1. 簡述 airway 和 alveolus 的 defense mechanisms。(10%)
2. 簡述 cough reflex 的 affect、central replay 的位置和 efferent pathways。(15%)
3. 試由文章中所提供的資訊歸納使用 High Flow Nasal Cannula 對呼吸協助的生理機制。(25%)

文章摘自【Sharma S, Danckers M, Sanghavi D, et al. High Flow Nasal Cannula. Available from: https://www.ncbi.nlm.nih.gov/books/NBK526071/】

High Flow Nasal Cannula: Basic components include a flow generator providing gas flow rates up to 60 liters per minute, an air-oxygen blender that achieves escalation of FIO_2 from 21% to 100% irrespective of flow rates, and a humidifier that saturates the gas mixture at a temperature of 31 to 37°C. To minimize condensation, the heated humidified gas is delivered via heated tubings through a wide-bore nasal prong. Physiological dead space accounts for approximately one-third of the tidal volume of breathing. This allows for the accumulation of CO_2 and a decrease in available oxygen (O_2) for diffusion when ventilation is not effective in cycling inspired air with retained air within dead spaces. The high flow rates involved in high-flow nasal cannula delivers volumes of air over what a patient ventilates physiologically, which increases ventilation and allows for displacement of excess CO_2 with excess O_2. This allows for an increased PAO_2 creating a greater oxygen diffusion gradient and potentially improving patient oxygenation. A high-flow nasal cannula accomplishes a reduction of nasopharyngeal airway resistance, leading to improved ventilation and oxygenation through the application of a positive pressure environment. The resistance of an airway follows the Hagen–Poiseuille law and is calculated as:

【$R = 8\eta l / \pi r4$】 Where l equals the length of the airway, η equals the dynamic viscosity of air, and r equals the radius of the airway. Physiologically, the nasopharynx is a dynamic environment that allows for expansion and constriction of the airway radius. By creating a positive pressure environment, high-flow nasal cannula presses from the interior of the nasopharynx outwards. This dilates the radius of the nasopharyngeal airways and dramatically reduces the resistance to airway flow, thus increasing ventilation and oxygenation potential. In addition to providing positive pressure support to the nasopharynx, a high-flow nasal cannula creates a positive end-expiratory pressure to the lower airways. This effect acts similarly to continuous positive airway pressure support in that it

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applies a splinting force to keep alveolar airways from collapsing under increased surface tensile stresses during exhalation. Additionally, this allows for improved alveolar recruitment, increasing the effective available surface area within the lungs for gaseous diffusion both to and from the blood. However, it is important to note that patients keep their mouths closed to gain the maximum benefit of PEEP from high-flow nasal cannula therapy. The approximate magnitude of PEEP generated with a closed mouth is about 1 cm of water pressure for 10 liters flow. There is a resultant increase in end-expiratory volume with an increase in PEEP. One of the challenges and potential pitfalls of this hypothesis is that it is difficult for patients to keep their mouths closed when they are in respiratory distress. Humidification and warming of inspired air are essential in creating an effective oxygenation system. Primarily, this is due to the human factor of comfort. Traditional low-flow nasal cannula blows cool, dry air directly into the nasal passages. This leads to drying of the mucosa, irritation, epistaxis, and cracking of the tissue barriers, which is uncomfortable and leads to poor compliance to therapy. Many high-flow nasal cannula systems are designed with inline warming and humidification systems that provide appropriately humidified and body temperature air that is non-irritating to the mucosa, increasing patient comfort (31 to 37°C). Increased comfort leads to improved compliance and, therefore, better outcomes of therapy.

4. 請說明第二型糖尿病的診斷標準（9%），及胰島素阻抗（insulin resistance）和胰島素敏感度（insulin sensitivity）的定義（6%）。
5. 請說明末期心衰竭患者（end-stage heart failure）的處置流程建議（10%）。
6. 請閱讀下列節錄文章後，說明脂肪組織的結構、解剖和生理功能（25%）。

The adipose tissue in the human body can be broadly divided into two main anatomical depots, visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT). VAT in turn can be classified on the basis of its anatomical location as intrathoracic, abdominal and so on, and intrathoracic adipose tissue can be further classified as epicardial adipose tissue (EAT) and pericardial adipose tissue on the basis of its location within or outside the human pericardium, respectively.

The importance of this classification is highlighted by studies revealing distinct transcriptomic and proteomic profiles between different adipose tissue depots, as well as epidemiological studies that reveal a close link between VAT

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expansion and cardiometabolic risk, as opposed to the neutral or even cardioprotective profile of SAT. However, regional biological variability has also been described within the same depots. For instance, when compared with gluteal SAT, abdominal SAT has a distinct transcriptomic signature, which resembles that of VAT depots. Substantial variability exists even within the abdominal SAT, with deep SAT (below the Scarpa fascia) exhibiting a metabolic phenotype closer to that of VAT, which is more closely associated with insulin resistance and cardiometabolic risk, than that of superficial SAT. Similar regional heterogeneity has been described in EAT, with distinct transcriptomic signatures in the periventricular, peri-atrial and peri-coronary sites.

On the basis of its phenotype, functional role and gene expression profile, the adipose tissue can be further classified as white or brown. White adipose tissue (WAT) represents most of the adipose tissue mass in humans, whereas brown adipose tissue (BAT) accounts for ~4.3% of the total fat mass in adults and is located in several regions, predominantly in the interscapular and supraclavicular area. An inducible form of BAT, namely beige adipose tissue (also known as brite adipose tissue), can be found interspersed in WAT depots and occurs in response to cold exposure and pharmacological modulation of WAT. Although BAT or beige adipose tissue activation is traditionally linked to thermoregulatory thermogenesis, this activation might also have an important role in promoting weight loss and insulin sensitivity.

Although adipocytes account for most of the volume of a given adipose tissue depot, being responsible for energy storage in the form of triglycerides, several other cell types exist in the stromal fraction of the adipose tissue. These cell types include inflammatory cells such as macrophages, lymphocytes and eosinophils, fibroblasts, pre-adipocytes, vascular cells that form the adipose tissue microvasculature and multipotent mesenchymal stem-like cells known as adipose-derived stromal or stem cells. Most adipose tissue-resident cells produce and secrete adipocytokines and other mediators that exert autocrine, paracrine and/or endocrine effects on neighbouring cells or remote tissues and organs. Of note, the composition of the adipose tissue secretome is largely depot-specific and can also be affected by systemic and local factors linked to inflammation, insulin resistance and obesity. For instance, analysis of adipose tissue-resident cells from different depots has revealed distinct patterns, with visceral adipose-derived stem cells secreting higher levels of pro-inflammatory factors, such as IL-6 and C-C-chemokine ligand 2 (CCL2), and lower levels of anti-inflammatory mediators such as adiponectin and IL-10 than subcutaneous adipose-derived stem cells.

(以上摘要修改自 Oikonomou EK, et al. The role of adipose tissue in cardiovascular health and disease. Nature Reviews Cardiology 2019;16:83-99.)

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