COVID-19社區化呼吸道治療的因應

2023.09.22

台大醫院綜合診療部呼吸診療科

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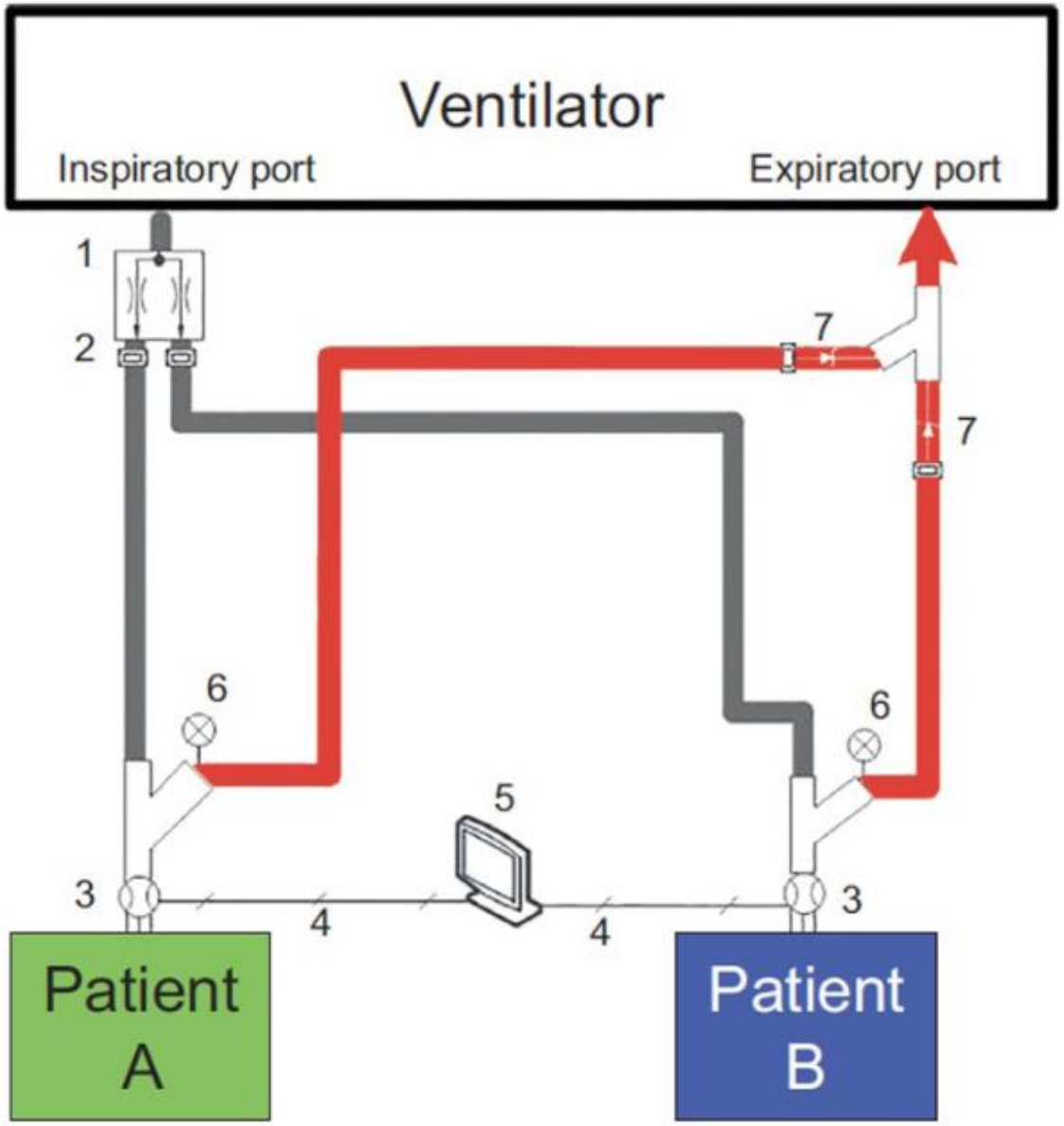
Outlines

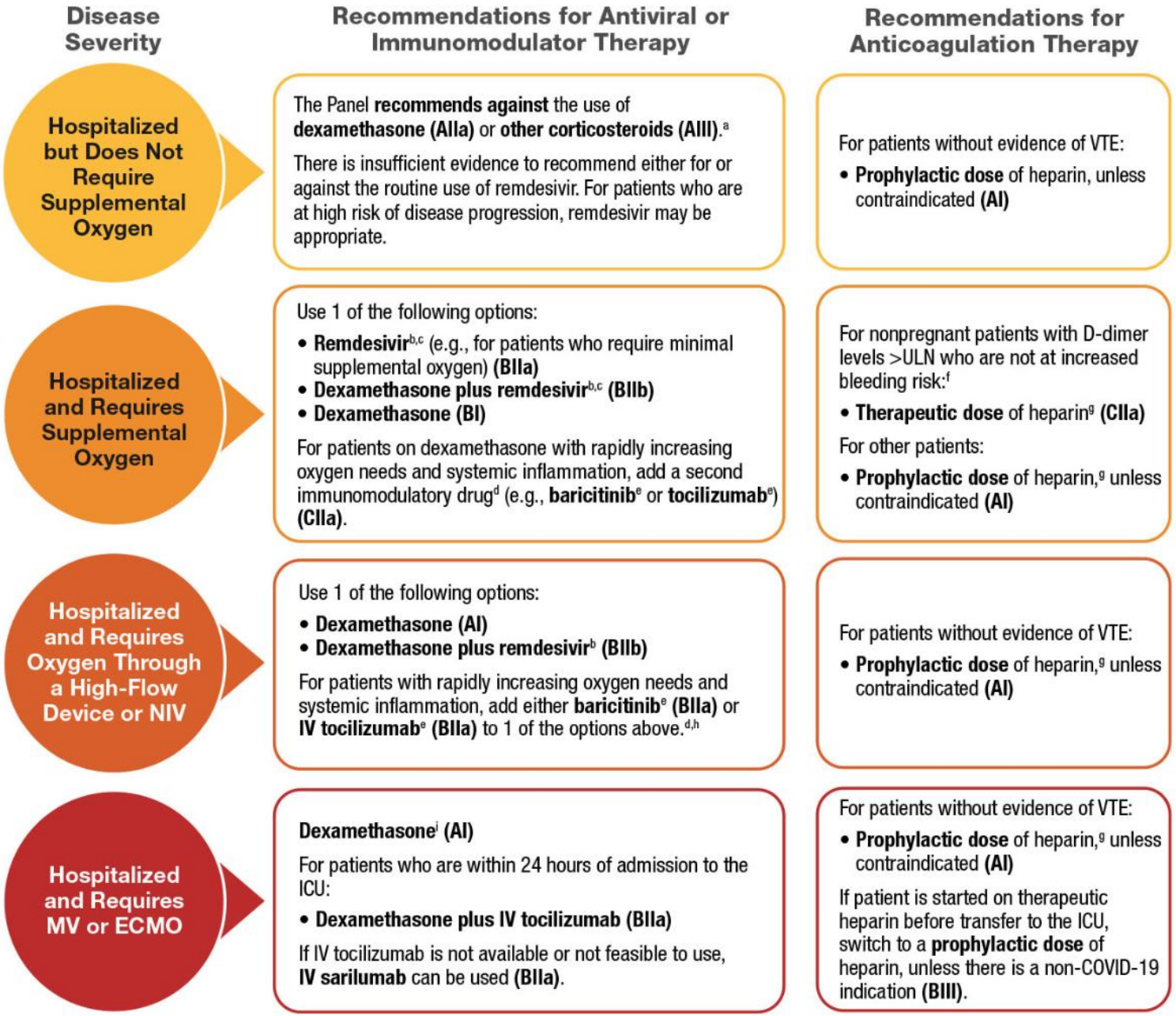
- 前言
- 標準氧氣治療
- 高流量鼻導管& 非侵襲性呼吸器
- 侵襲性呼吸器病人照護
- 病人轉送
- 呼吸治療設備與管路之消毒

Table 1. Cases, hospitalizations, deaths, and vaccinations in the US during the COVID-19 pandemic. On May 31, 2022, 258,586,526 Americans had received at least one dose of vaccine (78% of the population). Data from https://COVID.cdc.gov/COVID-data-tracker

	March 1, 2020	Sept 1, 2020	Peak 2020	March 1, 2021	Sept 1, 2021	March 1, 2022	Peak 2022
New Cases **(7-day average)**	18 7	39,075 42,489	246,614 218,004	61,328 165,742	135,103 134,224	42,498 54,891	475,193 809,496
Hospitalizations – New Admissions (7-day moving average)	unknown	4,067	15,121	5,646	7,103	4,291	22,920
Deaths daily **(7-day moving average)**	0	864	3,425	1,788	1.992	1,788	2,712
Vaccinated Americans > 5 years of age (7-day moving average)	0	0	405,469 (Dec 31)	2,209,444	663,920	285,668	505,271

Shared Ventilation 共用呼吸器




Disease Severity
Recommendations for Antiviral or Immunomodulator Therapy
Recommendations for Anticoagulation Therapy
Hospitalized but Does Not Require Supplemental Oxygen
The Panel recommends against the use of dexamethasone (AIIa) or other corticosteroids (AIII).[a]
There is insufficient evidence to recommend either for or against the routine use of remdesivir. For patients who are at high risk of disease progression, remdesivir may be appropriate.
For patients without evidence of VTE:
• Prophylactic dose of heparin, unless contraindicated (AI)
Hospitalized and Requires Supplemental Oxygen
Use 1 of the following options:
• Remdesivir[b,c] (e.g., for patients who require minimal supplemental oxygen) (BIIa)
• Dexamethasone plus remdesivir[b,c] (BIIb)
• Dexamethasone (BI)
For patients on dexamethasone with rapidly increasing oxygen needs and systemic inflammation, add a second immunomodulatory drug[d] (e.g., baricitinib[e] or tocilizumab[e]) (CIIa).
For nonpregnant patients with D-dimer levels >ULN who are not at increased bleeding risk:[f]
• Therapeutic dose of heparin[g] (CIIa)
For other patients:
• Prophylactic dose of heparin,[g] unless contraindicated (AI)
Hospitalized and Requires Oxygen Through a High-Flow Device or NIV
Use 1 of the following options:
• Dexamethasone (AI)
• Dexamethasone plus remdesivir[b] (BIIb)
For patients with rapidly increasing oxygen needs and systemic inflammation, add either baricitinib[e] (BIIa) or IV tocilizumab[e] (BIIa) to 1 of the options above.[d,h]
For patients without evidence of VTE:
• Prophylactic dose of heparin,[g] unless contraindicated (AI)
Hospitalized and Requires MV or ECMO
Dexamethasone[i] (AI)
For patients who are within 24 hours of admission to the ICU:
• Dexamethasone plus IV tocilizumab (BIIa)
If IV tocilizumab is not available or not feasible to use, IV sarilumab can be used (BIIa).
For patients without evidence of VTE:
• Prophylactic dose of heparin,[g] unless contraindicated (AI)
If patient is started on therapeutic heparin before transfer to the ICU, switch to a prophylactic dose of heparin, unless there is a non-COVID-19 indication (BIII).

COVID-19傳播途徑

Particle	SARS-CoV-2 transmission	Precautions
Droplets >5 μm	1) Produced by cough or sneeze. 2) Vulnerable mucosa infected by droplets. 3) Close contact within 1 m. 4) Direct or indirect physical contact with pathogens from patients' secretions.	Droplet and contact
Aerosol ≤5 μm	1) AGMPs (induced and mechanical type). 2) Fomites formed by toilet flushing. 3) Deposition and resuspension. 4) Respirable particle aerosols via natural respiratory activities	Airborne

AGMP: aerosol-generating medical procedures.

Wang et al. Respir Med. 2021 Sep;186:106516.

COVID患者之呼吸治療

立即對呼吸窘迫，低血氧症或休克的患者給予氧氣治療，使其 $SpO_2 \geq 94\%$。

- 開始建議給予 5 L / min 氧氣治療並適時調整流速
- 病人穩定後，目標血氧飽和度為：

  (1) 非懷孕之成年患者 $SpO_2 \geq 90\%$

  (2) 懷孕患者 $SpO_2 \geq 92–95\%$

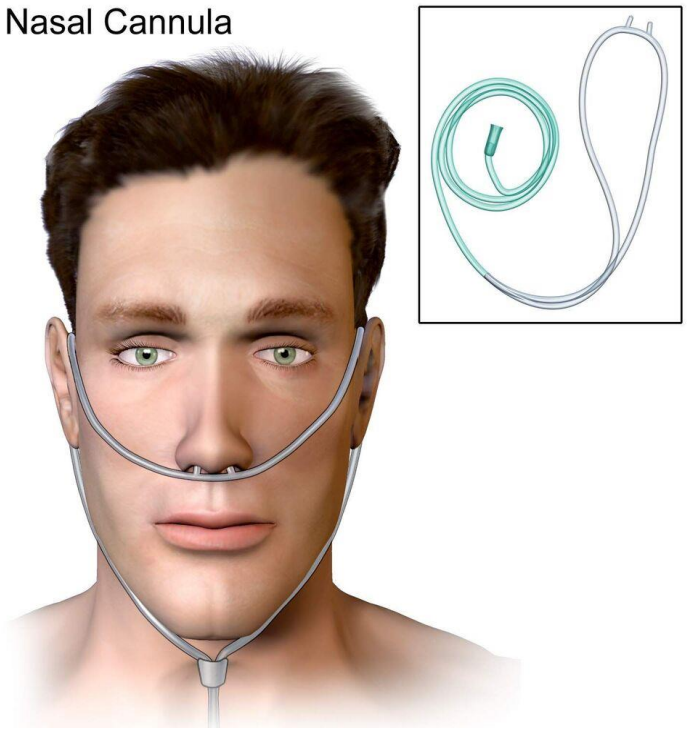
  (3) 出現危急徵候的兒童應在救治過程中 $SpO_2 \geq 94\%$

  (4) 無危急徵候之兒童則應達 $SpO_2 \geq 90\%$
- 住院患者進行照護的所有診療區域均應配備脈搏血氧儀

新型冠狀病毒（SARS-CoV-2）感染臨床處置指引
2023年7月28日 第二十四版

SUPPLEMENTAL OXYGEN

- **Nasal cannula**



- Up to ~6 liters per minute (LPM) flow
- Consider humidification at 4-6 LPM if longer term
- Roughly 4% FiO_2 increase per LPM (highly dependent on minute ventilation)
- Wearing a procedure mask over the nasal cannula is recommended for patients with COVID-19 when in close contact with healthcare providers.

SUPPLEMENTAL OXYGEN

- **Simple mask**

- provide supplemental oxygen with flow rates up to approximately 5–10 L/min. FiO_2 < ~50%
- Respiratory rate and exhalation are controlled by the patient and these individually affect the actual FiO2 delivered.

SUPPLEMENTAL OXYGEN

- **Non-rebreathing masks（非循環呼吸面罩 ）**

- provide supplemental oxygen up to a level of approximately 90% at flow rates approaching 15 L/min.
- reservoir bag must remain inflated at all times; this requires flow rates of at least 8–10 L/min.

高流量鼻導管& 非侵襲性呼吸器

COVID患者之呼吸治療

當標準氧氣治療無效，患者出現嚴重的低血氧性呼吸衰竭時，需及時介入給予進一 步的呼吸支持。

可考慮

- 使用高流量鼻導管(high-flow nasal oxygen, HFNO)給氧，防護措施等同執行可能產生飛沫微粒(aerosol)之醫療處置並應密切監視患者臨床狀況變化
- 非侵襲性呼吸 器(non-invasive ventilation, NIV)則須由醫師判斷後依臨床狀況使用

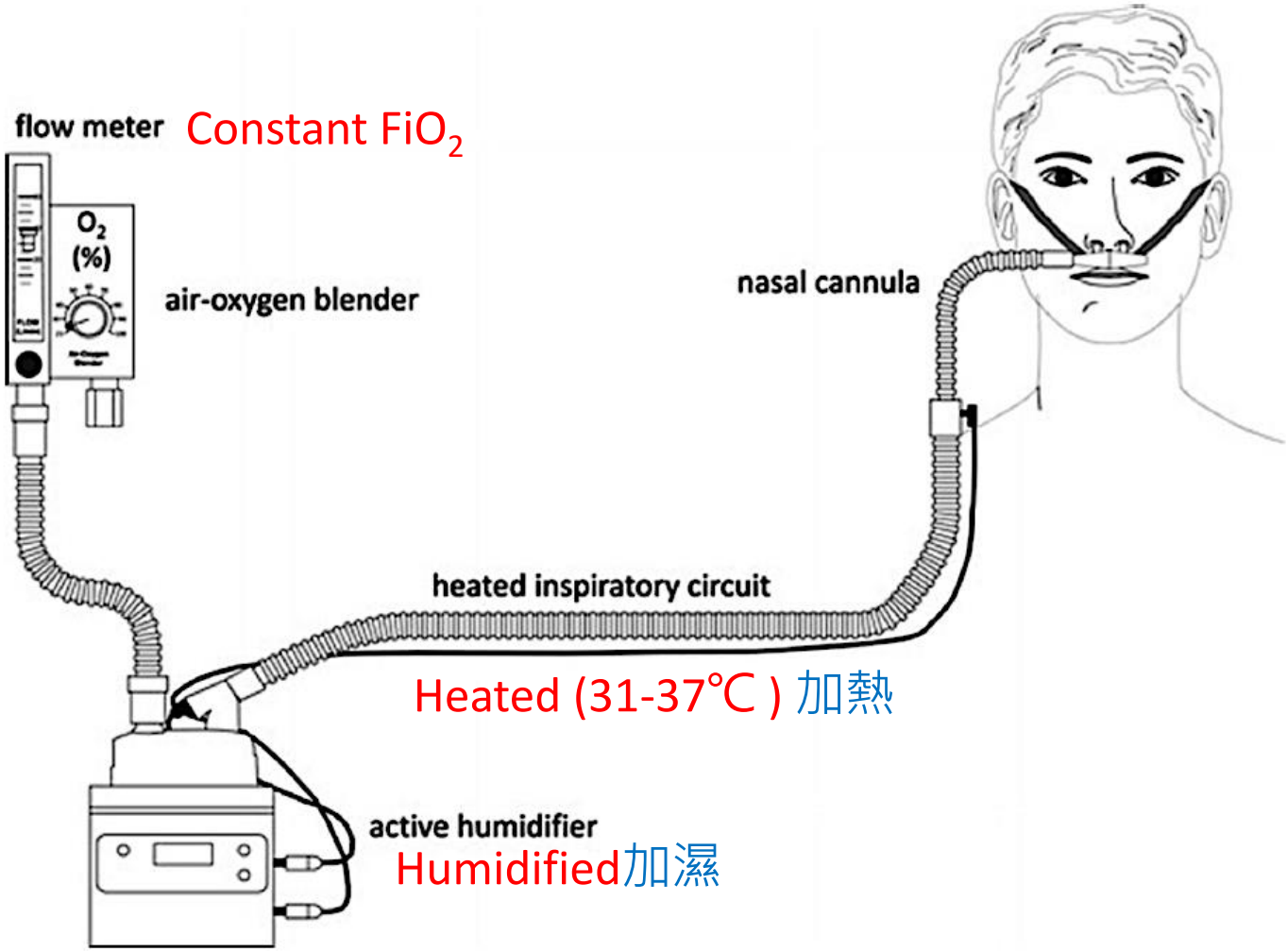
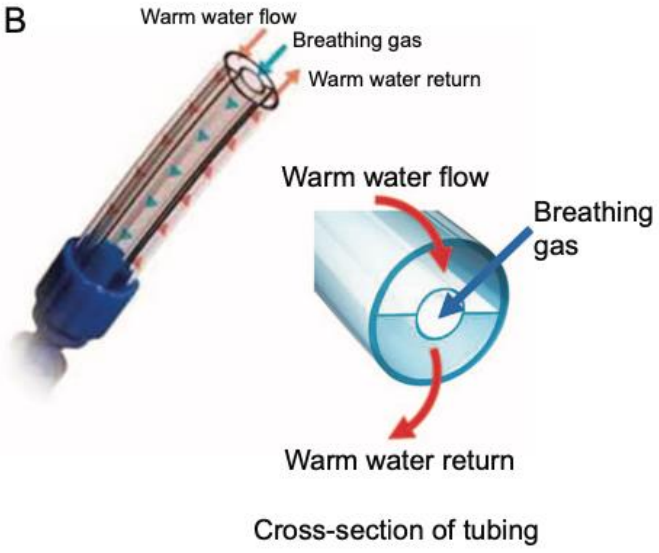
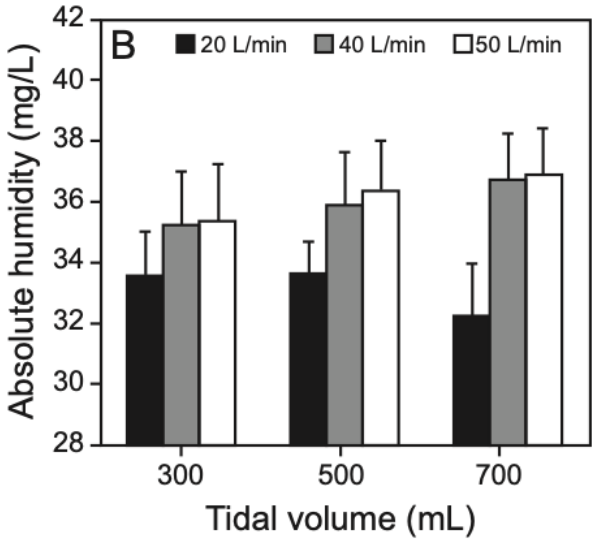


Fig. 1 High-flow nasal cannula oxygenation (HFNCO) device. An air/oxygen blender, allowing FiO_2 ranging from 0.21 to 1.0, generates flows of up to 60 L/min. The gas is heated and humidified by an active heated humidifier and delivered via a single limb

Papazian et al. Intensive Care Med . 2016 Sep;42(9):1336-49.

管路外圈包覆隔熱圈





Nishimura et al. Respir Care . 2019 Jun;64(6):735-742.

High-flow device: at least 60 L/min total flow

(peak inspiratory flow rate about three times the minute ventilation)

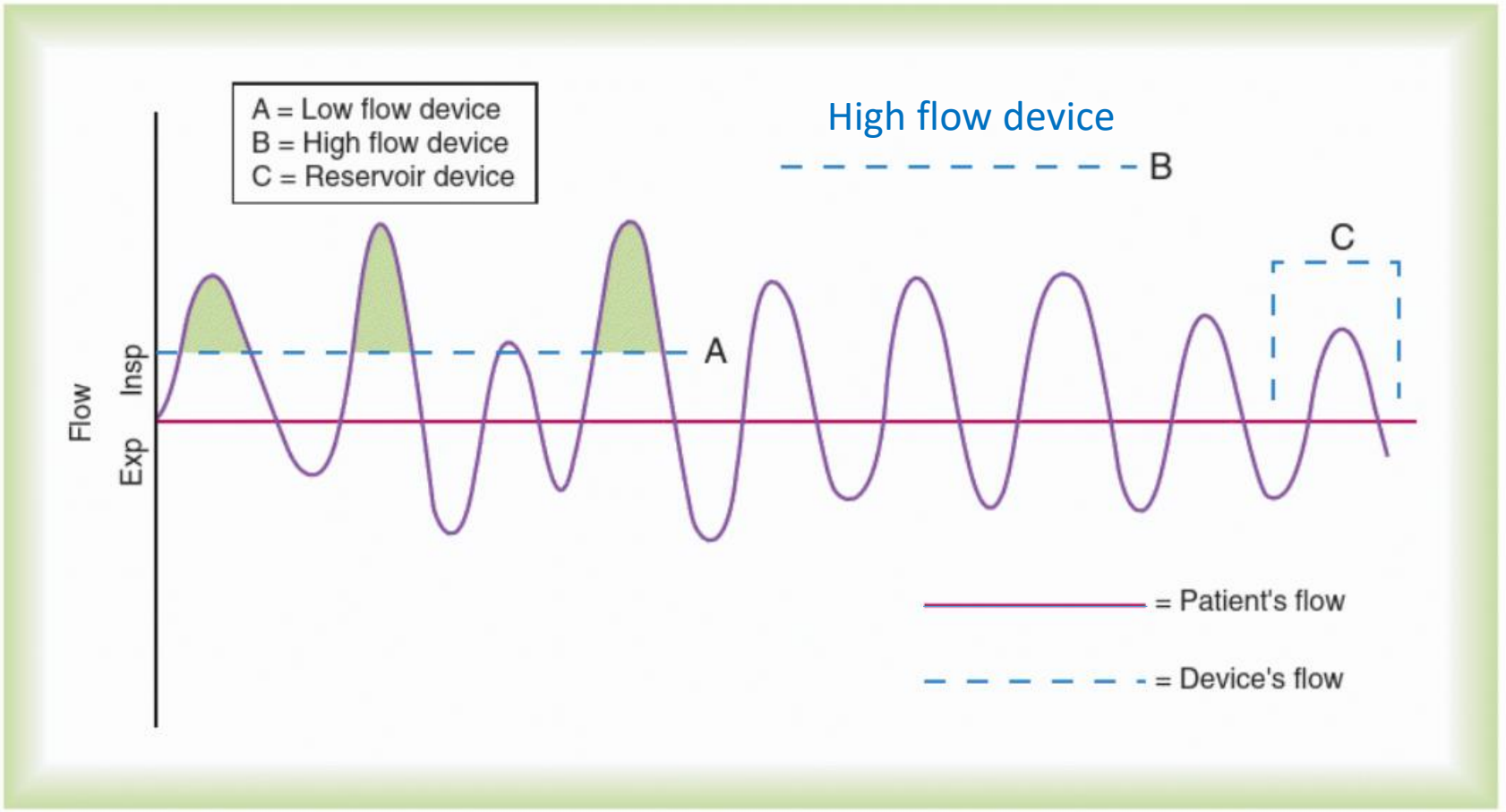


FIGURE 41-4 Differences between O_2 delivery systems. *A*, Low-flow device. *B*, High-flow device. *C*, Reservoir device.

Egan's fundamentals of respiratory care 11th edition

absolute humidity 絕對濕度

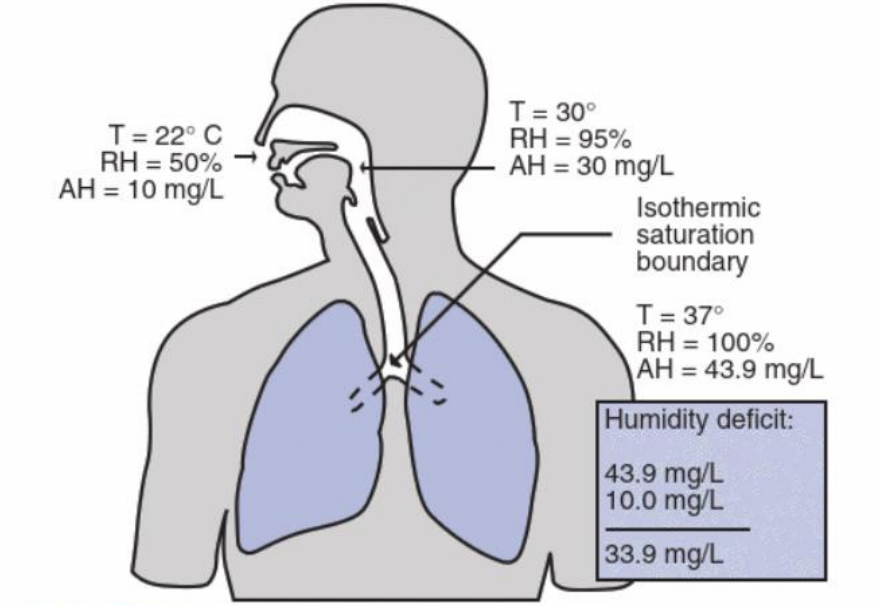


FIGURE 38-1 As a person breathes typical ambient air, the upper airway adds 20 mg/L of water vapor and the lower airway adds 13.9 mg/L. If all of that humidity were exhaled, this would represent a 33.9 mg/L humidity deficit. *AH,* Absolute humidity; *RH,* relative humidity; *T,* temperature. (From Fink J: Humidity and aerosol therapy. In Cairo J, Pilbeam S, editors: Mosby's respiratory equipment, ed 8, St. Louis, 2010, Mosby.)

Heat and moisture exchange: primary function of upper respiratory tract , esp **nose**

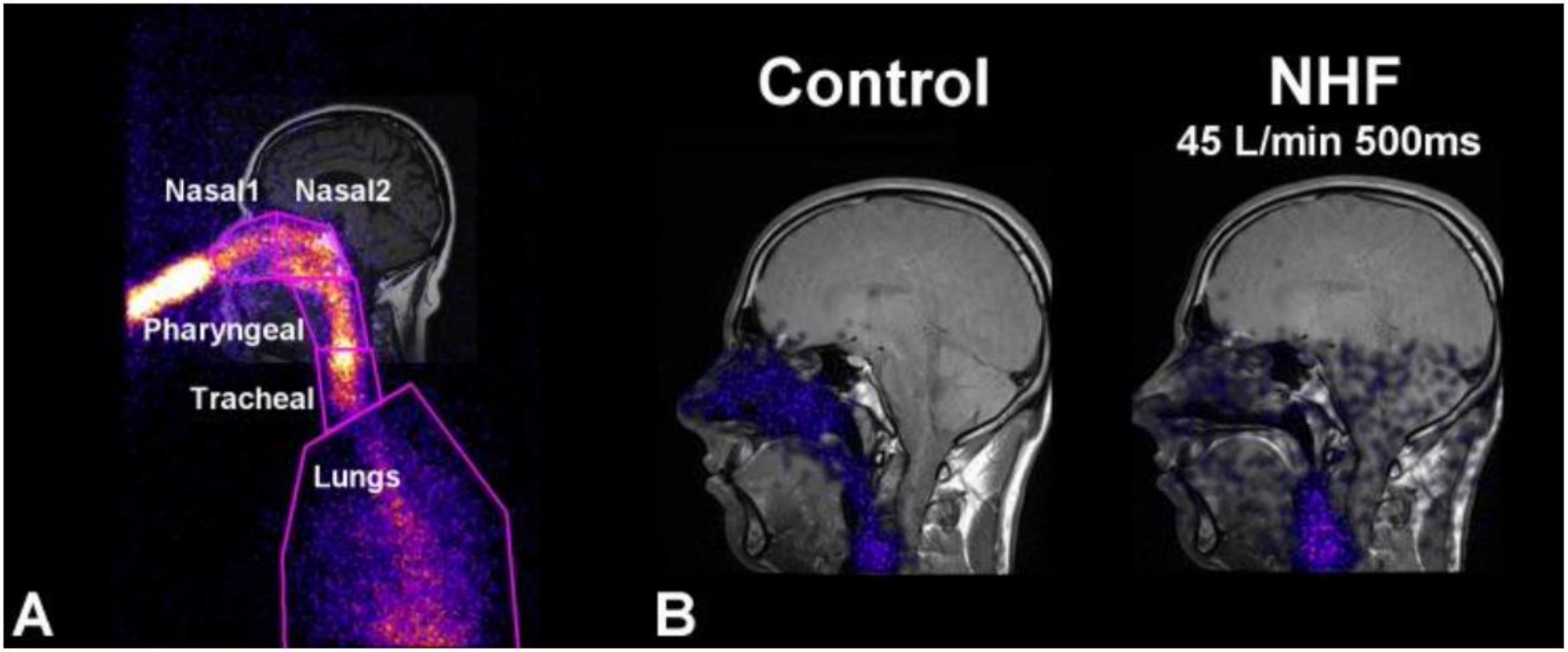
Dry medical gases (> 4 L/min) to upper airway causes immediate heat and water loss

Humidification therapy

- Humidifying dry medical gases: ensuring normal function of the **mucociliary clearance**

Egan's fundamentals of respiratory care 11th edition

Decrease in Anatomical **Dead Space** (about 50 ml) in less than 1 second



Möller et al. J Appl Physiol. 2015 Jun 15; 118(12): 1525–1532.
Möller et al. J Appl Physiol. 2017 Jan 1; 122(1): 191–197.

Physiologic effect of HFNO

Mechanism	Clinical benefits
loose-fitting nasal prongs	Enhance comfort
High flow rate	Maintenance of **constant FiO_2**
Heat and humidification	Improved **Mucociliary Clearance; Enhanced comfort**
Generation of a **Low PEEP** (**3-5 cmH_2O, by flow rate and mouth open/closed**	Counterbalance auto-PEEP; Decreased work of breathing
Decrease in Anatomical **Dead Space** (**50ml, and a small decrease in PaCO2**)	Improved efficiency of ventilation; Enhanced oxygen delivery

Spoletini et al. Chest . 2015 Jul;148(1):253-261.
Helviz et al. Crit Care. 2018 Mar 20;22(1):71.

High-flow Nasal oxygen

由於有可能增加病毒氣溶膠 (aerosol) 產生，增加病毒傳播可能性，醫療人 員應穿戴高效過濾口罩 (N95 或相當等級[含]以上口罩)、 戴手套、防水隔 離衣、配戴護目裝備、髮帽;且應在負壓病室或換氣良好獨立房間，來照顧 使用高流量鼻導管的新冠肺炎病人

新型冠狀病毒（SARS-CoV-2）感染臨床處置暫行指引
台灣胸腔暨重症加護醫學會 編輯 2020年5月4日 第二版

Figure 4. Patient wearing procedural mask over high flow nasal cannula to minimize aerosol dispersion.

密切監視HFNO患者臨床狀況

$$\text{ROX Index} = \frac{SPO_2/FIO_2}{\text{Respiratory Rate}}$$

Respiratory rate - OXygenation

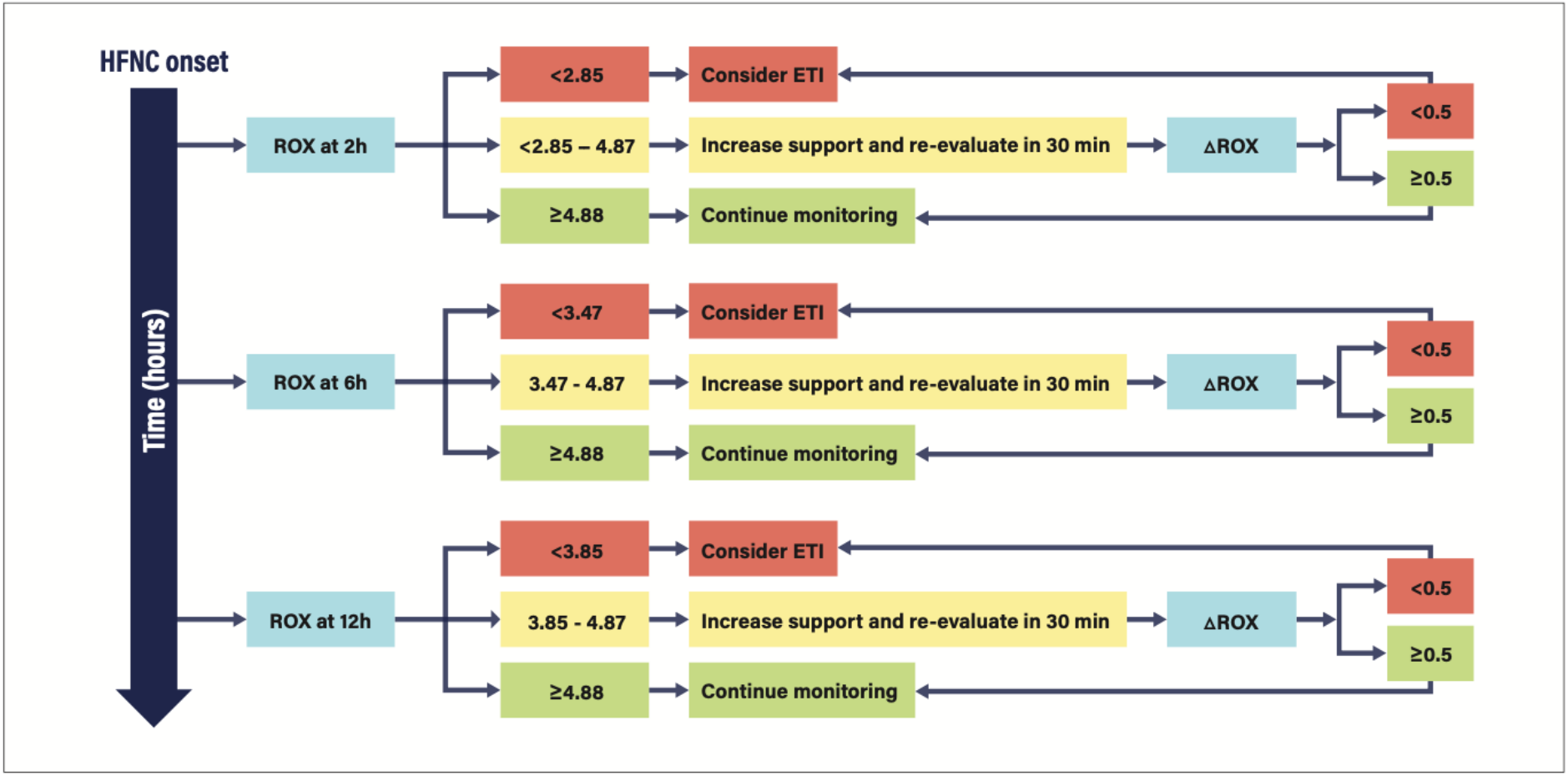
ROX Index = $\frac{SpO_2/FiO_2}{RR}$				
Time post intervention	2 hours	6 hours	12 hours	All times
ROX Index	< 2.85	< 3.47	< 3.85	> 4.88
Decision	Intubate	Intubate	Intubate	Observe

- 須密切監測呼吸速率、血氧及呼吸型態
- 若無明顯效果，應考慮及早插管

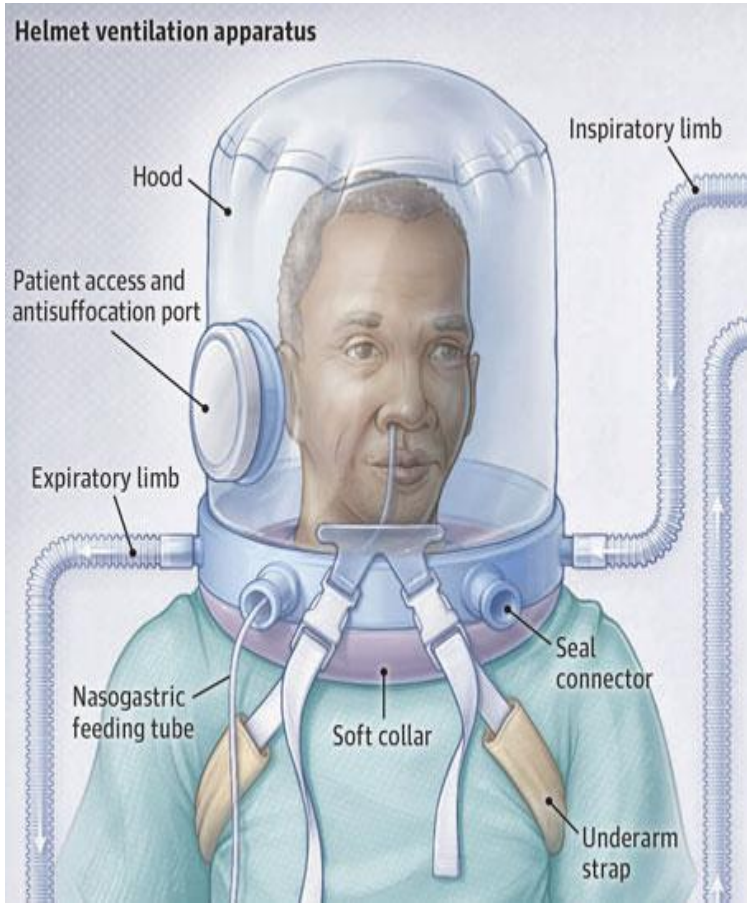
- 流量60 LPM且持續需FiO2 >60%上升
- 1-2 小時內病人 惡化 P/F < 150 mmHg
- 呼吸窘迫持續加重
- 合併其他器官功能不全

$$\text{ROX Index} = \frac{SPO_2/FIO_2}{\text{Respiratory Rate}}$$

Respiratory rate - OXygenation



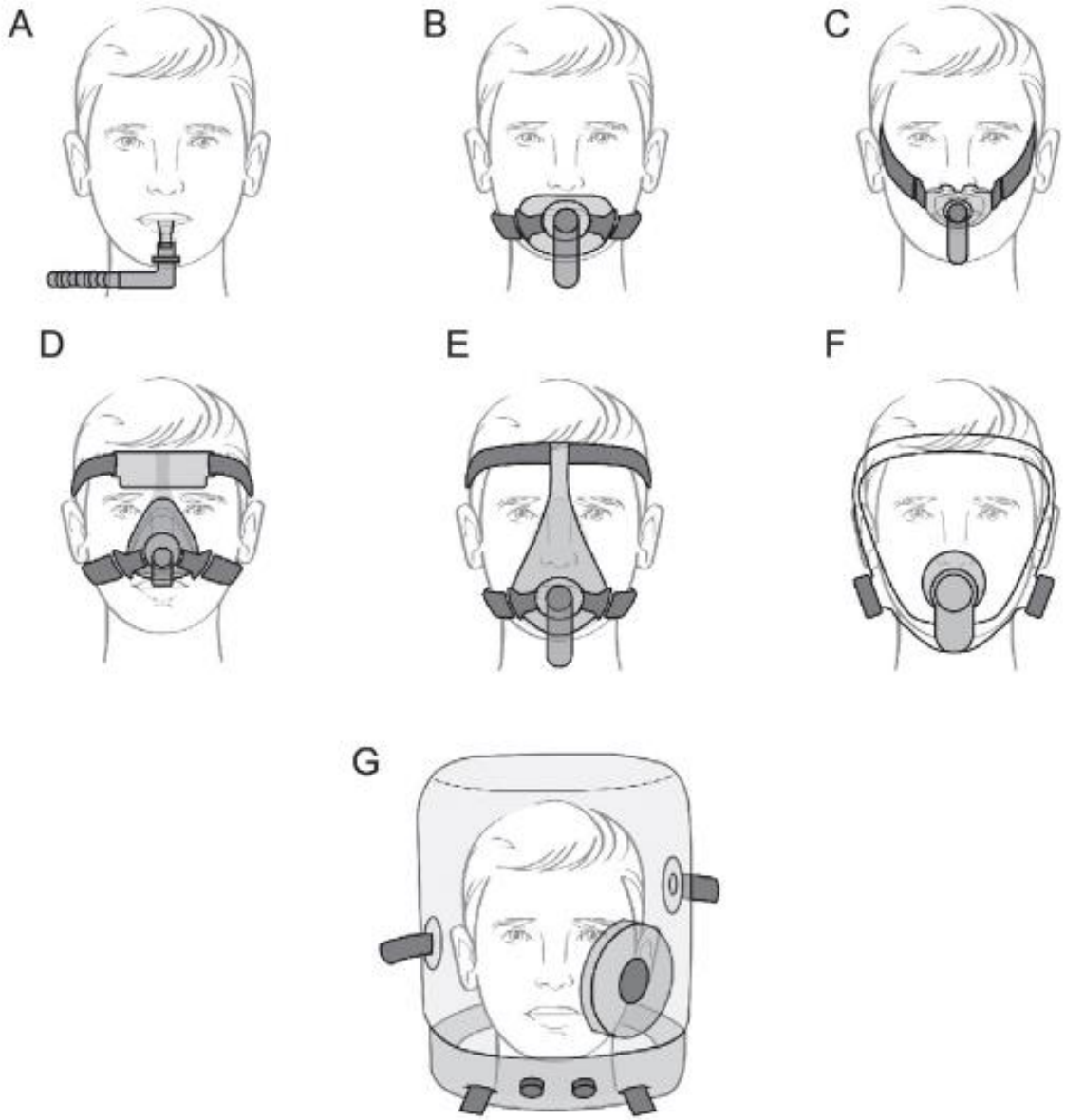
非侵襲性呼吸 器
(non-invasive ventilation, NIV)



非侵襲性正壓呼吸器 (NIPPV)

適用於：

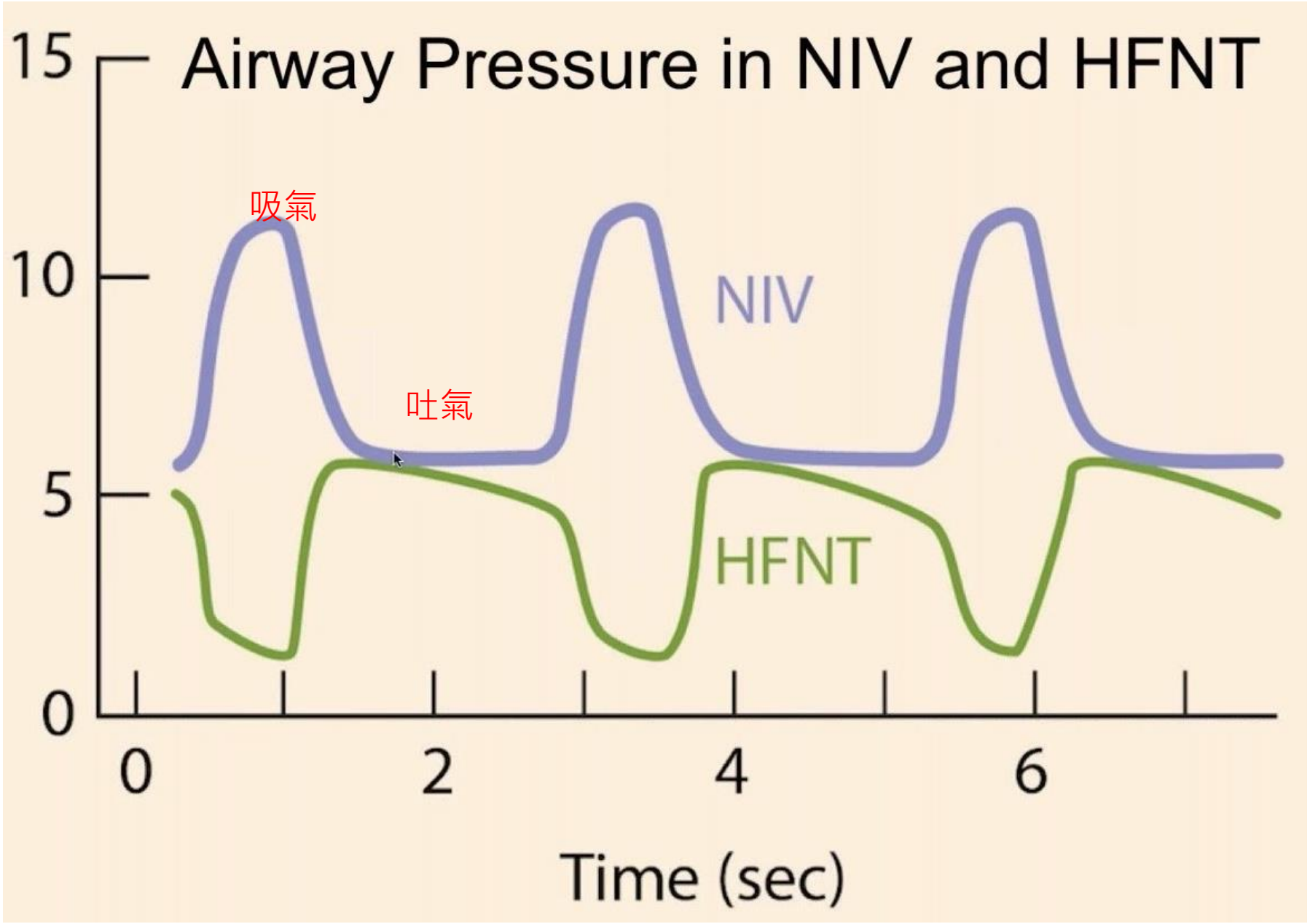
- 慢性阻塞性肺病急性惡化合併高二氧化碳性呼吸衰竭
- 心因性肺水腫
- 對於使用HFNC失敗，可能提供比較好的呼吸輔助
- 拔管後呼吸急促的病人
- 建議在負壓隔離室或單人病室內使用
- 要有生理監視設備
- 不可因使用而延遲氣管內插管



Oronasal mask or total face mask are preferred over a nasal interface
in the setting of COVID-19 due to the risk of bioaerosol dispersion with mouth leak

NIPPV vs. HFNO

	NIPPV	HFNO
Circuit	Close; single or double	Open, single-heated
Heat	Variable	31-37℃
Humidity	Variable	Saturated
Pressure	Pre-set Insp and Exp	Variable
Flow	Variable (max ~200 L/min)	30-60 L/min (continuous)
Oxygen	Bled-in or blender	Blender (0.21-1)

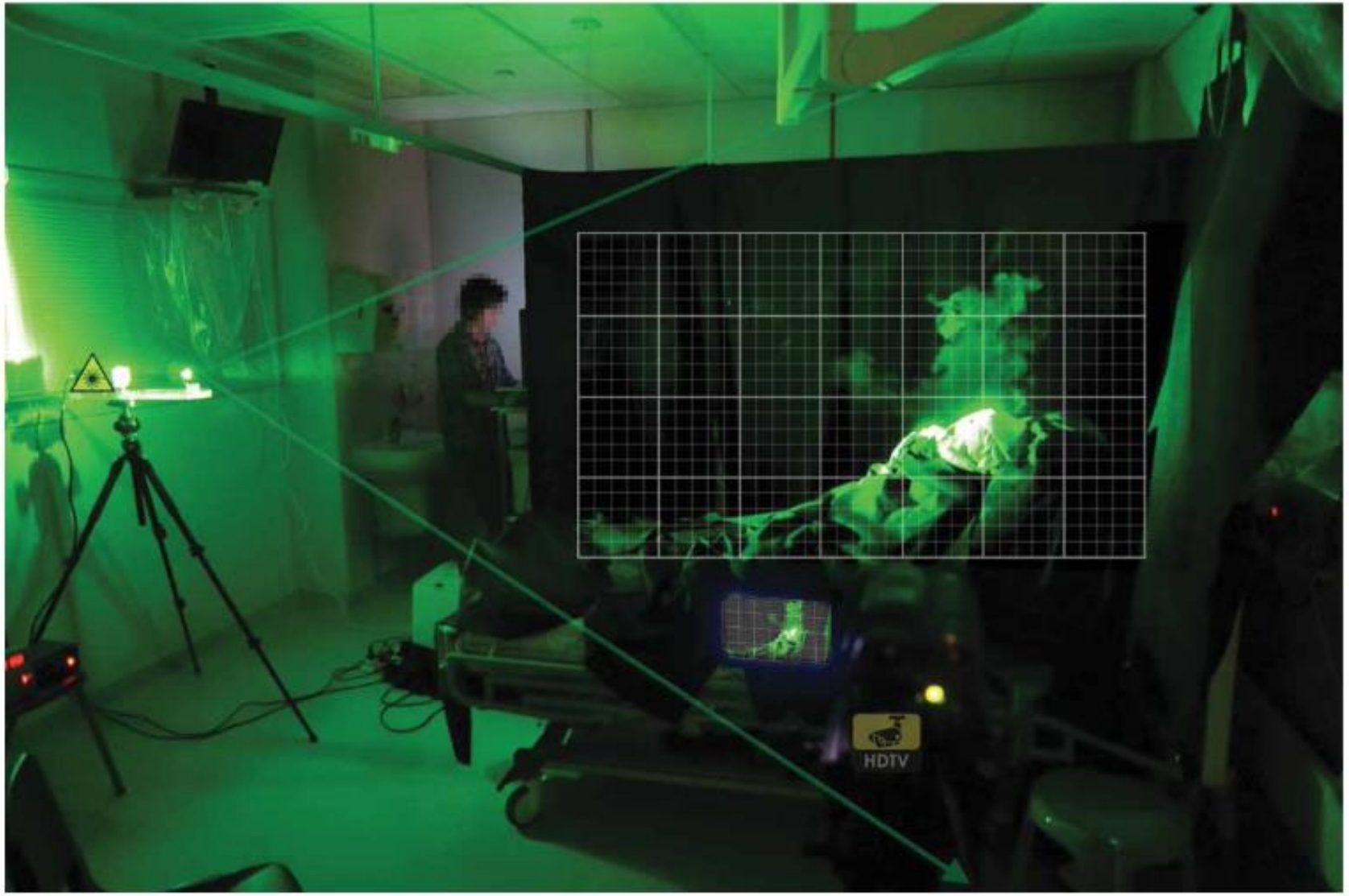

Airway Pressure in NIV and HFNT
15
10
5
0
吸氣
吐氣
NIV
HFNT
0
2
4
6
Time (sec)

COVID-19 transmission

- HFNC was avoided at the beginning of the SARS CoV-2 pandemic in favor of **early intubation** for fear of disease transmission by exhaled aerosol
- **Patient's outcome** vs. **healthcare worker safety**
- Large observational studies suggest that patients with COVID-19-associated ARDS have similar respiratory system mechanics to patients with ARDS from other causes (COVID-19-associated ARDS is **ARDS**)

Fan et al. Lancet Respir Med . 2020 Aug;8(8):816-821.

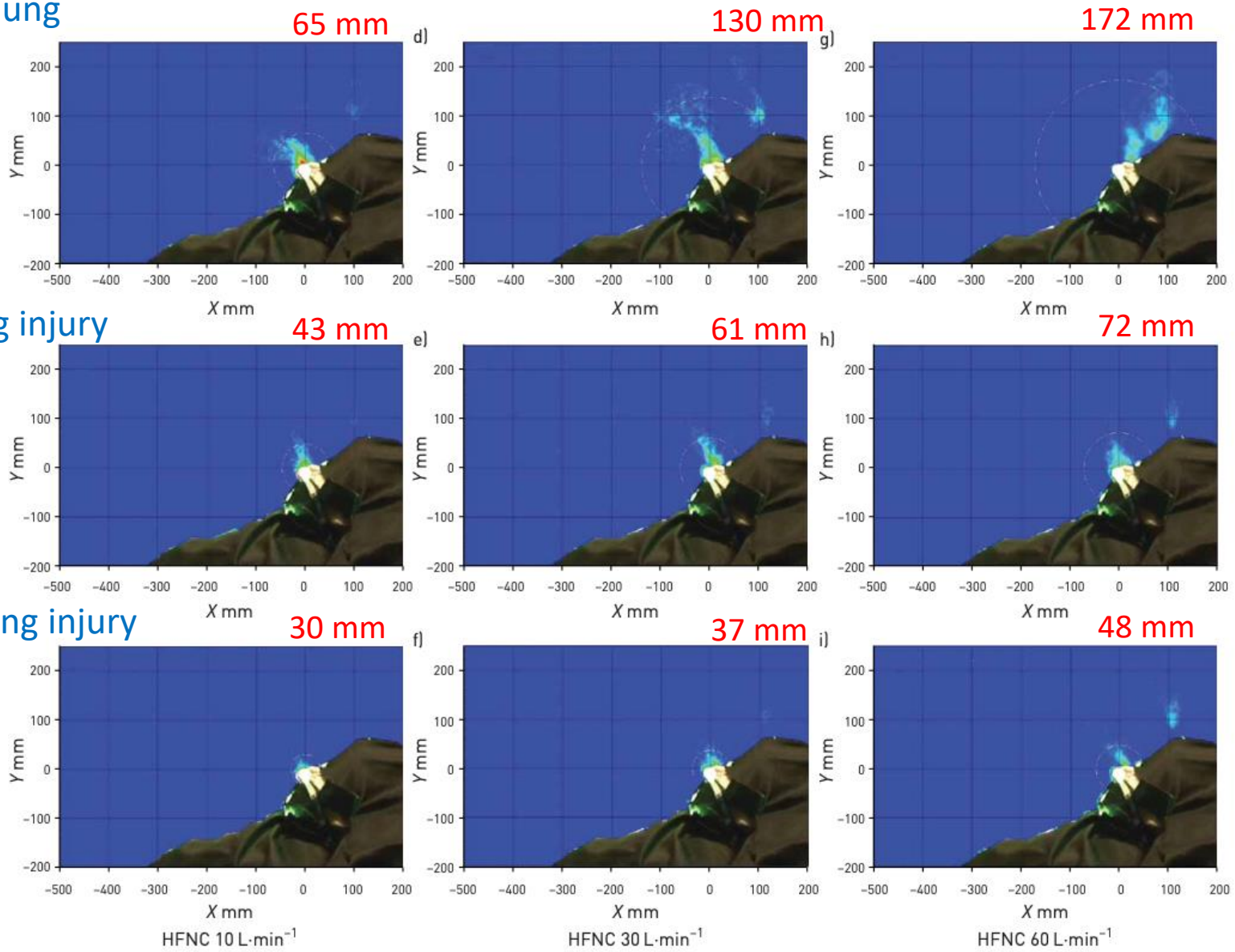
Attaway et al. BMJ . 2021 Mar 10;372:n436.



Hui et al. Eur Respir J . 2019 Apr 11;53(4):1802339.

HFNC 10 L/min 30 L/min 60 L/min

Normal lung



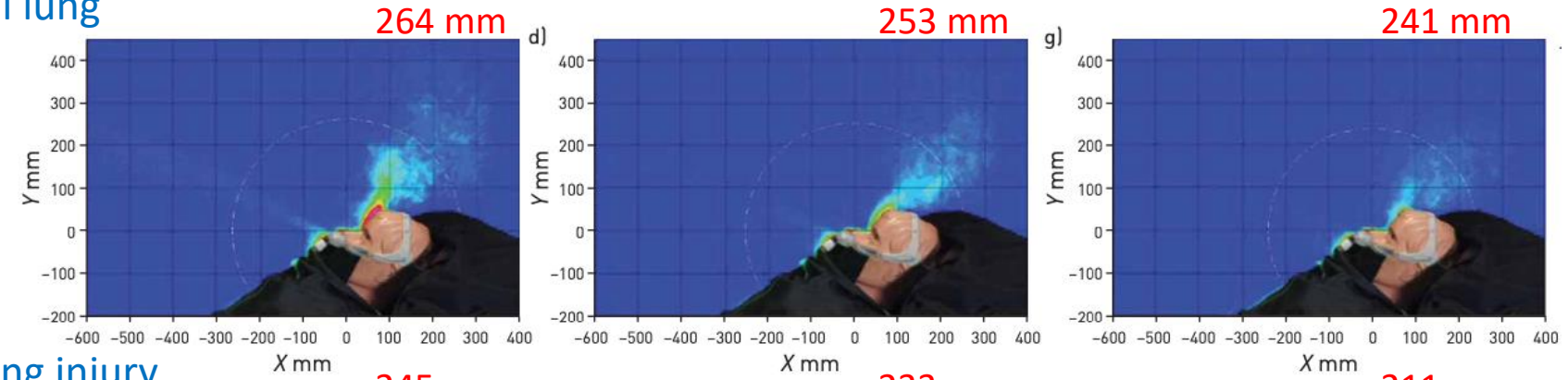
Mild lung injury

Severe lung injury

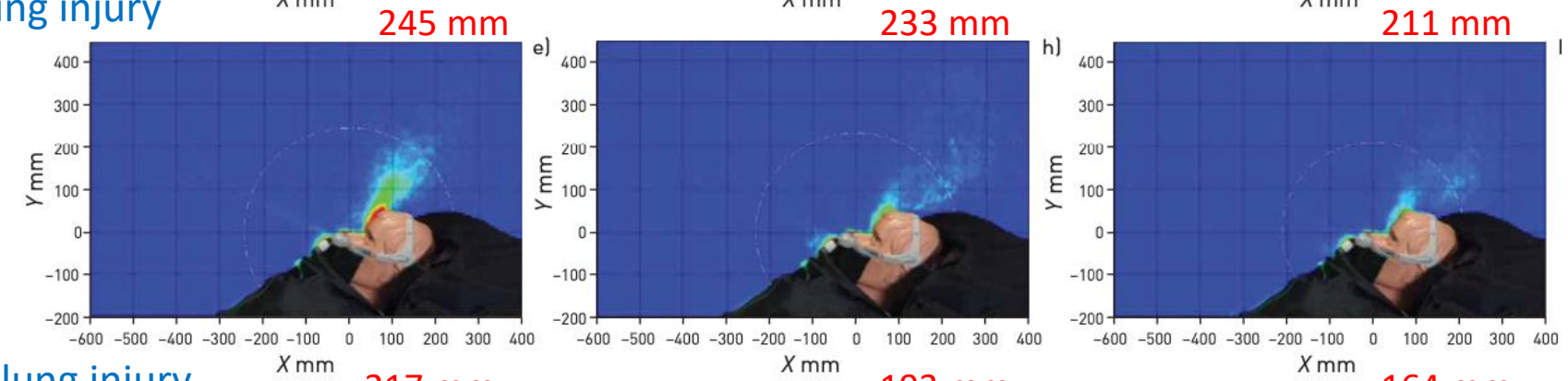
Hui et al. Eur Respir J . 2019 Apr 11;53(4):1802339.

CPAP 20 cmH_2O 15 cmH_2O 10 cmH_2O

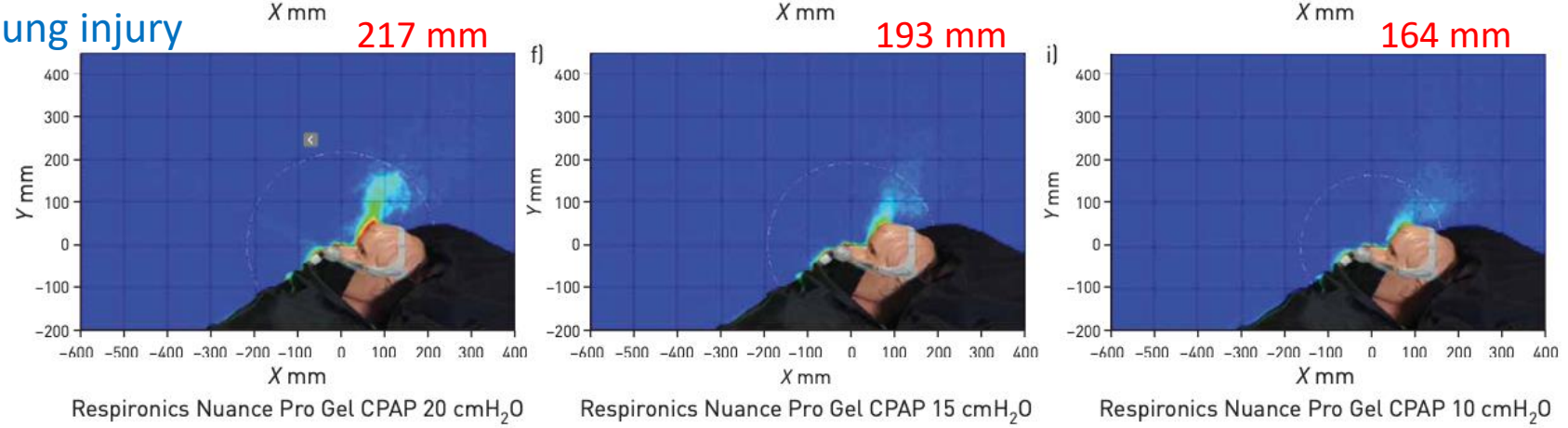
Normal lung



Mild lung injury



Severe lung injury



Hui et al. Eur Respir J. 2019 Apr 11;53(4):1802339.

TABLE 1 Summary of exhaled smoke dispersion distances with different oxygen devices

Oxygen device	Flow rate L·min^{-1}	Dispersion distance cm
HFNC	60	17.2±3.3
	30	13.0±1.1
	10	6.5±1.5
Simple mask	15	11.2±0.7
	10	9.5±0.6
Non-rebreathing mask	10	24.6±2.2
Venturi mask at F_{IO_2} 0.4	6	39.7±1.6
Venturi mask at F_{IO_2} 0.35	6	27.2±1.1

Li et al. ur Respir J 2020; 55: 2000892.

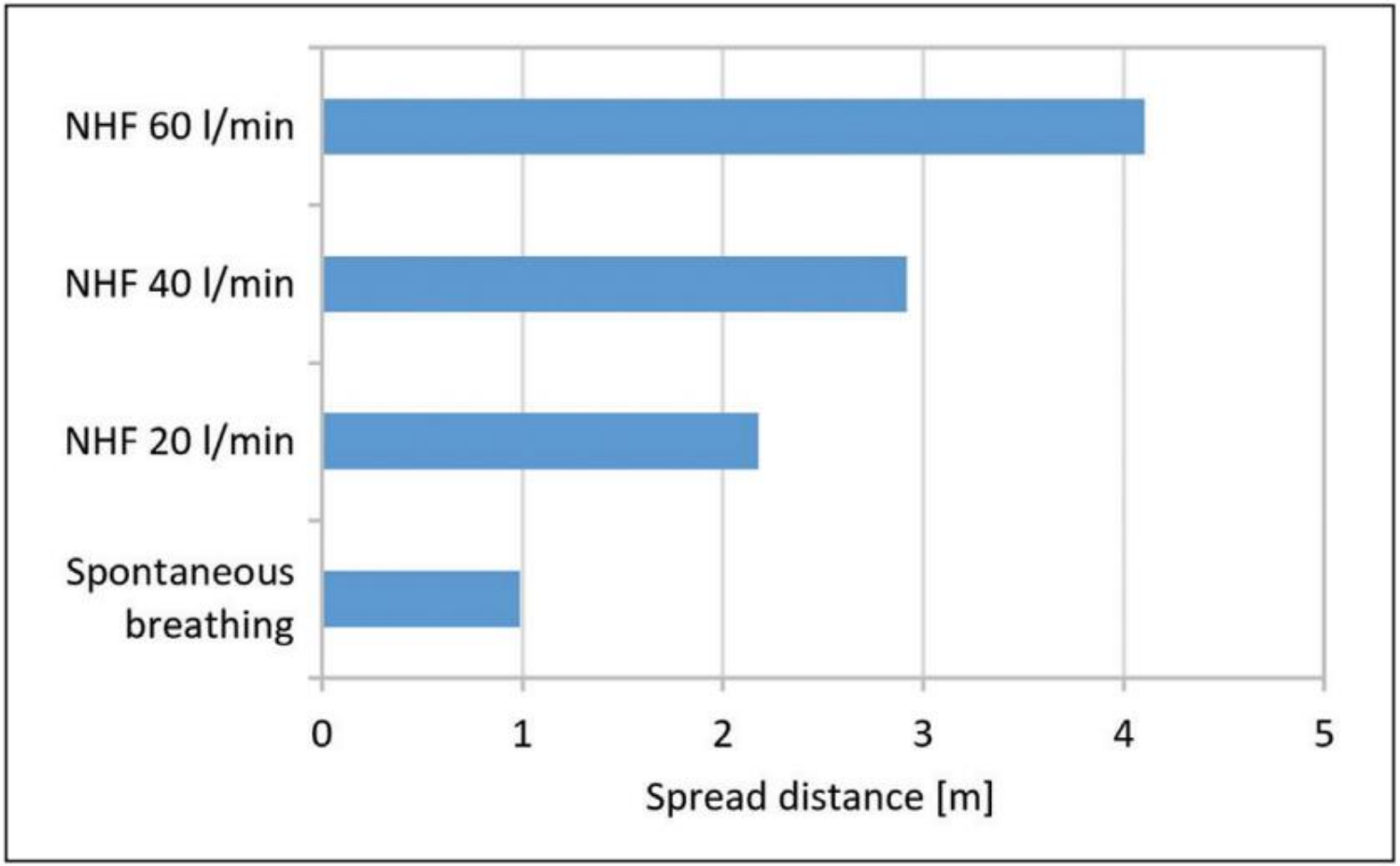
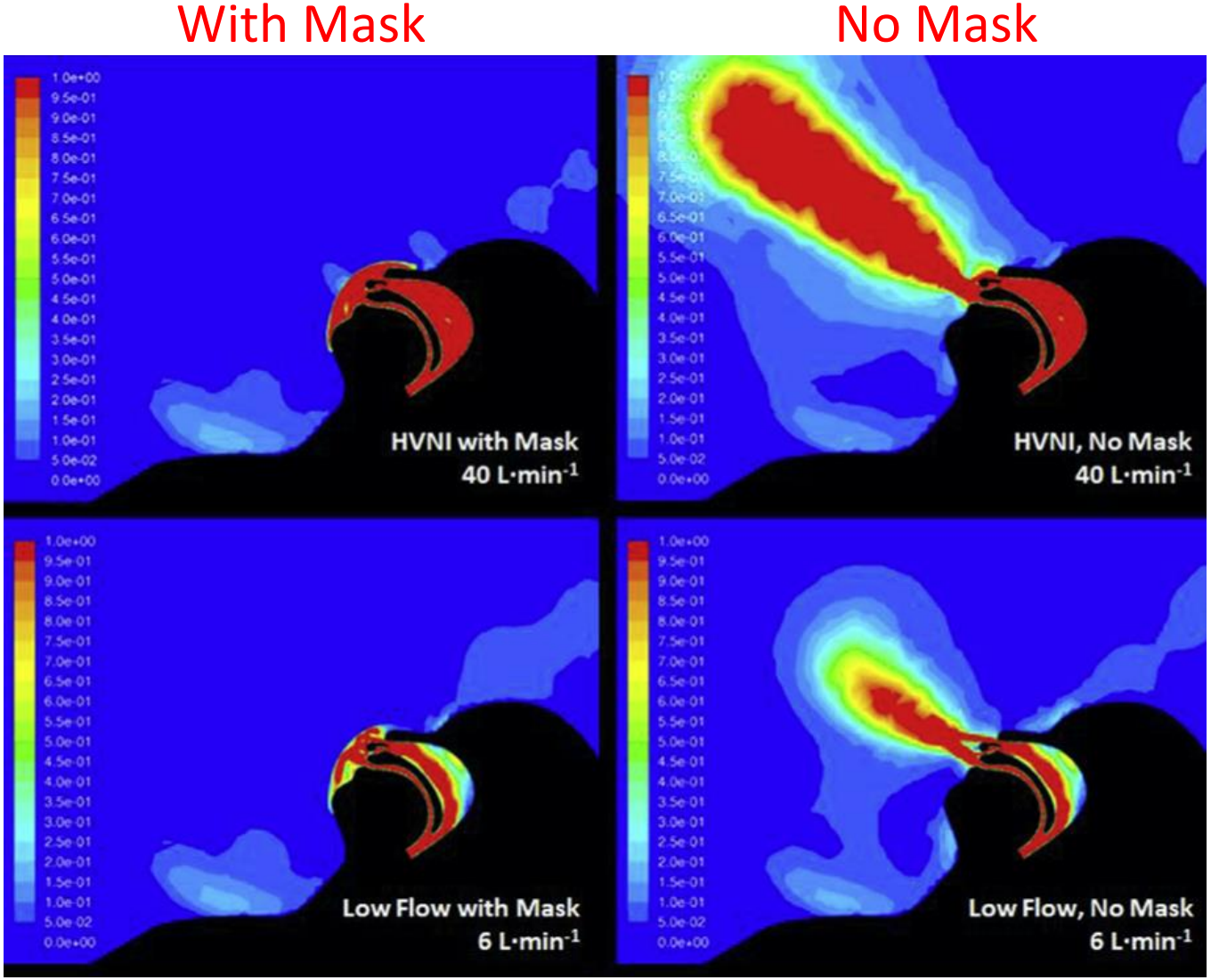


Figure 4. The calculated spread distance of nasal high-flow without surgical masks.

Dellweg D, et al. Crit Care Med. 2021 Jul 1;49(7):e693-e700.

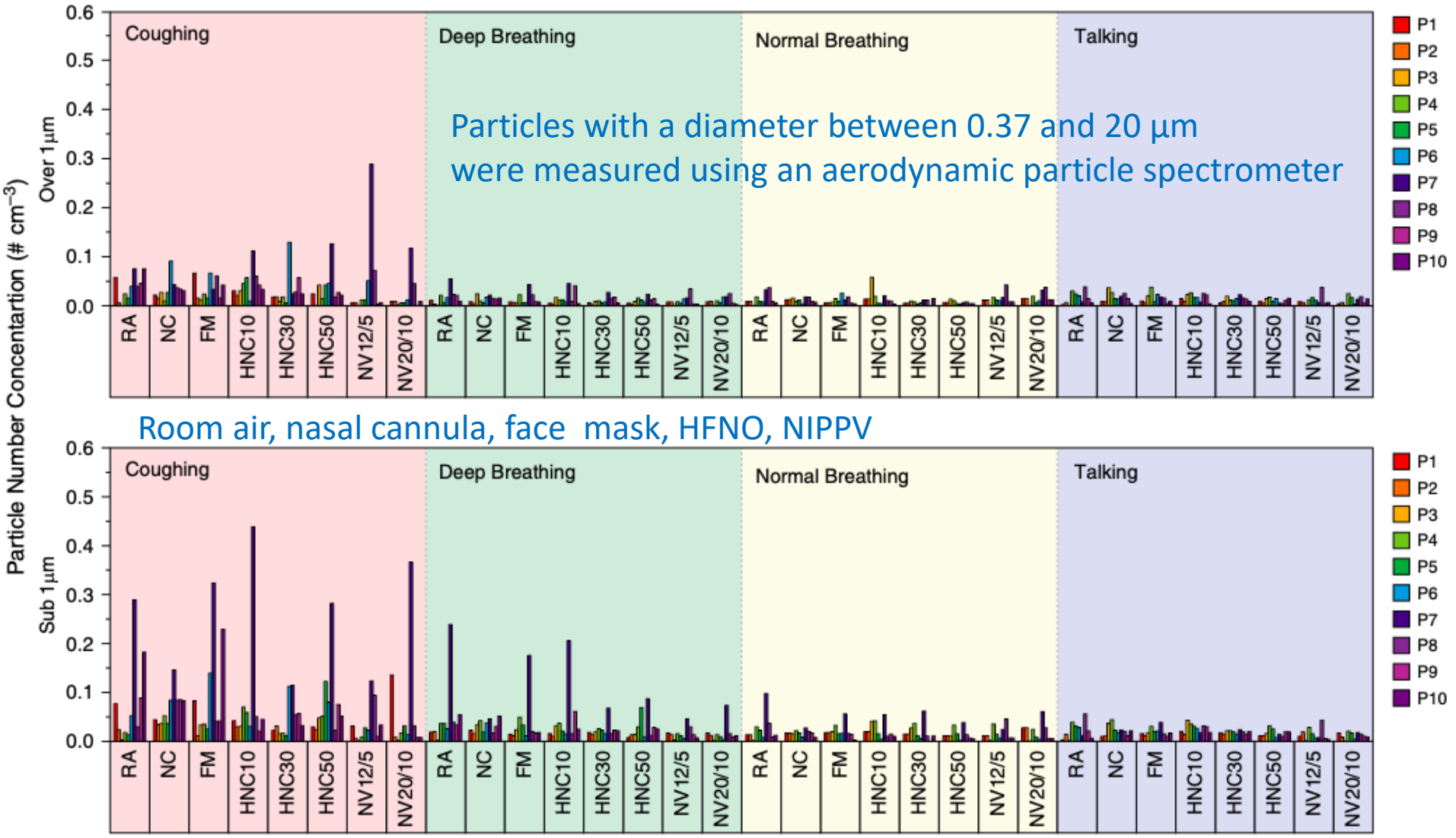
Control of Dispersion of Aerosols and Droplets **Using a Simple Surgical Mask**



Leonard et al. Chest. 2020 Sep;158(3):1046-1049.

Aerosol Generation from the Respiratory Tract with Various Modes of Oxygen Delivery

Ten healthy participants



Particles with a diameter between 0.37 and 20 µm were measured using an aerodynamic particle spectrometer

Room air, nasal cannula, face mask, HFNO, NIPPV

Gaeckle et al. Am J Respir Crit Care Med . 2020 Oct 15;202(8):1115-1124.

Aerosol dispersing / generating

- Bioaerosols (containing micro-organisms)
  - Procedures that irritate the airway of an infected individual, such as bronchoscopy, intubation, suctioning, or sputum induction, can stimulate cough and generate bioaerosols
- Medical aerosols generated from aerosol devices, including nebulizers, do not carry micro-organisms unless contaminated
  - Respiratory support devices such as HFNC or NIV do not cause patients to generate additional bioaerosols; they carry the exhaled gas and aerosols from subjects further

Li et al. Respir Care. 2022 Aug;67(8):1022-1042.
Li et al. Am J Respir Crit Care Med. 2020 Oct 15;202(8):1069-1071.

Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected

Interim guidance

13 March 2020

World Health Organization

The following recommendations pertain to adult and paediatric patients with ARDS who are treated with non-invasive or high-flow oxygen systems.

- **High-flow nasal oxygen (HFNO) should be used only in selected patients with hypoxemic respiratory failure.**
- **Non-invasive ventilation (NIV) should be used only in selected patients with hypoxemic respiratory failure.**
- **Patients treated with either HFNO or NIV should be closely monitored for clinical deterioration.**

Remark 1: Adult HFNO systems can deliver 60 L/min of gas flow and FiO_2 up to 1.0. Paediatric circuits generally only handle up to 25 L/min, and many children will require an adult circuit to deliver adequate flow.

Remark 2: Because of uncertainty around the potential for aerosolization, HFO, NIV, including bubble CPAP, should be used with airborne precautions until further evaluation of safety can be completed.

Remark 3: Compared with standard oxygen therapy, HFNO reduces the need for intubation *(42)*. Patients with hypercapnia (exacerbation of obstructive lung disease, cardiogenic pulmonary oedema), hemodynamic instability, multiorgan failure, or abnormal mental status should generally not receive HFNO, although emerging data suggest that HFNO may be safe in patients with mild-moderate and non-worsening hypercapnia *(42, 43, 44)*. Patients receiving HFNO should be in a monitored setting and cared for by experienced personnel capable of performing endotracheal intubation in case the patient acutely deteriorates or does not improve after a short trial (about 1 hour). Evidence-based guidelines on HFNO do not exist, and reports on HFNO in patients infected with other coronaviruses are limited *(44)*.

NIH COVID-19 treatment guidelines

Oxygenation and Ventilation

Last Updated: December 17, 2020

The COVID-19 Treatment Guidelines Panel's (the Panel's) recommendations below emphasize recommendations from the Surviving Sepsis Campaign Guidelines for adult sepsis, pediatric sepsis, and COVID-19.

Nonmechanically Ventilated Adults With Hypoxemic Respiratory Failure

Recommendations

- For adults with COVID-19 and acute hypoxemic respiratory failure despite conventional oxygen therapy, the Panel recommends high-flow nasal cannula (HFNC) oxygen over noninvasive positive pressure ventilation (NIPPV) **(BIIa)**.

Strength of Recommendation	Quality of Evidence for Recommendation
A: Strong recommendation for the statement	**I:** One or more randomized trials without major limitations
B: Moderate recommendation for the statement	**IIa:** Other randomized trials or subgroup analyses of randomized trials
C: Optional recommendation for the statement	**IIb:** Nonrandomized trials or observational cohort studies
	III: Expert opinion

Society of Critical Care Medicine (Surviving sepsis campaign)

For adults with COVID-19 and acute hypoxemic respiratory failure despite conventional oxygen therapy, we suggest using HFNC over conventional oxygen therapy.	**Weak**
In adults with COVID-19 and acute hypoxemic respiratory failure, we suggest using HFNC over NIPPV.	**Weak**
In adults with COVID-19 and acute hypoxemic respiratory failure, if HFNC is not available and there is no urgent indication for endotracheal intubation, we suggest a trial of NIPPV with close monitoring and short-interval assessment for worsening of respiratory failure.	**Weak**
We were not able to make a recommendation regarding the use of helmet NIPPV compared with mask NIPPV. It is an option, but we are not certain about its safety or efficacy in COVID-19.	**No recommendation**
In adults with COVID-19 receiving NIPPV or HFNC, we recommend close monitoring for worsening of respiratory status and early intubation in a controlled setting if worsening occurs.	**Best practice statement**

Alhazzani et al. Crit Care Med. 2021 Mar 1;49(3):e219-e234.

A European Respiratory Society living guideline

- We suggest HFNC for patients with COVID- 19 and hypoxaemic acute respiratory failure (conditional recommendation, very low quality of evidence)
- HFNC is classified as aerosol generating and should therefore be delivered in **a safe environment with staff wearing appropriate personal protecting equipment**
- HFNC **should not delay mechanical ventilation** in patients who are not responding to treatment

Chalmers et al. Eur Respir J . 2021 Mar 10;2100048.

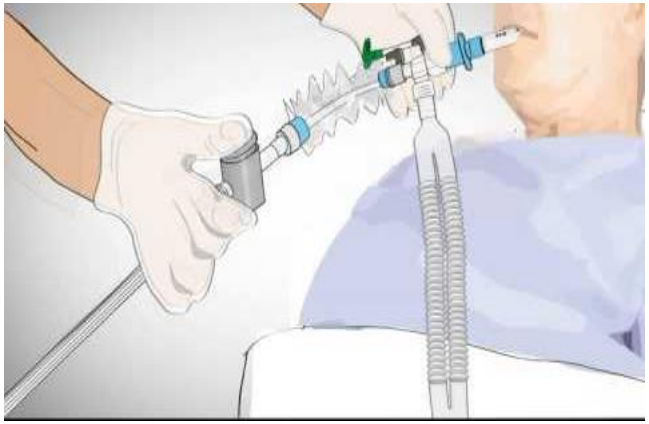
Guidelines for COVID-19

Guidelines	HFNC	NIPPV
WHO	Selected (closely monitored)	Selected (closely monitored)
NIH	HFNC over NIPPV in hypoxemic respiratory failure despite COT	
SCCM	HFNC over NIPPV in hypoxemic respiratory failure; closely monitoring	
ERS	Suggested; safe environment; appropriate PPE; don't delay intubation	Suggested; safe environment; appropriate PPE; don't delay intubation
Taiwan CDC	Not routine (closely monitored)	Not routine (closely monitored)

呼吸器病人照護

Mechanical ventilation

- 使用拋棄式管路
- 吸氣及吐氣端須裝置過濾器
- 密閉式抽吸系統



呼吸治療設備與管路

1. 呼吸器之吸氣端入口和吐氣端出口需加裝高效率過濾裝置，以降低病毒散佈之機率。
2. 須使用密閉迴路系統的抽痰管(Closed system suction)。
3. 儘可能使用可拋棄式的呼吸治療相關用物，包括氧氣治療用物、呼吸器管路、急救甦醒球等。
4. 所有管路應維持完整密閉系統，若需斷開呼吸器應調整於 stand-by，避免斷開呼吸器時高流量噴出，造病毒汙染範圍擴大。

呼吸器相關設定

接受機械通氣輔助的 ARDS 成人及孩童患者

1. 較低的潮氣量（4-8ml/kg預測體重）
2. 吐氣末陽壓(Positive End Expiratory Pressure, PEEP)則應依據氧合狀態、 血行動力學、及個別病人特性設定
3. 較低的吸氣高原壓力(Plateau pressure < 30 cm H_2O）
4. 對於重度 ARDS 的成人患者，強烈建議每天應進行至少 12-16 小時俯臥式通氣(prone ventilation)

呼吸器相關設定

接受機械通氣輔助的 ARDS 成人及孩童患者

5. 對沒有組織灌注不足的 ARDS 患者使用保守性的液體管理策略
6. 在中度或重度 ARDS 患者中，建議使用較高的 PEEP 而不是較低的 PEEP（孩童患者建議 PEEP 不超過 15 cm H_2O ）
7. 對肺部保護性通氣後仍有低血氧症的患者，是否需使用體外生命支持 (extracorporeal membrane oxygenation, ECMO)，應由具有相關醫療專業的團隊評估
8. 避免中斷患者與呼吸機的連接管路，否則會導致 PEEP 消失和肺擴張不全

呼吸器病人相關照護

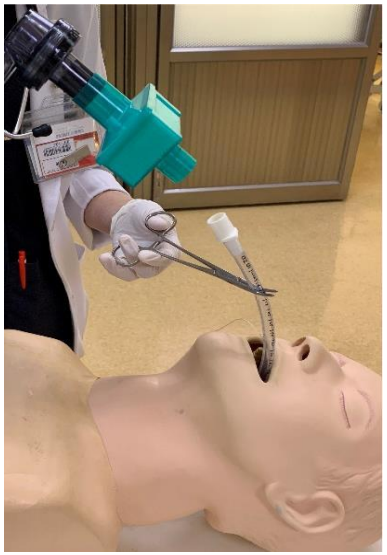
- 考量傳染風險
  1. 不測氣管內管氣囊壓力(cuff pressure) 、如有漏氣請用空針充填；解隔離後即恢復正常測量方式。
  2. 減少decuff的動作，不執行cuff leak test。
  3. 測量weaning parameter：不執行open method，改以呼吸器用low Pressure support或Automatic tube compensation (ATC)測Rapid shallow breathing index (RSBI)
  4. 執行spontaneous breathing test :不用T-tube tiral, 以呼吸器ATC或low pressure support執行

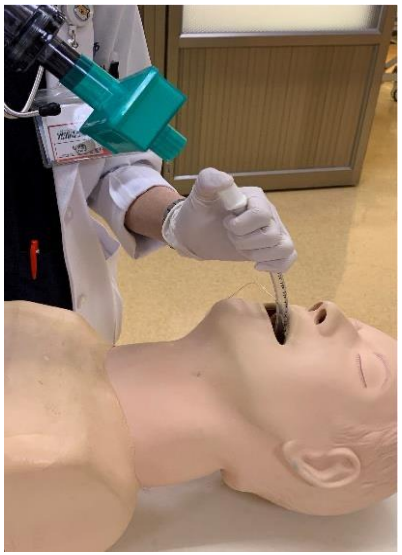
病人轉送

插管病人

- 經風險評估及與團隊討論，確認採運送型呼吸器或 Ambu Bagging（甦醒球加裝高效率過濾器）
- 路線要事先規劃好，運送前請務必先抽好痰及口水，確認氧氣鋼瓶是否滿桶足夠運送時使用， 運送過程中要確保管線的安全

必要斷開呼吸器與氣管內管連接時，須在氣管內管連結高效能氣體過濾器(例如 HEPA、HMEF 等)的遠端斷開，確保氣管內管與過濾器不要斷開





新型冠狀病毒（SARS-CoV-2）感染臨床處置暫行指引
台灣胸腔暨重症加護醫學會 編輯 2020年5月4日 第二版

甦醒球加裝高效率過濾器（NTUH）





掃QR code看組裝影片

病人轉送

未插管

- 經風險評估及與團隊討論，確認是當氧氣裝置運送(nasal cannula ,simple mask. NRM)
- 病人戴上外科口罩或以枕頭套輕輕蓋住臉與mask依O_2流速、路程距離，準備足夠的氧氣桶

Nebulizer therapies

Medication cup is in close contact with the patient's mouth, can be easily contaminated by saliva or secretions during the use

治療疑似或確診 SARS-CoV-2 感染病患時，應避免使用 Nebulizer 等氣霧式治療，可 使用 Dry-powder inhaler 或 Metered-dose inhaler(MDI)

新型冠狀病毒（SARS-CoV-2）感染臨床處置指引
2023年7月28日 第二十四版

呼吸治療設備與管路之消毒

1. 儘可能使用拋棄式管路及的相關呼吸治療用物
2. 呼吸器之每日消毒:依各醫院訂立之感控標準操作
3. 呼吸器之終期消毒:病人卸機後可於負壓病室內以紫外燈直接照射消毒再依每日消毒之方法消毒再依據製造商產品說明書所 提供的方式執行消毒
4. 紫外線對呼吸器的消毒效果缺乏文獻證實不建議做為呼吸器之單一方式消毒

Take home message

- Medical aerosols and bioaerosols are different
- Wearing a procedure mask over the nasal cannula /HFNO for patients with COVID-19 when in close contact with healthcare providers
- Small volume jet nebulizers should be avoided, if possible, for COVID-19 patients
- When patients are coughing or sneezing, they should be encouraged to cover their mouth and nose with a tissue or a mask
- Clinicians need to **wear appropriate personal protective equipment** and stay at a greater distance from patients when patients are coughing or sneezing, and keep time within proximity at a minimum

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