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林新醫學年報 JANUARY


中華民國 112 年 01 月份醫教會編製

# 目　　錄

# 林新年報

林新年報為收集院內醫師、醫事人員及行政人員，最近一年的論文，其來源來自於投稿林新年報的論文及已刊登於國內外雜誌論文，期待本院同仁儘量發表，提高本院醫療、護理及醫管專業的水準。論文的電子稿，請 E-mail 至教研部秘書。




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# 序

林新醫院自民國 88 年遷院以來，以「創新、溫馨、效率、品質」的理念，於三年內由地區醫院升格為區域教學醫院，全體同仁的努力有目共睹。醫院的角色也由「全方位的社區醫療服務」另須兼顧「教學的任務」。

「全面醫療品質提昇」及「以病人為中心的服務導向」為本院既定的方針，院方希望全體同仁能提高自己專業的能力，除接受繼續教育訓練外，更鼓勵將寶貴的經驗、想法寫成論文發表。因此除了本院原已制定的論文獎金制度外，更於民國 91 年開始籌劃成立林新醫學年報～LinShin Medicial Annual Report～，鼓勵全院同仁投稿。

很欣慰的林新醫學年報創刊號終於出版了。

一種高水準雜誌的形成是非常不容易的，林新醫學年報創刊號，不論其內容水準如何，畢竟是大家努力的心血。我很誠心的希望「林新醫學年報」能夠長久持續下去，內容更豐富，水準更高。

最後我要感謝全院同仁的支持，在我們共同的努力之下，使夢想成真，踏出了第一步。同時也希望全院同仁共同努力，持續將研究成果投稿於林新醫學年報。

林新醫院 院長 林仁卿

JAN.16, 2023

# 編者的話

林新年報自民國 92 年創刊以來，如今已進入了第 19 年。回顧過去，在院長、歷任副院長、部主任及所有院內同仁的努力下，這本屬於林新醫院的年報，終能按時一期又一期的出版。在院長的帶領及鼓勵下，每一年投稿的件數及論文的品質皆有顯著的進步。希望藉著林新年報，能提高院內同仁論文寫作的動機，將臨床寶貴經驗及想法付諸文字，以達流傳保留目的，提升同仁專業水平，並為醫院留下重要的醫學資料，以利後進學習。希望有朝一日，這份年報能成為同儕審查的醫學期刊，這是我們的目標，也將是林新醫院向醫學中心水平邁進的重要里程碑之一。

106 年起我們已將林新年報電子化，取消紙本印刷，除了響應環保議題外，亦可讓員工在院內任何一台電腦經院內網路讀取年報資料，增加閱讀可近性。

最後我們感謝院內同仁在忙碌的醫療服務之中，還能踴躍的寫作及投稿，才能使這份年報順利出刊。期望未來每一年的年報，都能有更豐富的內容。

林新醫院教研部副院長 張光遠

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REVIEW ARTICLE

# Allergy from perspective of environmental pollution effects: from an aspect of atopic dermatitis, immune system, and atmospheric hazards—a narrative review of current evidences

**Su Boon Yong[1] · Shuo-Yan Gau[2] · Yu-Chen Guo[2] · James Cheng-Chung Wei[3,4,5]**

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## Abstract

Environmental pollution has become more diversified in recent years as technologies for urbanization is increasingly more advanced. Several environmental factors such as air and water pollutants have been linked to allergic symptoms. For instance, because of industrialization for city development in many countries, polluted soil or tiny particles in the air could result in an even more hazardous environment for people to reside. Aside from the aspects of environmental issues, other newly emerging factors such as the electromagnetic field (EMF) also require further investigation. Here, in this narrative review, we focused on allergens from atmospheric and water pollution, hygiene improvement, changes in food trend, and residential environmental pollution. Current evidences regarding the association between various pollutants and the potential clinical diseases could be induced. For people with high skin exposure to air pollutants such as PM 2.5, PM 10, or sulfur dioxide, potential onset of dermatological allergic events should be alerted. The mechanisms involved in allergic diseases are being discussed and summarized. Interactions between immunological mechanisms and clinical implications could potentially provide clearer view to the association between allergic status and pollutants. Moreover, understanding the mechanistic role of allergens can raise awareness to global environment and public health.

**Keywords** Environmental pollution · Allergens · Electromagnetic field · Public health · Immunology · Tiny particles · Atopic dermatitis

## Introduction

Issues regarding environmental factors in the influence of immune system has become clinically critical. The present study discussed aspects including risk factors in atmospheric and water environment, public health improvement, changes of food trend, and living environment to elucidate the importance of environmental allergen. In Table 1 and Fig. 1, we

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**Table 1** Summarization of recent findings on allergen and allergy-related disease

| Allergen/related disease | Approach | Findings | Ref |
|---|---|---|---|
| DEP | Nasal passage in mice | Mice inoculated with DEP showed increased level of IgE | (Takafuji et al. 1987) |
| PM; $O_3$; $NO_2$ | Air Quality Health Index and urticaria prevalence | Poor air quality is related to increased urticaria patients | (Kousha and Valacchi 2015) |
| Dioxin-like compound | Case study for mother and child before and 18 months after birth | Level of dioxin-like compound 2,3,4,7,8-pentachlorodibenzofuran in mother`s blood is associated with otitis media development in infant | (Miyashita et al. 2011) |
| Dust mite | Airway smooth muscle (ASM) cells | Rabbit ASM exposed to *Der p 1* increased ERK ½ and p38 MAPK signaling pathways | (Grunstein et al. 2005) |
| Sulfur dioxide | Population study | Individuals with methacholine hypersensitivity were highly allergic to sulfur dioxide | (Nowak et al. 1997) |
| Herbicide | Prospective study of farmers for a 5-year period | 2,4-D and simazine were significantly related to allergy-associated wheeze | (Hoppin et al. 2017) |
| Bullous systemic lupus erythematosus | Case study | Systemic lupus erythematosus was reported in children with recurrent vesiculobullous lesions with or without systemic autoimmune symptoms | (Lourenco et al. 2014) |
| Sjögren syndrome | Case report | The destruction of exocrine glands (primary salivary and lacrimal) pertained to autoimmunity via lymphocytes infiltration | (Jadhav et al. 2015) |

summarized recent findings on allergen and allergy-related disease to provide a clearer view on the current development in the field. In Table 2, allergens and their physicochemical characteristics and clinical relevance were described. Types of allergies mentioned in this article referred to the related allergic reactions and diseases aroused by specific allergens, including dermatological allergy and respiratory allergy, etc.

## Atmospheric hazards

The environment has become ever more hazardous due to industrialization for city development in many countries. This includes the sky and the soil where humans reside (Baldacci et al. 2015). Tiny particles from vehicles (e.g., diesel exhaust particles, particulate matters (PM)), dusts containing ultrafine particles (e.g., diameter below 0.1 μm), smoking (e.g., first- and second-hand smoke), chemicals from factories (e.g., coloring dyes, cotton, epoxy resins, isocyanates), and the emerging electromagnetic field (EMF) in telecommunications (e.g., use of 4G or even higher electromagnetic waves) (Lucas et al. 2001; Wu et al. 2018).

Tiny particles such as particulate matter 2.5 (PM 2.5) and 10 (PM 10) have diameter 2.5 μm and 10 μm, respectively or below can pass through and be trapped in our lung cells. The trapped PM affects breathing rate as it agglomerates into insoluble particles in the lungs that obstruct airway, thereby inducing breathing difficulties linked to chronic obstructive pulmonary disease (COPD) (Ni et al. 2015; Lamichhane et al. 2018; Wen and Gao 2018). Previous study showed that traffic-related PM 10 reduces lungs' expiratory flows in children residing near traffic-polluted region (Peters et al. 1999; Schindler et al. 2009; Guo et al. 2018). Another study confirms that PM 10 from traffic pollution is significantly linked to asthma development (Braback and Forsberg 2009; Kunzli et al. 2009). However, PM 10 concentration below 150 $\mu g/m^3$ did not cause any nasal allergic symptoms (Kim et al. 2017). Other studies showed that PM is associated with skin problems such as urticaria and allergic rhinitis (Kang et al. 2015; Kousha and Valacchi 2015).

Tiny particles of chemical sources such as coloring dyes have been reported to be allergic to some people. Carmine (e.g., red), tartrazine (e.g., yellow), and annatto (e.g., orange or yellow) have been used in food coloring for meat, or peanuts, and many other types of foods (Bhatia 2000). Of the three coloring dyes, tartrazine has been mostly reported to be allergic and might cause pruritus and urticaria (Neuman et al. 1978). The common symptoms of allergic associated with food coloring include severe headache, itchy skin, breathing difficulty, and chest tightness.

Meanwhile, EMF has been an emerging new topic associated with allergies. EMF includes the broadcasting devices such as power station, television, radio, LASER, and most importantly, mobile phones. Power and phones range from $10^1$ to $10^4$ Hertz (Hz), radiowaves range from $10^4$ to $10^9$ Hz,

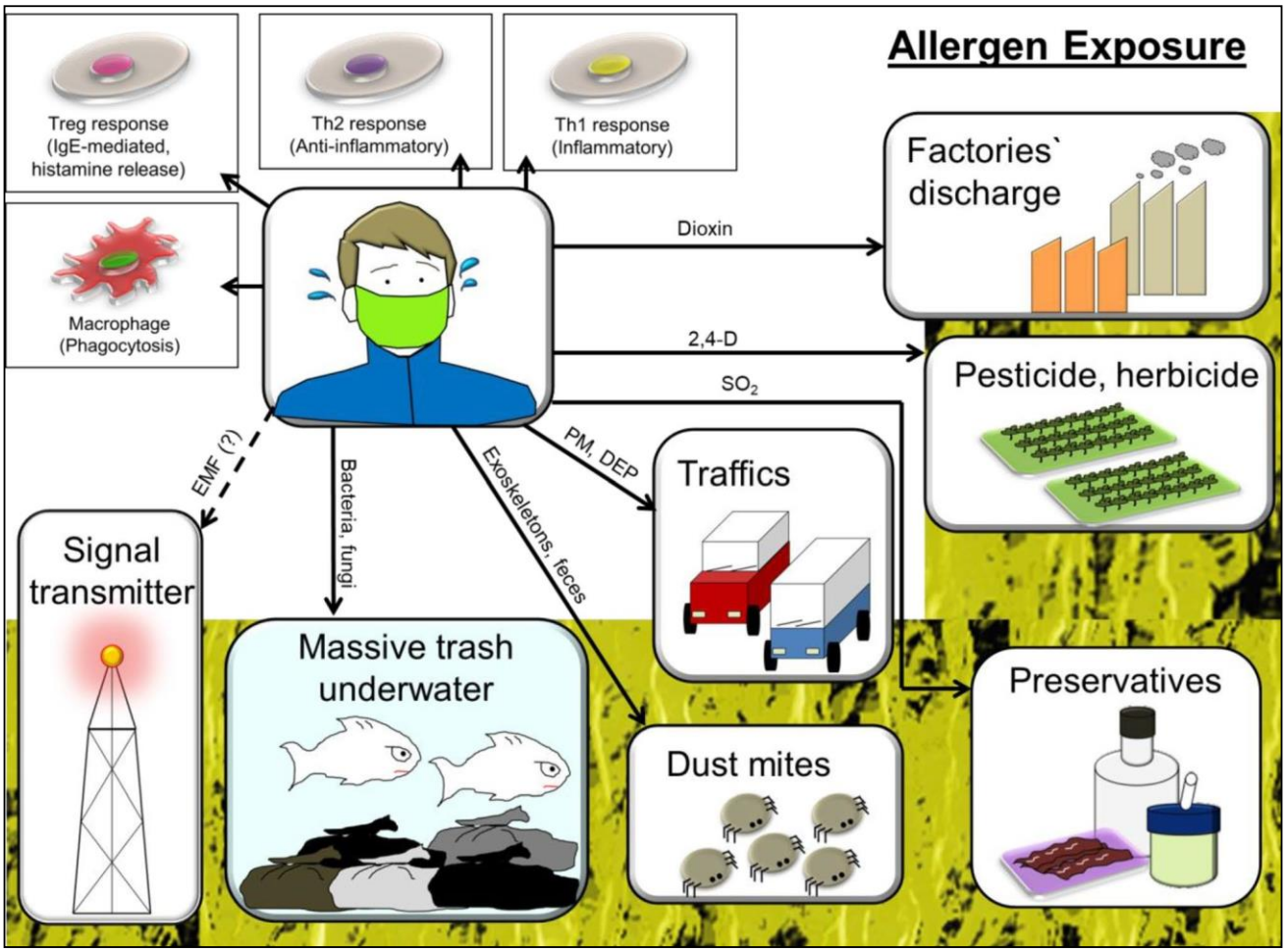


**Fig. 1** Summarization of currently known allergen exposures

and LASER communication is at $10^{14}$ Hz. Some reports on "triggered sensitivity" have been linked to mobile phones which lie in the 2–4 GHz. However, the future is 5 GHz with yet unknown effect on our health. Previous study reported that weak magnetic field shares similarity with chemical reactions from drug, indicating that magnetic field may affect humans at molecular level (Whissell and Persinger 2007). Symptoms that have been reported include headache, nausea, and dermatological symptoms. However, the reported symptoms are yet to be medically diagnosed.

## Water pollution

The pollution does not stop in the atmosphere, but continues in the sea. Since a decade ago, global warming has become a concern for health and environment (Schiermeier 2012). On the lands, human civilizations thrive as new products along with heat-trapping air pollutants (e.g., PM 2.5) are being manufactured (Wang et al. 2021a, b). To solve the heat trap in atmosphere, some countries have used aerosols that reflect the heat (Rawlinson et al. 2017; Ren et al. 2019). The amount of wastes include plastics, heavy metals, alloys, chemicals (e.g., pesticides from farmland), nuclear materials (e.g., uranium-238 (half-life of 4.47 billion years), hydrogen-3 (half-life of 12.3 years), and carbon-14 (half-life of 5,730 years)), and various other materials are increasing quickly. However, for some of the wastes such as plastics, burning could potentially cause severe influence on the environment and thus could not be fully relied on (Simoneit et al. 2005). Some of the wastes such as heavy metals were not easy to be decomposed (Sall et al. 2020). To save the lands from being drowned by massive trash, the trash are in fact submerged in water (Agamuthu et al. 2019). The atmospheric pollution and the wastes that are kept underwater help breed bacteria, fungi, and other microorganisms that are yet to be discovered (Jacquin et al. 2019).

The health concern due to sea pollution arises from the fact that fishes are being consumed worldwide. In some nations, aquatic lives are staple foods; in other nations, people live on the water as a lifestyle. The metals found

**Table 2** Summarization of involved allergens from various sources

| Sources | Involved allergens or reasons potentially causing allergies | Physicochemical characteristics and clinical relevance |
|---|---|---|
| Atmospheric hazards | ➢**Tiny particles from vehicles**<br>→Diesel exhaust particles and particulate matters<br>➢ **Dusts containing ultrafine particles**<br>➢ **Smoking**<br>➢ **Chemicals from factories**<br>→Coloring dyes, cotton, epoxy resins and isocyanates<br>➢ **Emerging electromagnetic field** | ➢ Could agglomerate into insoluble particles in the lungs that obstruct airway, thereby inducing breathing difficulties<br>➢ Could be allergic for some people due to the chemical adding, leading to neurological, dermatological or respiratory symptoms |
| Water pollution | ➢**Wastes**<br>→Plastics, heavy metals, alloys, agricultural chemical wastes and nuclear materials | ➢ Could cause accumulation of contaminated substances via food chain, leading to clinical allergic diseases such as eczema |
| Hygiene improvement | ➢**Decreased number of encountered microbes in immune system**<br>→Potential influences in Th1/Th2 balance | ➢ Could cause reduced ability against pathogens and autoimmune responses due to Th1/Th2 imbalance |
| Changes in food trend | ➢**Herbicides**<br>→2,4-Dichlorophenoxyacetic acid and glyphosate<br>➢ **Pesticides**<br>→ Rodenticide warfarin, permethrin and carbaryl<br>➢ **Others**<br>→ plasticizers | ➢ Could cause dermatological symptoms such as dermatitis, urticaria, purpura, hemorrhagic necrosis, and purple toe syndrome |
| Residential environment | ➢**Dust mites**<br>→ *Dermatophagoides farinae, Dermatophagoides pteronyssinus, Euroglyphus maynei*, and *Blomia tropicalis* | ➢ Could lead to allergic diseases including rhinitis, asthma, and atopic dermatitis |

in contaminated water such as chromium, mercury, and tin are consumed by fish at the top of food chain (Langard and Vigander 1983; Pujol et al. 2014; Nguyen et al. 2016). Contaminated water has been linked to asthma in the Salton Sea in the USA (Marshall 2017). In addition, fish contaminated with heavy metals has been associated with eczema in children (Hon et al. 2012). However, one of the most toxic by-products from industrial waste is dioxin which is manufactured during paper bleaching, metal refining, and incineration. According to the US Environmental Protection Agency, dioxin can be found in the drinking water from factories discharge and waste incineration, and has been associated with allergy (Miyashita et al. 2011; Takano and Inoue 2017).

## Hygiene improvement

As modernization grows worldwide, we have increased ways of sanitation which results to improved hygiene in personal and public environment. The applications of bactericidal agents, pesticides, have reduced bacterial and parasitic infections. Reduction in microorganism infections also reflects the fact that we encounter less microbes invasion in our immune system. An immune system that experiences reduced or no foreign invasion might be unable to act rapidly against foreign pathogen while being attacked the second time (Chaplin 2010). However, previous study suggested that the gut microbiota is linked to an IgE-mediated food allergy, rather than microorganism infection (Molloy et al. 2013).

Our adaptive immune system can be modulated by T helper 1 (Th1) (e.g., fighting against intracellular invaders such as virus and bacteria) or Th2 cells (e.g., triggered by extracellular invaders). The Th1 response activates macrophages to kill the invaders. Th1 cells secrete interferon-gamma (IFN-γ) to trigger Th1 development and suppress Th2 response. The Th2 is known as a humoral response which produces antibodies to generate isotype switch to fight against foreign pathogens. While Th1 cells secrete IFN-γ, Th2 cells secrete interleukin-10 (IL-10) to trigger Th2 response while inhibiting Th1 development. Since the antibodies are triggered from a humoral response, the immune system can store a memory of the pathogens that have been encountered in an earlier period, such that identical pathogens can be killed efficiently upon the second encounter. Evidence has shown that reduced microorganism infection can affect the Th1/Th2 response. If the Th2 response is less triggered, the immune system has reduced ability to fight various pathogens, the immune system is inclined to Th1 response, causing an autoimmune response (Redecke et al. 2004).

## Changes in food trend

Nowadays, manufacturing of food products has become modernized in many ways. To prolong storage period, or to make foods taste better, foods are chemically processed.

Preservatives such as antioxidants (e.g., sulfur dioxide, sodium benzoate, and nitrates) are added in meat products and beverages to prevent bacterial infection. The beer and wines, sausages, meat patties for burgers, and even pickled vegetables can be preserved with sulfur dioxide to restrict oxidation. Unfortunately, some people are allergic to the added antioxidant.

To grow foods more efficiently, seedlings are cultivated with herbicides (e.g., 2,4-dichlorophenoxyacetic acid and glyphosate) or pesticides (e.g., rodenticide warfarin, permethrin, and carbaryl). The 2,4-dichlorophenoxyacetic acid (2, 4-D) is an active ingredient in herbicides for removing unwanted vegetation. The 2,4-dichlorophenoxyacetic acid has been linked to allergic wheezes as it is widely used in public parks, playground, and crops (Fukuyama et al. 2009). The pesticide warfarin is widely being used to kill rats. Since the 1970s, even stronger type of warfarin was being developed to overcome rats that were resistant to warfarin which was then called "Superwarfarin." The molecule brodifacoum is found in the superwarfarin which restricts the function of vitamin K by stabilizing the inactive form of vitamin K, vitamin K epoxide (Nelson et al. 2006; Card et al. 2014). Furthermore, warfarin was found to induce skin conditions such as dermatitis, urticaria, purpura, hemorrhagic necrosis, and purple toe syndrome (Adams and Pass 1960; Kwong et al. 1978).

In addition to food making, plasticizers are used in various cooking utensils, plastics, which can be dissolved after a period of time and be mixed in the lipids of foods during cooking. Phthalate ester is a plasticizer commonly used for increasing flexibility in plastics and has been associated with atopic dermatitis (Takano and Inoue 2017). As a result, we consume various types of molecules apart from the original foods themselves.

### Residential environment

Dust mites are prevalent in residential areas worldwide regardless of geographical locations. The factors that determine mites prevalence are dependent on their need to humidity and to avoid light. The prevalences of dust mites are added on by pets inside the residential areas. In addition to pets, the use of air conditions can stabilize humidity in the living environment. Clinical symptoms for dust mite-associated allergy include wheezing and breathing difficulty. *Dermatophagoides farinae*, *Dermatophagoides pteronyssinus*, *Euroglyphus maynei*, and *Blomia tropicalis* belong to the arachnid class. Components from the mites (e.g., exoskeletons, feaces) can affect skin through proteolytic effect on epithelial cells (Hilger et al. 2014; Erban et al. 2016). The dust mites can activate the pattern recognition receptors which recognize conserved pathogen associated molecular patterns (PAMPs) to induce innate immune system. Clinical symptoms from dust mites include rhinitis, asthma, and atopic dermatitis.

## Discussion

### Mechanisms involving allergic disease and environmental pollution

The adaptive immune system, also known as acquired immune system, is mainly regulated by B and T cells. During an attack by foreign particles, naïve T cells are activated into CD4-expressing T helper cells: Th1, Th2, T reg, Th17, and $T_{FH}$.

Inflammatory mechanisms could greatly influence the comorbidity status of autoimmune diseases (Gau et al. 2021; Gau et al. 2022a). Previous study showed that autoimmune diseases are inclined to be Th1-dependent. Th1 response is pro-inflammatory, increases IL12, IFN-γ, IL18, and IL27 production to combat intracellular pathogens: bacteria and viruses. The Th1 response leads to activation of phagocytes including macrophages, neutrophils, and natural killer cells. When the cells are infected by bacteria, the lipopolysaccharides (LPS) bind to the endotoxin receptor CD14 on CD14-expressing antigen presenting cells (e.g., dendritic and macrophages). The LPS are being presented to immune cells through interaction with Toll-like receptor-4 (TLR-4) expressed on immune cells. As a result, the TLR-4 can induce IL-12 production which promotes Th1 development (Pålsson-McDermott and O'Neill 2004).

On the contrary, atopy diseases are more likely Th2-dependent. Th2 response is antibody-mediated, anti-inflammatory, increases IL-4, IL-5, and IL-13 production to fight against extracellular parasites. The Th2 response activates eosinophils (Watanabe et al. 2022). Asthma has been reported to be Th2-mediated, enhances B7RP-1, IL-13, IL-1β, and GM-CSF production (Finn and Bigby 2009). Previous study suggested that early exposure to a specific environment can affect development of children's Th1/Th2 immune response (Duramad et al. 2006). In addi- tion, the atmospheric pollutants such as diesel exhaust particles, PM2.5, ozone, and nitrogen dioxide are also linked to asthma development. Exposure to these air pol- lutants increases IL-4, IL-5, IL-6, and IL-10 mRNA levels to enhance the Th2 response (Sasaki et al. 2009; Lee et al. 2013). Previous study demonstrated that exposure of PM to rats increased number of macrophages which can either promote Th1 or Th2 response, and caused mucus metaplasia in the airways where mucous cells were absent (He et al. 2017). In Fig. 2, we summarized environmental allergens triggering pro-inflammation, anti-inflammation, or allergen tolerance through activation (Fig 3).

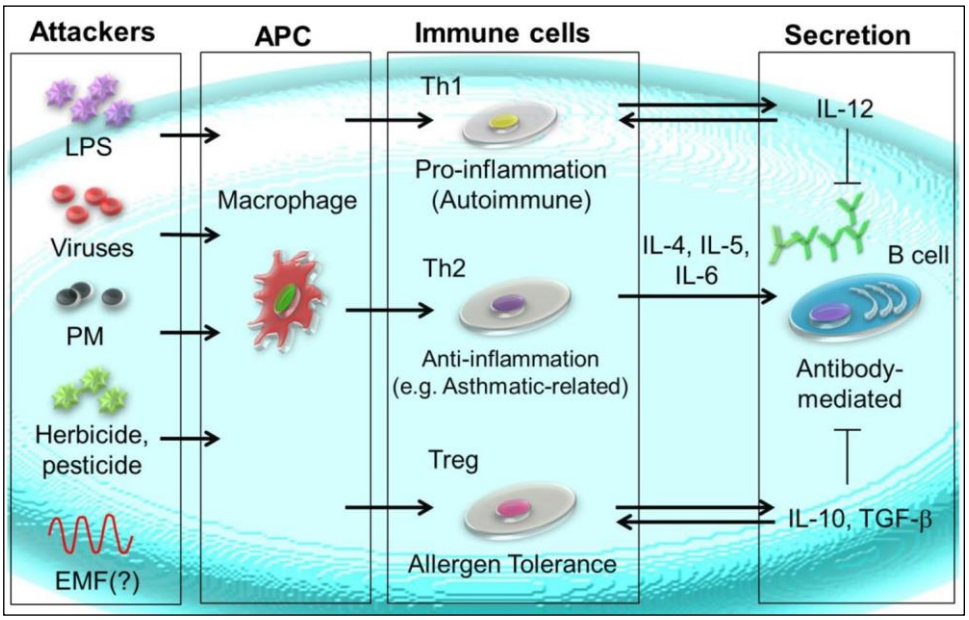


**Fig. 2** Respective environmental allergens trigger pro-inflammation, anti-inflammation, or allergen tolerance through activation of Th1, Th2, and Treg

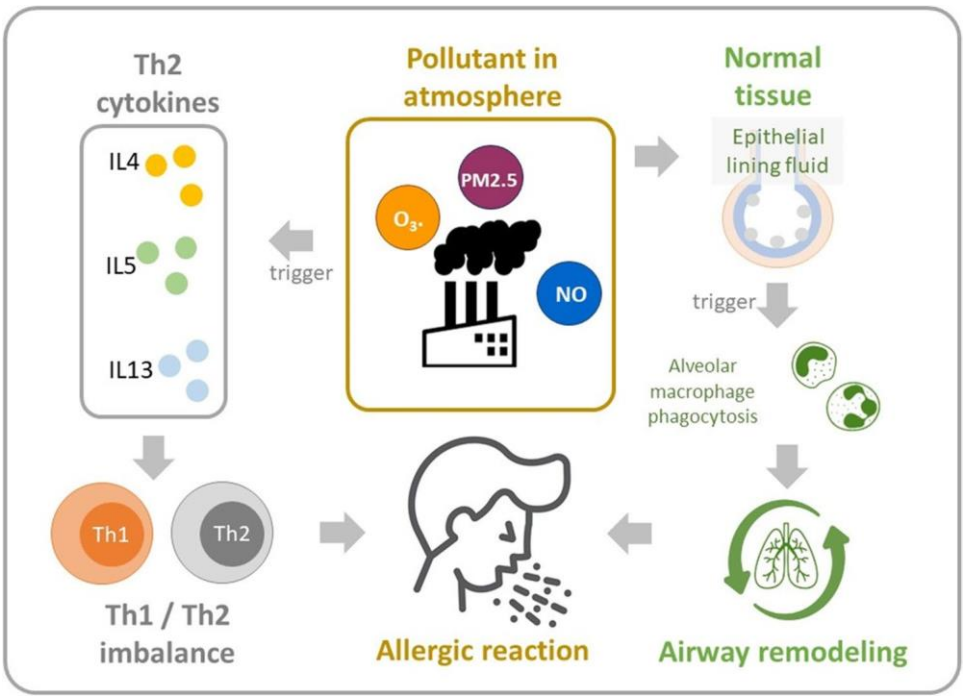


**Fig. 3** Mechanisms involving allergic disease and environmental pollution

The epithelial lining fluids in the lungs contain surfactant proteins which protect alveolar cells from harmful tiny particles (Hohlfeld 2002). The PM diffused into the epithelial lining fluids to form larger, agglomerated particles with diameter 5 μm that promote phagocytosis by alveolar macrophages (AM). However, the AM-dependent phagocytosis is reduced when alveolar cells become overloaded with agglomerated particles (Ling and van Eeden 2009). The PM further induces oxidative stress and affects gene transcription for pro-inflammation in the AM by unwinding deoxyribonucleic acid (DNA) (MacNee and Donaldson 2003). Long-term PM exposure was found to cause remodeling and fibrosis of airway cells in individuals who are non-smokers (Churg et al. 2003). In addition, ultrafine particles that can be found alongside larger particle PM promote inflammation by encouraging particle agglomeration and reducing AM phagocytosis (MacNee and Donaldson 2003).

The use of herbicides and pesticides for public parks and agriculture has been demonstrated to trigger Th2-dependent response (Duramad et al. 2006). Furthermore, chemicals

from various organic products such as paints and nail polish are found to cause allergic and respiratory problems through Th2-dependent mechanism (Zheng et al. 2011).

Anaphylaxis is caused by allergen that binds to B cells which produce the IgE, and the released IgE further binds to mast cells or basophils upon primary exposure (Ebisawa et al. 2017). When the individual encounters a second exposure to same allergen, the allergen then binds to the IgE-bound mast cells or basophils from the primary exposure, triggering histamine production and release. The released histamine quickly dilates blood vessels, promoting the anaphylaxis symptom. Furthermore, allergen tolerance is shown to be modulated by regulatory T helper cells (Treg). Treg increases IL-10 and TGF-β production. Evidence shows that allergen tolerance reduced IgE production and is characterized by Foxp3, CD25 expressions on the Treg cells (Noval Rivas and Chatila 2016; Martín-Orozco et al. 2017).

The status "allergy" refers to allergen-specific serological changes and symptoms aroused by the exposure to specific allergen (Salo et al. 2011; Stokes and Casale 2022). Allergy could be a long-time exposure effect since many evidences indicated that after long-term exposure to allergen or pollutant, allergic event could have increased incidence (Bracken et al. 2015; Liu et al. 2021). In this case, the attribution of allergy could not be easily determined. Clinically, though understanding the serological changes in patients with allergic diseases could be helpful in clarifying the pathogenesis and immunological mechanisms behind the disease, the presence of related antibodies, T helper cells, and cytokines might not be enough for diagnosis (Fanta 2022; Weston and Howe 2022). Therefore, to determine a clinical status being allergic or not, clinical symptoms, history taking, and physiological functions were critical indicators for evaluation for allergic disease diagnosis (Williams 2005; NHLBI 2021).

## State-of-art knowledge: air pollution and atopic dermatitis

### Risk factors in the air

Recent evidences have indicated that atmospheric hazards could cause negative effect on dermatological allergies. According to a guideline published by European Academy of Dermatology and Venereology (EADV), cigarette and volatile organic compounds were identified as provocation factors of atopic dermatitis (Wollenberg et al. 2018; Damevska et al. 2021). In a Korean population-based study, long-term exposure of particles smaller than 2.5 μm in diameter was associated with an increased risk of atopic dermatitis incidence, with a 1.42-fold hazard ratio (Park et al. 2021). Hazardous substances in the air that have been identified as potential risk factor for arousing or aggravating the onset of atopic dermatitis includes ozone, sulfur dioxide, nitrogen dioxide, hydrocarbons, non-methane hydrocarbons, and methane (Wang et al. 2021a, b; Ye et al. 2022). A previous observational study conducted in Shanghai, China also reported that aside from air pollution, extreme weather conditions including dry air and low temperature could also lead to aggravation of the onset of atopic dermatitis symptoms (Ye et al. 2022). Aside from atopic dermatitis, increased medical burden of other inflammatory dermatological diseases, such as psoriasis and seborrheic dermatitis, was observed in the population exposed in higher PM 2.5 and PM 10 concentration in the atmosphere (Park et al. 2022). Aside from gas-phase pollutants, some pollutants in the air such as lead, mercury, and organic carbon could cause impairment in via particulate approach (Damevska et al. 2020).

### Strategies for treatment

Exacerbation of atopic dermatitis could be associated with air pollution induced Th1/Th2 imbalance or aryl hydrocarbon receptor activation, leading to subsequent IgE generation (Damevska et al. 2021). Previous studies have identified potential approaches for human skin to absorb air pollutants. Direct contact and exposure to pollutants were regarded as factors to influence the onset of pollutant-associated skin diseases (Damevska et al. 2020). Fadadu et al. stated that a present-day topical therapeutic modulating agent targeting aryl hydrocarbon receptor for atopic dermatitis, Tapinarof (Paller et al. 2021), could be potentially effective for the treatment of air-pollution-exacerbated atopic dermatitis (Fadadu et al. 2021). However, given that some of the anti-pollution components could be irritative and serve possible risk factor of allergic status, topical products for air-pollution-exacerbated atopic dermatitis were scarce (Damevska et al. 2021).

## Potential prevention approaches of allergen-related allergy and interaction with public health

Preventions for the allergen-related allergy could be practiced through various approaches. In prevention of respiratory diseases aroused by air pollution, approaches could be applied in the aspects of environmental policy and personal prevention (Pfeffer et al. 2021). Policies strengthening the regulation of air pollution (i.e., emission of PM 2.5) were reportedly showing potential positive effect of respiratory function of residents (Laden et al. 2006; Gauderman et al. 2015; Guan et al. 2016). As for personal prevention, avoidance of places with high risk of allergen exposure could be effective in lowering the adverse influence in respiratory system (McCreanor et al. 2007). Moreover, antioxidants could also serve as feasible option as pharmacotherapies for allergen-associated allergic reaction prevention (Whyand et al.

2018; Pfeffer et al. 2021). For instance, in a previous translational study, vitamin D was reported to play a protective role in the pathogenesis of pollutant-induced inflammation (Pfeffer et al. 2018). Other substances or medications such as vitamin C, vitamin E, N-acetylcysteine, and sulforaphane could also provide similar effect on antioxidant response (Pfeffer et al. 2021). However. given that there were many risk factors regarding the development of allergic diseases, it is important to consider the effect of confounders while setting allergic diseases as observational outcomes in studies (Gau 2022; Paller et al. 2022). Therefore, while considering the preventive effect to pollutant-induced allergic reaction, potential influence of confounding biases should be noticed in studies.

The mechanistic role of allergens has gradually influenced global environment and public health. The early care and education (ECE) program in the USA is an important example to demonstrate the correlation between environmental toxicants, policies, and practices (Hoang et al. 2017; Querdibitty et al. 2021). Participants of ECE programs are children that could be chronically exposed to pollutants in the environment (Breysse et al. 2004; Querdibitty et al. 2021). Risk of developing clinical diseases were monitored and protective policies could be enforced based on the structure of ECE program. Improvements brought about by management practicing were also evaluated in the program (Alkon et al. 2016; Stephens et al. 2017). However, based on the variation of policy enforcement and the amount of caring facilities, difference could exist between different regions (Querdibitty et al. 2021). To further clarify the interaction between public health and allergens, future studies should focus on the effectiveness of different policy implement and the influence on environmental toxicant-associated pediatric allergic diseases.

## Conclusion

The current review provided current evidences regarding the association between various pollutants and the potential clinical diseases that could be induced. For people with high skin exposure to air pollutants such as PM 2.5, PM 10, or sulfur dioxide, potential onset of dermatological allergic events should be alerted. The detailed immunological mechanisms and clinical implications could potentially provide readers with clearer view to the interaction between allergic status and pollutants. Moreover, potential prevention approaches have also been provided in this review. For personal prevention, avoidance of contacting potential pollutant and consuming antioxidants could be possible approaches.

As a conclusion, different environmental allergens pose various extent of risk in people. The influence does not only limited in respiratory system but also could potentially lead to systemic influence and changes in the comorbidity status (Gau et al. 2022b). Identifying potential interaction between environmental pollution effects and allergy could be protective for future allergic statuses. Clarifying interactions between allergens, pollutions, and microbiomes could be effective in understanding the influence to the severity and onset time of allergic diseases (Burbank et al. 2017).

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## Declarations

**Ethics approval and consent to participate** Not applicable.

**Consent for publication** Not applicable.

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# 心因性休克病患使用葉克膜治療的呼吸照護經驗

Respiratory care experience of a cardiogenic shock patient on ECMO.

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## 前言

臺灣108年十大死因中，心臟疾病位於第二位。研究指出癌症、慢性呼吸道疾病、糖尿病、吸菸者，比一般人罹患心血管疾病的死亡風險高達2~7倍。本文描述一位診斷為急性冠狀動脈症候群患者，呼吸衰竭插管使用呼吸器，行冠狀動脈繞道手術(coronary artery bypass graft；CABG)後因心因性休克使用體外膜氧合(Extra-corporeal membrane oxygenation；ECMO)，於照護過程中呼吸器設定使用肺部保護策略(lung protection)避免肺部損傷之呼吸照護經驗。

## 呼吸治療評估

54歲男性，體重60公斤，因胸痛、胸悶至急診求治，呼吸衰竭插管使用呼吸器，心導管檢查顯示冠狀動脈性心臟病合併三條冠狀動脈狹窄(Coronary artery disease；CAD-3VD)，行冠狀動脈繞道手術後因心電圖呈現心室性心搏過速(Ventricular tachycardia；VT)給予多次電擊，仍出現心因性休克情形，最後使用靜脈-動脈體外膜氧合(Veno-arterial extra-corporeal membrane oxygenation；V-A ECMO)。過程中呼吸器使用肺部保護策略維持肺部擴張避免呼吸器導致的肺損傷，最後病人成功移除體外膜氧合且進行呼吸訓練嘗試脫離呼吸器。

## 確認問題

1.氣體交換障礙 2.呼吸道清除功能失效

## 呼吸治療措施

1-1機械通氣時，配合鎮靜藥物的使用，呼吸器依每公斤體重4-6ml設定潮氣容積。1-2監測肺部壓力使$P_{plat} \leqq$ 30 $cmH_2O$。2-1給予姿位引流、確實執行胸腔物理治療及抽痰。2-2維持床頭抬高30-45度以利肺擴張。2-3排空管路積水，避免吸入性肺炎及減少呼吸器相關肺炎。2-4定期追蹤胸腔X光變化。

## 結果評值

病人在治療過程中使用肺保護策略，潮氣容積維持在200-300ml，胸腔X光無出現新增浸潤及肺炎情形。移除ECMO後開始進行呼吸器脫離訓練，使用PSV模式潮氣容積可達450ml,但呼吸次數淺快約每分鐘30-35次，測量MIP/MEP:-8cmH2O/+12cmH2O，痰液可自咳至氣管內管可見範圍。

## 結論與討論

病人因心肌梗塞及心因性休克進行冠狀動脈繞道手術後使用ECMO幫助病人輔助心肺功能，呼吸器設定使用肺保護性策略，來避免造成肺損傷；個案心輸出量及血壓改善後移除ECMO，呼吸器改為潮氣容積6-8ml/kg的設定，並在個案病況穩定後嘗試脫離呼吸器。文獻指出呼吸器天數每增加一天，呼吸肌力量會消退5%，評估此個案因長時間使用呼吸器導致呼吸肌較無力，建議在病況穩定下可執行主動或被動運動來加強呼吸肌力，可利用儀器坐支持性運動，如使用手搖車在床上定速間歇性訓練，而非支持性上肢運動為舉起手臂至少高於肩膀並維持抵抗重力、手臂舉重、擴胸運動等，以利早日脫離呼吸器。

關鍵字

心因性休克(cardiogenic shock)、肺部保護(lung protection)、體外循環維生系統 (ECMO)

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# 從實證觀點探討肺高壓病人執行肺復原之成效

# Evidence-base Effect of Pulmonary Rehabilitationin Adult with Pulmonary Hypertension

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## RT 評估與問題確立

肺高壓定義為休息狀態時，以右心導管測得的平均肺動脈壓力大於或等於25mmHg，依據歐洲心臟學會公告之準則，造成肺高壓的病因可分成五大類，無論為哪一類病因導致，肺高壓的臨床表徵都是運動受限和逐漸增加的呼吸困難。根據世界衛生組織(WHO)以及紐約心臟協會(NYHA)分為四級，最嚴重者甚至於休息狀態下也有呼吸困難和胸痛等症狀。臨床上觀察到肺高壓病人，會因為漸趨嚴重的症狀而影響日常生活，故憑藉實證手法探討是否能藉由肺復原運動改善其生活品質，作為日後治療之參考依據。

## 文章搜尋步驟

依據實證醫學的角度，提出 PICO 以架構臨床問題，P：成人(Adult)、肺高壓(Pulmonary hypertension)，I：肺復原(Pulmonary rehabilitation)，C：一般照護(Usual medical therapy)，O：運動能力(Exercise capacity)、生活品質(Health-related quality of life)，本實證為治療型問題，採用 PICO 同義字以及 MeSHterm 作為搜尋關鍵字，於 PubMed、Uptodate、Clinicalkey、Cochrane Library 資料庫中進行搜尋五年內文獻，排除重複且完全符合的 PICO 後，僅一篇系統性回顧和統合分析(Systematic Review and Meta-Analyses)，此篇為 2017 出版之 Exercise-based rehabilitation programmesfor pulmonary hypertension(Review)，Critical Appraisal Skills Programme(CASP)評讀證據等級為 Level 1。

## 文獻整理

此篇作者資料庫搜尋了 Cochrane Airways Register of Trials、Cochrane Central Register of Controlled Trials、MEDLINE、Embase、PEDro、Pubmed、CENTRAL，搜尋年份截至截稿前，未限制出版類型及語言，並且搜尋了所有參考文獻以及相關會議摘要，共搜尋了 2451 篇，扣除掉重複和明顯無關的文獻，選出共 29 篇全文論文後，排除非隨機對照試驗、沒有運動訓練和錯誤的介入措施後，最後篩選出共 6 項研究(11 篇報告)。過程中執行肺復原，不限頻率、時間及運動內容。其主要結果為：在執行肺復原後，於六分鐘走路測試(6MWD)中有顯著差異(P<0.0001，I2=64%)，平均增加 60.12 公尺(MD 30.17 ~ 90.07)，於心肺運動最大能力測試(CPET)中，VO2 peak 明顯增加(MD 2.4 ml/kg/min，95% CI 1.4 ~ 3.4)，亦顯示有顯著差異(P<0.0001，I2=37%)。本篇研究的生活品質由生活品質量表(SF-36)進行評估，其中生理功能問卷(PCS)統計(MD 4.63，95% CI 0.8 ~ 8.47)、心理功能問卷(MCS)統計(MD 4.17，95% CI 0.01 ~ 8.34)、角色限制(Role physical)統計(MD 21.8，95% CI 14.40 ~ 29.23，I2=0%)和社會功能(Social function)統計(MD 14.01，95% CI 9.82 ~ 18.21，I2=0%)皆表示生活品質提高；使用 CAMPHOR 問卷進行評估，其中症狀表現(MD -3.08，95% CI -7.78 ~ 1.62)和整體生活質量(MD -5.42，95% CI -8.03 ~ -2.81，I2=29%)亦表示生活品質提高，綜合上述問卷結果顯示運動介入後相關生活品質提高。此外本篇作者提出研究過程中僅有一例不良事件，為暈眩而中止肺復原運動訓練。

## RT 措施及評值、反思

經上述實證結果顯示病人進行肺復原後，於運動測試結果中觀察到在六分鐘走路測試(6MWD)和 VO2 peak 皆增加，顯示運動能力的改善，而透過生活品質

的問卷(SF-36 和 CAMPHOR)評估，也顯示肺復原可以使肺高壓病人的生活品質獲得改善。因此當臨床上遇到肺高壓病人，因為症狀漸趨嚴重而影響生活時，可以建議執行肺復原運動，幫助病人改善運動能力和提升生活品質。

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# 祖父母以對話式閱讀教學方案提升認知發展遲緩兒童之聽覺理解及口語表達能力–個案報告

呂智源 、高立瑋

## 前言

對話式閱讀可有效提升兒童的聽覺理解及口語表達能力，但國內目前無關於祖父母實施對話式閱讀的研究，因此本研究將探討祖父母實施對話式閱讀，是否可提升認知發展遲緩兒童的聽覺理解及口語表達能力。

## 方法

此篇為個案研究，研究對象為 3 歲 2 個月認知發展遲緩兒童，由祖父母帶來醫院接受早療服務，並於研究期間帶領研究對象閱讀繪本，每週閱讀一本繪本，每本閱讀兩次，每次 15-20 分鐘，介入時間總共 12 週。前測與後測以華語兒童理解與表達詞彙測驗(以下簡稱 REVT)、林寶貴老師之修訂學齡前兒童語言障礙評量表及非正式化評估、進而評估研究對象聽覺理解及口語表達能力的進展。

## 結果

研究對象在 REVT 理解分數前測為 0 分、後測為 8 分；表達分數前測為 2 分、後測為 2 分，顯示研究對象在詞彙理解能力上有提升。林寶貴老師之修訂學齡前兒童語言障礙評量表分數上，前測總分為 6 分，後測為 7 分，較無明顯進展。非正式化測驗上對於整體語言理解及口語表達能力上有進步。

## 結論

依據研究結果，祖父母實施對話式閱讀可提升認知發展遲緩兒童的聽覺理解及口語表達能力，但因研究時間有所限制，導致 REVT 理解分數上有學習效應，可能有高估的情況需再留意。本研究根據上述結果提出建議，以供未來研究之參考。

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# Comparison of Improving Uptake of Mammography Screening by Using Two Types of Short Message Service Reminders: A Randomized Controlled Trial

Y.-T. Huang

## Introduction

Previous investigations show that sending Short Message Service (SMS) reminders is associating with the rate of ongoing mammography screening, but it is unknown whether different reminder content can affect the rate of ongoing mammography screening. Therefore, the purpose of this study is to compare two types of SMS reminders for increasing the uptake of mammography screening. .

## Methods

Two hundred twelve female subjects whose age were between 45 and 69 were recruited and randomly assigned into two groups. One group got SMS reminders informing promotional materials was offered as completing mammography (SMS, N = 108). The other group got SMS reminders informing female technicians conducting exam and promotional materials offered as completing mammography (SMSf, N = 104). All the subjects were under the Health Insurance Plan in Taiwan. In addition, they did not get mammography in the past two years. Their phone numbers were released from electronic medical charts by authority's approval. The outcome measurement was the rate of receiving mammography screening in six months since getting SMS reminders. Chi-square tests were used to compare the rate between groups after getting SMS reminders in six months. SPSS 24 (IBM, NY), with a significant level of 0.05, was used.

## Results

The rate of getting mammography screening was comparable between groups. Chi-square test was conducted ($p = .338$). The results didn't showed statistically significant. Rate of receiving mammography in SMSf group was about 11% lower than SMS group (50% vs. 39.8%).

## Discussion and Conclusions

The increasing in the rate of receiving mammography screening could be resulted from SMS reminders informing that mammography screening is conducted by female technicians. Although there is no statistical significance between groups, the small sample size between groups could be a reason. A large number of sample size is needed to confirm the effect of different content of SMS reminders. screening.

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# 隱翅蟲蜂窩性組織炎急診案例

# A case of Paederus cellulitis-Case report

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## Introduction

Skin and soft-tissue infections are a frequent problem frequently in clinical practice. Often with wide spectrum of clinical presentations, ranging from simple cellulitis to rapidly progressive illness, it may lead to complications that require prompt treatment: such as necrotising fasciitis, gas gangrene, severe sepsis. Early diagnosised of the disease, appropritate antimicrobilas, and timely surgical intervention as soon as, is critical the successful treatment. The course of the disease is rapid, typically progressing to septic shock and death, so we have to attach to this issue.

## Case Report

This 48-year-old woman denied any past medical history, suffered from rapidly expanding symptoms with erythema, warmth, and tenderness over trunk, associated with chillness and fatigue form 3 days ago. At ER course, GCS:E4V5M6, Vital signs BP:89/42 mmHg, pulse 102 ,RR 24,BT 38.4, Spo2:96%, acute illness looking, huge painful skin lesions are on the posterior trunk, erythema, warm, accociated some vesicles and necrotic tissue formation. The history of Paederus bites at 3 days before.

Laboratory revealed severe leukyosis with left shifting, raised CRP16.49, abnormal electrolyte including: BUN 73.8 mg/dl, Creatine 2, eGFR 28.26, sodium 117 meq/L, Glucose 452 mg/dl, hypoalbuminemia.

She was admission for further treatment. Hospitalization, prescripted with Tigecycline, isotonic solution resuscitation, control blood sugar, maintain fluid balance. After fluid supply, adequate urine output with stable blood pressure. Early surgical intervention with incision, drainage, and debridement. Improving of lab data: WBC 24110 to 9330, CRP 16.49 to 3.47. Pus sample from surgery growed OSSA. We de-escalation antibiotics theaty to Oxacillin. Wound care with wet-to-dry dressing changes. Wound shows less purulent discharge and less necrosis tissue formation. Staging debridement also performed for her. The patient discharge for 14 days later.

## Discussion

1. Using antimicrobials based on the severity of local and systemic signs and the presence or absence of comorbid conditions for patient and on the early prescription of shorter antibiotic treatment courses.
2. Source control for drainage of infected fluids, debridement of infected soft tissues, removal of infected devices or foreign bodies.

圖一：急診入院時蜂窩性傷口

圖二：第一次清創傷口

圖三：第二次清創口傷口

# 一位乳癌患者於骨骼檢查意外發現有薦骨壓力性骨折：SPECT/CT 之臨床價值

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## 背景

我們報告一名 75 歲乳癌患者，患者抱怨有嚴重下背痛(約 2 年)和椎間盤突出病史。臨床安排全身骨骼掃描檢查做定期追蹤。在 SPECT/CT 之 CT 影像意外發現有薦骨和左側恥骨處有骨折壓力性骨折。之後，安排患者進一步評估及治療壓力性骨折。此案例說明 SPECT/CT 中 CT 可提供臨床額外輔助診斷價值。

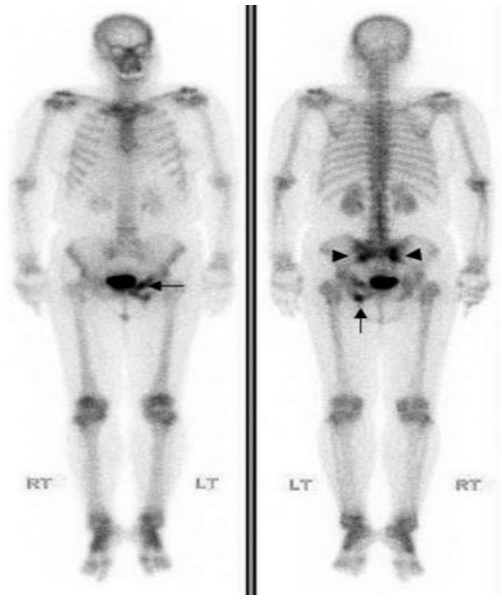
## 方法

一名 75 歲乳癌女性患者，臨床安排全身骨骼掃描檢查做定期追蹤。靜脈注射 740MBq(20mCi)的 99mTc-MDP 後 3 小時進行全身骨骼掃描檢查，全身骨骼掃描檢查發現在薦骨和左側恥骨有不明放射性活性聚積。為了準確定位和定位骨盆區域解剖形態，執行 SEPCT/CT 檢查。SEPCT/CT 檢查參數如下：The CT apparatus operates at 140kV and up to 2.5 mA.A step-and-shoot protocol of 25 s/3° for a total of 60 views per camera head was used。

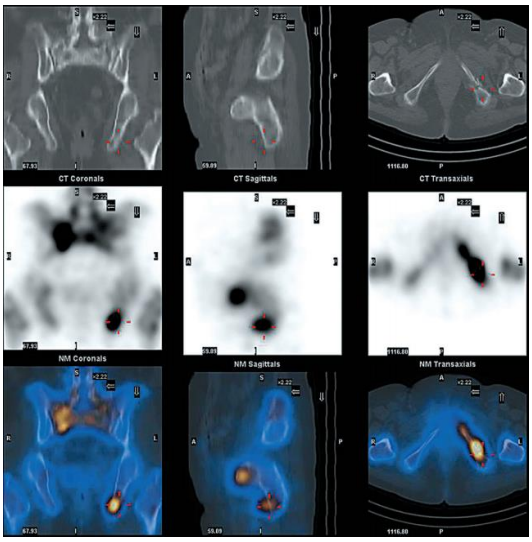
## 結果

骨骼攝影顯示在薦骨和左側恥骨有放射活性聚集(圖一)。SPECT/CT 中 CT 骨骼攝影發現，在薦骨和左側恥骨處有骨折線，圖像顯示放射性藥品在左側恥骨上異常攝取(圖二)。SPECT/CT 中 CT 發現，在薦骨處有骨折線，SPECT/CT 圖像顯示放射性藥品在薦骨異常攝取(圖三)。

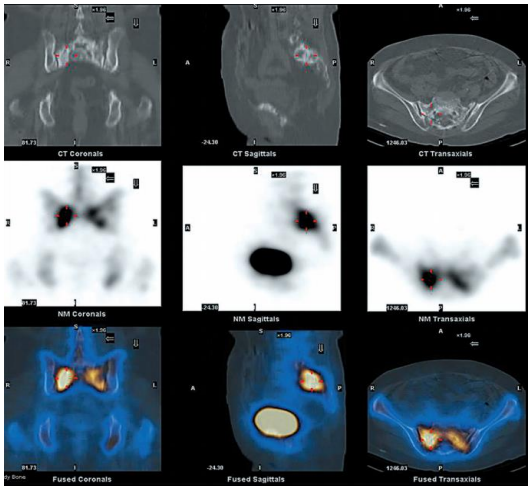
綜合 SPECT/CT 之影像，上述影像是壓力性骨折所造成。




圖一、在薦骨和左側恥骨有放射活性聚集




圖二、在薦骨和左側恥骨有放射活性聚集




圖三、在薦骨處有骨折線，圖像顯示放射性藥品在薦骨異常攝取

## 結論

薦骨之壓力性骨折 sacral insufficiency fractures (SIF)常見於骨質疏鬆的老年婦女，通常是沒有外傷或輕微撞傷後出現腰背和骨盆疼痛。SIF 屬於一種特殊類型的壓力性骨折，發生原因是礦物質含量減少和彈性降低。骨骼攝影之薦骨處典型特徵為 Honda sign (HS)；SPECT/CT 優點是可以針對懷疑的病灶同時準確定位並觀察解剖形態。骨骼攝影顯示在薦骨和左側恥骨有放射活性聚集，CT 發現在薦骨和左側恥骨處有骨折線。造成上述影像懷疑是壓力性骨折所造成。本病例報告強調 SPECT/CT 中 CT 影像在影像判讀上可以提供臨床額外輔助診斷價值。