**Table 1** Clinical characteristics and microbiological findings of 231 patients with community acquired pneumonia

| | Enterovirus (n = 12)* | Rhinovirus (n = 7) | Influenza A (n = 17)* | Other respiratory viruses (n = 12) | Other or undetermined aetiology (n = 184) |
|---|---|---|---|---|---|
| Age (y) (mean (SD)) | 45.9 (18.5) | 44.6 (19.9) | 64.2 (16.7) | 50.3 (23.4) | 48.8 (17.7) |
| Males (n (%)) | 6 (50) | 6 (86) | 5 (29) | 7 (58) | 103 (56) |
| Underlying disease (n (%)) | 4 (33) | 4 (57) | 9 (53) | 3 (25) | 73 (40) |
| COPD or asthma (n (%)) | 2 (17) | 3 (43) | 4 (24) | 1 (8) | 23 (13) |
| Cardiovascular disease (n (%)) | 2 (17) | 1 (14) | 3 (18) | 2 (17) | 29 (16) |
| Smoker (n (%)) | 4 (33) | 4 (57) | 3 (18) | 1 (8) | 59 (32) |
| PSI class IV–V (n (%)) | 2 (17) | 2 (29) | 8 (47) | 2 (17) | 35 (19) |
| Died (n (%)) | 0 | 1 (14) | 3 (18) | 0 | 1 (5) |
| *Streptococcus pneumoniae* (n (%)) | 3 (25) | 4 (57) | 6 (35) | 2 (17) | 50 (27) |

COPD, chronic obstructive pulmonary disease; PSI, Pneumonia Severity Index.
*Two patients with enterovirus and influenza A.

important viruses causing this disease. Collectively, our findings corroborate those of Jennings and colleagues[1] and support their conclusion that the importance of both viral pneumonia and mixed viral/bacterial pneumonia may be greater than previously realised.

**U Hohenthal,[1] R Vainionpää,[2] J Nikoskelainen,[1] P Kotilainen[1]**

[1] Department of Medicine, Turku University Hospital, Turku, Finland; [2] Department of Virology, University of Turku, Turku, Finland

**Correspondence to:** Dr U Hohenthal, Department of Medicine, Turku University Hospital, Kiinamyllynkatu 4-8, 20520 Turku, Finland; ulla.hohenthal@tyks.fi

**Competing interests:** None.

**Ethics approval:** Ethics approval was obtained

## REFERENCES

1. **Jennings LC,** Anderson TP, Beynon KA, *et al*. Incidence and characteristics of viral community acquired pneumonia in adults. *Thorax* 2008;**63**:42–8.
2. **Hohenthal U,** Vainionpää R, Meurman O, *et al*. Aetiological diagnosis of community acquired pneumonia: Utility of rapid microbiological methods with respect to disease severity. *Scand J Infect Dis* 2008;**40**:131–8.
3. **Vuorinen T,** Vainionpää R, Hyypiä T. Five years' experience of reverse-transcriptase polymerase chain reaction in daily diagnosis of enterovirus and rhinovirus infections. *Clin Infect Dis* 2003;**37**:452–5.
4. **Ishizuka S,** Yamaya M, Suzuki T, *et al*. Effects of rhinovirus infection on the adherence of Streptococcus pneumoniae to cultured human airway epithelial cells. *J Infect Dis* 2003;**188**:1928–39.
5. **Angeles Marcos M,** Camps M, Pumarola T, *et al*. The role of viruses in the aetiology of community-acquired pneumonia in adults. *Antivir Ther* 2006;**11**:351–9.
6. **Jennings LC,** Anderson TP, Werno AM, *et al*. Viral etiology of acute respiratory tract infections in children presenting to hospital: role of polymerase chain reaction and demonstration of multiple infections. *Pediatr Infect Dis J* 2004;**23**:1003–7.

# Leptin and regulatory T cells in obese patients with asthma

Taylor and colleagues[1] demonstrated a significant association between asthma severity and obesity. However, the mechanisms underlying this association are not fully understood. We suggest that the increase in asthma severity in obese patients might also be related to a defective function of regulatory T cells (Tregs).

Tregs play an essential role in immune homeostasis and protection against autoimmunity, and it has been suggested that the function of Tregs may be defective in patients with asthma.[2] On the other hand, leptin, a known hormone marker for obesity, exerts actions on multiple organ systems, including the immune system. Indeed, it has been shown that leptin signalling negatively modulates Treg function.[3]

Therefore, the increase in asthma severity observed in obese patients might by caused, in part, by a decreased immunological tolerance induced by a decreased function of Tregs mediated by leptin. Moreover, it has been suggested that induction of Treg development might be a useful tool for asthma treatment.[2] However, Treg increases might also increase cancer risk by impairing host antitumor immune response.[4] Thus the safest way to improve asthma in obese patients is to lose weight.

**L Mascitelli, F Pezzetta, M R Goldstein**

Comando Brigata Alpina Julia, Udine, Italy

**Correspondence to:** Dr L Mascitelli, Comando Brigata Alpina Julia, 8 Via S Agostino, Udine 33100, Italy; lumasci@libero.it

**Competing interests:** None.

## REFERENCES

1. **Taylor B,** Mannino D, Brown C, *et al*. Body mass index and asthma severity in the National Asthma Survey. *Thorax* 2008;**63**:14–20.
2. **Larché M.** Regulatory T cells in allergy and asthma. *Chest* 2007;**132**:1007–14.
3. **Taleb S,** Herbin O, Ait-Oufella H, *et al*. Defective leptin/leptin receptor signaling improves regulatory T cell immune response and protects mice from atherosclerosis. *Arterioscler Thromb Vasc Biol* 2007;**27**:2691–8.
4. **Yakirevich E,** Resnick MB. Regulatory T lymphocytes: pivotal components of the host antitumor response. *J Clin Oncol* 2007;**25**:2506–8.

# Thunderstorm associated asthma in Atlanta, Georgia

Associations between thunderstorm activity and asthma morbidity have been reported in numerous locations around the world.[1] The most prominent hypotheses explaining the associations are that pollen grains rupture by osmotic shock in rainwater, releasing allergens, and that gusty winds from thunderstorm downdrafts spread particles and/or aeroallergens, which may ultimately increase the risk of asthma attacks. A full understanding of "thunderstorm asthma" is crucial, especially with projections of increases in heavy rainfall, thunderstorm events and aeroallergen concentrations as the climate system warms.[2 3] Many existing studies of this phenomenon have been limited in power and scope.[1] Our study seeks to conduct the most extensive investigation of thunderstorm occurrence and asthma morbidity to date in a region, the Southeast US, that has not previously been examined but where thunderstorms are highly prevalent.

We capitalised on the availability of an extensive emergency department (ED) visit database, consisting of data on over 10 million ED visits collected from 41 of 42 hospitals in 20 county Atlanta, Georgia, between 1993 and 2004. We selected visits for asthma (identified using the primary International Classification of Disease, 9th revision diagnosis codes 493, 786.07) by patients residing in zip codes located wholly or partially in the study area. Thunderstorm occurrence data were obtained from the automated surface observing system station at the Atlanta Hartsfield–Jackson airport, which recorded 564 thunderstorm days (12.9% of 4383 total study days). In order to test the mechanistic hypotheses of thunderstorm asthma, we also obtained total daily rainfall and maximum 5 s wind gust data. The wind gust data were used as a surrogate for thunderstorm downdrafts and to indicate the maximum wind speed of the storm. We assessed the association between thunderstorms and next day asthma ED visits using Poisson generalised linear models.[4] We controlled for long term temporal and seasonal trends and meteorological conditions with cubic splines,[5] which allow for flexible control of temporally varying confounding factors. We examined effect modification by levels of rainfall and wind speed, defined a priori by quartiles of their respective distributions.

We observed 215 832 asthma ED visits during the study period; 24 350 of these visits occurred on days following thunderstorms. In our epidemiological models, we observed an association between daily counts of asthma ED visits and thunderstorm occurrence ($p<0.001$, fig 1). Overall, asthma visits were 3% higher on days following thunderstorms. When thunderstorms were stratified by rainfall amount, associations with asthma were observed for thunderstorms with rainfall but not for thunderstorms with no recorded rainfall.

Thorax: first published as 10.1136/thx.2007.092882 on 27 June 2008. Downloaded from http://thorax.bmj.com/ on April 19, 2024 by guest. Protected by copyright.

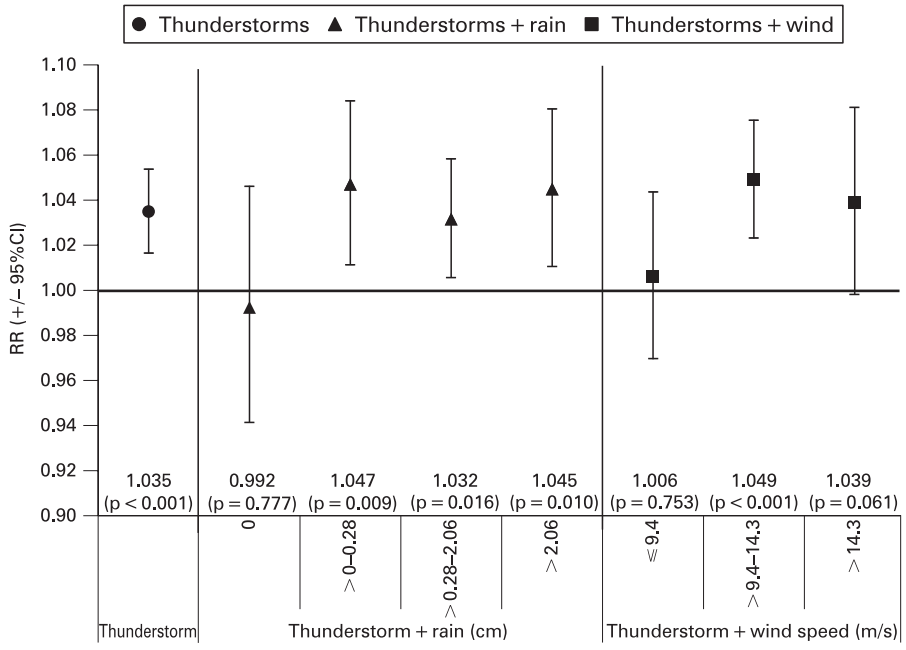


**Figure 1** Relative risk of asthma emergency department visits following days with thunderstorms, thunderstorms in combination with rainfall (in four categories) and thunderstorms in combination with wind speed from maximum 5 s wind gusts (in three categories), compared with days with no thunderstorms. Relative risks (RR) and p values are presented for each model result.

When thunderstorms were stratified by wind gust levels, associations with asthma were strongest when wind gusts were intermediate and high.

Our findings corroborate previous reports of an association of thunderstorm activity with asthma exacerbation. Furthermore, our results provide preliminary evidence in support of rainfall and wind gusts playing important roles in this association. While a 3% increase in risk may seem modest, asthma is quite prevalent in Atlanta and a modest relative increase could have a significant public health impact in the population. This analysis used meteorological data from one weather station. However, thunderstorms are small scale phenomena, and these data may only represent events in close proximity to the station. Planned analyses will take advantage of data from other local stations, radar data on thunderstorm characteristics and spatial resolution of the outcome data to conduct a more refined assessment of the mechanistic basis of the observed association.

**A Grundstein,[1] S E Sarnat,[2] M Klein,[2] M Shepherd,[1] L Naeher,[3] T Mote,[1] P Tolbert[2]**

[1] University of Georgia, Department of Geography, Climatology Research Laboratory, Athens, Georgia, USA; [2] Emory University, Department of Environmental and Occupational Health, Rollins School of Public Health, Atlanta, Georgia, USA; [3] University of Georgia, Department of Environmental Health Science, Athens, Georgia, USA

**Correspondence to:** Dr A Grundstein, University of Georgia, Department of Geography, Climatology Research Laboratory, GG Building, Room #204, Athens, GA 30602, USA; andrewg@uga.edu

**Funding:** This work was supported by grant No R01ES11294 from the National Institute of Environmental Health Sciences, STAR Research Assistance Agreement No R82921301-0 from the US Environmental Protection Agency and grant No EP-P4353/C2124 from the Electric Power Research Institute. Although the research described in this article has been funded in part by the NIEHS and USEPA, it has not been subjected to peer and policy review by these agencies and therefore does not necessarily reflect the views of the agencies.

**Competing interests:** None.

**Ethics approval:** Ethics approval was obtained.

*Thorax* 2008;**63**:659–660. doi:10.1136/thx.2007.092882

## REFERENCES

1. **D'Amato G,** Liccardi G, Frenguelli G. Thunderstorm-asthma and pollen allergy. *Allergy* 2007;**62**:11–16.
2. **Intergovernmental Panel on Climate Change 2007**. Summary for policymakers. In: Solomon S, Qin D, Manning M, *et al*, eds. *Climate Change 2007: The Physical Science Basis. Contribution of Working Group I to the Fourth Assessment Report of the Intergovernmental Panel on Climate Change*. Cambridge: Cambridge University Press.
3. **Ziska LH,** Epstein PR, Rogers CA. Climate change, aerobiology, and public health in the Northeast United States. *Mitig Adapt Strat Glob Change* 2007 (doi 10.1007/S11027-007-91341).
4. **Kleinbaum DG,** Kupper LL, Nizam A, *et al*. Poisson regression analysis. In: *Applied regression analysis and other multivariable methods*, 4th Edn. Belmont, CA: Duxbury, 2008:661–92.
5. **Peel JL,** Tolbert PE, Klein M, *et al*. Ambient air pollution and respiratory emergency department visits. *Epidemiology* 2005;**16**:164–74.

## Prolonged survival of neutrophils from patients with ΔF508 CFTR mutations

Cystic fibrosis (CF) is an autosomal recessive "channelopathy" characterised by aberrant CFTR and ENaC function resulting in widespread epithelial cell dysfunction and persistent airway infection. Studies indicating that airway inflammation precedes infection[1] and that patients with CF display exaggerated neutrophilic responses to pathogens have suggested a primary defect in innate immune responses in CF. Given the importance of apoptosis to the resolution of neutrophilic inflammation,[2] we sought to determine whether circulating CF neutrophils display normal apoptotic capacity.

Peripheral blood neutrophils were isolated from 12 clinically stable *Pseudomonas* colonised ΔF508 homozygote adult patients with CF and 12 age and sex matched healthy controls using discontinuous plasma/Percoll gradients.[3] Blood neutrophil counts were in the normal range for all subjects (CF mean 4.1 (range 5.4–8.3), controls 2.5 (3.7–6.6) $\times 10^9$/l); none of the patients with CF were taking azithromycin. CF and control neutrophils were isolated in parallel and handled identically. Cells were cultured ($5\times10^6$/ml, 5% $CO_2$, 37°C) in Iscove's Dulbecco's medium with 10% autologous serum for 6 and 20 h, as detailed previously.[3] These incubations were conducted with or without tumour necrosis factor α (TNFα 10 ng/ml) or granulocyte macrophage-colony stimulating factor (GM-CSF 10 ng/ml), which have defined proapoptotic and antiapoptotic effects, respectively.[3] Apoptosis was assessed by blinded morphological assessment of May–Gründwald–Giemsa stained cytospins, confirmed by quantification of annexin-V–fluorescein isothiocyanate binding and propidium iodide staining.[3]

Neutrophils from patients with CF had delayed constitutive apoptosis and were resistant to the normal early proapoptotic effects of TNFα,[3] yet remained fully sensitive to the antiapoptotic effects of GM-CSF (fig 1A–C). Incubation of control neutrophils with 10% serum from patients with CF mimicked exactly the enhanced survival effect seen in CF cells, suggesting an acquired rather than intrinsic defect (fig 1D). These data indicate that blood neutrophils from clinically well patients with CF display a relative resistance to spontaneous and death ligand induced apoptosis when cultured with autologous serum. Using the Luminex FlowMetrix system to compare protein and cytokine profiles in CF and control sera, only C reactive protein (CRP) differed, with a 3.6-fold increase in CF sera (controls 1.6 (0.3) μg/ml, CF 5.8 (1.3) μg/ml; $p<0.05$, $n=4$). Although no direct measures of neutrophil activation were performed, there were no differences in proinflammatory cytokines or growth factors present in control and CF sera, including interleukin (IL)8, TNFα, IL6 and GM-CSF. Previous data reporting that migration inhibitory factor can inhibit CF neutrophil apoptosis may reflect lipopolysaccharide contamination of

Thorax: first published as 10.1136/thx.2007.092882 on 27 June 2008. Downloaded from http://thorax.bmj.com/ on April 19, 2024 by guest. Protected by copyright.