



奇美醫療
財團法人

奇美醫院

Chi Mei Medical Center



奇美醫院 COVID-19照護經驗分享

朱育陞藥師

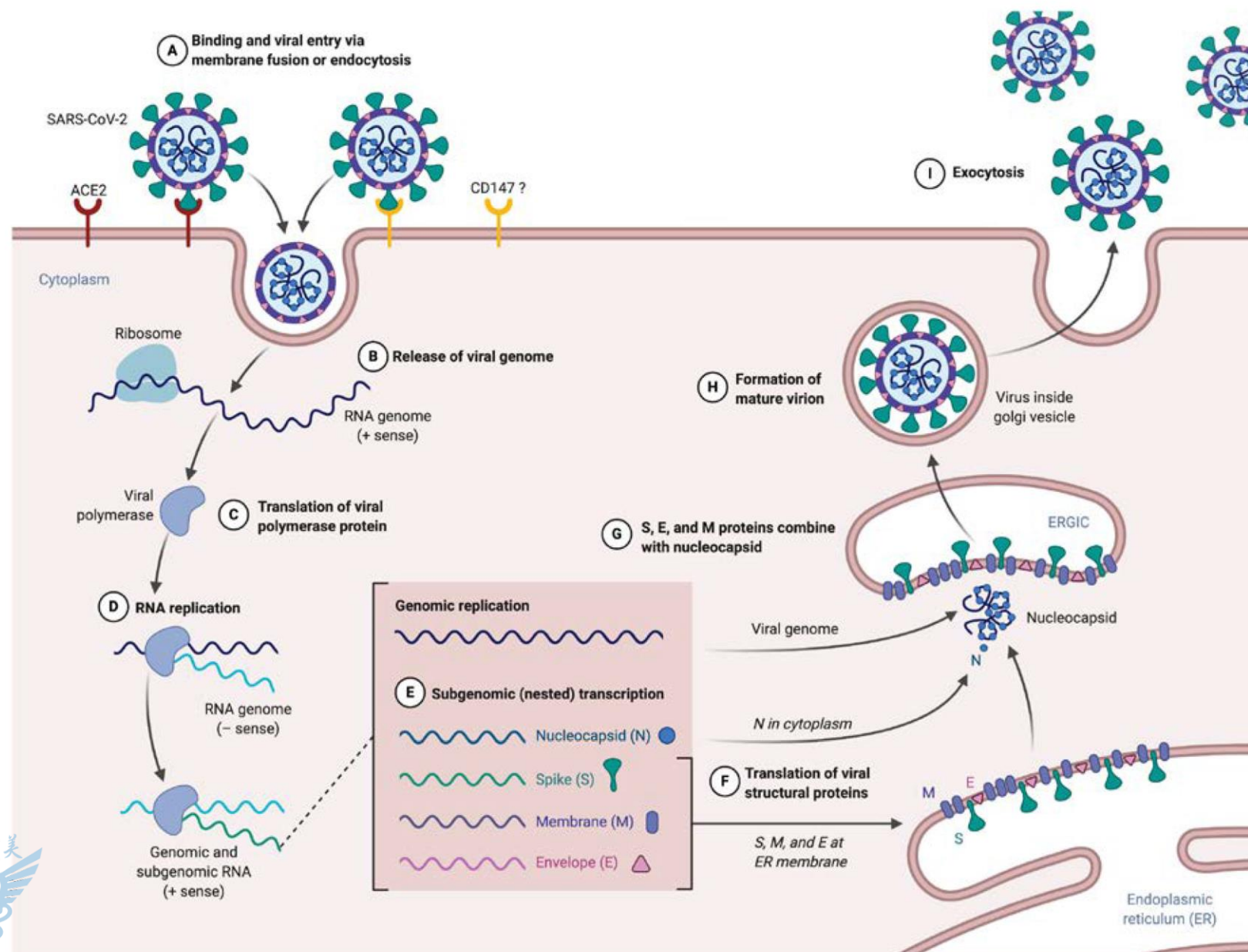
2021/8/21



Outline

- Overview of COVID-19
- Pharmacotherapy of COVID-19
- Difference between international guidelines
- Experience sharing

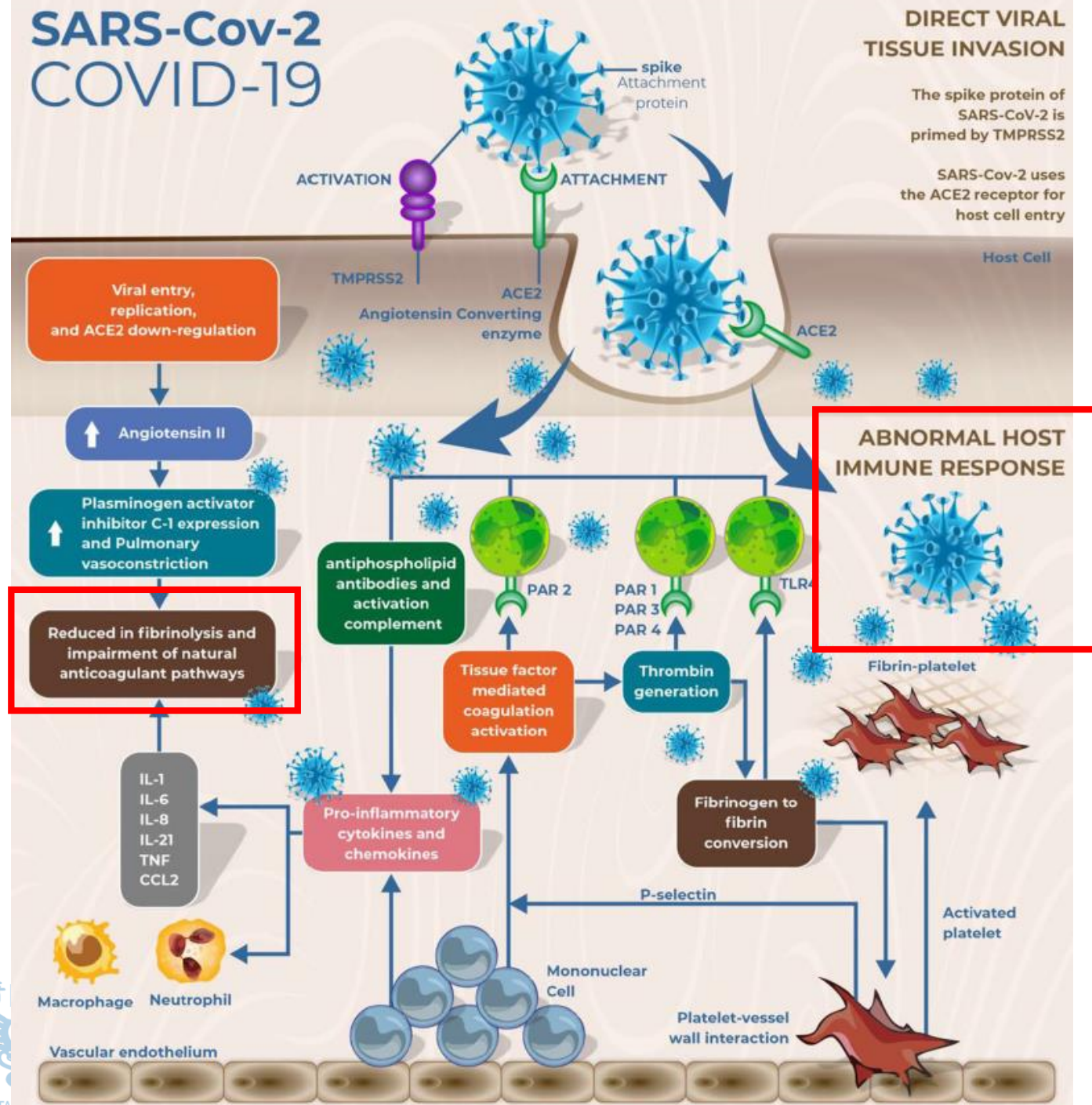
Life Cycle of SARS-CoV-2



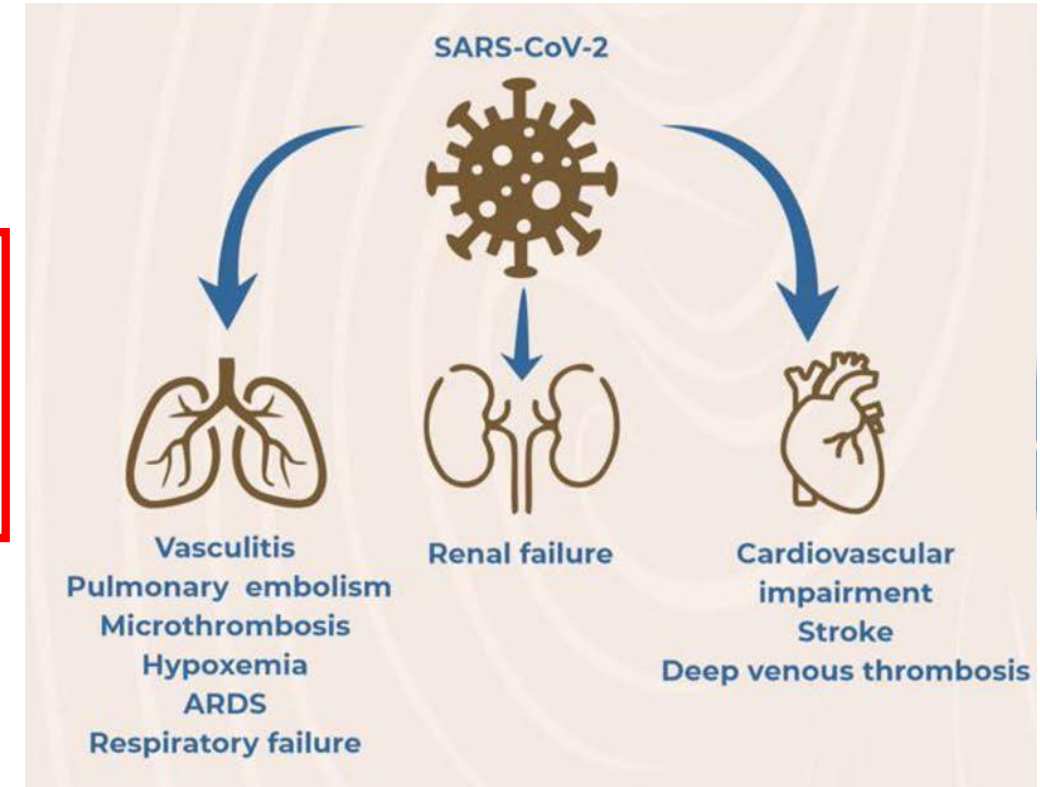
潛伏期：1-14天
(多數為5至6天)

可傳染期：始於發病前2天

SARS-CoV-2 COVID-19

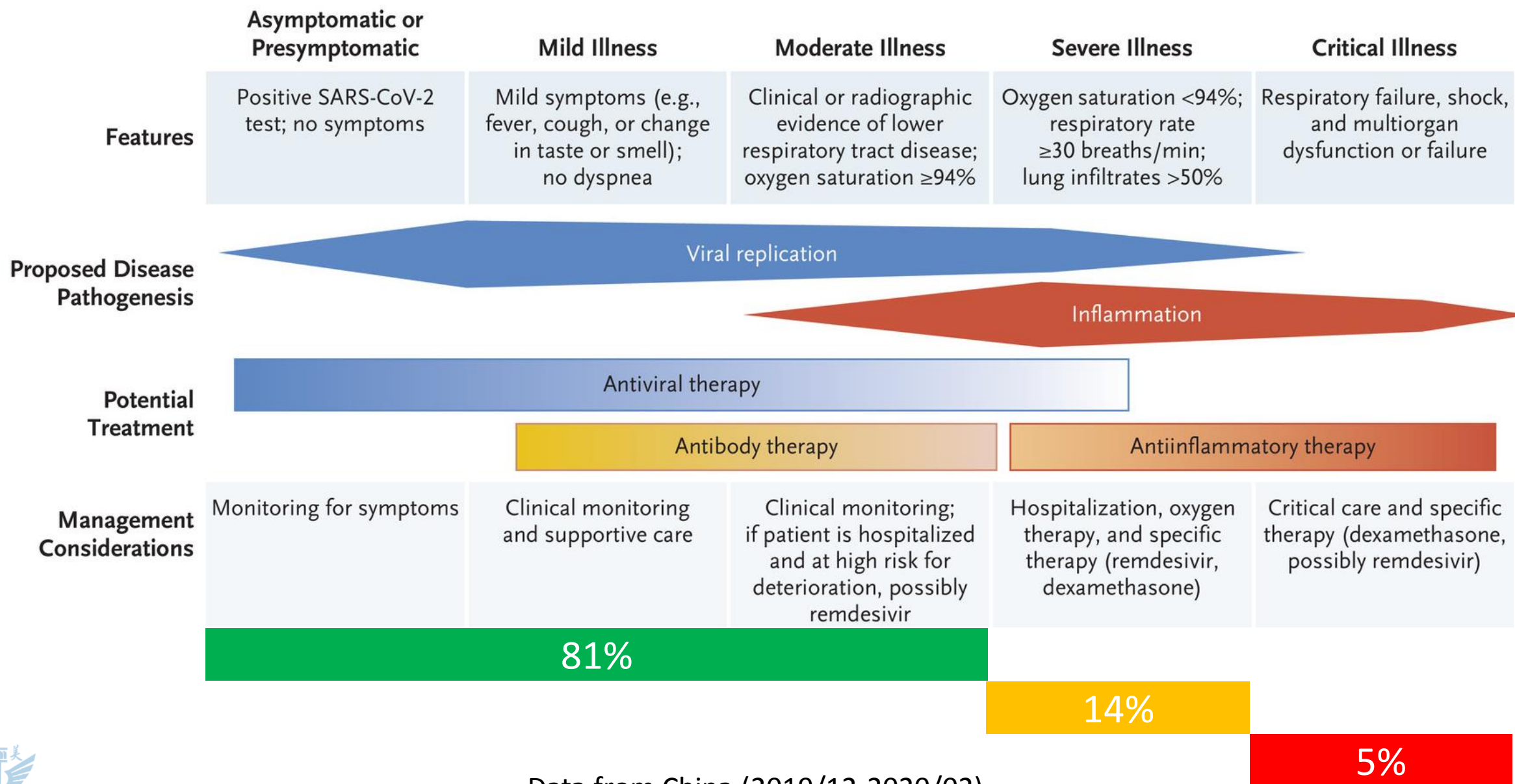


Ann Intensive Care . 2021 Feb 18;11(1):36.



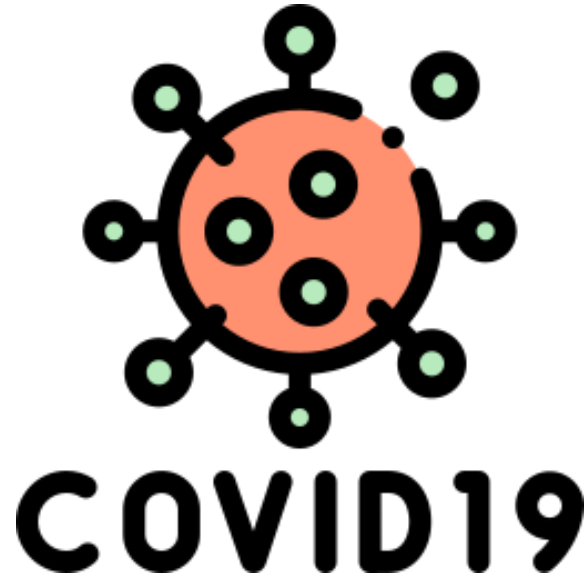
Disease Stage or Severity of COVID-19

N Engl J Med 2020; 383:1757-1766
JAMA. 2020 Apr 7;323(13):1239-1242



Data from China (2019/12-2020/02)

Virus



- Monoclonal Antibodies
- Convalescent Plasma
- Antiviral Drugs

Inflammation



- Steroid
- Interleukin-6 Inhibitors
- Janus Kinase Inhibitors

Coagulation



- LMWH
- Heparin
- Fondaparinux
- NOACs

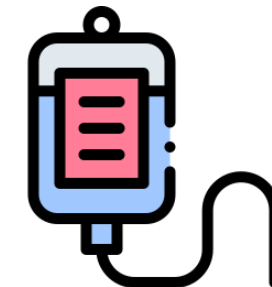
- Monoclonal Antibodies
 - Bamlanivimab + Etesevimab (\downarrow susceptibility to γ - or β -variants)
 - Casirivimab + Imdevimab
 - Sotrovimab
- COVID-19 convalescent plasma
 - High-titer plasma (USA EUA for immunity-impaired hospitalized P't)
- Antiviral Drugs
 - Remdesivir (not for P't w/o supplemental O_2)



- Monoclonal Antibodies

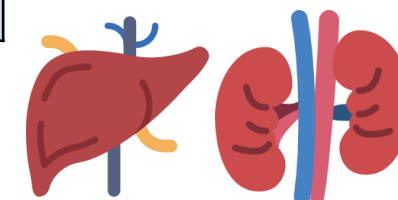
- Bamlanivimab 700 mg + Etesevimab 1400 mg IV once

NS	50mL	100mL	150mL	250mL
≥50 kg	≥21 min	≥31min	≥41min	≥60min
<50kg				≥70min



- Casirivimab 600 mg + Imdevimab 600 mg IV once

NS	50mL	100mL	150mL	250mL
All weight	≥20 min	≥21min	≥31min	≥50min



SBEC D

- Antiviral Drugs

- Remdesivir : In 100-250mL NS run 30-120 min

Adults or children ≥ 40 kg	Infants and Children ≥ 3.5 kg
Day 1 : 200 mg IV	Day 1 : 5mg/kg IV
Day2-5 : 100 mg IV QD	Day2-5 : 2.5mg/kg IV QD

- Steroids
 - Dexamethasone as 1st line
 - Equivalent dose of Prednisone, Methylprednisolone, Hydrocortisone
- Interleukin-6 Inhibitors
 - Tocilizumab (add on for critical illness P't)
- Janus Kinase Inhibitors
 - Baricitinib (add on for critical illness P't but not on MV or ECMO)



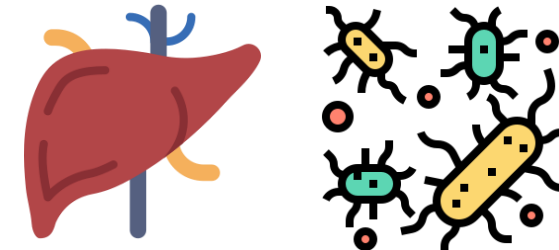
- Steroids

- Dexamethasone 6mg QD PO or IV for 7-10 days
- Prednisone 40mg QD, Hydrocortisone 80mg Q12H, Methylprednisolone 16mg Q12H

- Tocilizumab : Give once, in 100mL NS or 0.45%NS, run >60 min

Recommended Intravenous Dosage for COVID-19	
Patients less than 30 kg weight	12 mg/kg
Patients at or above 30 kg weight	8 mg/kg

- MAX dose: 800mg



- Baricitinib : PO

	eGFR>60	eGFR 30-60	eGFR 15-30	eGFR <15 or dialysis
>9 y/o	4 mg QD	2 mg QD	1 mg QD	not recommended
2-9 y/o	2 mg QD	1 mg QD	not recommended	not recommended

*use for 14 days or hospital discharge (whichever comes first)

Timing of prophylaxis

- Western : All hospitalized patients, at least 14 days
- Taiwan : May not use routinely, consider D-dimer and patient mobility



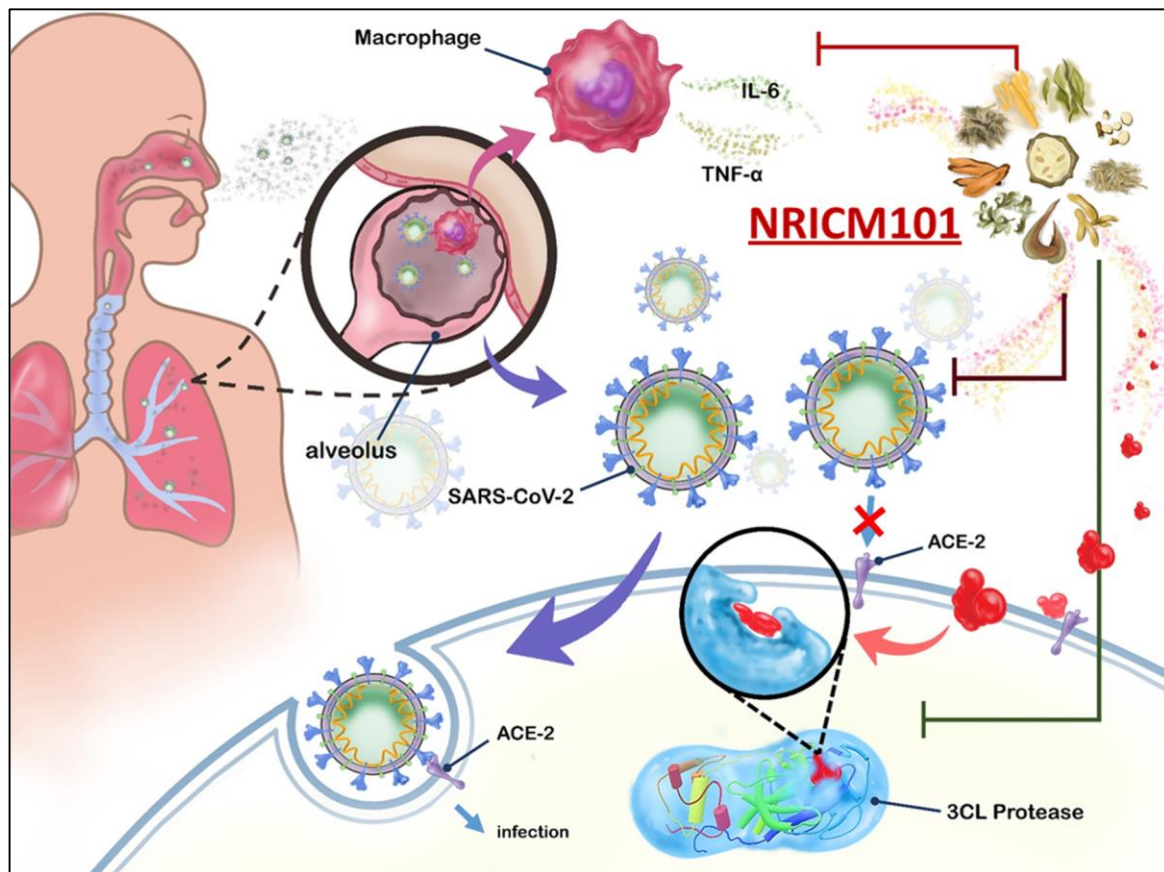
Drug	Dose	Note
Enoxaparin (Clexane)	40 mg SC QD (if CrCl 15-30, 30 mg QD)	May titrate dose in obesity P't
Dalteparin (Fragmin)	5000 units SC QD	
Heparin	5000 units SC Q8-12H	for CrCl <15 mL/min or on dialysis
Fondaparinux	2.5 mg SC QD (if CrCl 20-50, 1.5 mg QD)	for P't w/ history of HIT
Low dose NOACs	Rivaroxaban 10 mg QD	For outpatient w/ thrombosis risk

- COVID-19臨床主要表現：病邪入肺化熱
- 組成：
 - 辛散解表：荊芥、防風、甘草
 - 清熱宣肺解毒：薄荷、桑葉、黃芩、板藍根、魚腥草
 - 寬胸祛痰：全瓜蒌
 - 降氣平喘：厚朴
- 成年人使用方式：
 - 確診者：一天三次，每次10公克
 - 檢疫隔離者：一天一次，每次10公克
- 常見副作用：腹瀉、嘔吐等

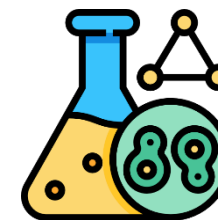


> *Biomed Pharmacother.* 2021 Jan;133:111037. doi: 10.1016/j.biopha.2020.111037. Epub 2020 Nov 19.

A traditional Chinese medicine formula NRICM101 to target COVID-19 through multiple pathways: A bedside-to-bench study



1. 抑制 SARS-CoV-2 的 Spike Protein與ACE2的結合
2. 抑制3CL蛋白酶的活性，阻斷病毒在細胞內的複製。
3. 抑制 Macrophage 分泌的 TNF- α 、IL-6





Difference between international guidelines

分期		Low-Flow Device	High-Flow Device or Noninvasive Ventilation	Invasive Mechanical Ventilation or ECMO
NIH	Dexamethasone	建議使用		
	Remdesivir	可使用	may add on	insufficient evidence
	Baricitinib	insufficient evidence, may add on	併用 Remdesivir 於 Steroid 不可用者 or Add on 需氧疾速上升和 CRP ≥75 mg/L 者	insufficient evidence
	Tocilizumab	insufficient evidence, may add on	Add on 需氧疾速上升, CRP ≥75 mg/L 或 24hr 內進 ICU 者	
NICE 未提到 Baricitinib	Dexamethasone	建議使用		
	Remdesivir	建議使用 5 天療程	不建議 (use only in research settings)	
	Tocilizumab	CRP≥75 時使用	建議於 48hr 內 add on	
ERS 未提到 Baricitinib	Corticosteroids	建議使用		
	IL-6 receptor antagonist	建議 add on		
	Remdesivir	No recommendation		不建議
Taiwan CDC	Dexamethasone	建議使用		
	Remdesivir	可考慮 add on (5 天療程)		沒有提到
	Tocilizumab	建議 add on (與 Baricitinib 不可併用)		
	Baricitinib	沒有提到	add on CRP ≥ 7.5 mg/dL 者	沒有提到
分期		SpO2 ≤94% or on supplemental oxygen (Severe)	On mechanical ventilation or ECMO (Critical)	
WHO 未提到 Baricitinib	Dexamethasone	建議使用		
	Remdesivir	Beneficial effects are likely to be small and the possibility of important harm remains. However, the values and preferences are likely to vary, and some p't and clinicians who may use it given the evidence hasn't excluded the possibility of benefit.		
	Tocilizumab	建議使用		
IDSA	Dexamethasone	建議使用		
	Remdesivir	建議使用 5 天療程	不建議常規使用	
	Baricitinib	發炎指數上升時 add on 或併用 Remdesivir 於 Steroid 不可用者	uncertain	
	Tocilizumab	發炎指數上升時 add on		

建議使用

需要再用

無建議

不建議

- Monoclonal Antibodies

- 具任一風險因子*，未使用氧氣且於發病十天內之 ≥ 12 歲且體重 ≥ 40 kg 病患

- *年齡 ≥ 65 歲、糖尿病、慢性腎病、心血管疾病、慢性肺疾、BMI ≥ 25 (或 12-17 歲 BMI 超過同齡第 85 百分位)、懷孕、其他影響免疫功能之疾病或已知重症風險因子者

- Remdesivir

- 嚴重肺炎以上但未插管病患

- Steroids

- 嚴重肺炎以上病患

- Tocilizumab

- 與 Dexamethasone 合併用於嚴重肺炎以上病患

- 與 Dexamethasone + Remdesivir 合併用於嚴重肺炎以上但未插管病患

- Baricitinib

- 與 Dexamethasone \pm Remdesivir 合併用於需使用高流量氧氣或非侵襲性呼吸器但未插管，同時發炎指數上升 (CRP ≥ 7.5 mg/dL) 之病患



- CRP ≥ 75 mg/L
- rapidly increasing oxygen needs
- admitted to ICU within 24 hours

Brief Indications of COVID-19 drugs

- Monoclonal Antibodies：疾病初期的高風險患者
- Dexamethasone：所有需要供氧的患者
- Remdesivir：低流量供氧患者，需氧量更高但未插管者可考慮使用
- Tocilizumab：需要供氧合併有惡化傾向或高度發炎(CRP ≥ 75 mg/L)的患者
- Baricitinib：需要高流量供氧或非侵入性呼吸器的Tocilizumab alternative.
- Baricitinib+Remdesivir：使用於無法使用Steroid者 (Taiwan已移除)

	不需用氧	需吸氧治療	高流量氧或NIV	插管
可降低死亡率， 建議使用		Dexamethasone	Dexamethasone	Dexamethasone
		+Tocilizumab	+ Baricitinib或tocilizumab	+Tocilizumab
	Casirivimab+imdevimab或 Bamlanivimab+etesevimab			
加速臨床改善， 考慮使用		+ Remdesivir		

- Monoclonal Antibodies

1. VS評估個案是否符合條件，並與其居住地傳染病防治醫療網區指揮官討論
2. 確認用藥需求後，填寫「個案治療同意書」、「單株抗體申請暨領用檢核表」、「單株抗體領用切結書」，向存放藥物之主責醫院領藥回院內注射
3. 主責醫院接受領用後，於當日將「治療同意書」及「申請暨領用檢核表」附件給所在地轄屬CDC區管中心(正本醫院留存醫院)，並至MIS登錄領用情形。

- Remdesivir

1. 向CDC區管中心申請領用 (填寫VEKLURY®申請暨領用檢核表)
2. CDC防疫醫師審核
3. 審核通過後醫療機構派員前往指定地點領取 (填寫領用切結書)
4. CDC區管中心於MIS登錄領用情形，申請書表及依據資料由區管中心存查

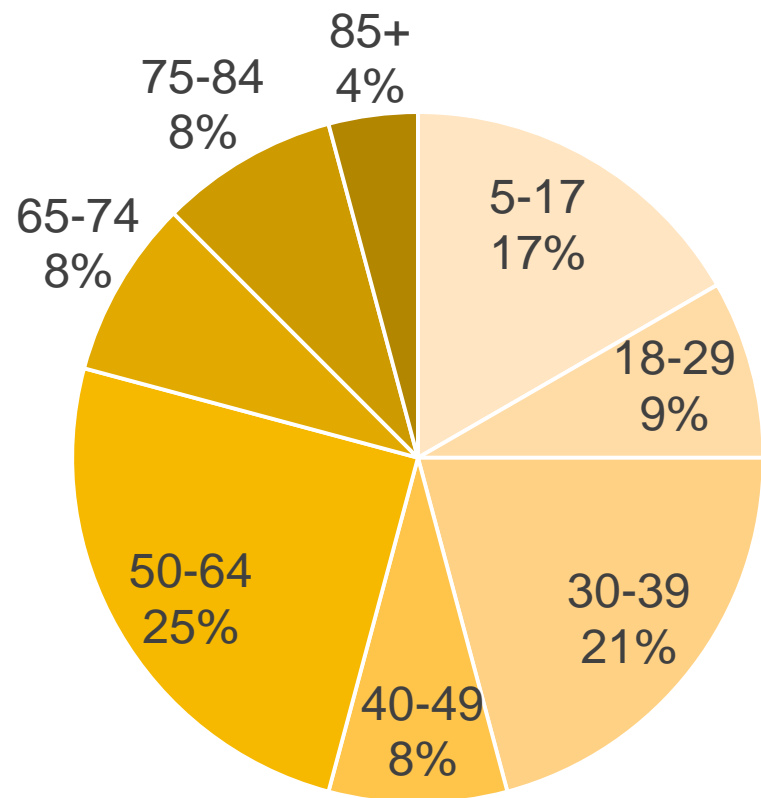


Experience sharing

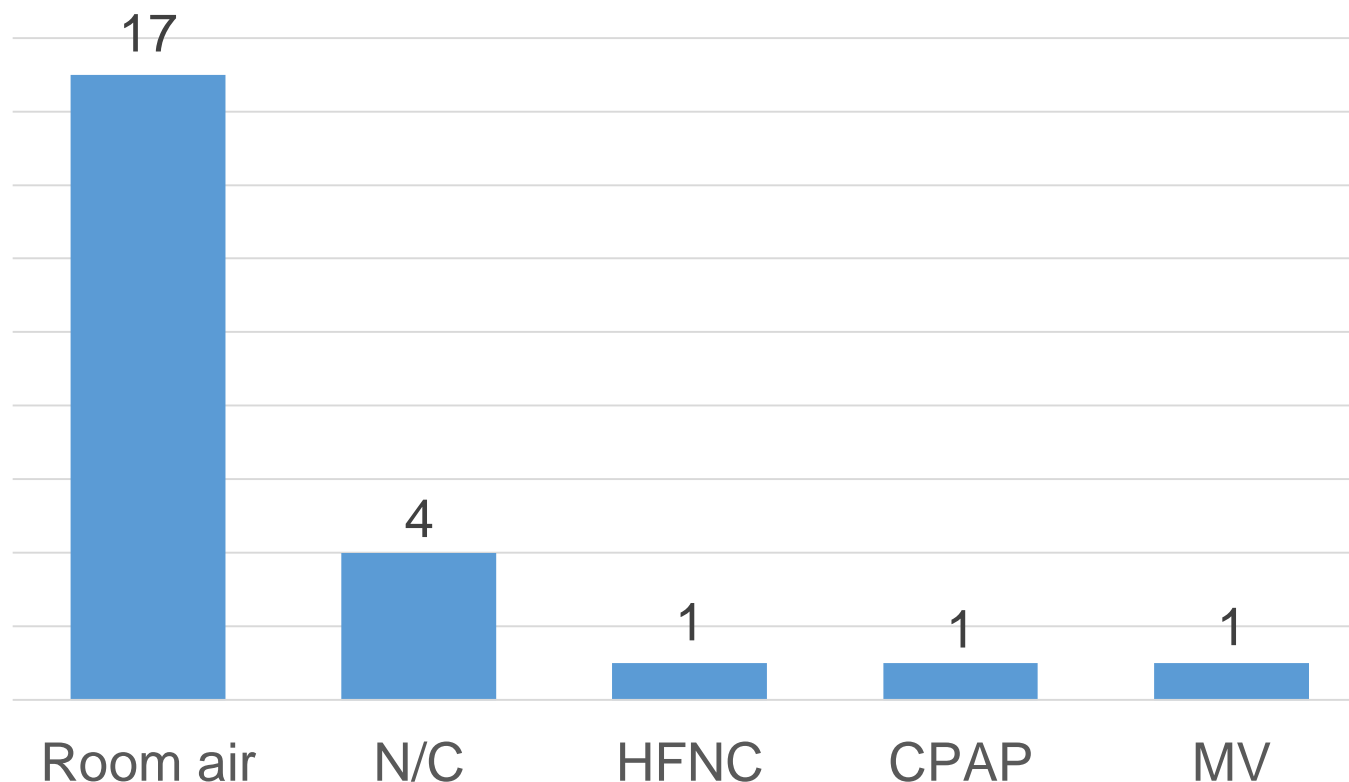
Profiles of COVID-19 Patients in Chi-Mei Hospital

- 24 patients was diagnosis of COVID-19 since 2021/05
平均住院15.28天 (中位數：13), all discharge alive

年齡比例



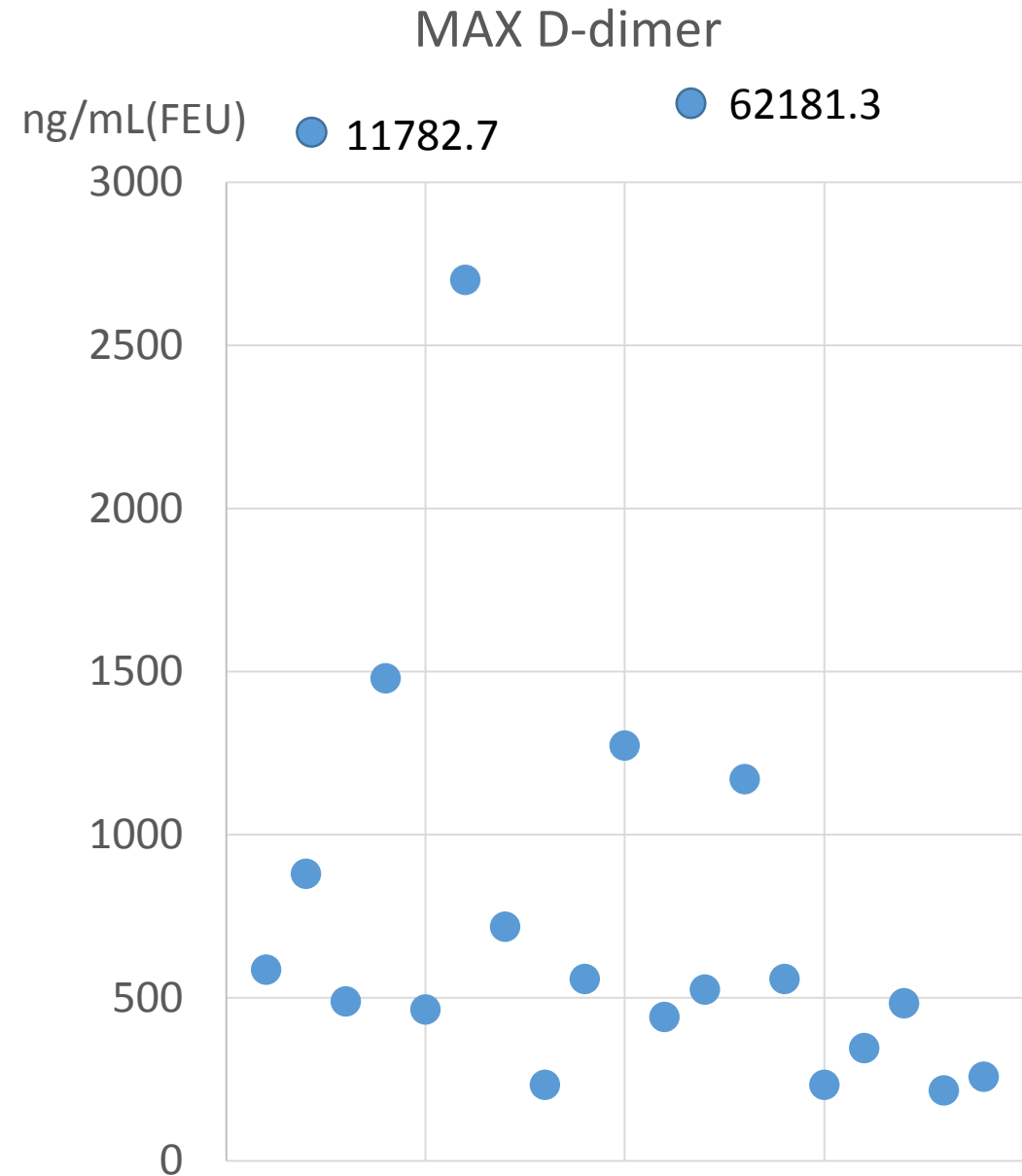
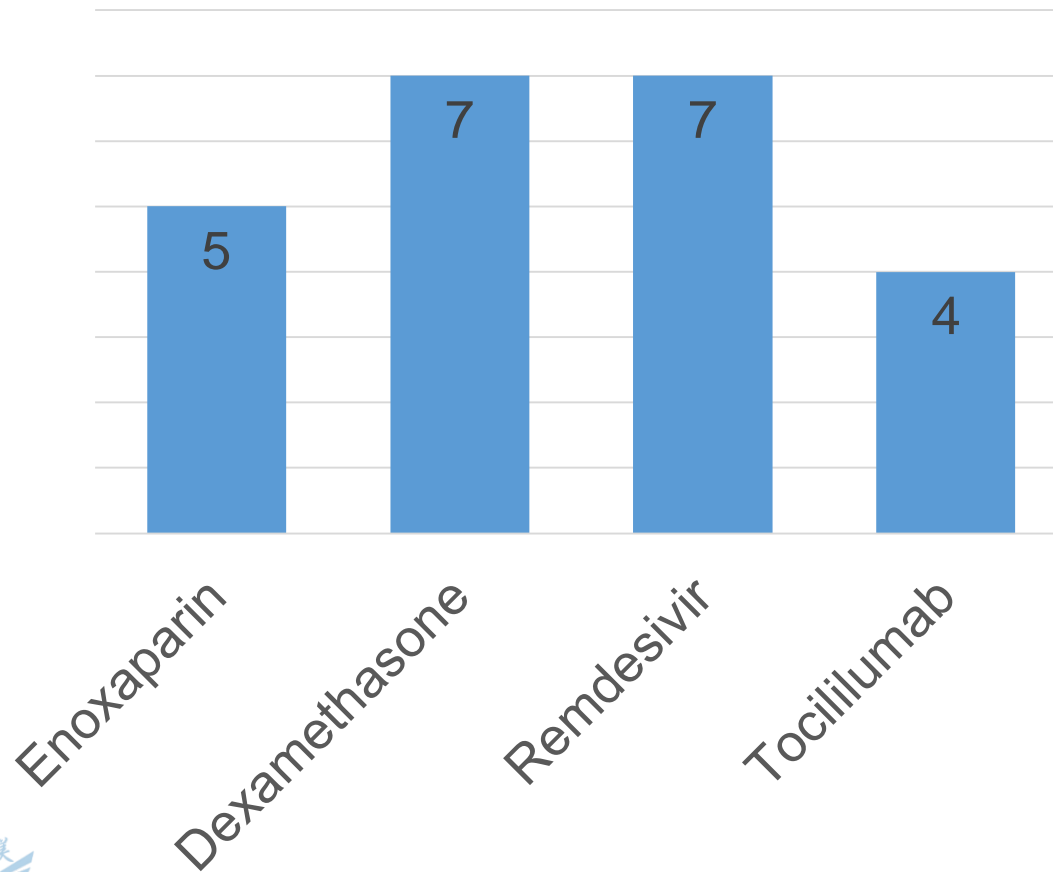
呼吸輔助



N/C:Nasal cannula | HFNC: High flow nasal cannula | CPAP:Continuous positive airway pressure

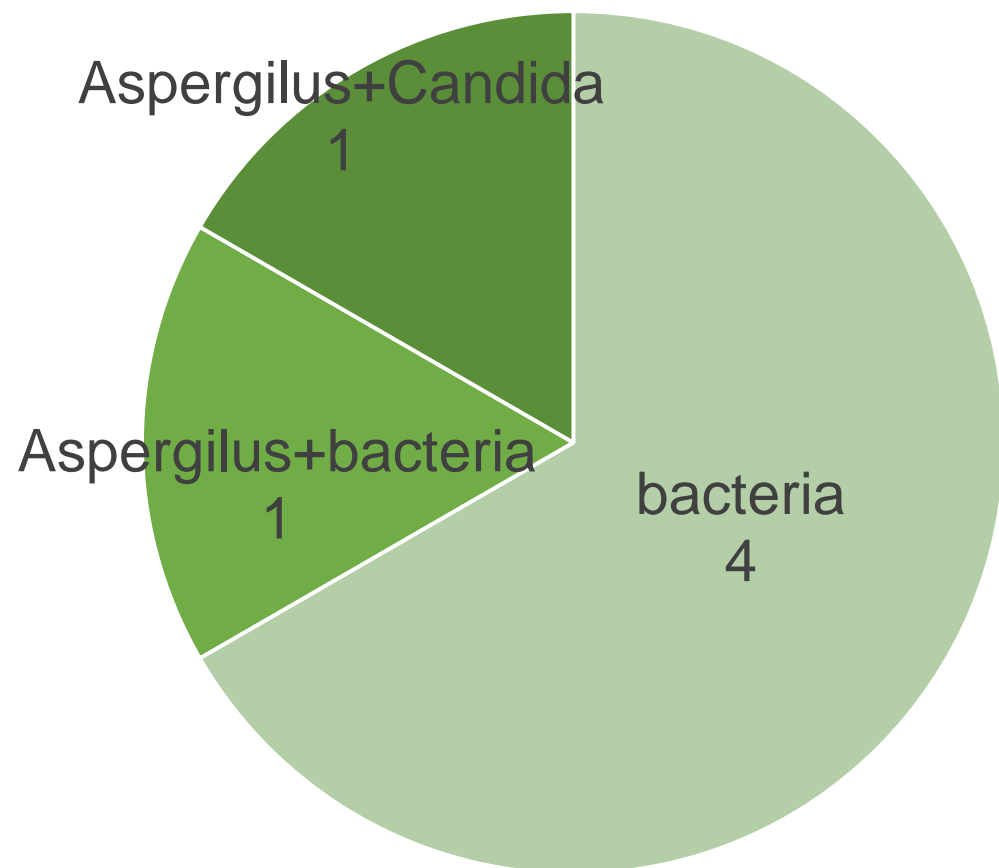
Use of COVID-19 Drugs in Chi-Mei Hospital

臨床處治

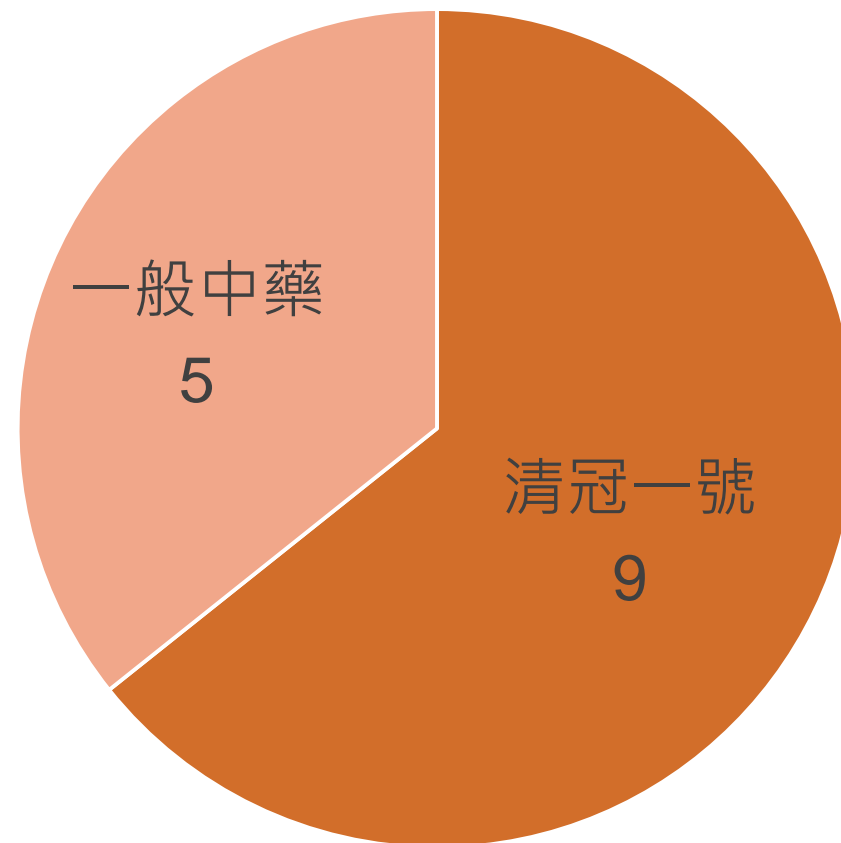


COVID-19 Patients in Chi-Mei Hospital

co-infection
(N=6)



Chinese medicine
(N=14)





Take Home Message

1. There are 3 targets of COVID-19 pharmacotherapy :
Virus 、 Inflammation 、 Coagulation
2. For severe to critical illness, **Dexamethasone** is the most important; Tocilizumab or Baricitinib should be considered for inflammation.
3. **Prophylactic-dose anticoagulation** should be considered in P't with high D-dimer and poor mobility.
4. Traditional Chinese medicine could be a thinkable adjuvant therapy.
5. Treatment of COVID-19 is ever-improving, and information update is important for all medical staff.



Thanks for your attention!