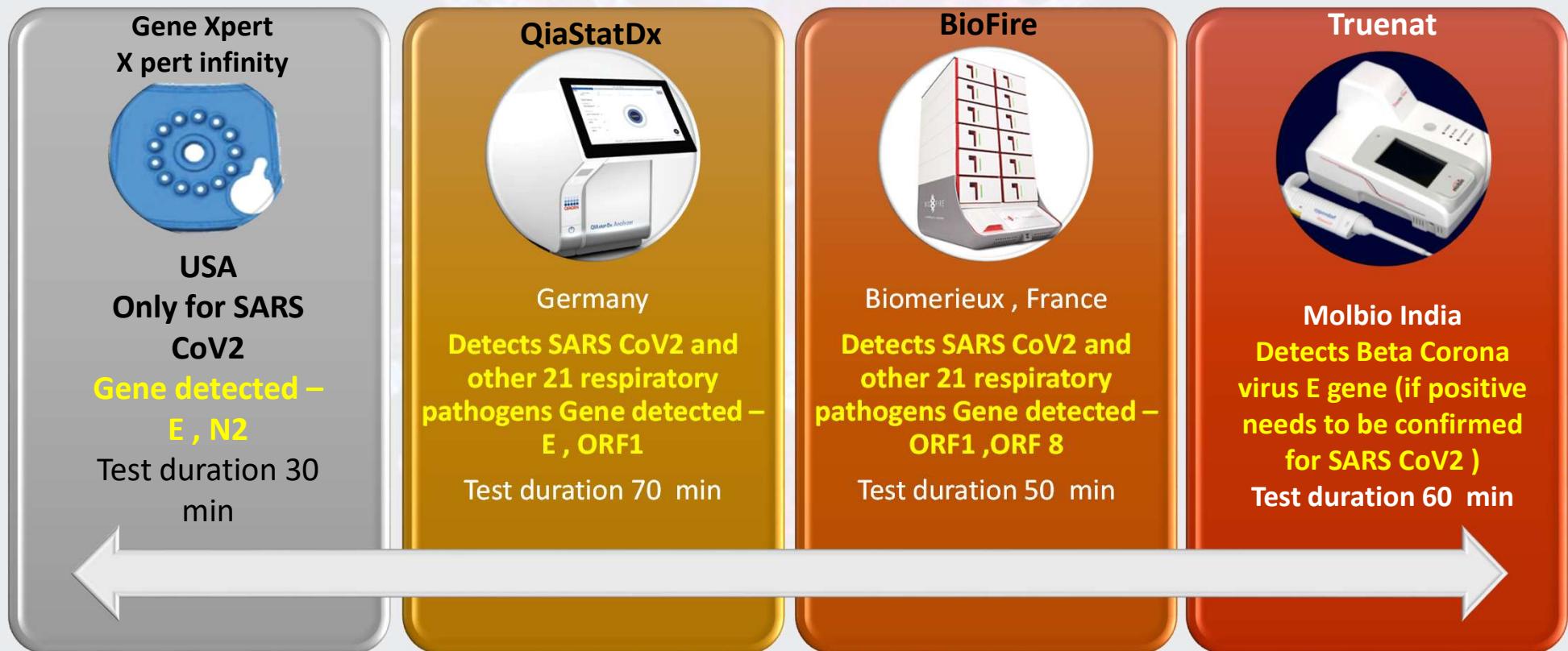


Which type of RTPCT ?

Real-time polymerase chain reaction (RT-PCR)

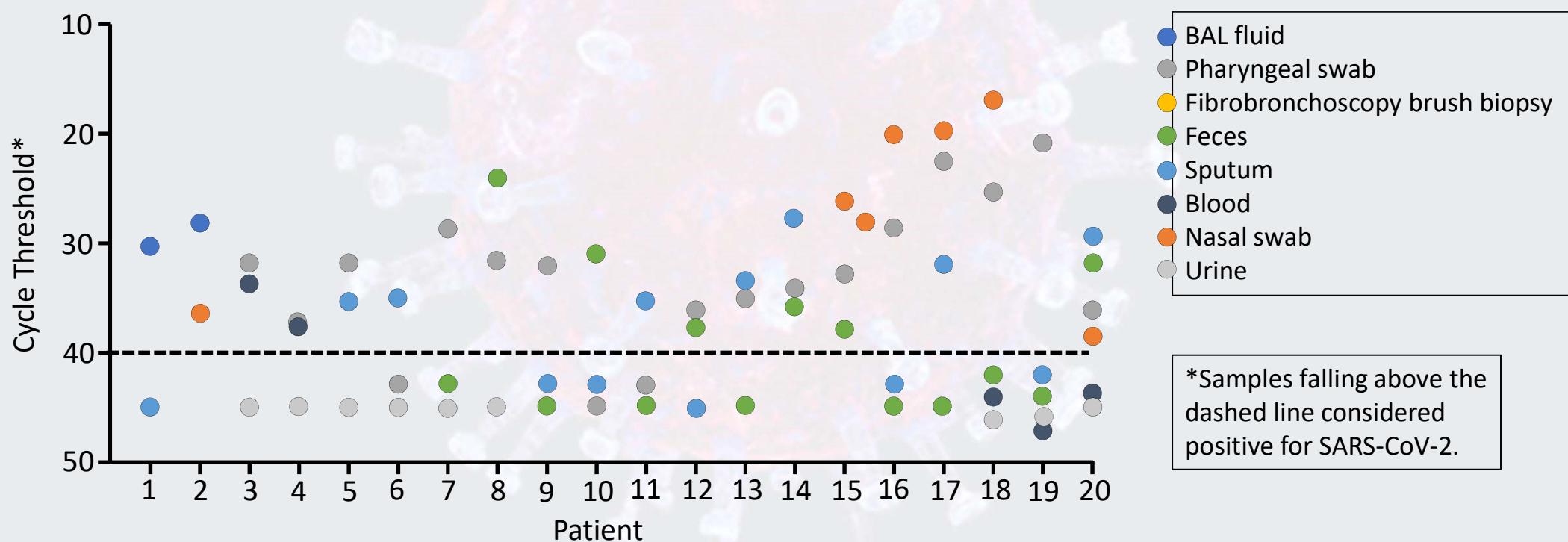
Portable and cartridge based systems – X pert ,
QiaStatDx , BioFire , Truenat

RT PCR - Portable and cartridge based systems



Which specimen gives maximum yield

- Among 1070 specimens from 205 COVID-19 patients in China, **highest SARS-CoV-2 positivity rates observed with BAL fluid (93%), sputum (72%), nasophyrngeal swab (70%)**

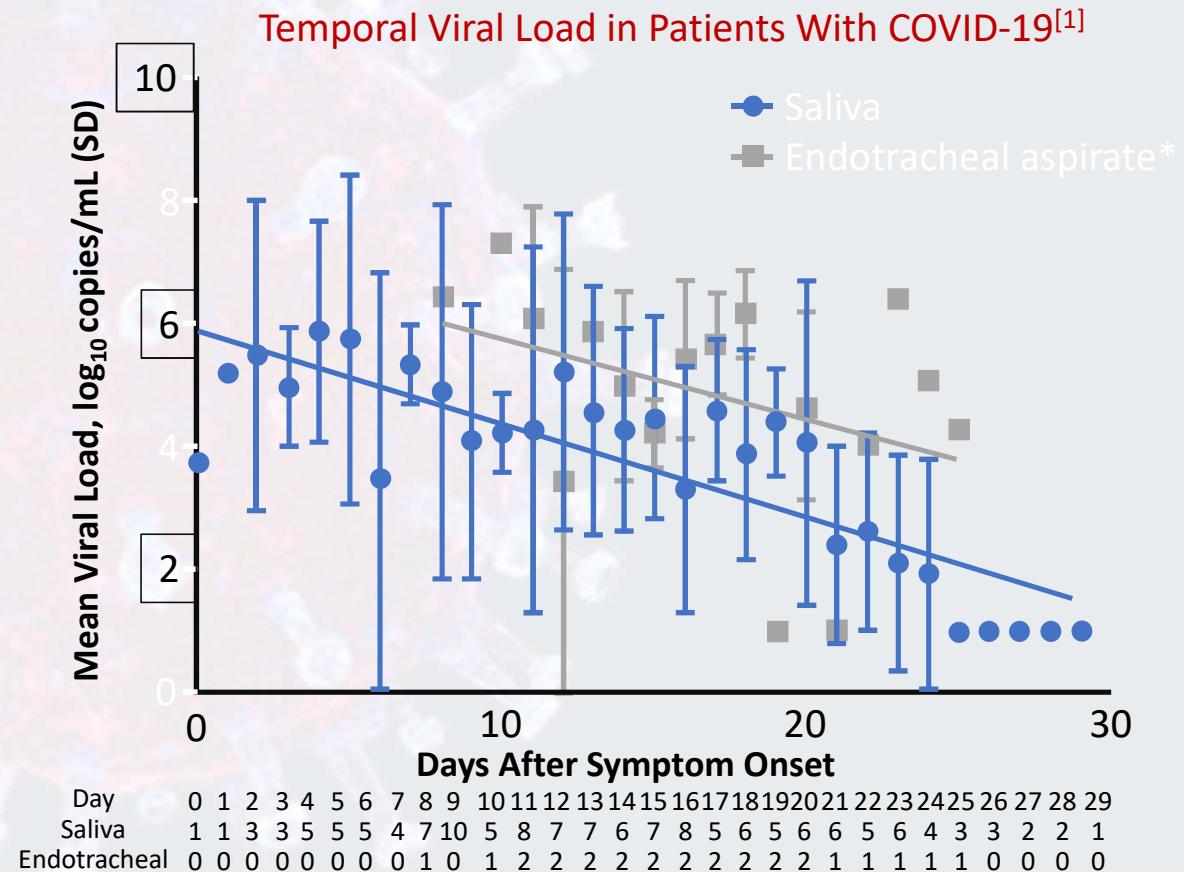


SARS-CoV-2 Test	Identification	Specimen	Se (%)	Sp (%)
rt-PCR	RNA	nasopharyngeal and/or oropharyngeal swabs and/or lower respiratory specimen	70 to 90	99
NP antigen detection test	Antigen (Ag) of SARS-CoV-2	nasopharyngeal and/or oropharyngeal swabs and/or lower respiratory specimen	40 to 50 %	95-97

SARS-CoV-2 Viral Load – CT value

- Viral loads highest during first wk following symptom onset^[1]
- Cycle Threshold - Ct refers to the number of cycles needed to amplify viral RNA to reach a detectable level
 - **Should not be used to describe severity of cases** as it depends on many parameters like day of collection , technique of collection , storage of sample
 - **No standardization for Ct values exists across RT-PCR platforms**

*Intubated patients.





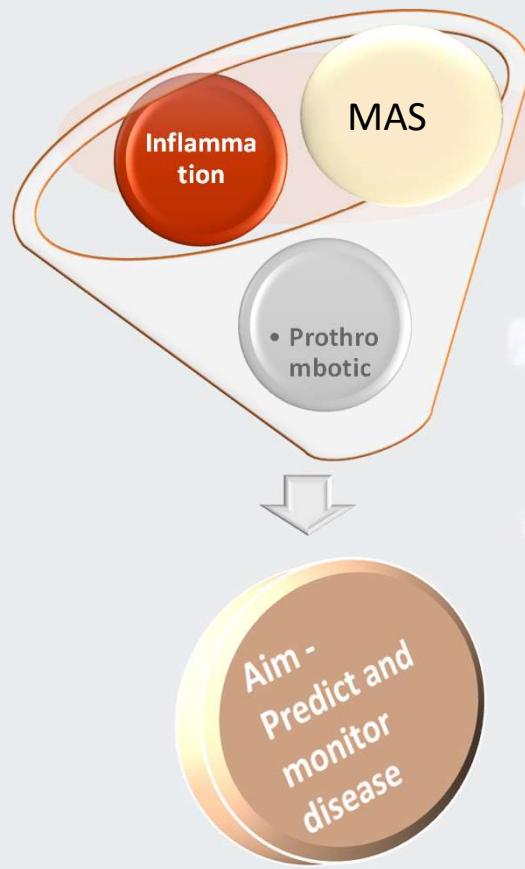
SARS-CoV-2 Antibody Tests

Type of Test*[1]	Time to Results[1]	Sensitivity ^[1]	Specificity ^[1]	What It Tells Us ^[1]	What It Cannot Tell Us ^[1]	Approved for Diagnostic Use ^[1,2]
Rapid diagnostic test (RDT)	10-30 mins	87.9% to 99.0%	95.6% to 100%	Presence of antiviral antibodies (qualitative)	Antibody titer, neutralizing activity	US (FDA EUA), EU, China, Australia
Enzyme-linked immunosorbent assay (ELISA)	2-5 hrs	13.9% (0-10 days) to 100% (\geq 21 days)	99% to 100%	Presence and level of antiviral antibodies (quantitative)	Neutralizing activity	US (FDA EUA), Australia
Neutralization assay	3-5 days	90%	Not stated	Presence of antibodies that can inhibit virus growth (ex vivo)	May miss antibodies to viral proteins not involved in replication	Singapore
Chemiluminescent immunoassay	1-2 hrs	65.5% (0-6 days) to 100% (\geq 14 days)	93.0% to 99.8%	Presence and level of antiviral antibodies (quantitative)	Neutralizing activity	US (FDA EUA)

*Some additional tests have been approved that do not fit these categories or are proprietary.

CDC: "Serologic testing by itself should not be used to establish the presence or absence of SARS-CoV-2 infection or reinfection."^[1]

Role of blood tests in management of COVID ?

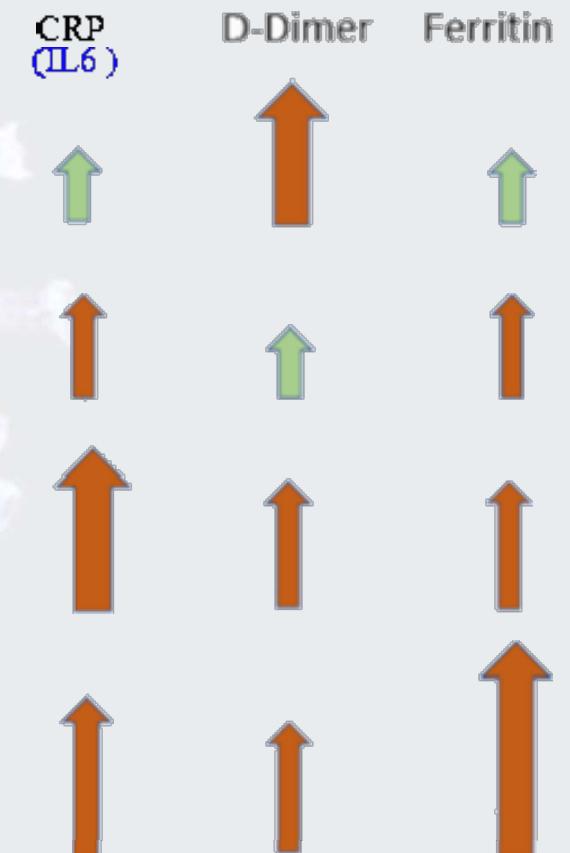


Thrombophilic

Early pulmonary

Late pulmonary: Inflammopathic

Late pulmonary/ MAS



Neutrophil lymphocyte ratio



< 4.5 predicts less severe disease with 82% sensitivity , > 6.5 predict mortality with 83 sensitivity

Systematic review and meta-analysis , Li et al. Predictive values of neutrophil-to-lymphocyte ratio for disease severity and mortality in COVID-19 patients: a systematic review and meta-analysis. *Crit Care* 24, 647 (2020). <https://doi.org/10.1186/s13054-020-03374-8>

Pearl - Alone NLR ratio should not be considered as major risk factor . Should combine with other factors . Steroids can alter the ratio

C Reactive protein

When
to be
done?

- Day 5 onward if symptoms persists in high risk individual

Not
indicated



- Day 1 as base line after symptoms onset

When CRP is significant ?



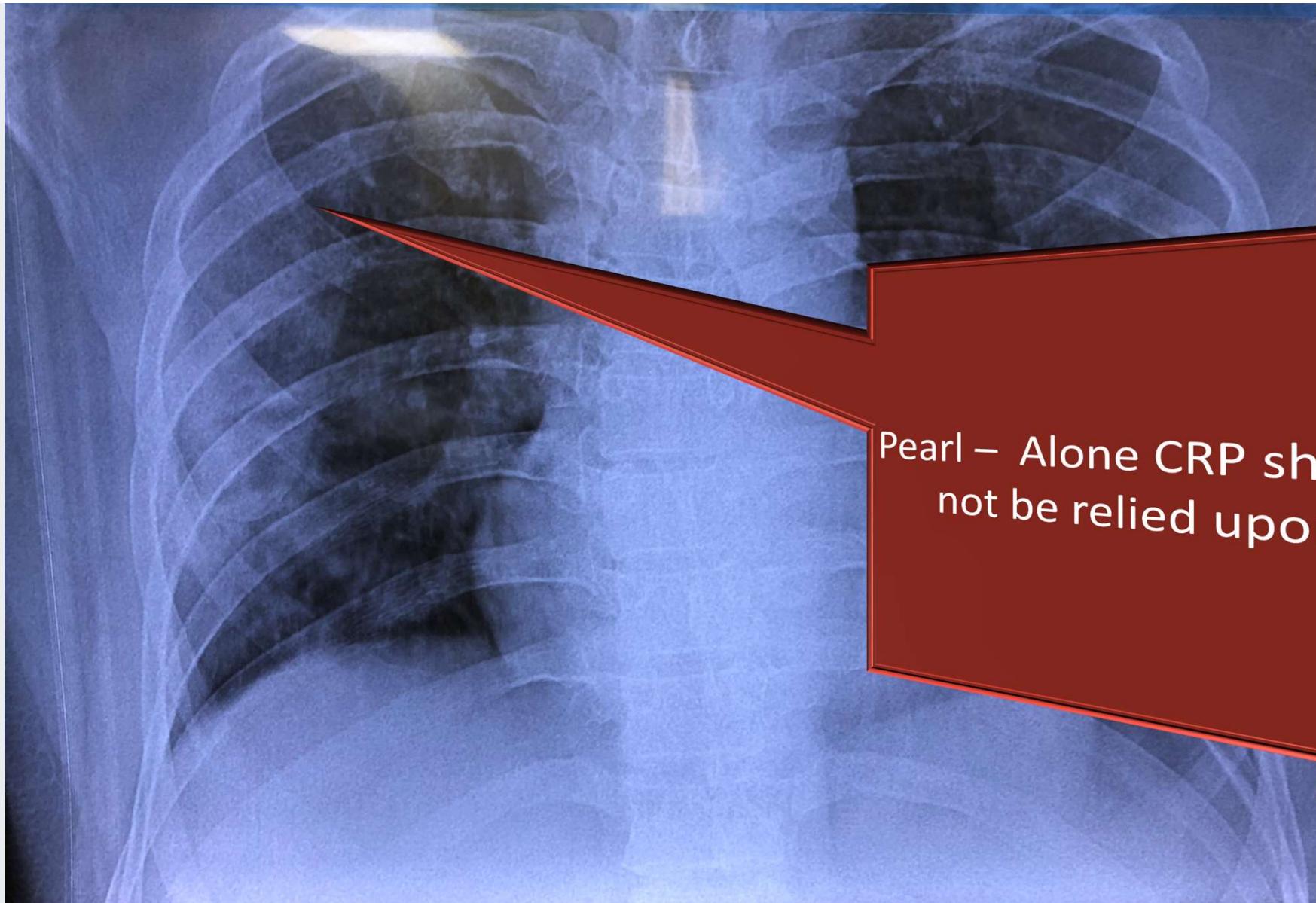
- CRP more than 70 mg/dl associated with low oxygen level

- Patients with 40 mg/L severe symptoms
- Mild symptoms 20 mg/L

- Trend of CRP with persistence of symptoms should be considered significant

J Med Virol 2020 Nov;92(11):2409-2411

Arch Pathol lab med .2020 Dec 1;144(12):1465-1474



Pearl – Alone CRP should
not be relied upon



D Dimer

- The normal reference concentration of D-dimer is < 400ng/mL or < 0.5
- D-dimer value on admission greater than 2.0 times the upper limit of normal mortality of COVID-19 patients with a sensitivity of 90%
- Helps in titrating anti coagulant therapy
- D-dimer levels may be elevated in the setting of pregnancy, trauma, postsurgical treatment, liver disease (decreased synthesis), and cancer.
- **False positive** - Lipemia, a high triglyceride level, an elevated bilirubin level, an elevated serum rheumatoid factor level, or hemolysis

It should be transported to the laboratory within 3 hours. If this is not possible, the plasma is separated , transported to the laboratory on dry ice.

Interleukin-6



- IL-6 does not always correspond to CRP (which is produced by hepatocytes in response to IL-6)
- **IL-6 over 25 pg/mL independent risk factor for the progression and/or in-hospital mortality.**
- **IL-6 > 80 pg/mL in combination with C-reactive protein > respiratory failure**

- Elevated interleukin-6 and severe COVID-19: A meta-analysis

J Med Virol. 2020 Jun 2 : 10.1002/jmv.25948

IL-6 levels rising trends especially more than three times important to predict complicated disease .
False positive if sample not processed properly



56 year male – Deteriorated on day 13 (fever)
with progressive hypoxemia on day 15

	CRP	Ddimar	Territin	DH	P
Day 1	4.99	38.23	199.04	21	21
Day 3	8.5	65.58	265.8	21	21
Day 6	6.51	79.82	323	380	380
Day 8	2.39	54.5	344.6	301	301
Day 11	4.25	56.01	309.5	354	354
Day 14	18.4	71.2	407	247	247
Day 15	31.4	67.4	479	311	311

Fever low grade

Trend of CRP , IL6
predicted the severe
disease before
hypoxemia sets in .
Remdesivir doesn't
guarantees " no
pneumonia)

Spo₂ 93 percent



Ferritin

- Ferritin is a marker of macrophage activity
- Increase in Ferritin value as a marker of prognostication / predictor - **thrombosis in diabetics**
- Ferritin is the last marker which return to normal (lag of 5 days after CRP)
- Trend rather than the threshold (700 plus)of the laboratory results provides the most information .
- Rising ferritin with deranged LFT and developing cytopenias – Predict Macrophage activation



REVIEW ARTICLE | Open Access |

Ferritin in the coronavirus disease 2019 (COVID-19): A systematic review and meta-analysis

Linlin Cheng, Haolong Li, Liubing Li, Chenxi Liu, Songxin Yan, Haizhen Chen, Yongzhe Li

First published: 19 October 2020 | <https://doi.org/10.1002/jcla.23618>

Case – 66 year male – DM , Chronic kidney disease , hypertensive

Symptoms	Ferritin	CRP	Lymphocyte count	IL6
Fever x 3 days	3364.69 ng /ml	6 mg /dl	%	Any persistent abnormal value of ferritin > 1000 should not be ignored
9 th day Afebrile (for 5 days) discharged Spo ₂ – 98 percent	5698.2	Negative for three days	LFT	
11 th Day readmitted ARDS , MODS	7621 (Raise to 72371 next 2 days)	Neg to 72 (next two days)	27500 , lympho 4%	2.5



LDH – Lactate dehydrogenase

Related to respiratory function ($\text{PaO}_2/\text{FiO}_2$) and be a predictor of respiratory failure in CoVID-19 patients

Strong inverse correlation between LDH and $\text{PaO}_2/\text{FiO}_2$ values



LDH showed that a cut-off value of 450 U/l had a sensitivity of 75% and a specificity of 70% in recognizing moderate and severe ARDS

Clin Chim Acta. 2020 Oct; 509: 135–138.



Chest imaging – Fact – Most inappropriately used modality



No routine use

Chest imaging

Least sensitive



Chest X ray

Most sensitive



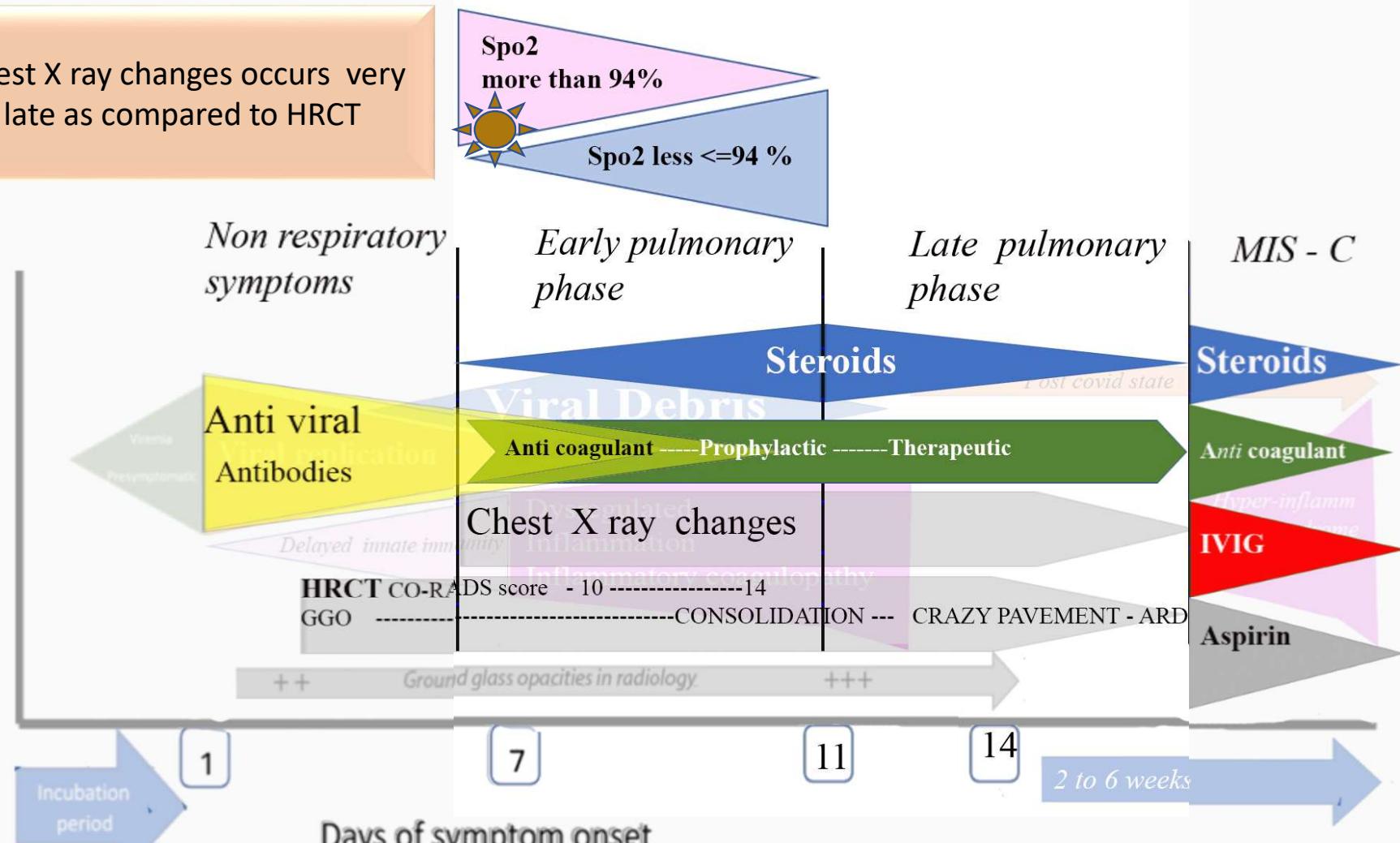
HRCT

Least evaluated



Ultrasound
Chest

Chest X ray changes occurs very late as compared to HRCT



Indication of chest imaging



- RTPCR neg , clinical suspicion



- Differential diagnosis / Complication



- Confusion in decision making



Case ashi family continued – Next 48 hours

CRP 18 , 9800
, L 5 , P 95% ,
D Dimer 211

Spo₂
95

77 M , DM day 8 ,
cough , weakness
persisted , HbA1C 6.0

CRP 8
No bed available
Next step ? Steroids ,
anti viral , anti
coagulant
Adv HRCT

5

HbA1C 8 .

Case ashi continued

CRP 18 , 9800 , L 5 , Hb 95% ,
D Dimer 211
CT SS 14 /25

Spo₂
95

77 M , DM day 8 ,
cough , weakness
persisted , HbA1C 6.0

CRP 8 . 12300 L 24

How to approach ?
Role of Imaging

5

afebrile



Chest X ray

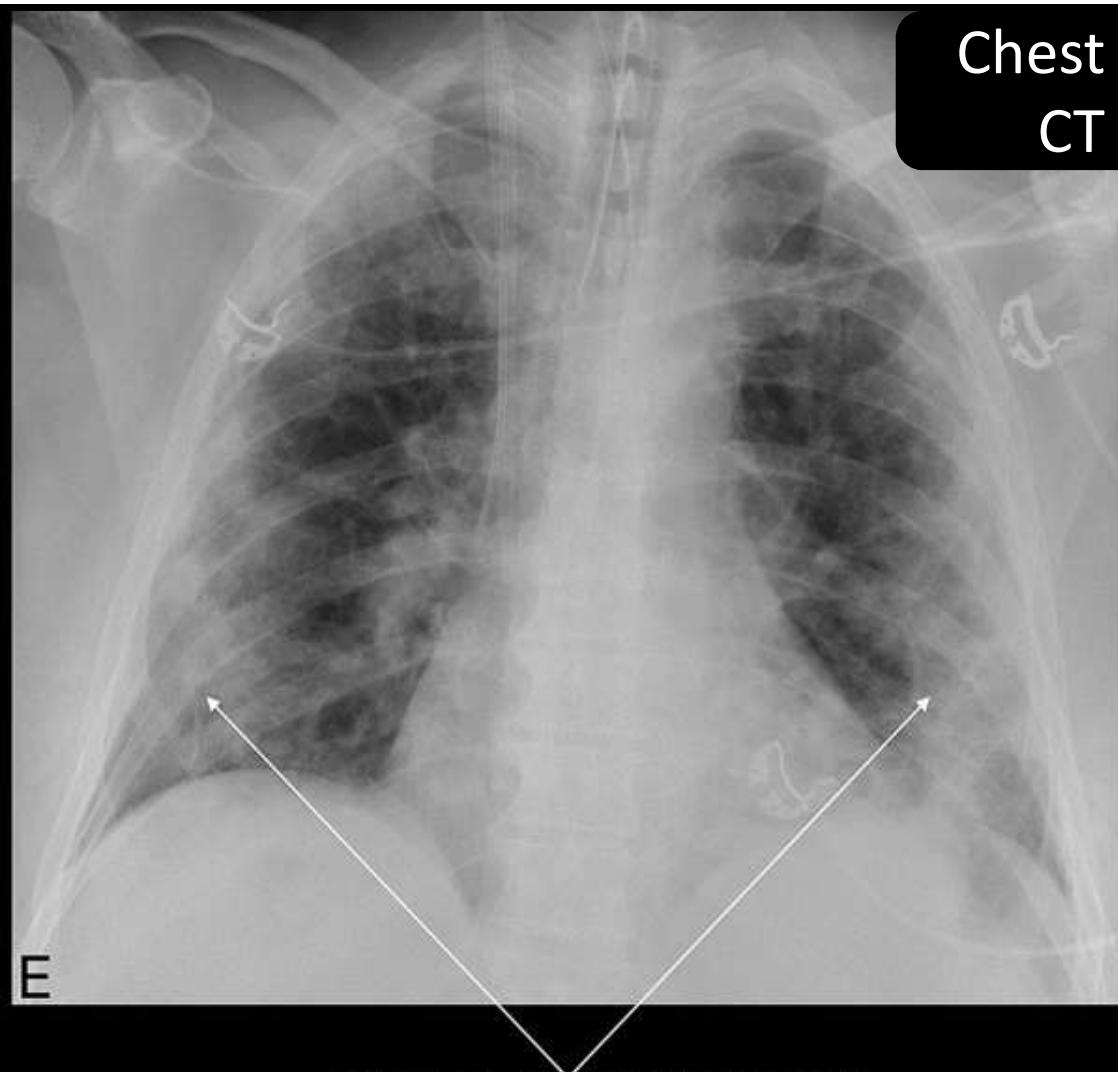
Less sensitive
than HRCT

Positive findings
after 6 th day after
symptom onset



Sensitivity 40
to 65 percent
Specificity –
70-80 %

Chest X ray vs CT scan



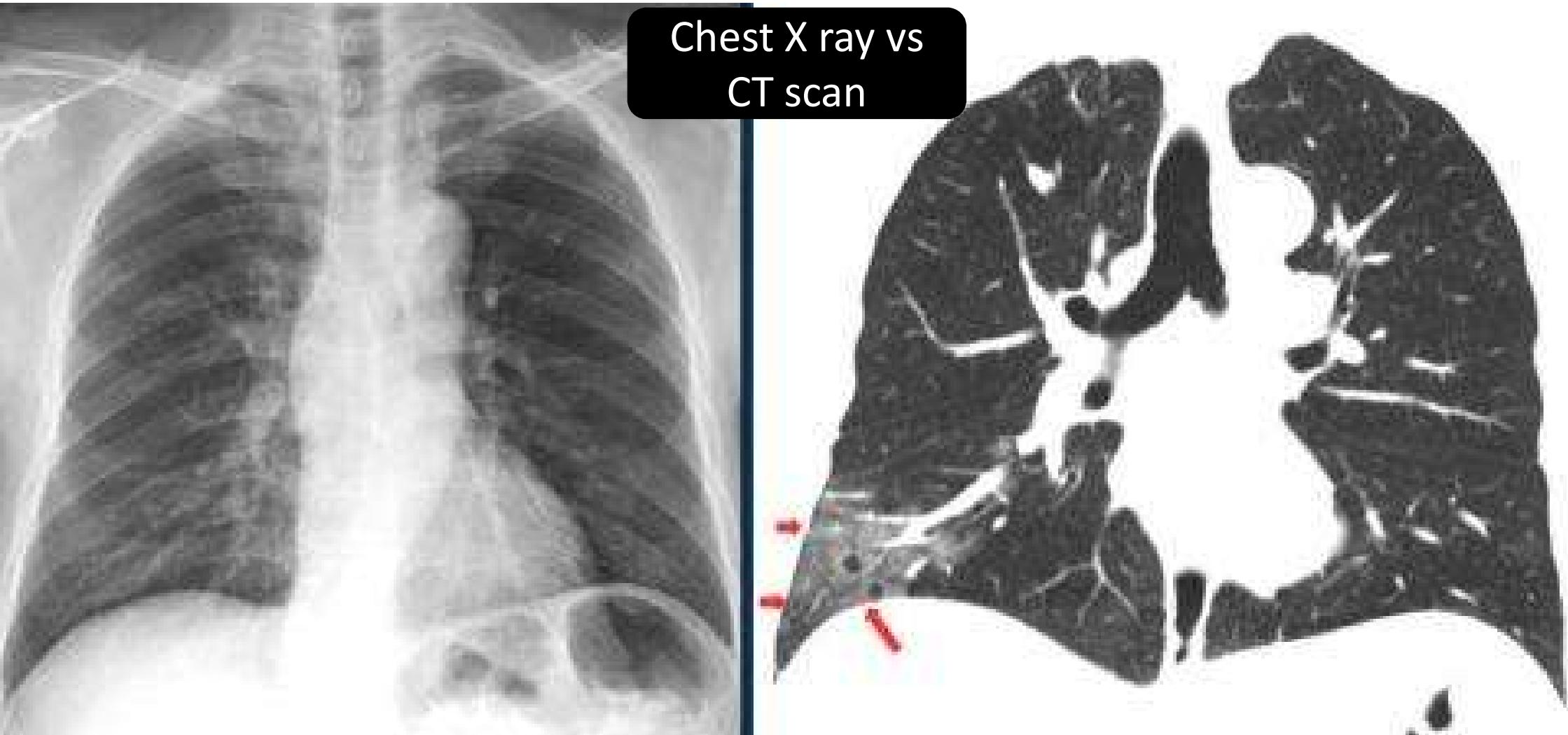
peripheral Consolidations



Organizing Pneumonia
- subpleural lines/bands
- perilobular thickening

peripheral Consolidations

Chest X ray vs
CT scan



The ground glass opacities in the right lower lobe on the CT (red arrows) are not visible on the chest radiograph, which was taken 1 hour prior to the CT-study

Chest X ray - semiquantitative severity score

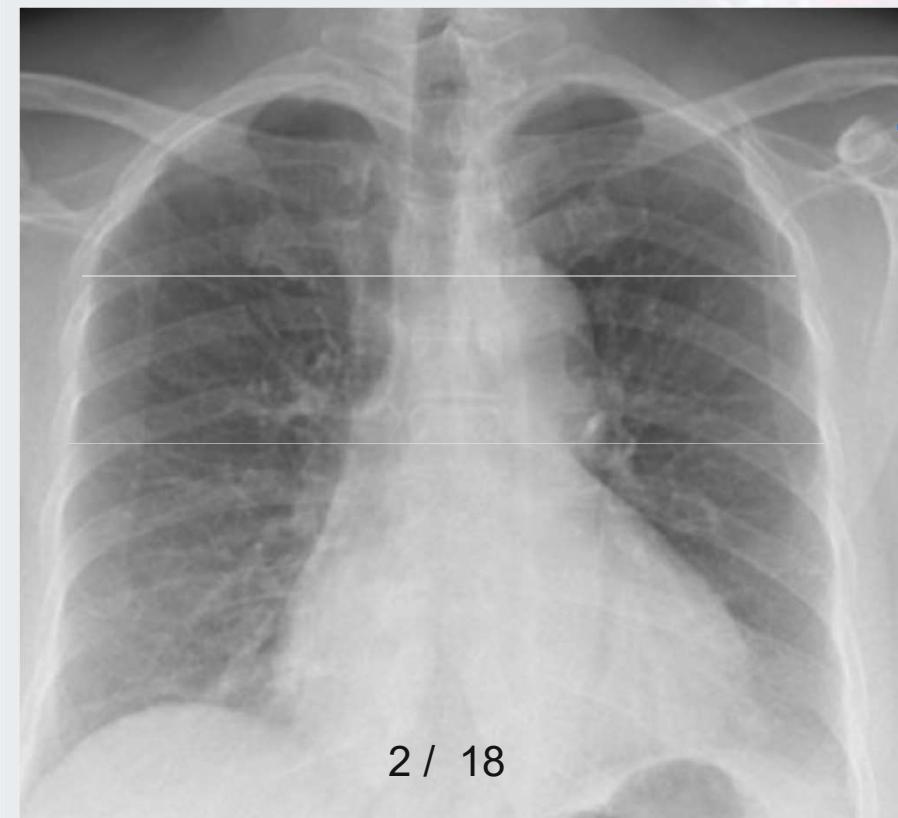


Superior zone (from the lung apex to the aortic arch profile)

Middle zone (lung hilum, from the aortic arch profile to the inferior margin of the left pulmonary hilum)

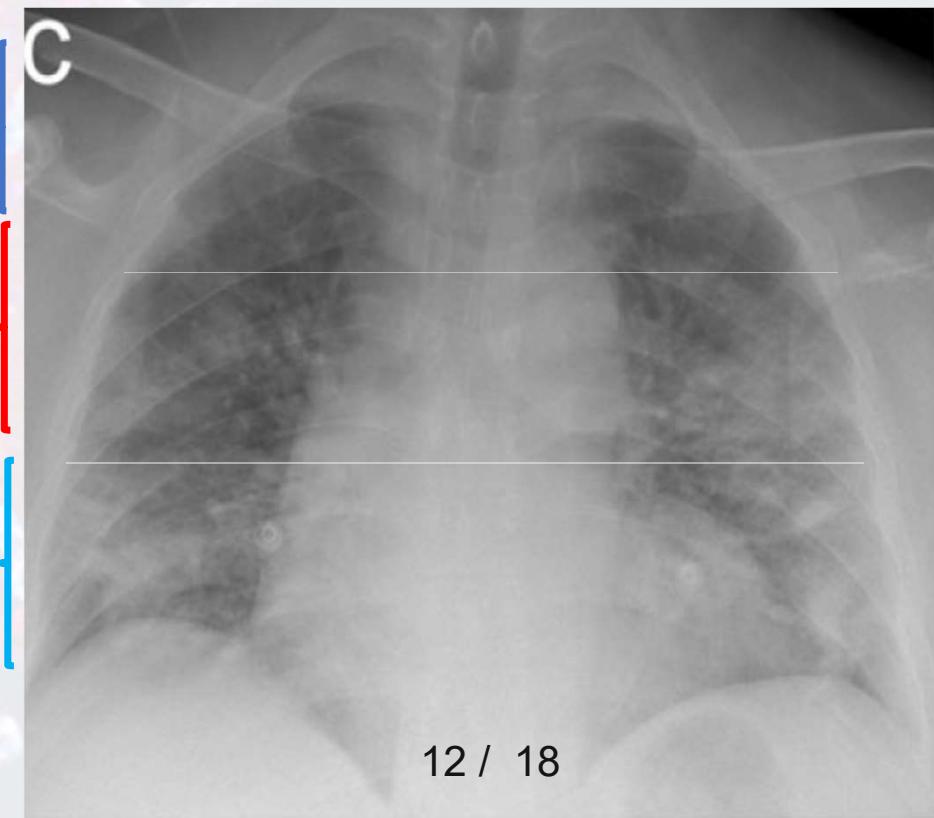
For each zone, a score on a scale from zero to three in 1-point increments assigned:
0, normal lung parenchyma; 1, interstitial involvement only; 2, presence of radiopacity for less than 50% of the visible lung parenchyma; 3, presence of radiopacity for 50% or more than 50% of the visible lung parenchyma

Severity score chest X ray



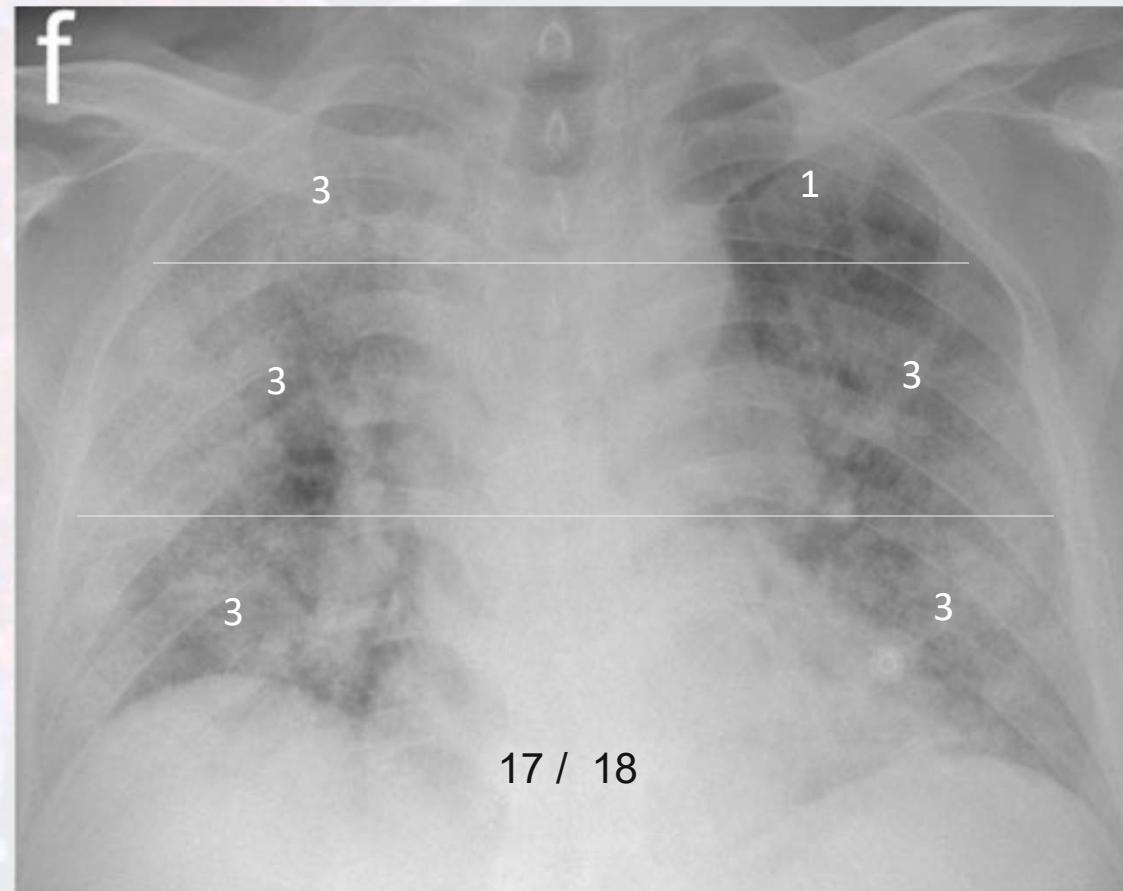
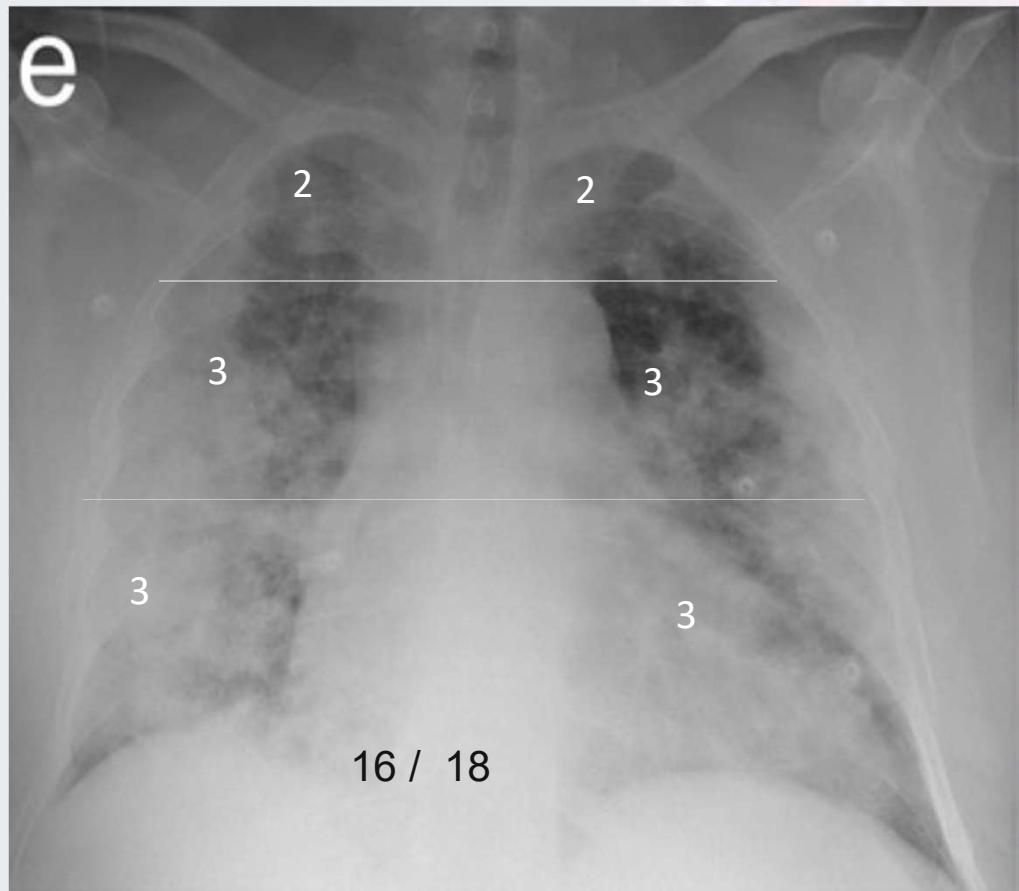
2 / 18

0	1
0	1
0	2
0	3
1	2
1	3



12 / 18

Severity score chest X ray



Chest CT Protocol

- **Non-contrast high resolution chest CT** unless CT pulmonary angiography is required to detect pulmonary embolism (PE).
- Low radiation as much as possible - CT images should be acquired during a single inspiratory breath hold (**no need of expiratory film**)



HRCT – what is expected ?

HRCT facts

Asymptomatic

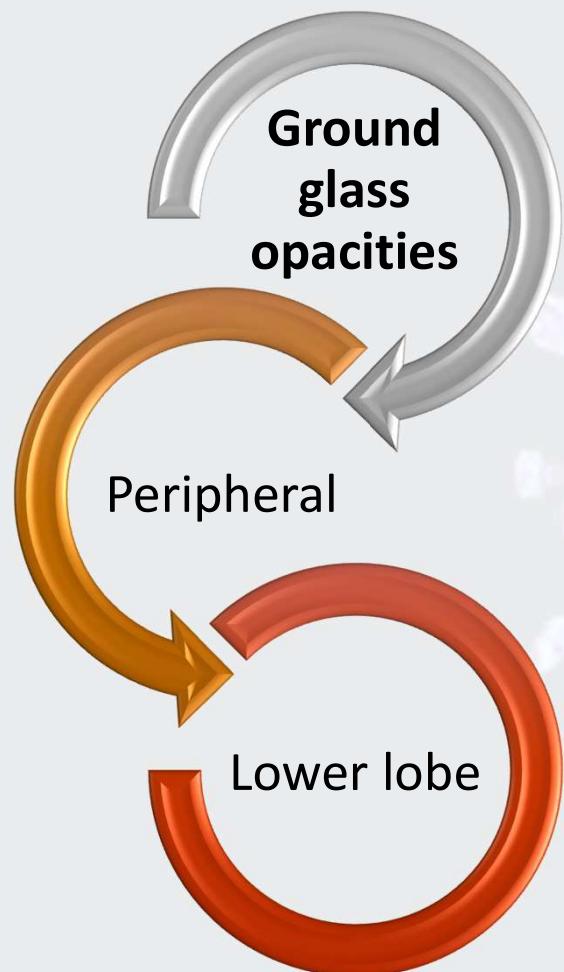
- 46% NORMAL

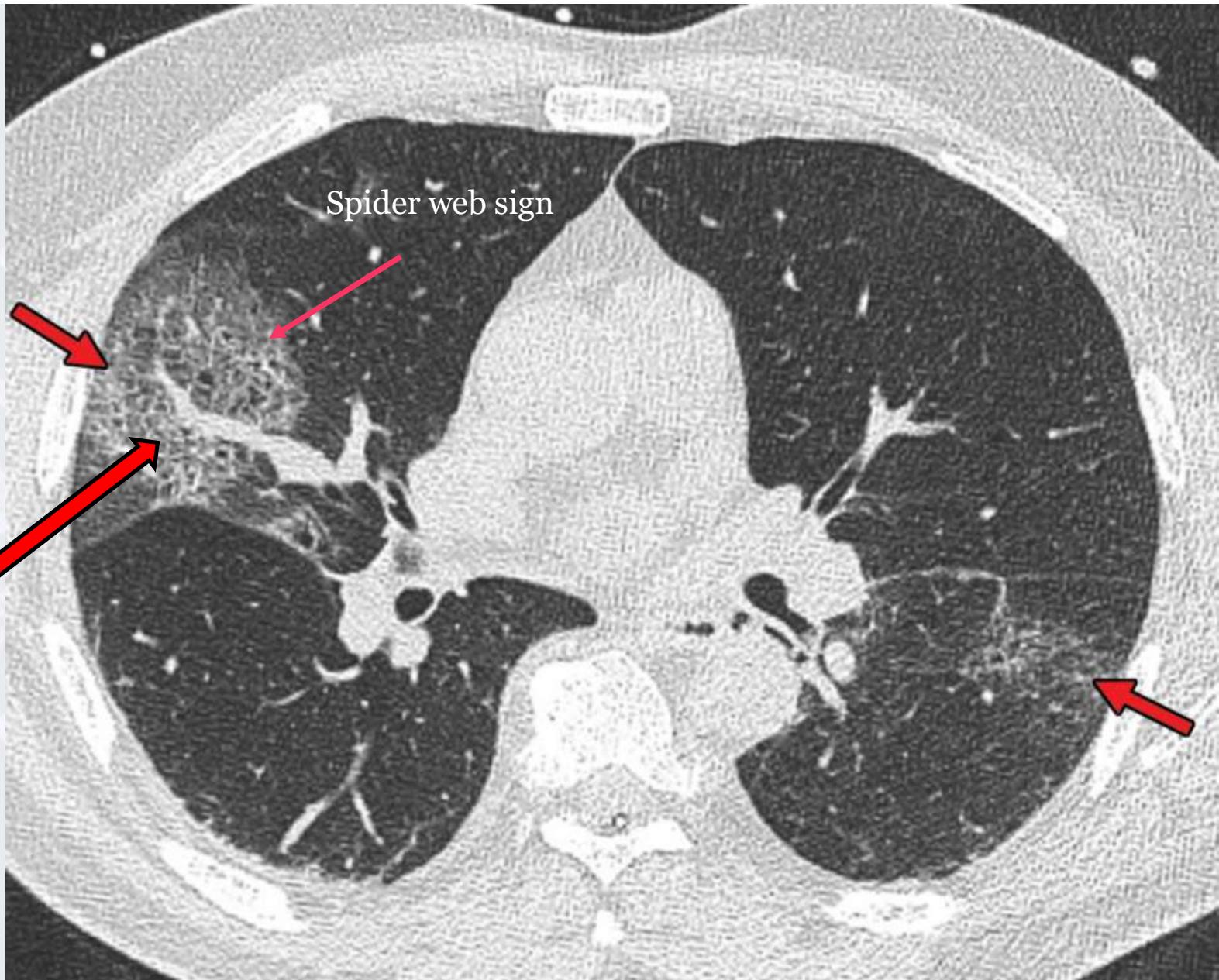
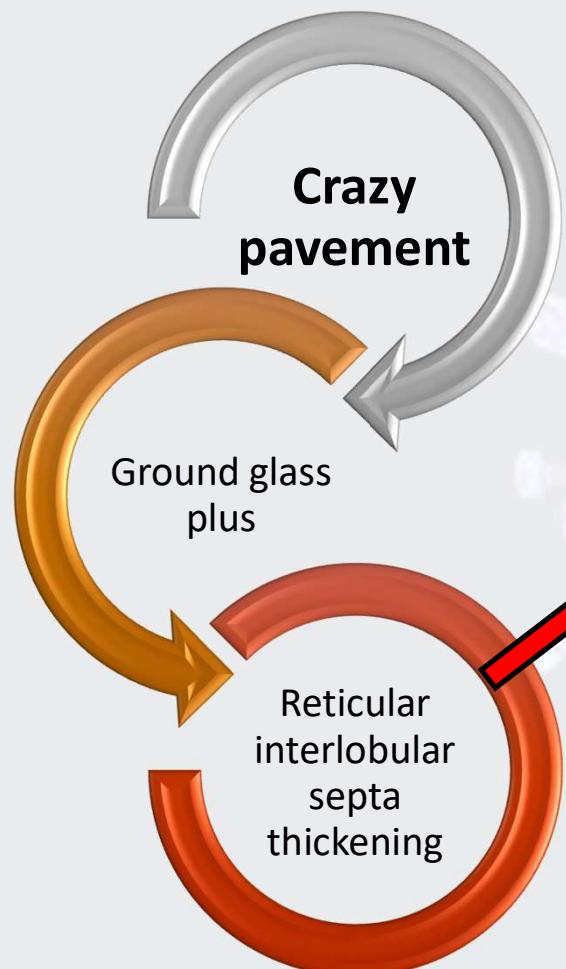
Symptomatic

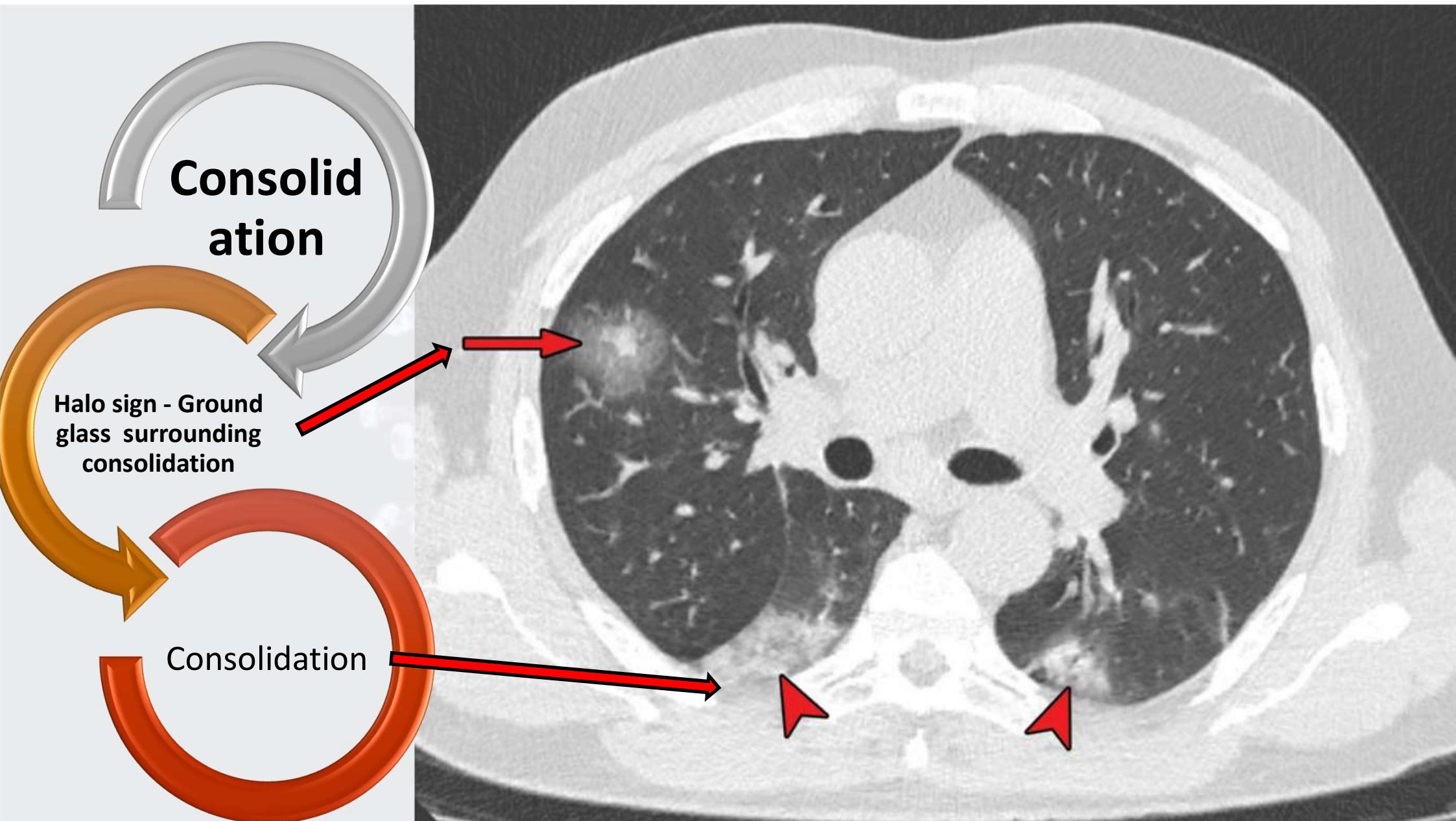
- 13% Normal if done in first 5 days

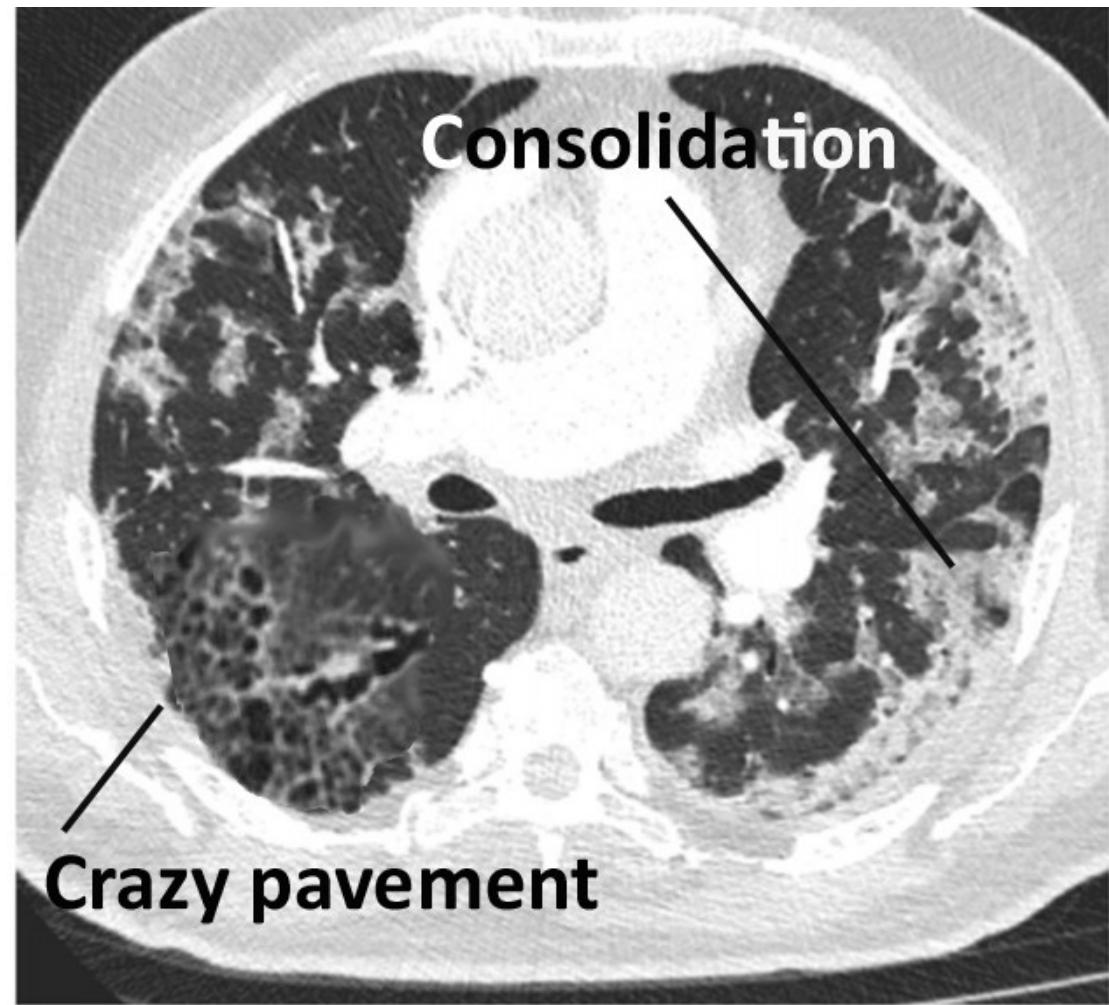
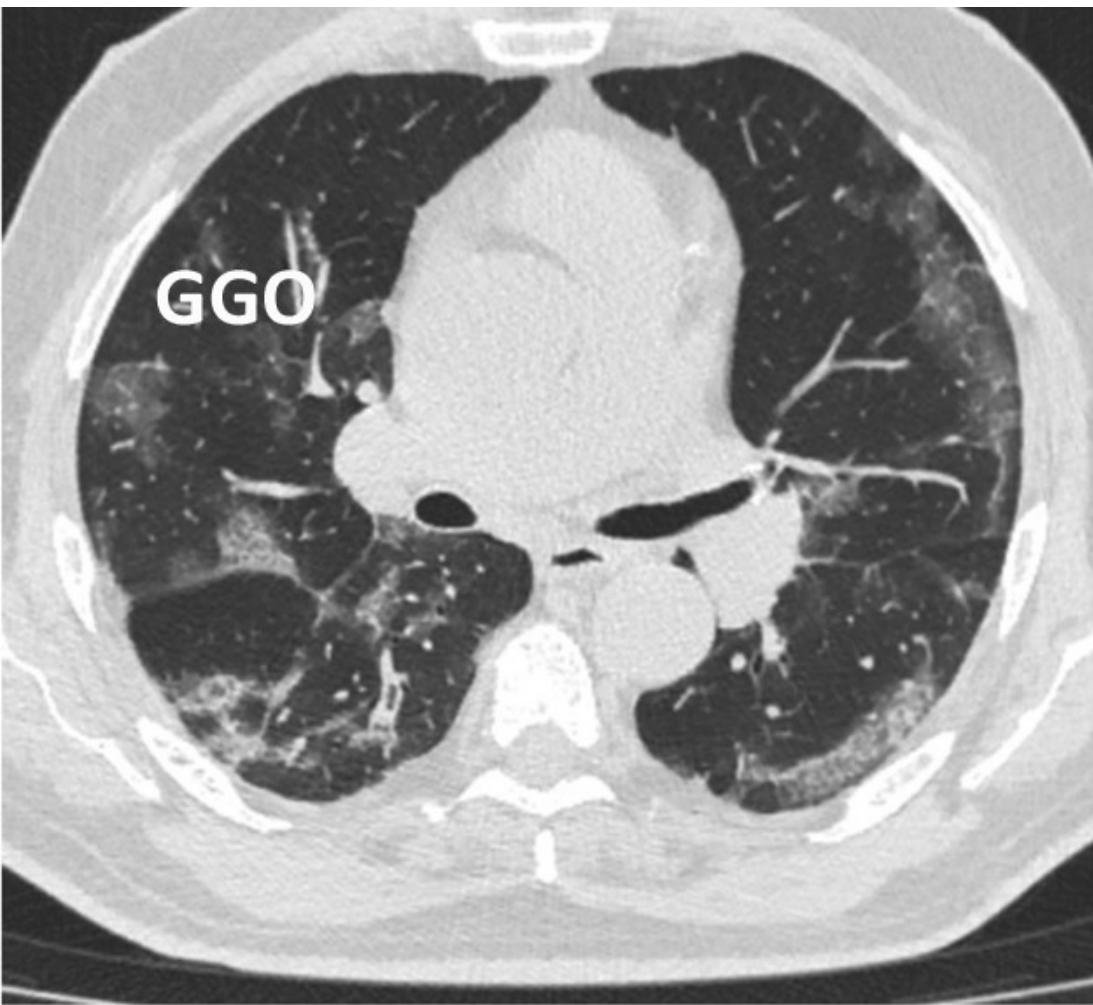
Symptomatic
after 5 days

- 97 percent sensitive after 5 days





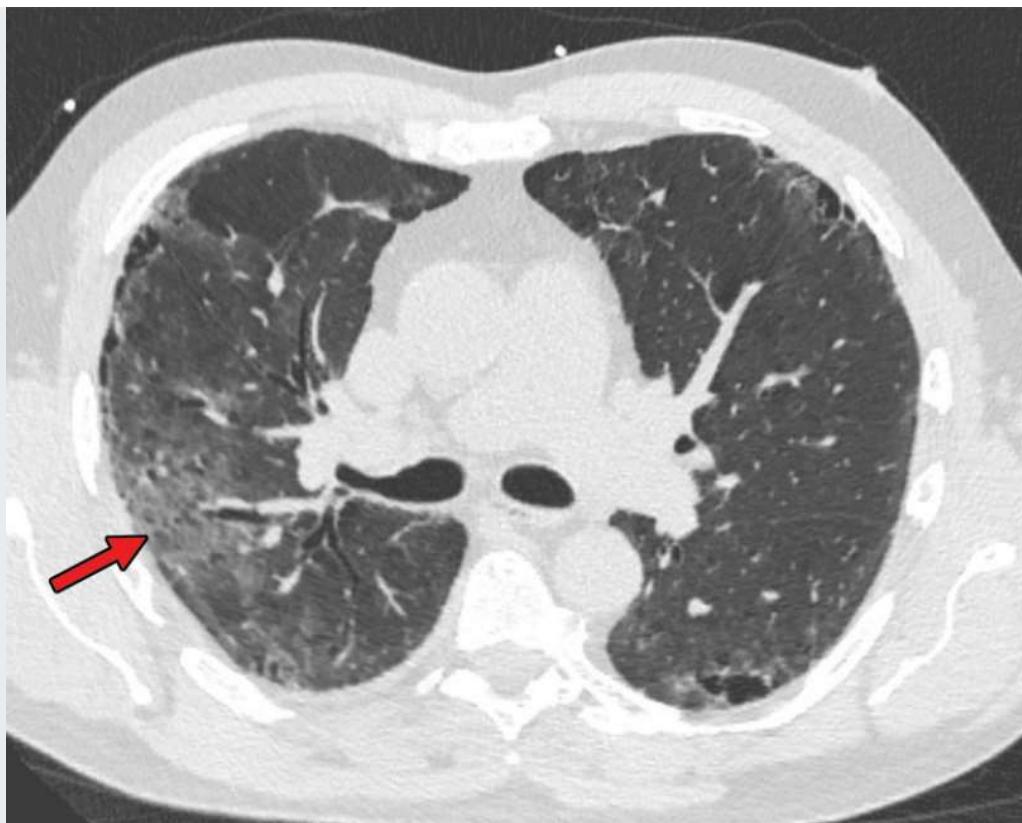




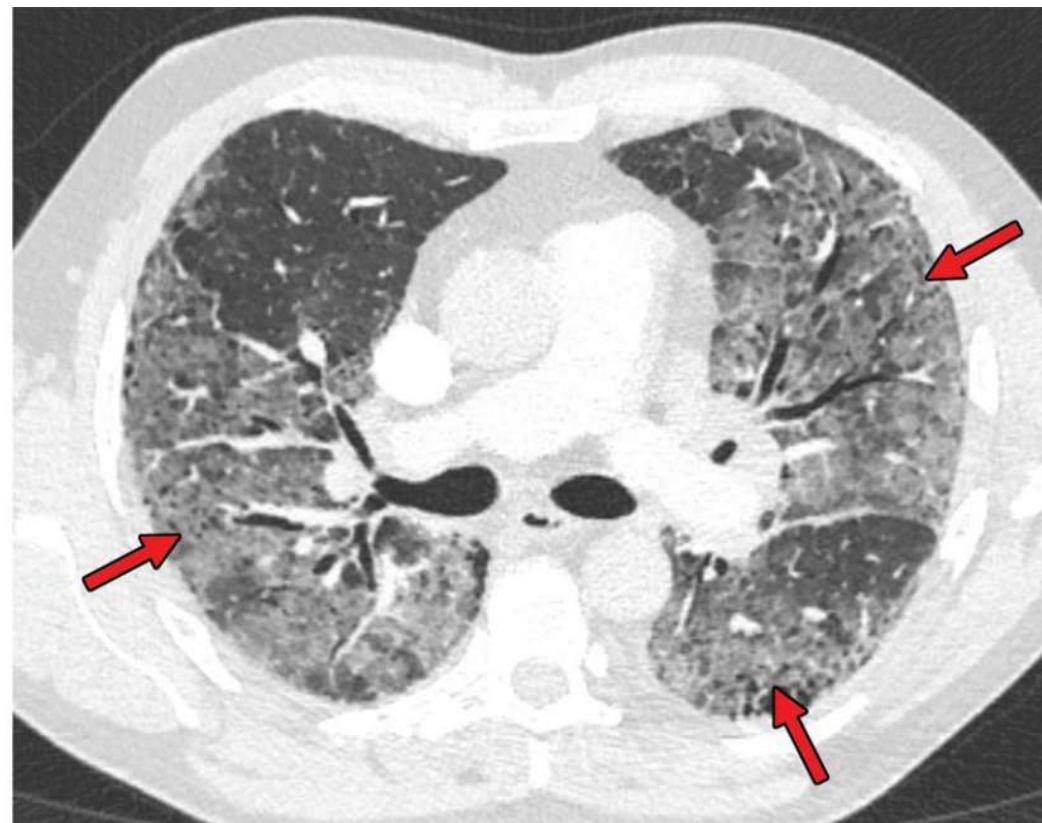
GGO – haziness with broncho-vascular markings seen in background

Crazy paving – Septal thickening superimposed over GGO

Consolidation -haziness with broncho-vascular markings not seen in background plus airbronchogram

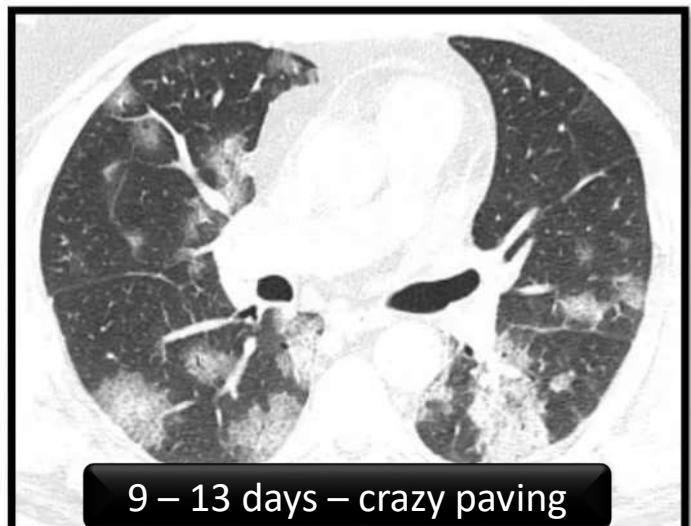
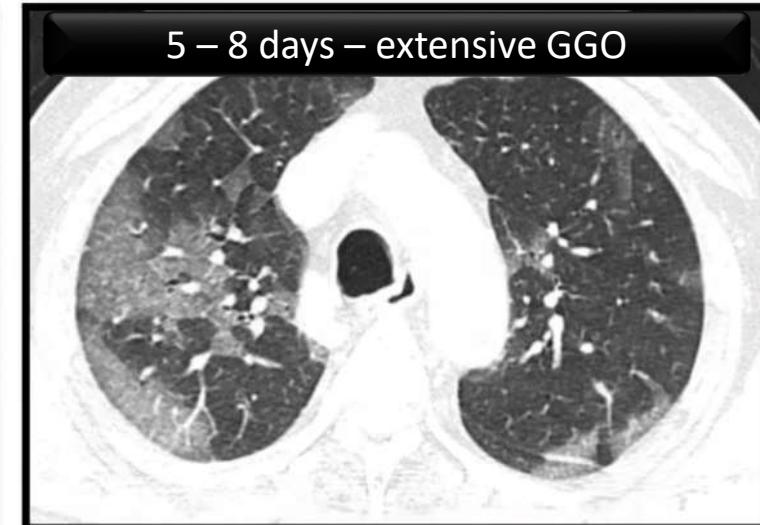
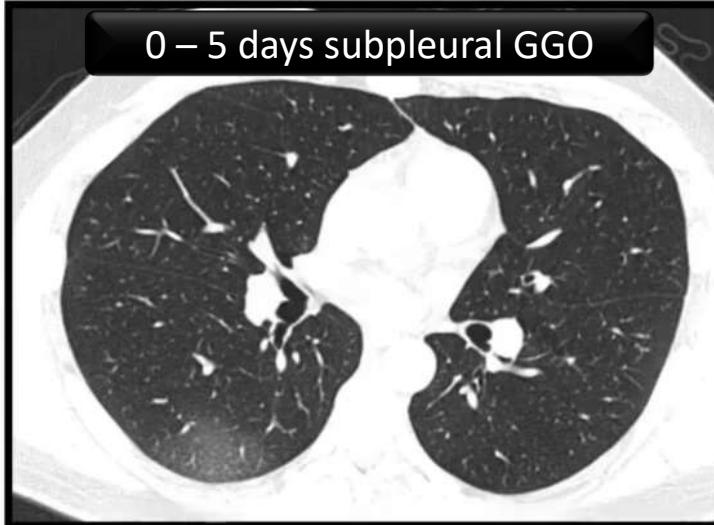


GGO

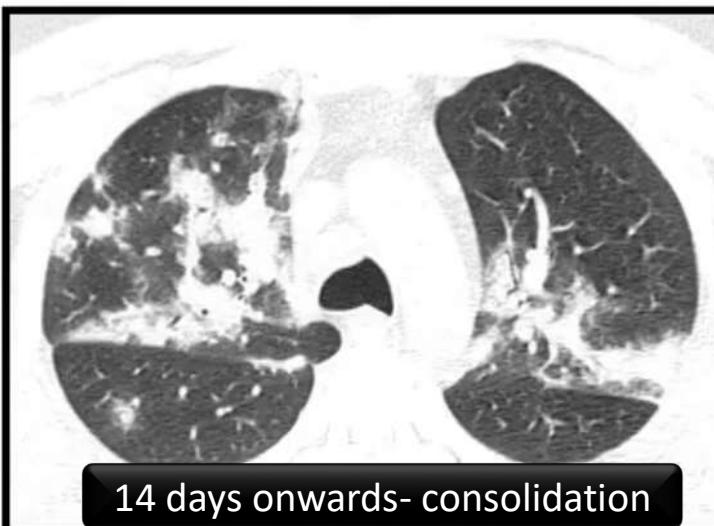


ARDS

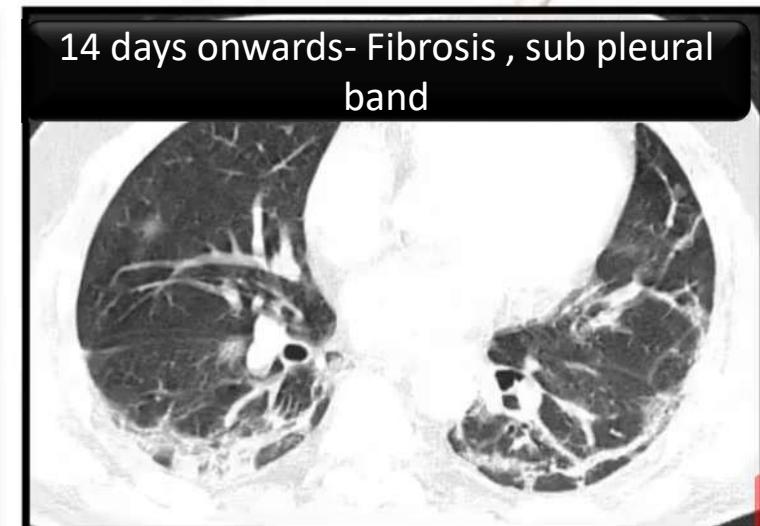
CT Changes over time



9 – 13 days – crazy paving



14 days onwards- consolidation





CT Chest - Four stages of COVID-19

Early stage 0 to 5 days - Normal or subpleural ground glass opacities



Progressive stage 5 to 8 days ground glass opacities



Peak stage 9 – 13 days – Ground glass opacities ± Crazy paving .



Late stage (>14 days after symptom onset) Ground glass opacities ±
Crazy paving ± Progressive Consolidation ± fibrosis

SCORING – Suspicion / Severity

CO-RADS

- The CO-RADS classification is a standardized reporting system for patients with suspected COVID-19 infection developed for a moderate to high prevalence setting

Severity score

- Severity score – Percentage of lung involved , lobe involvement (out of 25)

CO-RADS SCORING FOR DIAGNOSIS

	Level of suspicion	CT findings
CO-RADS 1	No	normal or non-infectious abnormalities
CO-RADS 2	Low	abnormalities consistent with infections other than COVID-19
CO-RADS 3	Indeterminate	unclear whether COVID-19 is present
CO-RADS 4	High	abnormalities suspicious for COVID-19
CO-RADS 5	Very high	typical COVID-19
CO-RADS 6	PCR +	



Similar findings overlap – DD

- H1N1 influenza
- Adenovirus, CMV
- Organizing pneumonia

Chest CT – What is least expected (<10%)

pleural effusion (5.2%)

tree-in-bud sign (4.1%),

lymphadenopathy (5.1%),

Pericardial effusion (2.7%),
and **cavitating lung lesions (0.7%)**



The percentage of lung involvement as per lobe

0 as normal,

1 point < 5% abnormality,

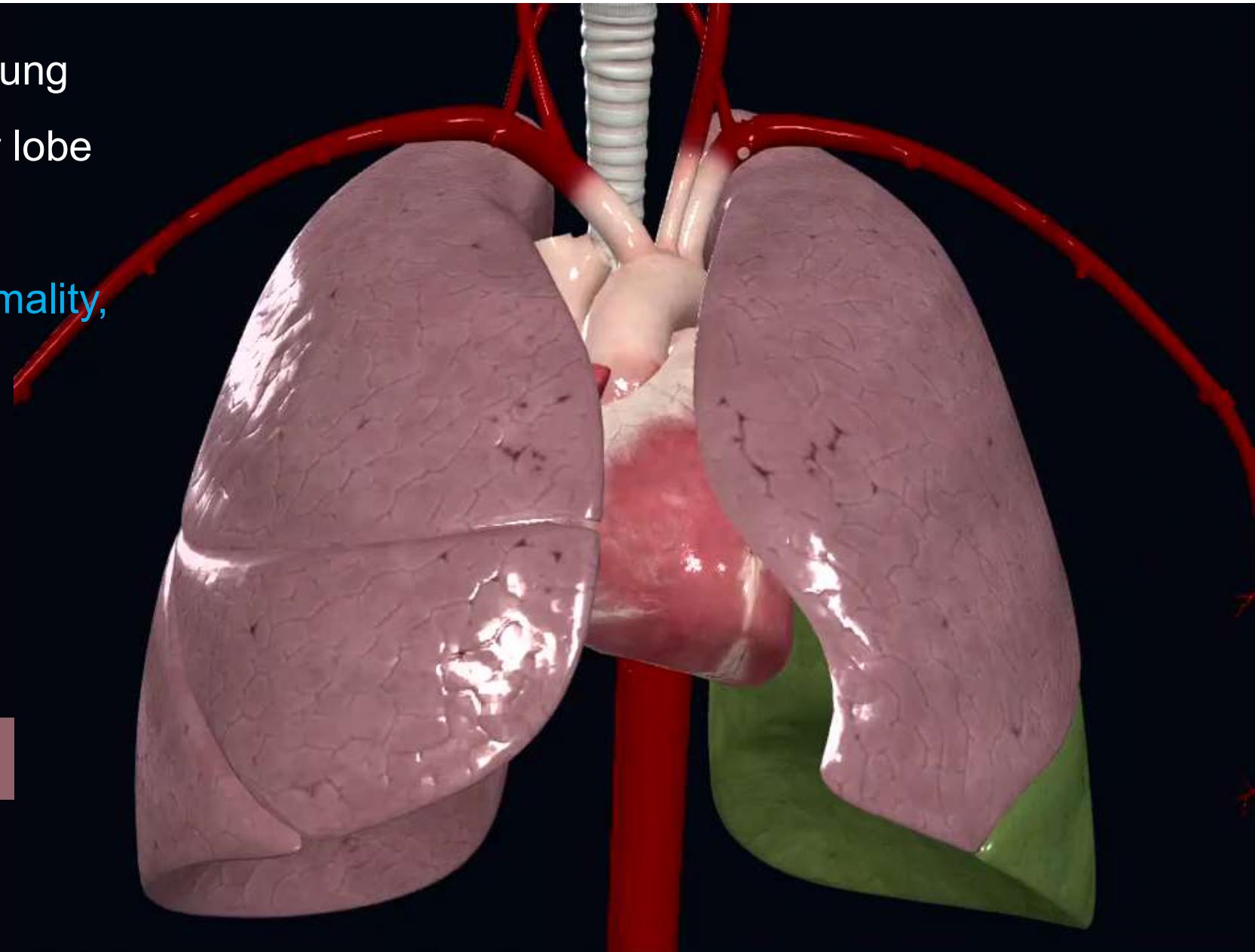
2 point 5 to 25%

3 as 25 – 50%

4 as 50 – 75%

5 ≥ 75% of lobe

5 lobes = 25 score

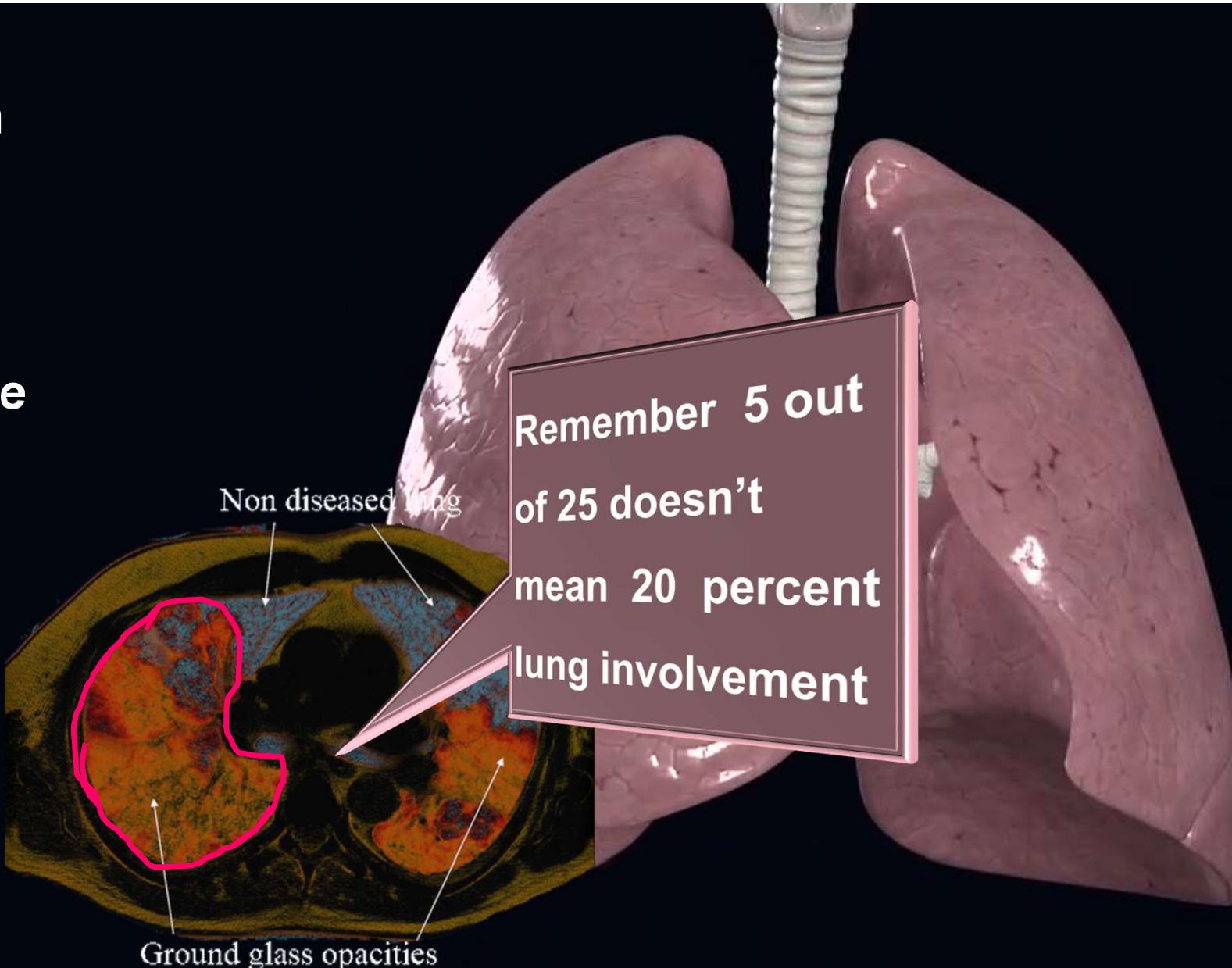


Select the lobe on
coronal plane

Give scoring per
lobe then calculate
complete scoring



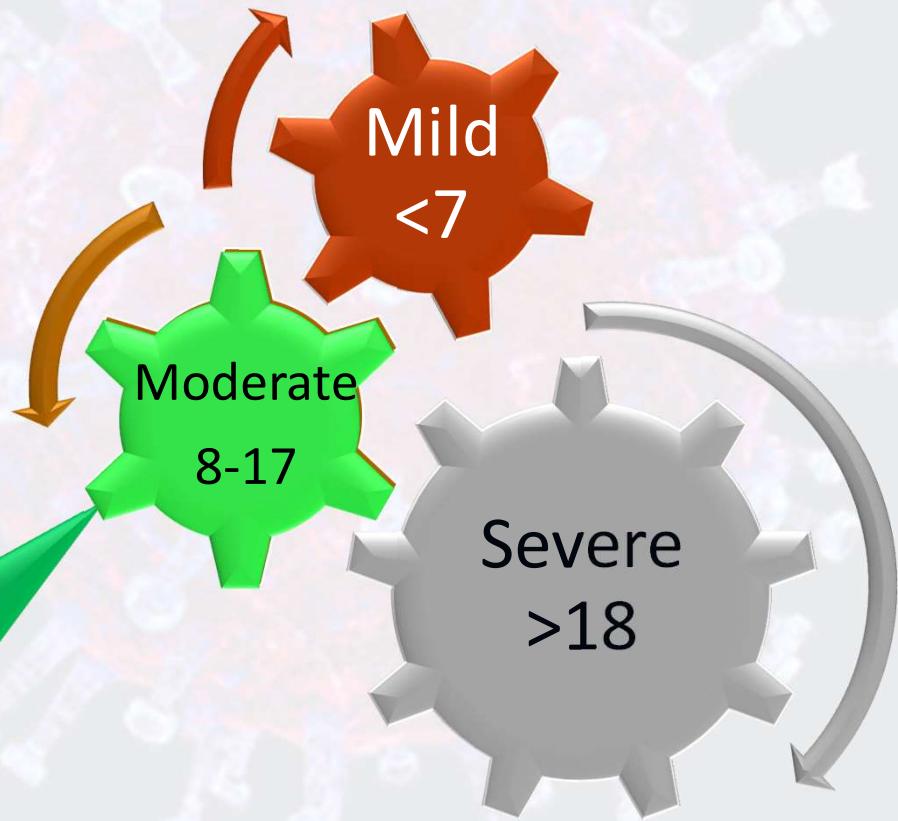
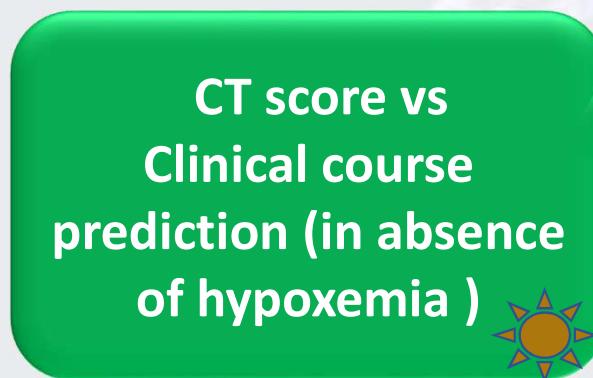
3 D Volume rendering



Can I predict clinical course on basis of imaging ?

CT Severity score classification

CT score vs
Clinical course
prediction (in absence
of hypoxemia)



Radiology Research and Practice Jan 2021 , Abu dabi Dubai
Volume 2021 |Article ID 6697677

		Max O2 requirement						
		None	Nasal canula	Facemask	Nonrebreather	HFNC/BIPAP	Intubation	Total
Moderate	Count	154	89	20	9	15	22	309
	% category	49.8%	28.8%	6.5%	2.9%	4.9%	7.1%	100.0
								%

No hypoxemia in
50 percent with
CT SS 8 to 17

Severe >18

Moderate 8-17

Mild <7

2 min break

*Radiology Research and Practice Jan 2021 , Abu dabi
Dubai*

**HRCT score more than 8
with no clinical features
(hypoxemia , fever ,
markers)**

Lung involvement >
50 percent
Consolidation +

Age >50 , co
morbidities

**Low risk
Intensive follow up
day to day basis**

Approach

Manage on case to case basis
Steroids , Anti coagulants ,
Antivirals

Case ashi continu ed



Medrol 12 mg OD , Enoxaparin
40 mg OD – close monitoring
for high risk features

No treatment – close
monitoring for high risk features

**CRP 18 , 9800 , L 5 , P 95% ,
D Dimer 211**

CT SS 14 /25

**Spo₂
96**

**77 M ,DM day 8 ,
cough , weakness
persisted , HbA1C 6.0**

**CRP 8 , 12300, L 34 , , D
Dimer 982**

CT SS 7/25

**Spo₂
96**

**57 F , DM , day 11 ,
afebrile , HbA1C 8.4**



Radiographic and Lab Abnormalities by Disease Severity

Radiographic or Lab Finding	All Patients (N = 1099)	Nonsevere Disease (n = 926)	Severe Disease (n = 173)
Abnormalities on chest radiograph,* n/N (%)	162/274 (59.1)	116/214 (54.2)	46/60 (76.7)
Abnormalities on chest CT,* n/N (%)	840/975 (86.2)	682/808 (84.4)	158/167 (94.6)
Median lymphocyte count per mm ³ (IQR)	1000 (700-1300)	1000 (800-1400)	800 (600-1000)
C-reactive protein ≥ 10 mg/L, n/N (%)	481/793 (60.7)	371/658 (56.4)	110/135 (81.5)

Group 1 EIM 270-272-2708

*Ground-glass opacity, local patchy shadowing, bilateral patchy shadowing, or interstitial abnormalities.



Government of India
Ministry of Health & Family Welfare
Directorate General of Health Services
(CMR Division)

Revised Guidelines on Clinical
Management of COVID - 19



Subset of patients with radiologically moderate disease can be missed if oxygen saturation alone taken as criteria of moderate disease



- **Mild**
- Asymptomatic
- Fever /URTI



- **Moderate**
- Pneumonia with SpO_2 94 to 90 percent
- RR 15 TO 30 /min



- **Severe**
- SpO_2 less than 90 percent
- $\text{RR} > 30 / \text{MIN}$

Clinical definition of severity – Fallacy



NIH definition

NIH severe disease is our moderate disease

A yellow circle icon with a smaller yellow segment at the bottom left, representing the Government of India's monitoring criteria.

Govt of India
 SpO_2 and RR

A green circle icon with a smaller green segment at the top right, representing the NIH's monitoring criteria.

NIH - Lung infiltrates
and oxygenation

The logo for the National Institutes of Health (NIH) COVID-19 Treatment Guidelines, featuring the NIH monogram and the text "National Institutes of Health (NIH) COVID-19 Treatment Guidelines".

Moderate Illness

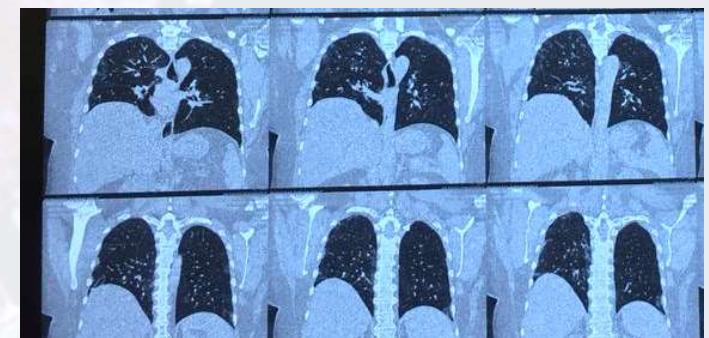
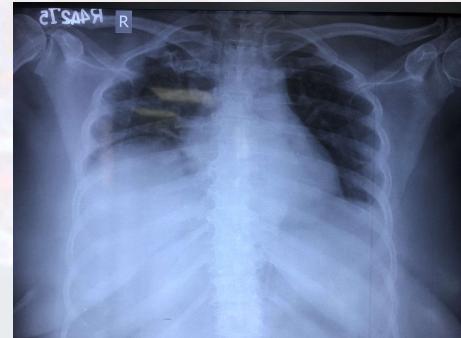
Moderate COVID-19 illness is defined as evidence of lower respiratory disease during clinical assessment or imaging, with $\text{SpO}_2 \geq 94\%$ on room air at sea level. Given that pulmonary disease can progress rapidly in patients with COVID-19, close monitoring of patients with moderate disease is recommended. If bacterial pneumonia or sepsis is strongly suspected,

Severe Illness

Patients with COVID-19 are considered to have severe illness if they have $\text{SpO}_2 < 94\%$ on room air at sea level, a respiratory rate of >30 breaths/min, $\text{PaO}_2/\text{FiO}_2 < 300$ mmHg, or lung infiltrates $>50\%$. These patients may experience rapid clinical deterioration. Oxygen therapy

59 year female - Obese , DM , HT , asthmatic

- Low grade fever plus cough x 8 days – **Favipiravir** plus doxy plus Ivermectin , Azithromycin , Cefuroxime , Spo2 > 97 % , CRP 6mg %
- HRCT on day 8
- Severity score 11/25
- Admitted due to CT CHEST



Case

- On admission – RR 20 , Spo2 96 under RA , CRP 25 IL 6 32.5
- Next 24 hours – desaturated to 88% oxygen
Oxygen 5 lt



High risk cases –
Clinical , laboratory ,
radiological
approach is essential

Therapeutic Classes Under Investigation

Antivirals

- Baloxivir
- Convalescent plasma**
- Antibodies**
- Favipiravir
- (Hydroxy)chloroquine
- Interferon
- Lopinavir/ritonavir
- Nitazoxanide
- Oseltamivir
- Remdesivir
- Ribavirin

Immunomodulators

- Corticosteroids (eg, dexamethasone)**
- IL-1 inhibitors (eg, anakinra)
- IL-6 inhibitors (eg, tocilizumab)
- Intravenous immunoglobulin
- JAK inhibitors (eg, baricitinib)**

Antibodies

- VIT C , VIT D , Ivermectin ,
- Azithromycin , Doxycycline , HCQ



Therapeutic Classes to be discussed

Antivirals

**Convalescent plasma
Remdesivir**

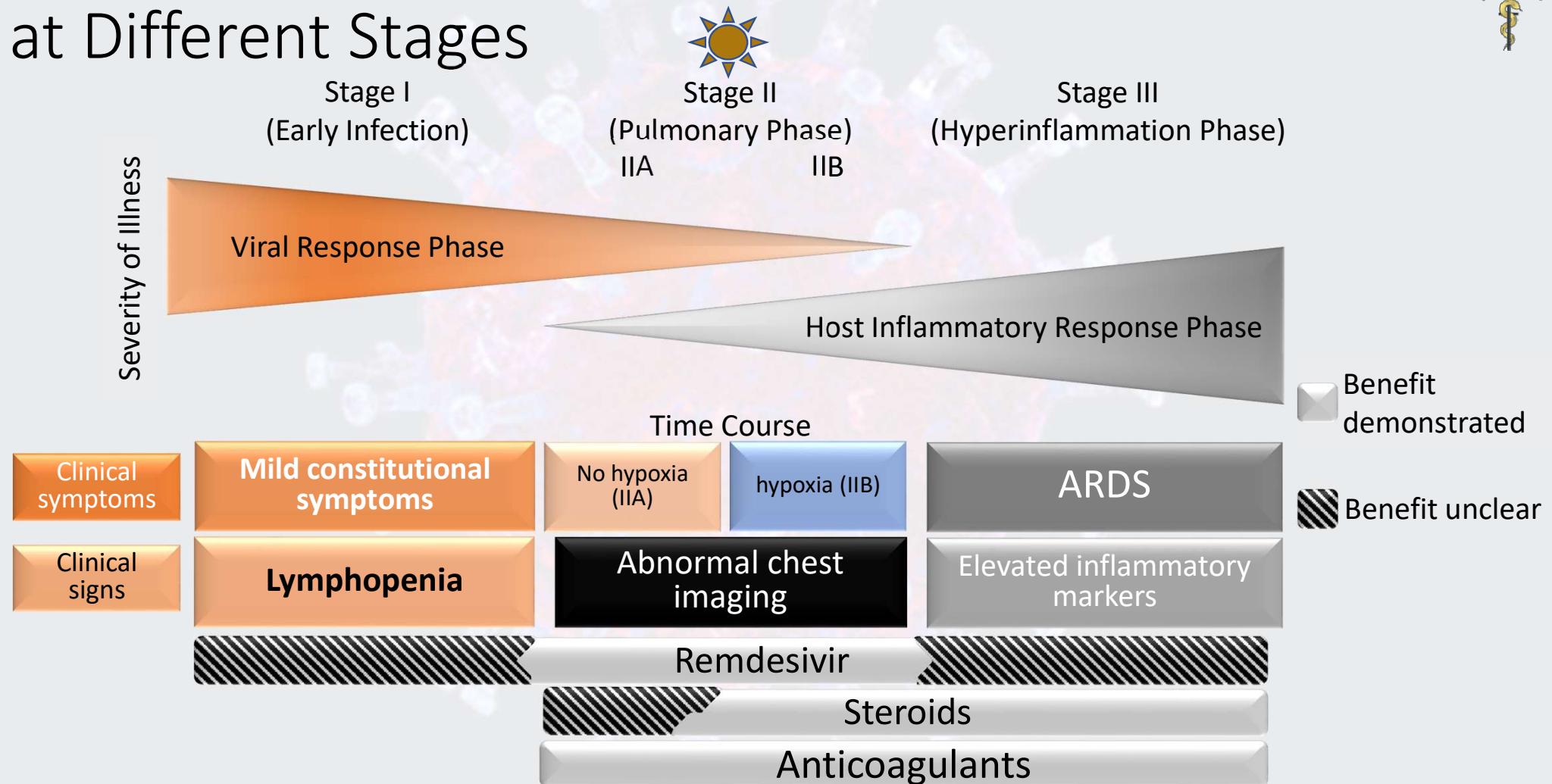
Antibodies

Immunomodulators

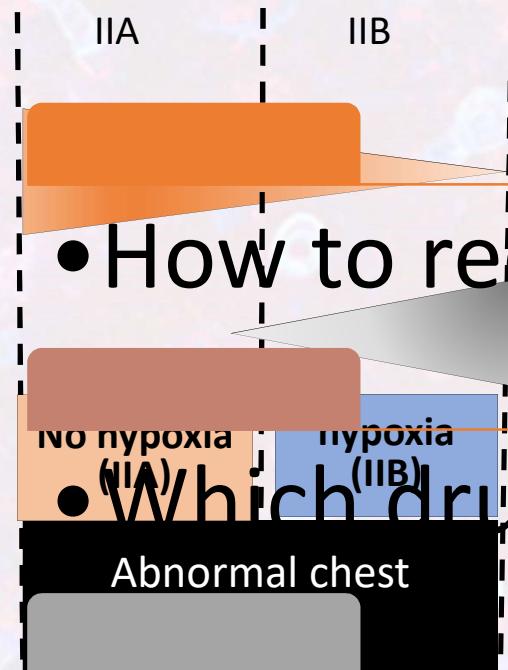
**Corticosteroids
JAK inhibitors (eg,
baricitinib)**

Anticoagulant

COVID-19 Therapies Predicted to Provide Benefit at Different Stages



Stage IIa (Pulmonary Phase)



Recognition and
prediction of
pulmonary
II a (window)

- How to recognise this stage?

- Which drugs to be used ?

Recognition

IIA

- Persistence of fever after 5 to 7 days , high grade fever with chills and rigor

Chest imaging

Significant chest infiltrates

Spo2 , CRP , D Dimer

Spo2 normal , Inflammatory markers ± , D Dimer ±

Clinical /
investigational
Approach

Fever grade

IIA

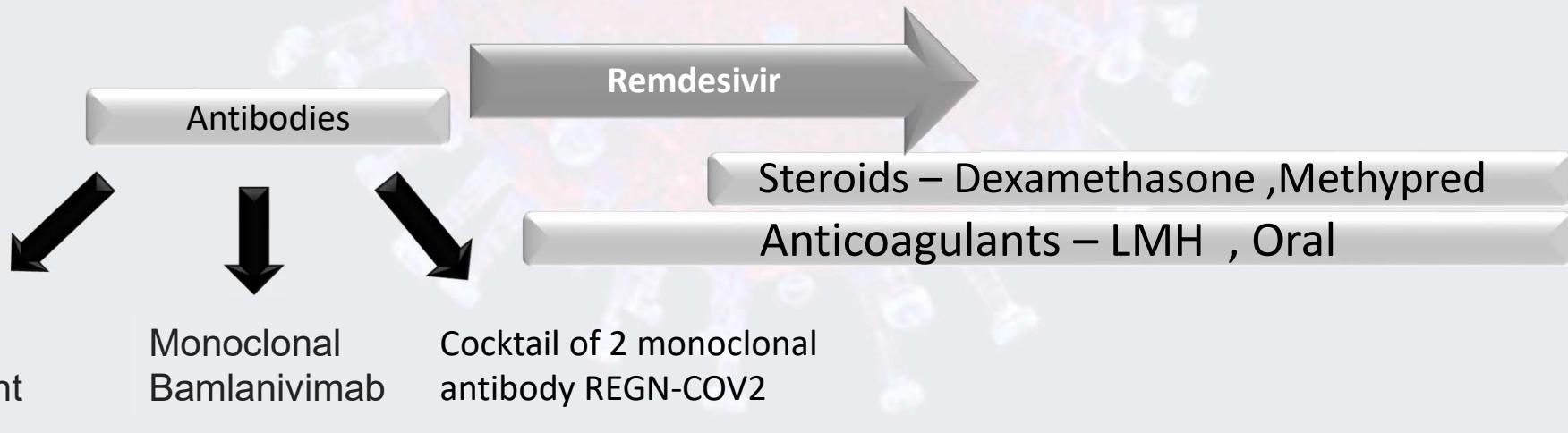
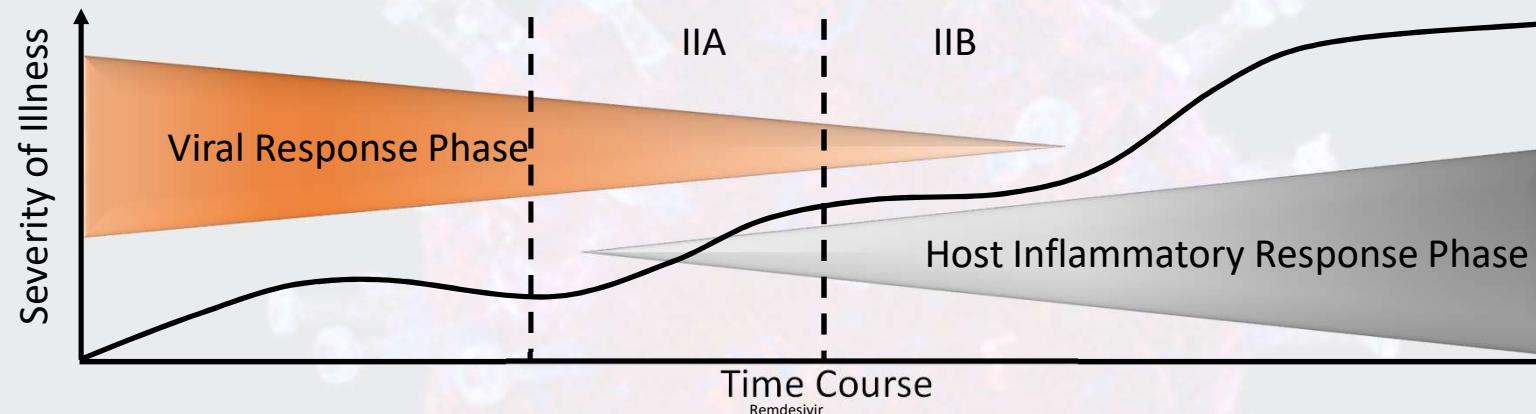
- Any fever more than 99 degree Fahrenheit especially with weakness , chills

Chest imaging – CT SS

Severity score 8/25 plus (with clinical features)

Clinical /
investigational
Approach

Drugs





Remdesivir

Indication ?

Contraindication

Controversy

Remdesivir – Indication

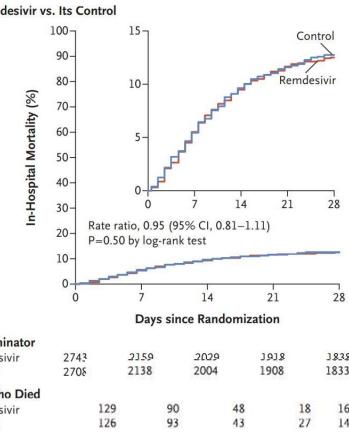
Progressive pneumonia – Minimum oxygen demand

High risk patient – significant chest infiltrates with symptoms , no oxygen requirement



Best results – if used early ie within first 12 days

Avoid in pregnancy , e GFR less than 30 , SGOT , SGPT > 5 times



WHO SOLIDARITY Trial: Antiviral Drugs to Treat Hospitalized Patients With COVID-19

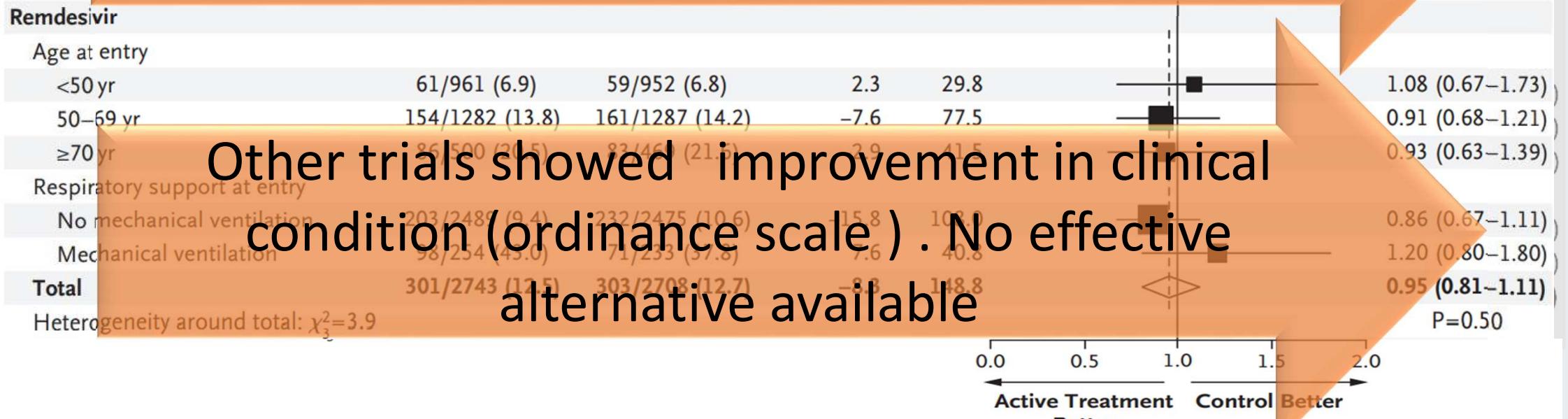
31st December 2020

ORIGINAL ARTICLE

Repurposed Antiviral Drugs for Covid-19 — Interim WHO Solidarity Trial Results

WHO Solidarity Trial Consortium*

Subgroup No mortality benefit but why clinicians still using it ?



Other trials showed improvement in clinical condition (ordinance scale) . No effective alternative available



ACTT 1 trial vs Solidarity trial

- Daniel Rubin, Ph.D.,
- Kirk Chan-Tack, M.D.,
- John Farley, M.D., M.P.H.,
- and Adam Sherwat, M.D.



ACTT-1 didn't demonstrated the mortality benefit but demonstrated robust results on time to recovery and odds of clinical improvement whereas Solidarity was not designed to rigorously assess these end points

FDA Approval of Remdesivir — A Step in the Right Direction

Daniel Rubin, Ph.D., Kirk Chan-Tack, M.D., John Farley, M.D., M.P.H., and Adam Sherwat, M.D.



Article



5 References 1 Citing Article

Metrics

December 31, 2020

N Engl J Med 2020; 383:2598-2600

DOI: 10.1056/NEJMp2032369

December 31, 2020

N Engl J Med 2020; 383:2598-2600

DOI: 10.1056/NEJMp2032369

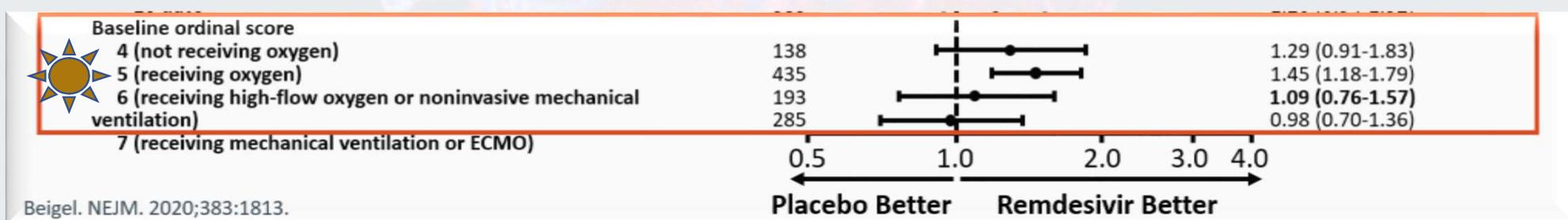
Adaptive COVID-19 Treatment Trial (NIAID ACTT-1): Study

Beigel. NEJM. 2020;383:1813. NCT04280705.



Less recovery time , benefit in patients with low flow oxygen

Outcome	Remdesivir (n = 541)	Placebo (n = 521)	RR/HR (95% CI)*	P Value
Mortality by 15 days, %	6.7	11.9	0.55 (0.36-0.83)	NR



Outcome if used early	Remdesivir	Placebo	HR (95% CI)
Randomized within 6 days of symptom onset			--
▪ Median time to recovery, days	10.0	24.0	1.92 (1.41-2.60)



SIMPLE-Moderate Study: Remdesivir in Patients With Moderate COVID-19 (normal oxygenation)

Spinner. JAMA. 2020;324:1048. NCT04292730.



Benefit if used in patients $\text{SpO}_2 > 94\%$ on room air and radiographic infiltrates by imaging
(N = 584)

Ordinal Scale Score, n (%)	Remdesivir 5-Day (n = 191)	Remdesivir 10-Day (n = 193)	SoC (n = 200)
5: Hospitalized, requiring ongoing medical care, not receiving supplemental oxygen	163 (84)	160 (84)	160 (80)



- Patients receiving 5-day remdesivir were 65% more likely to have clinical improvement at Day 11 vs SoC alone (OR: 1.65; 95% CI: 1.09-2.48; $P = .02$)



Remdesivir: Snapshot on Global Perspectives

FDA Indication

[Remdesivir] should only be administered in a hospital or healthcare setting capable of providing acute care comparable to inpatient hospital care."

The EMA's human medicines committee (CHMP) has granted remdesivir conditional marketing authorization for the treatment of COVID-19 in adults and adolescents from 12 yrs of age **with pneumonia who require supplemental oxygen¹**

¹ EMA European medical association Press Release. June 25, 2020.
<https://www.ema.europa.eu/en/news/first-covid-19-treatment-recommended-eu-authorisation>.



Antibody infusion - directed against the spike protein of SARS-CoV-2

Monoclonal antibody Bamlanivimab

IV infusion (700 mg over at least 60 mins); should be given as soon as possible after positive SARS-CoV-2 test and within 10 days of symptom onset

Casirivimab/imdevimab

REGN10933

Cocktail of two antibodies

Prophylactic within 3 days of symptom onset
Not indicated in hospitalised patients



Bamlanivimab EUA Provider Fact Sheet. November 2020.

Casirivimab and Imdevimab EUA Provider Fact Sheet. November 2020.

Patient selection

- Indication –
 - Those patients who are at high risk of disease progression 
 - Immunosuppressed

*FDA "... permits the emergency use of the unapproved product bamlanivimab or casirivimab and imdevimab (to be administered together) for the treatment of mild to moderate coronavirus disease 2019 (COVID-19) in adults and pediatric patients > 12 yrs , 40 kg, and **who are at high risk for progressing to severe COVID-19** *

Corticosteroids

Indication

- Hypoxemia

Dose /Duration

- Severity

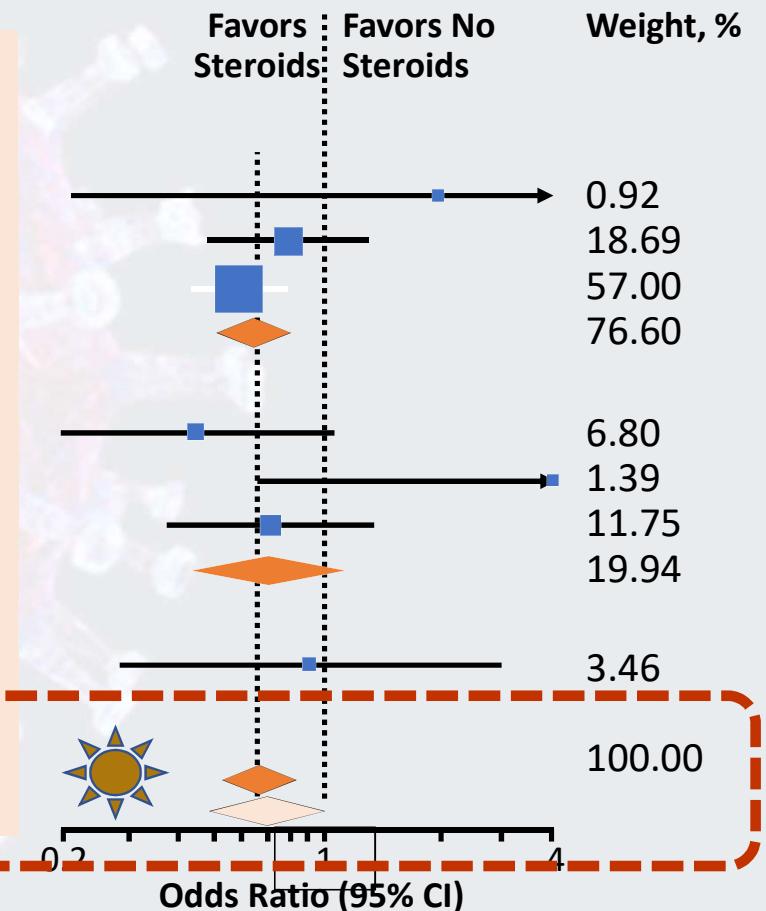
Tapering

- Slow

Systemic Corticosteroids and 28-Day All-Cause Mortality in Critically Ill Patients With COVID-19

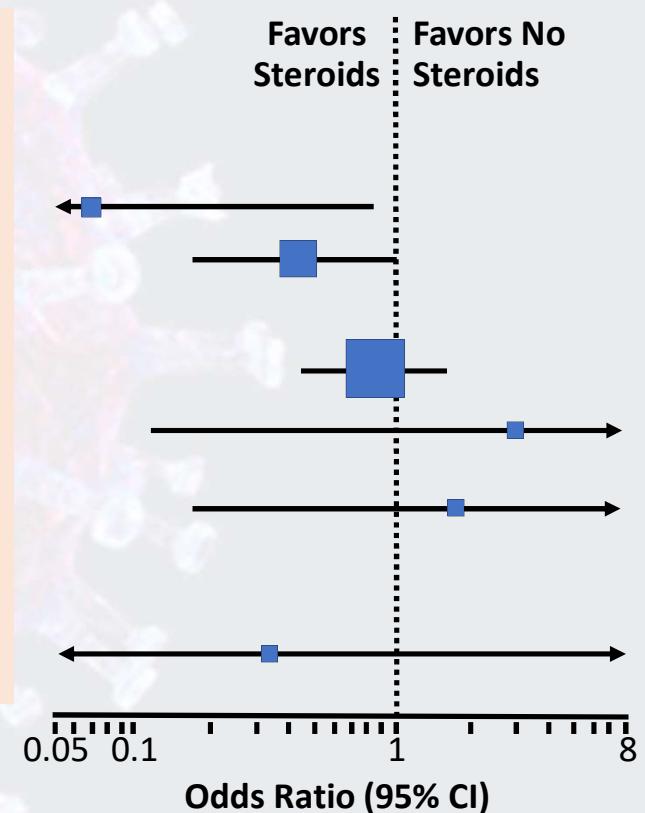
Drug/Trial	Initial Dose	Deaths/n		Odds Ratio (95% CI)	P Value
		Steroids	No Steroids		
Dexamethasone					
DEXA-COVID 19	High: 20 mg/day IV	2/7	2/12	2.00 (0.21-18.69)	
CoDEX	High: 20 mg/day IV	69/128	76/128	0.80 (0.49-1.31)	
RECOVERY	Low: 6 mg/day PO or IV	95/324	283/683	0.59 (0.44-0.78)	
Subgroup fixed effect		166/459	361/823	0.64 (0.50-0.82)	< .001
Hydrocortisone					
CAPE COVID	Low: 200 mg/day IV	11/75	20/73		
COVID STEROID	Low: 200 mg/day IV	6/15	2/14		
REMAP-COVID	Low: 50 mg every 6 hrs IV	26/105	29/92		
Subgroup fixed effect		43/195	51/179	0.69 (0.43-1.12)	.13
Methylprednisolone					
Steroids-SARI	High: 40 mg every 12 hrs IV	13/24	13/23	0.91 (0.29-2.87)	.87
Overall*					
Overall (fixed effects)		222/678	425/1025	0.66 (0.53-0.82)	< .001
Overall (random effects)		222/678	425/1025	0.70 (0.48-1.01)	.053

* $P = .31$ for heterogeneity; $I^2 = 15.6\%$



Systemic Corticosteroids and Serious Adverse Events in Critically Ill Patients With COVID-19

Drug/Trial	Initial Dose	Serious Adverse Events/n		Odds Ratio (95% CI)
		Steroids	No Steroids	
Dexamethasone				
DEXA-COVID 19	High: 20 mg/day IV	3/7	11/12	0.07 (0.01-0.86)
CoDEX	High: 20 mg/day IV	7/128	15/128	0.44 (0.17-1.11)
Hydrocortisone				
CAPE COVID	Low: 200 mg/day IV	28/75	30/73	0.85 (0.44-1.65)
COVID STEROID	Low: 200 mg/day IV	1/15	0/14	3.00 (0.11-79.91)
REMAP-COVID	Low: 50 mg every 6 hrs IV	2/105	1/92	1.77 (0.16-19.81)
Methylprednisolone				
Steroids-SARI	High: 40 mg every 12 hrs IV	23/24	23/23	0.33 (0.01-8.61)





Steroids recommendation

- WHO - Recommend systemic corticosteroids
 - ARDS, sepsis, septic shock
 - Severe disease ($O_2 < 90\%$ on room air* RR > 30 breaths/min)

WHO Living Guidance. Corticosteroids for COVID-19. September 2, 2020.

- NIH , IDSA – Recommend for those hospitalized and requiring supplemental oxygen – Dexona 6 mg once a day x 10 days or till discharge (or equivalent dose of methypred 32 mg , prednisolone 40 mg)

1. NIH COVID-19 Treatment Guidelines. Therapeutic management of patients with COVID-19. Last updated October 9, 2020.
2. IDSA. COVID-19 Guideline, Part 1: Treatment and Management. Version 3.5.0.

Use in practice

Hypoxia

Tapering
over 10 to
14 days



Moderate

Inj. Dexamethasone 0.1 –
0.2 mg /kg ≈ 6 mg IV OD
x 3 to 5 Days
or
Inj. Methyl Prednisolone
0.5 -1 mg/kg ≈ 40 to 60 mg
x 3 to 5 Days

Severe

Inj. Dexamethasone 0.2 – 0.4
mg /kg ≈ 6 mg IV BD x 5 to
7 Days
or
Inj. Methyl Prednisolone 1.0
mg x 5 to 7 Days
the dose if

2 min break

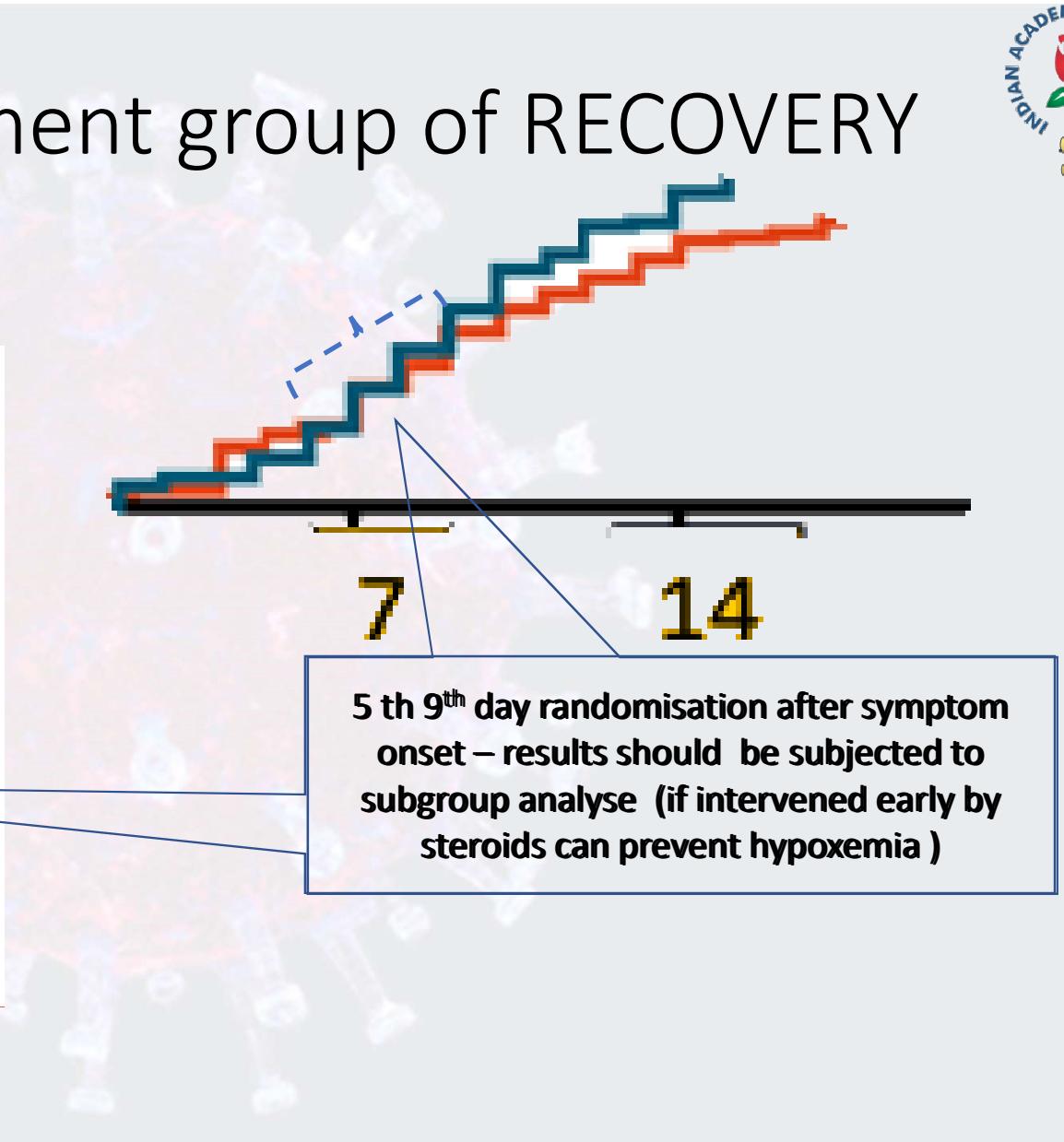
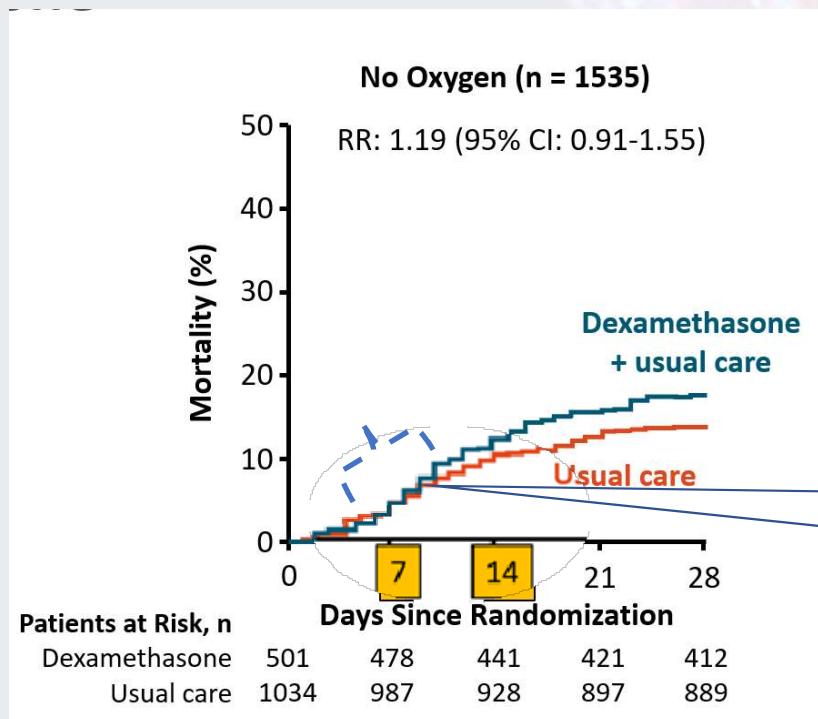
No use
days unless hypoxia

NATIONAL
(mohfw.gov.in)

VID-19

Investigational Therapies (Informed and shared decision making is essential before prescribing):
6 *In Remdesivir 200 mg IV on day 1 followed by 100 mg IV daily for next 5 days. Total 7 days therapy.
*Use of Convalescent plasma (200 ml single dose, may be repeated after 24 hrs) may be considered in selected cases.
7 Inj Tocilizumab 8mg/kg (max dose 800 mg once; usual dose 400 mg may be considered if no contraindications) in patients moderate-severe disease with progressively increasing oxygen requirement despite use of corticosteroids with raised inflammatory markers; dose can be repeated after 12 to 24 hours if no improvement occurs with the first dose.

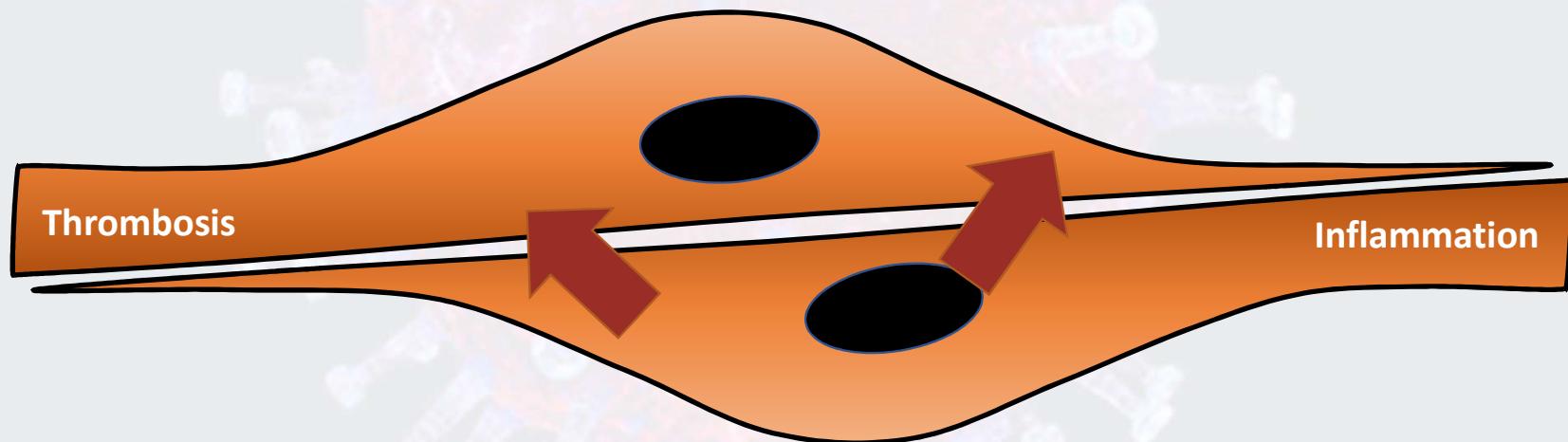
No oxygen requirement group of RECOVERY trial



dG1

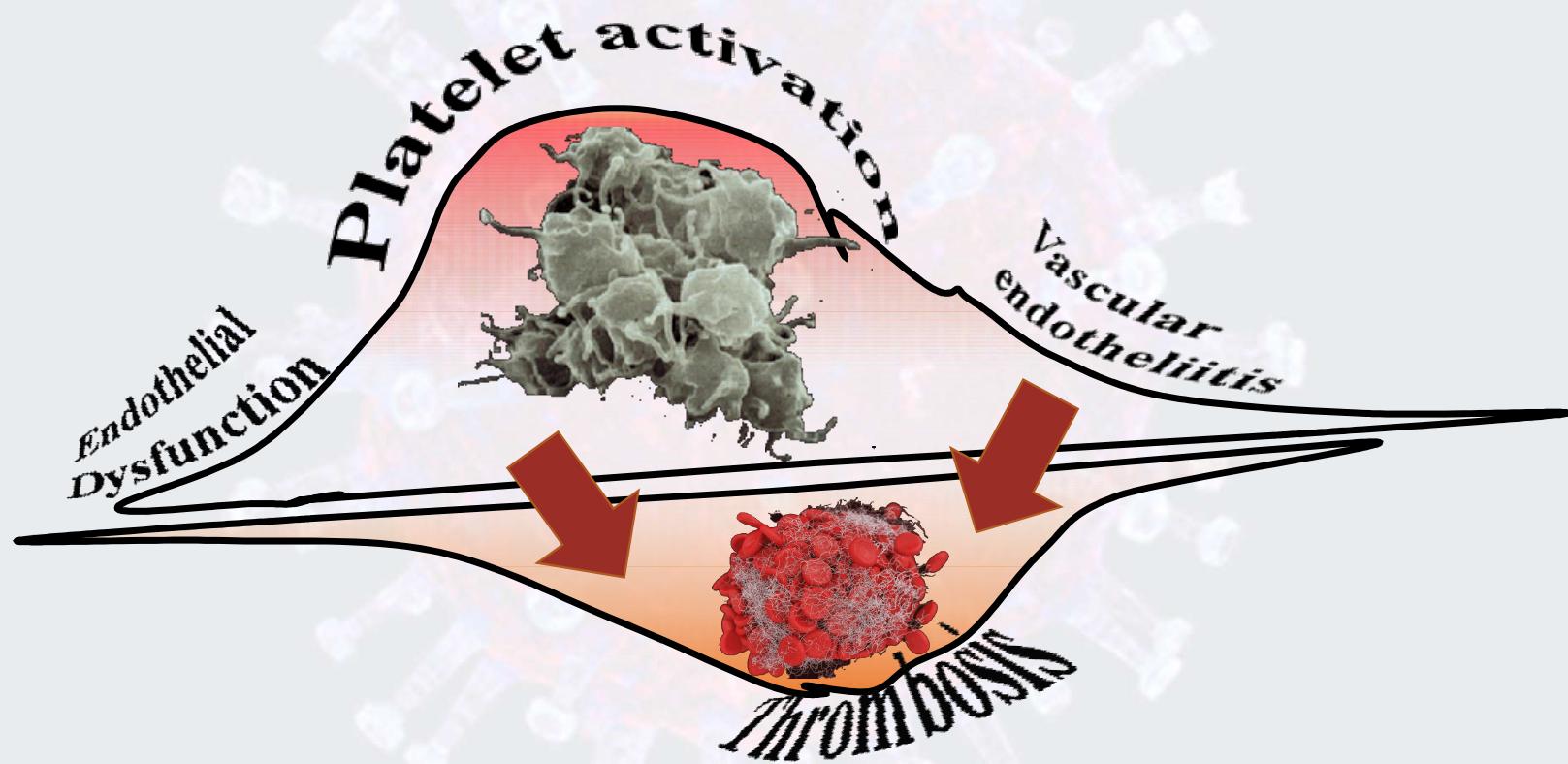
dhiren Gupta, 17-01-2021

COVID-19 Coagulopathy: Thromboinflammation



. Blood. 2019;133:906 , .
Becker. J Thromb Thrombolysis. 2020;15:1.

Virchow's Triad in COVID-19





Anticoagulant Therapy

Indication

- Clinical risk of thrombosis
- Lab markers

Dose /Duration

- Severity
- Prophylactic , Therapeutic

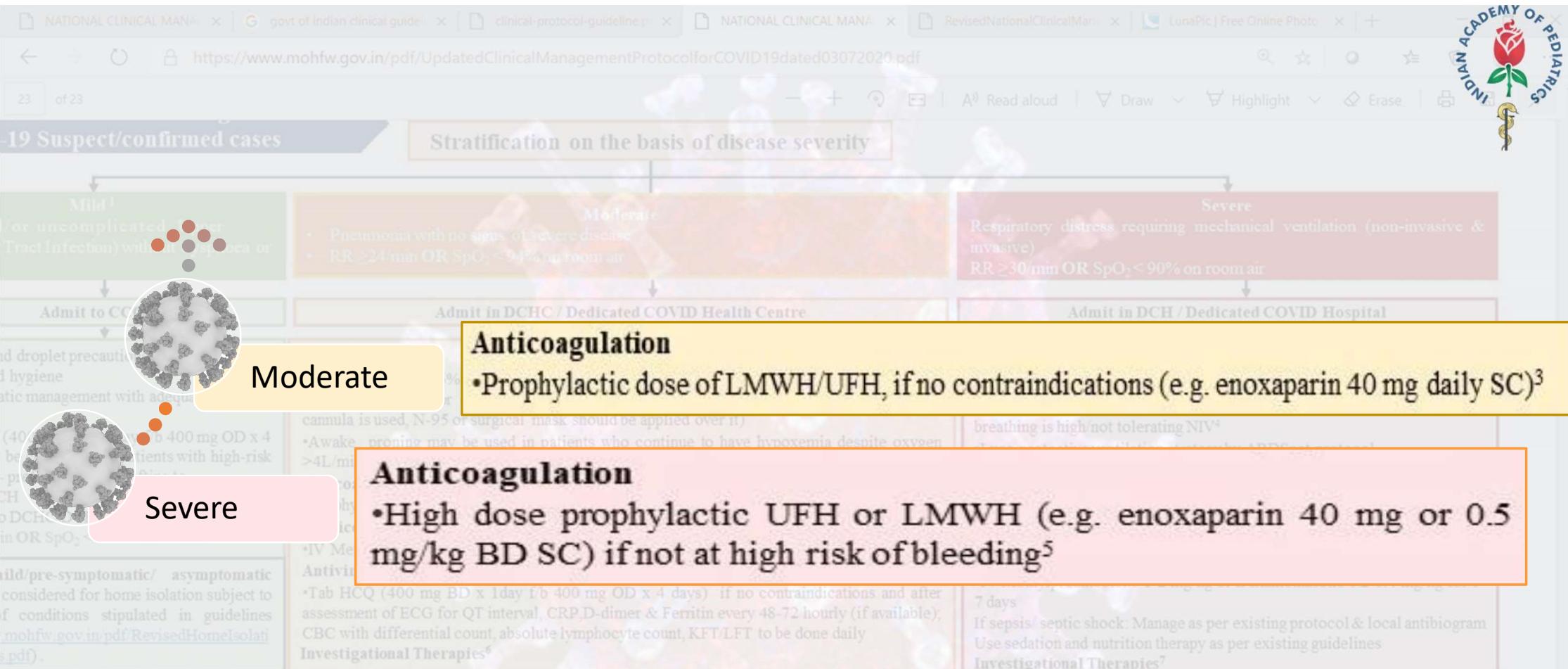
Duration

- 2 to 6 weeks



Laboratory Predictors of Thrombosis in COVID-19

Median Value	No Thrombotic or Bleeding Complication (n = 347)	Thrombotic Complication (n = 38)	P Value
D-dimer, ng/mL			
▪ Initial	891	1538	.0002
▪ Minimum	760	1336	.0006
▪ Peak	1377	4001	< .0001
CRP, mg/L			
▪ Initial	63.3	124.7	.0011
▪ Minimum	35.4	94.2	< .0001
▪ Peak	130.3	277.7	< .0001
Ferritin, µg/L			
▪ Initial	504	825	.015
▪ Minimum	453	750	.0056
▪ Peak	707	1182	.0020



While attending suspect cases, as per above protocol based on clinical assessment, testing shall be done, and if negative, manage in non-COVID facility according to clinical diagnosis.

Discharge: After clinical improvement, discharge as per revised discharge policy (available at:

NATIONAL CLINICAL MANAGEMENT PROTOCOL COVID-19 (mohfw.gov.in)

Patients for severe disease include:

≥ 65 years or more
on, DM (diabetes mellitus) & other immunocompromised states
(Color Disease and Obesity) BMI > 25 kg/m²)

3 LMWH: Low Molecular Weight Heparin: if no
contraindication or high risk of bleeding; UFH:
Unfractionated heparin

5 Risk of bleeding: use validated score for assessing bleeding risk (eg HAS-BLED
score). Use D-dimer and SIC score for further risk stratification (SIC score ≥ 4
portends high thrombotic risk). Follow AHA/ESC and ISTH guidelines in case
patient is on anti-platelet agents

49 year male

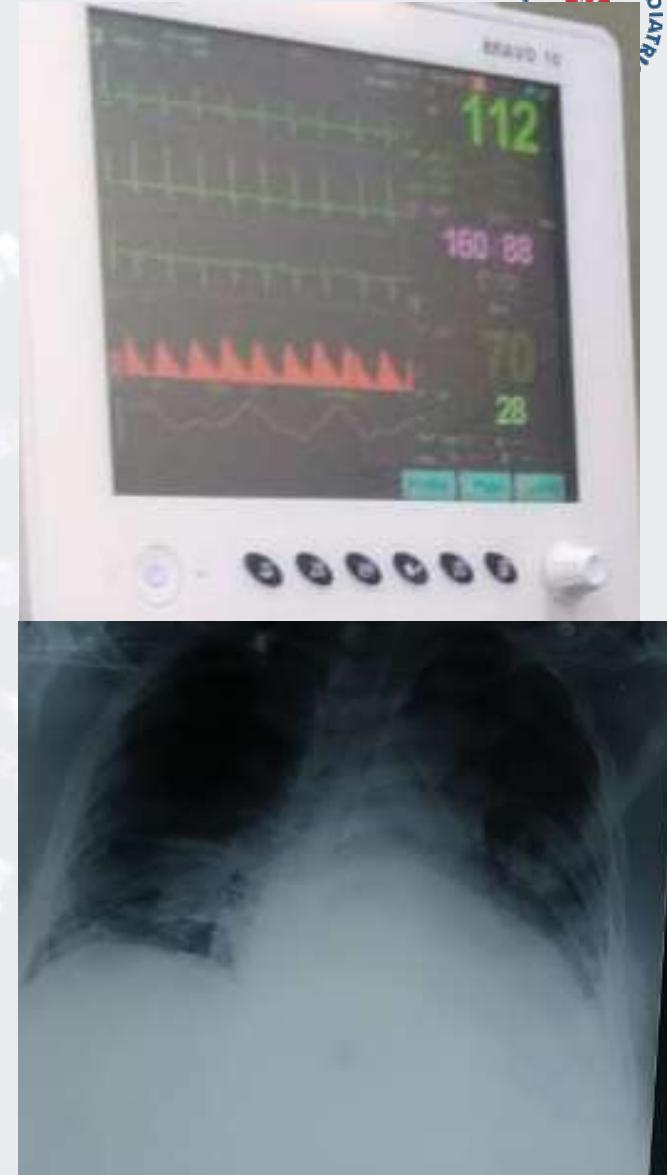
16 th of ICU stay , 5 days of invasive ventilation

Fully conscious

Stable

Extubated

SpO_2 dropped to 50 after 1 hour - reintubated – SpO_2 not increasing beyond 70 %



DD

- No major lung collapse
- Pulmonary hypertension
- Pulmonary thrombosis – D Dimer 10000 ng/ml plus (500 highest value) , High PaCO₂ dead space ventilation , normal looking Chest X ray



^R Tenecteplase (TNK-tPA)
for Injection Kit 40 mg

TenecteRel™

40 mg

For I.V. use.

40 mg

TenecteRel
40 mg

Each kit contains:

- 1 vial of Tenecteplase Lyophilized concentrate
- 1 Sterile Syringe of 10 ml
- 2 Sterile Needles 21G

3 Alcohol Swabs

reconstitute each vial with 8 ml Sterile Water for Injection IP

ecteplase is a sterile, preservative free lyophilized concentrate.

at 2-8°C. Do not freeze and shake once reconstituted with sterile WFI.

ard unused portion.

ut of reach of children.

pack insert prior to use.

Manufactured by:
Reliance Life Sciences Ltd.

25mg of tPA over 2 hours followed by a 25mg tPA infusion administered over the subsequent 22 hours, with a dose not to exceed 0.9 mg/kg followed by full anticoagulation

MFG. DATE : MAR 2020
EXP. DATE : AUG 2021
M.R.P. : RS. 44600.00
(Incl. of all taxes)

WFI:
Mfg. Lic. No. : DD/572
B. No. : C190701
MFG. DATE : JUL 2019
EXP. DATE : JUN 2024

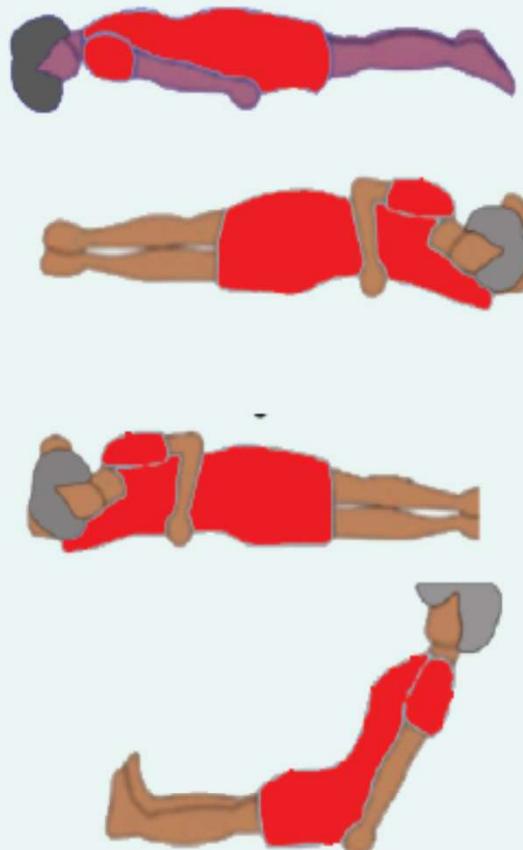
CAUTION:
Not to be sold by retail without
the prescription of a Cardiologist



Management of sick /critical covid 19 patient

- Any patient with saturation less than 90 percent , increased RR >30 , WOB , shock , MODS , requiring high oxygen (if Spo₂ < 90 despite of oxygen before treatment indicates poor prognosis – requires very aggressive treatment)

Prone ventilation



Awake proning if SpO₂ <94% on FiO₂ 40% by either venturi facemask or high flow nasal cannula

- 30 to 120 mins prone
- 30 to 120 mins left lateral
- 30 to 120 mins right lateral
- 30 to 120 mins upright
- Contraindicated in altered mental status and hemodynamic instability, pregnancy , vomiting, abdominal wound, unstable pelvic/spinal lesions.

Before proning increase fiO₂ to 100 percent for five minutes.

Prone Ventilation after intubation
(16 to 18 hrs / Day)

When to start proning ?
P/F ratio < 150, fiO₂ > 0.6 and PEEP > 5 cm H₂O.

When to stop proning ?
When P/F exceeds 150 on fiO₂ < 0.6 and < 6 PEEP

Controversial therapies

Within 7
days after
checking
antibodies

- Convalescent Plasma Therapy

- Tocilizumab



Case ashi continued

77 M ,DM day 8 , cough , weakness persisted , HbA1C 6.0 , started on oral methyl pred , **Enoxaparin**

Day 8	Day 12	Day 16
CRP 18	CRP 32	CRP 6
Fever + , Spo2 96	Afebrile , Spo2 94	Afebrile , Spo2 96
Medrol 24 , Enoxaparin 40	Medrol 32 , Enoxaparin	Tapering of Medrol , Enoxaparin 40 x 10 days then shift to oral x 4 weeks



CDC: Discontinuation of Transmission-Based Precautions for Patients With Confirmed SARS-CoV-2

Symptom-Based Strategy

≥ 24 hrs since resolution
of fever, last antipyretics

And

Improvement in symptoms
(eg, cough, shortness of breath)

And

≥ 10 days since symptom onset
for mild to moderate illness,
10-20 days for severe to critical illness
or those severely immunocompromised

- “*A test-based strategy is no longer recommended [except for rare situations] because, in the majority of cases, it results in prolonged isolation of patients who continue to shed detectable SARS-CoV-2 RNA but are no longer infectious.*”

Conclusion

- 1) Risk stratification – Most important
- 2) 85 percent patients do not need any treatment
- 3) Monitoring is the key to success
- 4) Laboratory and radiology to be used judiciously
- 5) Tests should be interpret in clinical context
- 6) Recognition of early pulmonary stage (before significant hypoxia) is key to success
- 7) Remdesivir recipients should be watched for pneumonia and development of hypoxemia

