A trans-disciplinary overview of case reports of thunderstorm-related asthma outbreaks and relapse

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There is evidence that, during the pollen season, thunderstorms can be associated with allergic asthma outbreaks in patients suffering from pollen allergy [1], and there are observations in favour of the possibility that thunderstorms disturb ground-level pollen grains, which may release allergenic particles of respirable size into the atmosphere after rupture by osmotic shock [2, 3].

During the first 20–30 min of a thunderstorm, patients suffering from pollen allergy may inhale a high concentration of the allergenic material that is dispersed into the atmosphere, which in turn can induce (severe) asthmatic reactions in some cases [3–6]. Even though thunderstorms can induce severe asthma attacks or exacerbations, they are neither frequent nor responsible for a high amount of disease exacerbation. However, physicians and pollen allergy patients should know the mechanisms involved in the release of allergens from airborne pollen grains during thunderstorms and the associated risk in view of prevention. Information about the risk of an asthma attack is also relevant in subjects affected only by seasonal allergic rhinitis who can inhale lower airways pollen aerosol. In addition, there is a potential risk of thunderstorm-related relapse of asthma attacks in some patients. This constitutes a major concern nowadays as the possibility of thunderstorm-associated asthma outbreaks have become of dramatic actuality due to the ‘highly likely’ increase in frequency of heavy precipitation events, including thunderstorms, projected by the climate change scenarios for the future decades [7].

The purpose of this article is to gather existing trans-disciplinary data on thunderstorm-related asthma attacks and potential relapse in the same patient.

ALLERGENIC POLLEN IN THE ATMOSPHERE AND POLLEN ALLERGY

Pollen grain, which is a causative agent of allergic respiratory responses, is among the commonest allergens and pollen allergy due to its elevated prevalence and associated costs is now a public health problem [8]. Worldwide, up to 40% of the general population are reported to suffer from hay fever [8, 9]. In the European Union countries, between 8% and 35% of young adults show immunoglobulin (Ig)E serum antibodies to the most commonly encountered grass pollen allergens [10] and the cost of pollen allergy in terms of impaired work fitness, sick leave, consulting physicians and drugs is very high [11].

The concentration of allergenic pollen influences the degree of symptoms, but the relationship between allergen exposure, inflammation of airways and clinical symptoms is complex, and factors other than allergens are involved [12]. Pollen grains penetrate into the upper respiratory tract but, because of their size, which is always >10 μm diameter, they rarely reach the bronchial regions. However, bronchial asthma and its equivalents, such as irritative cough, are not infrequent in people affected by pollen-induced allergy [8].

During natural pollination, mature pollen grains are dehydrated when they are released by anthers at the dispersal time. Once the pollen grains come into contact with a wet surface they absorb water undergoing rapid metabolic changes together with ultrastructural modifications. The pollinic allergens that are located in the pollen walls and/or in the cytoplasm are then rapidly released. This happens when the pollen grains come into contact with the oral, nasal or conjunctival mucosa that are humid, thereby inducing the appearance of pollinosis symptoms in sensitised patients [13]. Cytoplasmic allergens are also released into the atmosphere when the pollen bursts under osmotic shock and can create a respirable allergenic aerosol.

THUNDERSTORMS AND ALLERGIC ASTHMA EPIDEMICS IN POLLEN ALLERGY SUBJECTS DURING POLLEN SEASON

A PubMed search with MeSH terms “THUNDERSTORM” and “ASTHMA” resulted in 38 papers, 11 of which reported on cases of thunderstorm-related asthma that were considered to be of quality and included in the overview. The studies evaluated outbreaks of asthma during thunderstorms (table 1) and allowed the identification of associated characteristics (table 2).

Thunderstorm-related asthma outbreaks have been described in various geographical zones. One of the first observations regarding thunderstorms and asthma outbreaks was provided by Packe and Ayres [3] at the East Birmingham Hospital...
Other asthma outbreaks during thunderstorms have been described in Australia. In Melbourne, two large asthma outbreaks (rapid increase in hospital or general practitioner visits for asthma) coincided with thunderstorms [14]. In Wagga Wagga, 215 asthmatic subjects attended the local emergency department, 41 of whom required admission to hospital [18]. In south eastern Australia, Marks et al. [19] observed that the incidence of excess hospital attendances for asthma during late spring and summer was strongly linked to the occurrence of thunderstorm outflows and demonstrated that the arrival of a thunderstorm outflow was accompanied by a large increase in the concentration of ruptured pollen grains in ambient air.

Thunderstorm-related asthma was observed in Naples, Italy, on June 3 and 4, 2004, when six adults and one child received treatment in emergency departments. One patient was admitted to an intensive care unit for very severe bronchial obstruction and acute respiratory insufficiency following a sudden thunderstorm. All individuals were outdoors when the thunderstorm struck. In one severe case, a female sensitised only to *Parietaria* pollen allergen, soon began to show symptoms of intense dyspnoea, which gradually worsened. She was taken to hospital where she was intubated and given high intravenous doses of corticosteroids. She was discharged a few days later. This patient had previously suffered from seasonal asthma but had been asthma-free for the past few years and did not need continuous therapy. None of the other six subjects regularly took anti-allergic and/or anti-asthma drugs. All seven patients were sensitised with allergic

| Table 1: Thunderstorm asthma studies |
|--------------------------------------|
| **Country** | **Study year** | **Event** | **Comments** |
| UK [3] | 1983 | 26 sudden cases of asthma attacks | Increased risk of asthma in relation to thunderstorms |
| Australia [14] | 1992 | Hospital attendances and admissions because of asthma exacerbation | Late spring thunderstorms in Melbourne can trigger epidemics of asthma attacks (five to 10-fold rise) The seasonal nature of the phenomenon and the pattern of allergic responses found in affected patients suggests a possible aetiological role for rye grass pollen |
| UK [15] | 1997 | Asthma or other airways disease hospital visits | 640 cases who attended during a 30-h period from 18:00 h on June 24, 1994, nearly 10 times the expected number |
| Canada [16] | 1992–2000 | 18970 hospital ED asthma visits among children 2–15 yrs of age | Summer thunderstorm activity was associated with an OR of 1.35 (95% CI 1.02–1.77) relative to summer periods with no activity |
| USA [17] | 1993–2004 | 219832 asthma ED visits; 24350 of these visits occurred on days following thunderstorms | Significant association between daily counts of asthma ED visits and thunderstorm occurrence |
| Australia [18] | 2000 | Asthma visits during thunderstorms | Asthma visits were 3% higher on days following thunderstorms |
| Australia [19] | 2001 | Hospital attendances for asthma | History of hay fever and allergy to rye grass are strong predictors for asthma exacerbation during thunderstorms in spring |
| UK [20] | 2002 | A case-control study of 26 patients presenting to Cambridge University Hospital with asthma after the thunderstorm | The incidence of excess hospital attendances for asthma during late spring and summer was strongly linked to the occurrence of thunderstorm outflows |
| Italy [21] | 2004 | ED asthma | Alternaria alternata sensitivity is a compelling predictor of epidemic asthma in patients with seasonal asthma and grass pollen allergy and is likely to be the important factor in thunderstorm-related asthma |
| Italy [22] | 2010 | ED asthma | Six cases of thunderstorm-related asthma because of pollen (Parietaria) |
| Australia [23] | 2010 | Epidemics of “thunderstorm asthma” that occurred in Melbourne during spring 2010 | 20 cases of thunderstorm-related asthma because of pollen (olive tree) |

ED: emergency department; OR: odds ratio.
There is a link between asthma epidemics and thunderstorms. The epidemics related to thunderstorms are limited to seasons when there are high atmospheric concentrations of airborne allergenic pollens. There is a close temporal association between the start of the thunderstorm and the onset of epidemics. There are no high levels of gaseous and particulate components of air pollution during thunderstorm-related asthma outbreaks. Subjects with pollen allergy who stay indoors with the window closed during thunderstorms are not involved. There is a major risk for subjects who are not receiving anti-asthma treatment, but subjects with allergic rhinitis and without previous asthma can experience severe bronchoconstriction. There are no observations on the involvement of asthma in nonallergic subjects.

**TABLE 2** Characteristics of documented epidemics of thunderstorm-associated asthma

- There is a link between asthma epidemics and thunderstorms.
- The epidemics related to thunderstorms are limited to seasons when there are high atmospheric concentrations of airborne allergenic pollens.
- There is a close temporal association between the start of the thunderstorm and the onset of epidemics.
- There are no high levels of gaseous and particulate components of air pollution during thunderstorm-related asthma outbreaks.
- Subjects with pollen allergy who stay indoors with the window closed during thunderstorms are not involved.
- There is a major risk for subjects who are not receiving anti-asthma treatment, but subjects with allergic rhinitis and without previous asthma can experience severe bronchoconstriction.
- There are no observations on the involvement of asthma in nonallergic subjects.

**FIGURE 1.** Parietaria pollen.

asthma emergency department visits and thunderstorm occurrence (p<0.001). Overall, the number of emergency department asthma visits was 3% higher on days following thunderstorms. Rainfall and gusts of wind played a role, with higher risks of asthma associated with rainfall and strong gusts.

**Possible mechanisms for thunderstorm-related asthma**

Although much remains to be discovered about the relationship between an increase in the number of asthma attacks and thunderstorms, reasonable evidence exists in favour of a causal link between them in patients suffering from pollen allergy. Although rainfall is usually known to remove pollen from the air, that is not always the case. During a thunderstorm, dry updrafts entrain whole pollens into the high humidity at the cloud base where pollens may rupture and cold downdrafts carry pollen fragments (pollen grains are too large to penetrate the deeper airways) to ground level where outflows distribute them. As a consequence, there is a high respirable allergen load in the air. TAYLOR et al. [27] hypothesised that the turbulent front of the advancing outflow releases more pollen from flowering grasses. Due to strong electric fields that develop during thunderstorms, positive ions are released from the ground and could attach to particles and/or electric charge may enhance pollen rupture, thus, enhancing bronchial hyperresponsiveness. Moreover, grass pollen may release large amounts of paucimicronic allergenic particles, i.e. cytoplasmatic starch granules containing grass allergens (allergen-bearing starch granules), after rupture by osmotic shock during thunderstorms. In 1998, SUPHIOCU et al. [28] showed that rye grass pollen grains contain a large amount of starch granules coated with allergens. After being ruptured in rainwater by osmotic shock, each grain can release ~700 starch granules, which are small enough to penetrate the airways and trigger asthma attacks in previously sensitised subjects. Allergen-bearing starch granules obtained upon contact of pollen with water have been shown to create an inhalable allergenic aerosol capable of triggering an early asthmatic response in an experimental in vitro study. Starch granules were shown to be recognised by pollen sensitised in rat serum and to trigger lymph node cell proliferation in these rats [29]. These data provide new arguments supporting the implication of grass pollen starch granules in thunderstorm-related asthma. Other pollens, such as those of *Parietaria*, which do have not starch granules in the cytoplasm, can release other paucimicronic cytoplasmic component carrying allergens, as recently confirmed by JATO et al. [30]. Due to their very small size (<5 μm), these microparticles can penetrate the lower airways inducing the occurrence of bronchial...
allergic symptoms. In rats, it has been shown that pollen cytoplasmic granules (PCGs) containing allergens are able to deeply penetrate the respiratory tract and induce local and strong allergic and inflammatory responses more closely linked with asthma- than rhinitis-related allergic symptoms [31]. The proliferative responses of lymph node cells were similar in PCG- and pollen-sensitised rats. IgE and IgG1 levels were higher in pollen- than PCG-sensitised rats. However, eosinophils, lymphocytes and pro-allergy cytokines in bronchoalveolar lavage fluid were higher in PCG- than pollen-sensitised rats. Overall, significantly increased amounts of pollen and mould spore counts have been found during thunderstorms, although published data are scant [19, 21, 24]. However, to date, no experimental study reproducing thunderstorm conditions has been conducted to test the thunderstorm hypothesis in more detail. It is likely that there is no role for cold or thunderbolts as only patients with allergic sensitisation to pollen and not detail. It is likely that there is no role for cold or thunderbolts as only patients with allergic sensitisation to pollen and not patients suffering from intrinsic asthma have been involved. In the case of fungal spores, such as Alternaria, the prerequisites for asthma epidemics associated with thunderstorms have been described as follows [20, 25]: 1) a sensitised, atopic, asthmatic individual; 2) a sudden, large allergen exposure; 3) a large-scale thunderstorm with cold outflow occurring at a time and location during an allergen season in which large numbers of asthmatics are outdoors; and 4) sudden release of large amounts of respirable allergenic fragments, particularly fungal spores such as Alternaria.

### IS THERE A RISK OF RELAPSE OF THUNDERSTORM-RELATED ASTHMA?

Whereas there is increasing evidence of a possible link between thunderstorms and asthma, the fact that relapses of thunderstorm-related asthma are also possible, as shown by the following case report, is less well known.

A 35-yr-old female who experienced near fatal asthma in concomitance with a thunderstorm in June 2004 and who was treated in the emergency department of Cardarelli hospital in Naples was admitted to the emergency department of the same hospital 7 yrs later, on May 24, 2011, despite appropriate treatment with salmeterol 50 μg and fluticasone 250 μg b.i.d. She was immediately treated with a high concentration of oxygen and 2 g i.v. methylprednisolone on admission to the emergency department. Given the severity of respiratory failure, arterial blood gas analysis was performed under oxygen therapy, giving 70 mmHg. Since the first episode, the patient had avoided being outdoors when a thunderstorm was approaching. The second time, an unexpected thunderstorm occurred while she was driving her motorbike and she experienced increasing dyspnoea that had to be treated in the emergency department some hours later. Clinical parameters were similar to those during the first episode. On those days, the Parietaria pollen count was higher than in the past 10 yrs in Naples in the same period of the year (260, 113 and 79.4 pollen m⁻³ air in the previous 3 days, respectively), but no

### TABLE 3

| Hill’s criteria                                      | Application to the thunderstorm-related asthma                                      |
|------------------------------------------------------|--------------------------------------------------------------------------------------|
| Temporal relationship                                | Thunderstorms always precede asthma attacks                                          |
| Strength                                              | Increased risk of asthma attacks in relation to thunderstorms                         |
| Dose–response relationship                           | Increased amount of pollen and mould spores at the beginning of the thunderstorm     |
| Consistency                                          | Associated with increased probability of asthma attacks in pollen patients and other |
| Plausibility                                         | allergic patients                                                                     |
| Consistency of alternate explanations                 | Association between thunderstorm and asthma found in different studies and different |
| Experimental                                         | populations                                                                           |
| Specificity                                          | Evidence of biological plausibility at the basis of thunderstorm-related asthma through |
| Coherence                                            | pollen exposure (allergens and starch granules in the cytoplasm or other paucimicronic |
|                                                      | cytoplasmic-components carrying allergens)                                           |
|                                                      | Evidence to be established in the case of mould spores                                |
|                                                      | Alternate hypothesis involving chemical air pollution less explanatory than           |
|                                                      | thunderstorm-related asthma                                                           |
|                                                      | Evidence indicating that prevention is possible by avoiding exposure to thunderstorm   |
|                                                      | (at its beginning) in pollen patients                                                |
|                                                      | Poorly shown by experimental data (also sparse and heterogeneous)                    |
|                                                      | Existing theory and knowledge support the existence of thunderstorm-related asthma    |
air pollutants were observed. Her symptoms became stable within a couple of weeks following a short course of treatment with oral corticosteroids. She was offered specific immunotherapy treatment with *Parietaria* pollen extract but refused because of a possible pregnancy. Because this is a unique report, further investigations are needed to confirm thunderstorm-related asthma relapses.

### CRITERIA APPLIED TO THUNDERSTORM-RELATED ASThma

To better understand the existing evidence on thunderstorm-related asthma, we explored the nature of the relationship between thunderstorm and asthma attacks by applying the criteria of Hill [32], usually used in epidemiological research to identify causation between a risk factor and a health event. Most of the criteria of Hill [32], although not all, support the hypothesis of a causal link of thunderstorms to asthma attacks through pollen exposure (table 3). The main reason for uncertainty is that data are still scant, in particular experimental data, which challenges the specificity criterion according to which a single putative cause produces a specific effect. Marks et al. [19] demonstrated that the arrival of a thunderstorm outflow was accompanied by a large increase in the concentration of ruptured pollen grains in ambient air. Pulimood et al. [20] reported that in the thunderstorm in which they studied asthma, epidemics were associated with increased levels of *Alternaria, Cladosporium* and *Didymella* spp. but this has not been reproduced in any experiment.

**Public health dimension**

Depending on the size of the population at risk, thunderstorm-related asthma outbreaks may threaten the operative capacity of health services, as was the case in London [15]. Therefore, it is of interest to establish which risk factors may predict the occurrence of asthma outbreaks in such a way that early warning systems can be developed. With this approach, and using the same data set as above, Newsom et al. [33] identified 56 asthma epidemics defined as periods of exceptionally high asthma admission counts compared with predictions of a log-linear autoregressive model. Of note, the authors measured pollen counts and, for the first time, thunderstorms using densities of sferics (lightning flashes). However, the data from Newsom et al. [33] do not support the possibility of predicting asthma outbreaks by using meteorological data and pollen counts. In their study, thunderstorms and high grass pollen levels preceded asthma epidemics more often than expected by chance. However, most thunderstorms, even following high grass pollen levels, do not precede epidemics and most epidemics are not associated with thunderstorms or unusual weather conditions but to other factors, such as respiratory infections. An early warning system based on the indicators examined here would, therefore, detect few epidemics and generate an unacceptably high rate of false alarms. In addition, real-time data on both weather forecasting and pollination are not available in many countries at present. Finally, despite the increasing amount of data about allergen content of ambient air published in recent years [34, 35], to date, pollens or mould allergens have never been quantified during a thunderstorm. Hopefully, availability of pollen allergen count on a daily basis, as is planned in the frame of the European HIALINE project (www.hialine.eu), could provide conclusive data on the actual changes in the allergenic load of the air during such an extreme precipitative event. Preliminary data have shown that although pollen count and allergen in ambient air follow the same temporal trends, a 10-fold difference can exist in allergen potency of birch pollen, so that symptoms might be difficult to correlate with pollen counts, but perhaps better with allergen exposure [34].

### CONCLUSIONS

Thunderstorm-related asthma is a dramatic example of the allergenic potential of pollen antigens. Pollen allergic patients who encounter the allergenic cloud of pollen are at higher risk of having an asthma attack. Subjects allergic to pollen who are in the path of the thunderstorm outflow are likely to inhale airborne pollen allergens and experience an airway asthmatic response. Relapse is also possible. A similar phenomenon has been hypothesised for mould spores.

Thunderstorms are sudden and poorly predictable in nature and a specifically designed study is therefore a challenge for researchers. However, it is mandatory to analyse available and forthcoming data with a multidisciplinary approach in order to address the full spectrum of this issue.

In conclusion, patients suffering from pollen allergy should be alerted of the danger of being outdoors during a thunderstorm in the pollen season. Patients who experienced an episode of severe thunderstorm-related asthma could be at risk of a relapse during a heavy precipitation event, even if receiving treatment.

### STATEMENT OF INTEREST

None declared.

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