嚴重氣喘的挑戰與治療

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近年來，因為疾病診斷技術的進步與藥物研發的進展，使得我們對於嚴重氣喘的了解已經慢慢清楚。在診斷上，目前根據疾病的發炎型態可分為eosinophil asthma，neutrophilic asthma，IgE-mediated asthma and pauci-granunocytic asthma等endotypes；在臨床上的臨床表現型不同的研究也分為許多種表現型。以2016年新版的GINA將氣喘分為五種表現型: 包括allergic asthma、non-allergic asthma、late-onset asthma、asthma with fixed airflow limitation及asthma with obesity宇等五種。

同樣的，2016年的GINA診療指引在嚴重氣喘的部分，尤其是step 5 處理上，可以加上Tiotropium (LAMA)、Omalizumab (anti-IgE agent)或是mepolizumab (anti-IL-5 monoclonal Ab)等藥物治療。從這樣的建議治療上來看，氣喘的治療不再是簡單的ICS或LABA的治療了，已經走向個人化治療及生物製劑的時代了。這已意謂著我們需要更清楚知道每位嚴重氣喘的phenotypes 和endotypes，才能夠根據不同的情況來給予適當的治療。

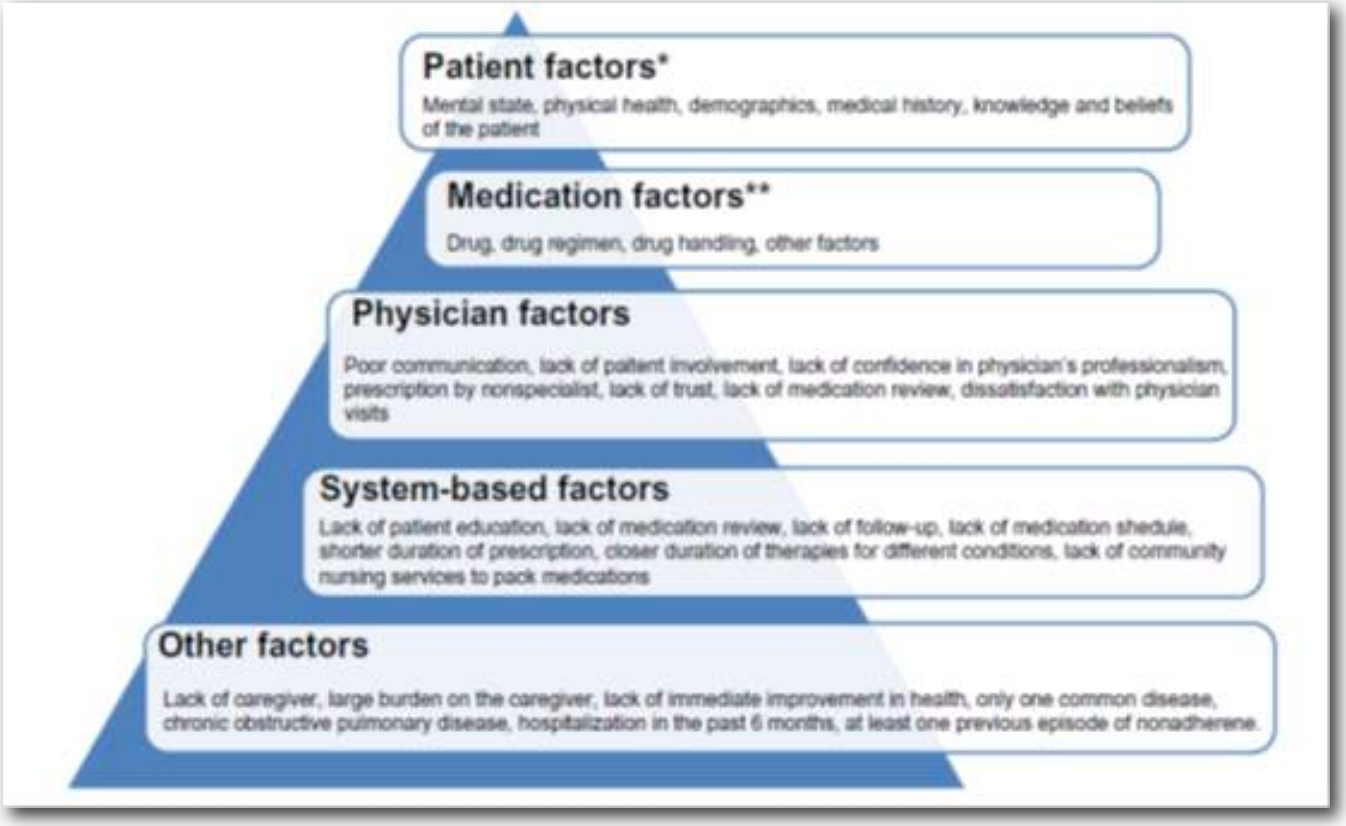
目前在治療嚴重氣喘時，有幾個步驟必須先釐清:

第一個步驟: 確診及定義

1. Confirmation of the diagnosis: 一定要明確診斷是氣喘，而非其他疾病如COPD、GERD、bronchiectasis或CHF等疾病造成。
2. Differentiation between severe asthma and mild asthma: 要先清楚嚴重氣喘的定義與症狀，這部分可參考ATS和ERS在2014年有發表嚴重氣喘的操作型定義。其中亦有包括使用藥物的劑量等。
3. Determination of whether severe asthma is controlled or uncontrolled: 下列四點都被認定為uncontrolled asthma，包括:
   (1). Poor control of symptoms (ACQ>1.5 or ACT<20)
   (2). Frequent severe exacerbation (defined as >=2 bursts of systemic corticosteroids [>3 days each] in the previous year
   (3). Serious exacerbation (defined as at least one hospitalization stay in the intensive care unit, or mechanical ventilation in the previous year
   (4). Airflow limitation (FEV1<80% predicted after withholding of short- and long-acting bronchodilators)

第二個步驟:病患評估

1. Assessment of contributory factors: 任何可能的加重因子都必須找出並加以改善或去除。這裡也包括了用藥與病患的醫囑性。(表一)



2. Interactions among the effects of aging, asthma and coexisting disease:可能的原因及共病都需要治療。

3. Special group: Asthma in patients with neuropsychological diseases: 特別是在老人家的嚴重氣喘，這部分更需要仔細評估。

4. Asthma-COPD overlap syndrome (ACOS):有抽菸的病患更需注意是否有ACOS的可能診斷。

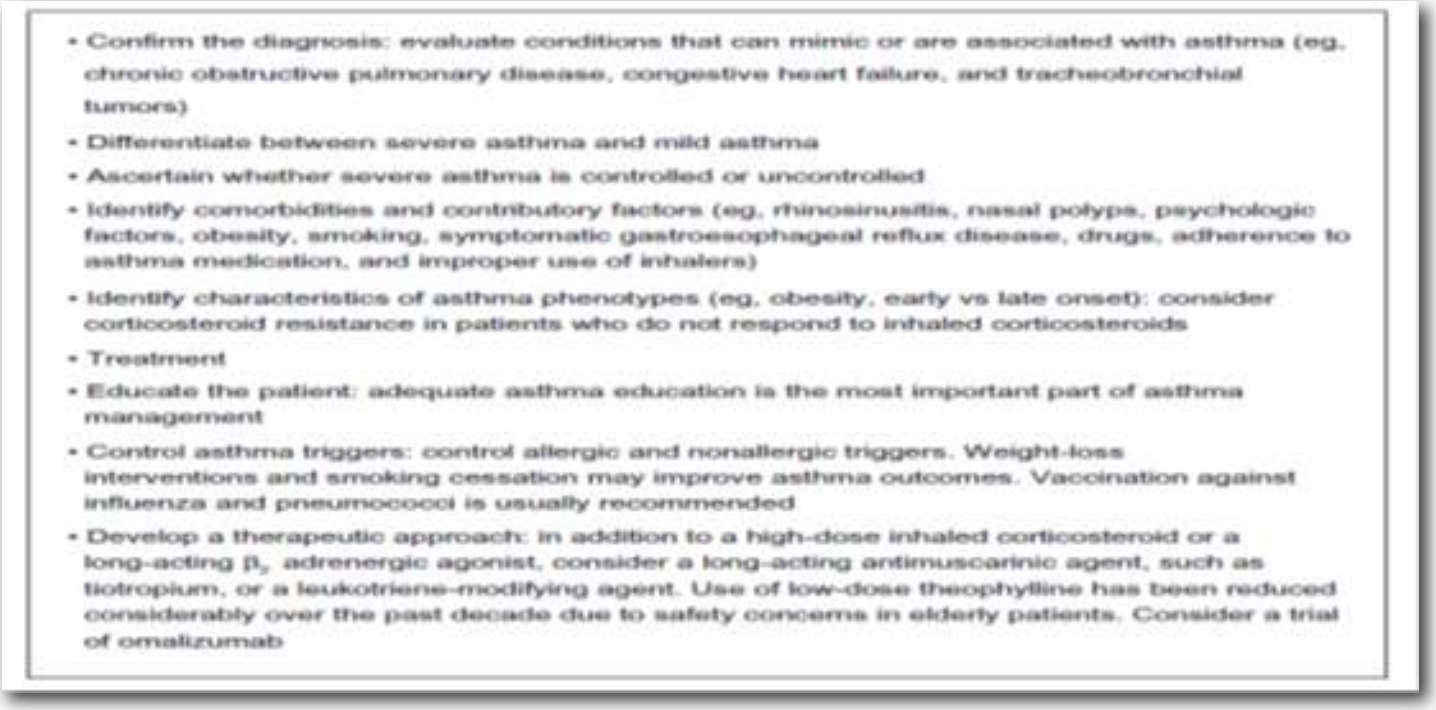
5. Approaches to asthma phenotyping: 包括Late-onset asthma、early-onset asthma、corticosteroid insensitivity、and obesity等等。

第三個步驟:治療

1. Non-pharmacologic intervention: 包括病患的衛教、控制誘發因子。

2. Pharmacological intervention: 在GINA的step 4和step 5的藥物需要考慮使用哪些藥物。

下表為統整的主要重點: (表二)



- Confirm the diagnosis: evaluate conditions that can mimic or are associated with asthma (eg, chronic obstructive pulmonary disease, congestive heart failure, and tracheobronchial tumors)
- Differentiate between severe asthma and mild asthma
- Ascertain whether severe asthma is controlled or uncontrolled
- Identify comorbidities and contributory factors (eg, rhinosinusitis, nasal polyps, psychologic factors, obesity, smoking, symptomatic gastroesophageal reflux disease, drugs, adherence to asthma medication, and improper use of inhalers)
- Identify characteristics of asthma phenotypes (eg, obesity, early vs late onset); consider corticosteroid resistance in patients who do not respond to inhaled corticosteroids
- Treatment
- Educate the patient: adequate asthma education is the most important part of asthma management
- Control asthma triggers: control allergic and nonallergic triggers. Weight-loss interventions and smoking cessation may improve asthma outcomes. Vaccination against influenza and pneumococci is usually recommended
- Develop a therapeutic approach: in addition to a high-dose inhaled corticosteroid or a long-acting β_2 adrenergic agonist, consider a long-acting antimuscarinic agent, such as tiotropium, or a leukotriene-modifying agent. Use of low-dose theophylline has been reduced considerably over the past decade due to safety concerns in elderly patients. Consider a trial of omalizumab

作者在此，希望能夠重視嚴重氣喘的未來衝擊，台灣到底嚴重氣喘的盛行率多少目前仍未知，也希望未來有更精確的診斷與更有效的藥物以嘉惠病患。

Reference:

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