Environmental Research 157 (2017) 60–63

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

Industrial air emissions, and proximity to major industrial emitters, are associated with anti-citrullinated protein antibodies

Sasha Bernatsky[a,*], Audrey Smargiassi[b,c], Lawrence Joseph[a], Phillip Awadalla[d], Ines Colmegna[e], Marie Hudson[a,f], Marvin J. Fritzler[g]

[a] Divisions of Rheumatology and Clinical Epidemiology, McGill University Health Centre, 687 Pine Avenue West, V-Building (V2.09), Montreal, Canada H3A 1A1
[b] Département de santé environnementale et de santé au travail, Université de Montréal, Pavillon Marguerite d'Youville, École de santé publique, Montréal, QC, Canada
[c] Institut National de Santé Publique du Québec, Montréal, QC, Canada
[d] Ontario Institute of Cancer Research, Unviersity of Toronto, ON, Canada
[e] Research Institute of McGill University Health Centre, Montreal, QC, Canada
[f] Jewish General Hospital and Lady Davis Institute for medical research, Montréal, Canada
[g] Unviersity of Calgary, Calgary, AB, Canada

ARTICLE INFO

Keywords:
Anti-citrullinated antibodies
ACPA
Air pollution
Particulate matter
$PM_{2.5}$
SO_2
Rheumatoid arthritis

ABSTRACT

Objective: To determine the association of anti-citrullinated antibodies (ACPA) with the ambient air pollutants fine particulate matter (PM2.5) and sulfur dioxide (SO2).

Methods: The CARTaGENE first-wave cohort includes 20,000 general population subjects from Quebec (Canada). On a sample of unselected 1586 subjects, we determined serum, ACPA and performed multivariable logistic regression, for the outcome of positive ACPA, assessing for independent effects of our air pollution variables, adjusting for age, sex, smoking, and French Canadian origin. Two models assessed distance to main industrial emitters of $PM_{2.5}$, and of SO2, and two models assessed tons of SO2 and of $PM_{2.5}$ annual emissions. We also assessed associations with PM2.5 regional ambient concentrations estimated with satellite imagery.

Results: Adjusted analyses suggested a positive association between annual industrial $PM_{2.5}$ and SO2 emissions and the presence of ACPA antibodies (OR: 1.02, 95%CI 1.00–1.04 per 10 t of PM2.5 and 100 t of SO2). The data were also consistent with a negative association between the presence of ACPA, and distance to a major industrial emitter of both $PM_{2.5}$ and SO_2. We found no association with PM2.5 estimates of ambient levels.

Conclusions: These analyses suggest that exposure to industrial emissions of air pollutants is related to ACPA positivity.

1. . Introduction

Rheumatoid arthritis (RA) is a serious autoimmune rheumatic disease affecting up to 1% of the population. Much remains to be learned about the risk factors for RA. During a pre-clinical course lasting up to several years, RA-related antibodies (particularly anti-citrullinated protein antibodies, ACPA), can be detected even prior to clinical manifestations. Rantapaa-Dahlqvist et al. (2003); Forslind et al. (2004).

Air pollution has also been associated with RA in a few studies, although this has not been consistent (Sun et al., 2016). Issues relating to measurement of air pollution, both in terms of types and timing, may in part explain the inconsistencies in previous reports. We therefore undertook this study to determine the association between industrial emissions of fine particulate matter ($PM_{2.5}$) and sulfur dioxide (SO_2) and the presence of ACPA, in a sample of a large population-based cohort. Most particulate matter is formed from gases emitted from industries and motor vehicles, although some particulate matter is directly emitted from smokestacks and other sources (EPA, 2009). Industrial activities are the largest sources of SO_2 emissions followed by fossil fuel combustion from motor vehicles. US EPA (2008).

2. Methods

Our analyses were based within the CARTaGENE cohort, 20,000 general population subjects drawn from four census metropolitan areas: Montreal, Quebec City, Sherbrooke, Saguenay–Lac-Saint-Jean, all in the province of Quebec, Canada. Participants were randomly selected from the provincial health insurance registries (fichier administratif des inscriptions des personnes assure´es de la Re´gie de l'assurance maladie

* Corresponding author.
E-mail address: sasha.bernatsky@mcgill.ca (S. Bernatsky).

http://dx.doi.org/10.1016/j.envres.2017.04.035
Received 28 February 2017; Received in revised form 23 April 2017; Accepted 24 April 2017

du Quebec, RAMQ). This excluded residents of First Nations Reserves or long-term health care facilities or prisons. The participants were selected according to the age distribution in these areas to obtain a representative sample. The CARTaGENE sample has an overall concordance in the distribution of socio-demographic characteristics as compared to the general population of Quebec, and the distribution of some common co-morbidity (e.g. hypertension, diabetes) is also comparable.

The baseline cohort data generated on enrolment of subjects (2008–2009) include demographics (age, sex, and self-reported French Canadian ancestry), health data (e.g. self-reported chronic diseases, including RA), smoking habits (current and past), and stored serum (taken at the baseline visit). Our analyses included a random sample of 3600 subjects. Of these, 1586 subjects provided data on residence, including a valid postal code, and these were used for our analyses. Serum ACPA was determined on biobanked sera using the Inova enzyme-linkeimmunosorbent assay (Quanta Lyte, CCP3 IgG: Inova Diagnostics Inc., San Diego, CA).

Within this subsample, we performed multivariable logistic regression models for the outcome of positive ACPA, assessing for independent effect of industrial air pollution exposure (see definitions below), adjusting for age, sex, smoking, and self-reported French Canadian ancestry(since race/ethnicity, age, and smoking have all been suggested as possible determinants of ACAP positivity, we considered them *a* priori). Miriovsky et al. (2010); Diaz et al. (2011); Kumagai et al. (2009). The smoking variable was categorical, capturing current versus past or never smoker status.

Pollution exposures were determined at the level of the postal code, which in Canada is a six-character alphanumeric string associated with one or more mail delivery points. One postal code serves on average about 20 households.

Exposure to industrial air pollutant emissions were determined from residential proximity (based on baseline six digit postal code of residence) to industrial $PM_{2.5}$ or SO2 emitters, estimated using the National Pollutant Release Inventory (NPRI). The NPRI is Canada's legislated, publicly-accessible database of pollutant releases, disposals and transfers by facilities. Over 8700 facilities report to the NPRI, providing comprehensive air pollutant emission data for contaminants affecting air quality, including $PM_{2.5}$ and SO_2.

Our analyses of the effects of pollution on ACPA antibodies were assessed with five logistic regression models as follows; using the baseline residential postal code for each subject, two separate models assessed distance to main industrial emitters of $PM_{2.5}$ and of SO_2, and two models assessed tons of $PM_{2.5}$ and SO_2 annual industrial emissions, while the remaining model assessed regional satellite $PM_{2.5}$. As has been done in the past (Brand et al., 2016) 'main' emitters were defined as any industry emitting more than an average of 100 t of either $PM_{2.5}$ or SO_2 for at least 5 continuous years from 2002 to 2010; all individuals at a distance larger than 7.5 km (km) from a main emitter were given the distance value of 7.5 km. Industrial emissions of $PM_{2.5}$ and SO_2 in 2008 were summed up for all industries (main emitters or not) within 2.5 km of each postal code.

We also used regional PM2.5 levels estimated from satellite imagery, produced with the Moderate Resolution Imaging Spectroradiometer and multi-angle imaging spectroradiometer systems. Information from these images has been interpreted using the chemical transport model of atmospheric compositions (Goddard Earth Observing System, GEOS-Chem) to estimate regional PM2.5 levels with a geographic resolution of 10×10 km units. Estimates of long-term PM2.5 averages (2001–2006) have been developed based on aerosol optical-depth data from satellite instruments. van Donkelaar et al. (2010) All six digit postal codes located within a 10×10 km cell were given the same regional PM2.5 levels.

Sensitivity analyses were done to decompose the exposure variables as suggested by Leffondre et al., 2002 (Leffondre et al., 2002) into two exposure variables, one binary (coded 1 for exposed and 0 for unexposed) and one continuous variable, centered to the mean exposure of those exposed (i.e. those with a value of one for the binary variable). Additional sensitivity analyses controlled for the four census metropolitan areas (Montreal, Quebec City, Sherbrooke, Saguenay–Lac-Saint-Jean) from which the subjects had been recruited.

Table 1
: Baseline characteristics of the sample (N = 1586), anti-citrullinated protein antibody (ACPA) positive and negative.

	ACPA positive (173)	ACPA negative (1413)
Mean age (standard deviation)	55.0 (7.3)	54.8 (8.0)
N (%) Female	89 (51.4)	738 (52.2)
N (%) French Canadian	111(64.1)	982 (69.5)
N (%) Never smokers	78 (45.1)	549 (38.9)
N (%) living within 2.5 km of any industrial emitter of PM2.5	66 (38.2)	560 (39.6)
N (%) living within 2.5 km of any industrial emitter of SO2	30 (17.3)	238 (16.8)
N (%) living within 7.5 km of a major industrial emitter of PM2.5	14 (8.1)	85 (6.0)
N (%) living within 7.5 km of a major industrial emitter of SO_2	84(48.6)	618 (43.7)

3. Results

Among the 1586 individual CARTaGENE subjects studied in these analyses, the mean age at baseline was 55 years (SD 7.8). Just over half (N = 827, 52%) were female and most (N = 1,093, 69%) were French-Canadian. Almost half (43%) were past smokers, 17% were current smokers and the remainder were never-smokers. Just over 75% (1200) of the subjects came from the Montreal CMA, with 248 subjects coming from the Quebec City CMA, 75 from the Sherbrooke CMA, and 63 from Saguenay–Lac-Saint-Jean.

Among the subjects living within 7.5 km of a main emitter to PM2.5, the mean exposure was 148.4 t/year (standard deviation, SD 291.0) and among subjects living within 7.5 km of a main emitter of SO2, the mean exposure to SO2 was 197.6 (SD 834.9).

Of the 1586 subjects, 173 (10.9%) were positive for ACPA. Table 1 provides univariate comparisons between the ACPA positive and negative subjects.

Adjusted analyses (Table 2) suggested positive associations between exposure to industrial emissions and ACPA. Every 10 t increase in the sum of annual PM2.5 emissions of industries located within 2.5 km of the residence was associated with a 2% (95% CI 1–4%) increase in the odds of ACPA. Similar results were found with exposure to SO_2 emissions (with the lower confidence limit extending to the null value). As for the models where the exposures were defined by distance to a major emitter, for those living within 7.5 km of a major industrial emitter of $PM_{2.5}$, every one-km decrease from the mean distance between the residences and the closest major emitter was associated with an OR of 0.81 (95% CI 0.69, 0.96) for ACPA positivity. The same trend was also suggested with the distance from major emitters of SO_2 per km (OR 0.92; 95% CI 0.84–1.00).

We did not see strong evidence of an association between ambient residential PM2.5 levels (as estimated by satellite imagery) and ACPA.

None of the sensitivity analyses produced appreciably different results for the exposure variables.

As can be seen in Table 2, in the adjusted analyses, there were no clear evidence that age, sex, smoking, or French ancestry were independently associated with serum ACPA positivity.

4. Discussion

Genetic risk factors associated with RA are known, such as the HLA-DRB1 'shared epitope' (Huizinga et al., 2005). However, since many

Table 2
: Effects of air pollution variables on anti-citrullinated antibody positivity: Odds ratios with 95% confidence intervals (CI).

	Adjusted odds ratio	95%	CI
$PM_{2.5}$ emissions[a]	1.02	1.01	1.04
Age (continuous)	1.00	0.98	1.02
Female	0.99	0.72	1.36
Current Smoker[b]	1.06	0.70	1.61
French Canadian	0.76	0.54	1.06
	Adjusted odds ratio	**95%**	**CI**
$PM_{2.5}$ distance[c]	0.81	0.69	0.96
Age	1.00	0.98	1.02
Female	0.99	0.72	1.36
Current Smoker	1.08	0.71	1.63
French Canadian	0.76	0.55	1.06
	Adjusted odds ratio	**95%**	**CI**
SO2 emissions[a]	1.02	1.00	1.04
Age	1.00	0.98	1.02
Female	0.99	0.72	1.36
Current Smoker	1.06	0.70	1.61
French Canadian	0.77	0.55	1.08
	Adjusted odds ratio	**95%**	**CI**
SO2 distance[b]	0.92	0.84	1.00
Age	1.00	0.98	1.02
Female	0.99	0.72	1.35
Current Smoker	1.07	0.70	1.61
French Canadian	0.78	0.56	1.08
	Adjusted odds ratio	**95%**	**CI**
Regional ambient $PM_{2.5}$ estimates[d]	0.97	0.92	1.03
Age	1.00	0.98	1.02
Female	0.98	0.71	1.35
Current Smoker	1.07	0.70	1.61
French Canadian	0.76	0.54	1.07

[a] $PM_{2.5}$ per 10 t increase or SO2 per 100 t increase in emissions exposures.
[b] Current (versus never or past) smoking.
[c] Average distance (kilometres) to a major industrial source, for those living within 7.5 km of an industrial emitter.
[d] Regional ambient $PM_{2.5}$ levels ($\mu g/m^3$) were estimated using satellite imagery.

people with these genetic markers never develop RA, interactions with the environment may also be critical in disease onset. The individual effects of susceptibility genes are likely to be small, and it is the combination of alleles along with strong effects on the specific pathways affected by these susceptibility genes that are essential for the development of RA. Ambient air pollution, as a trigger for the development of autoimmune rheumatic diseases like RA, has been the focus of recent studies, with conflicting conclusions. In 2009, analyses of the Nurses' Health Study, pollution emissions from road traffic were suggested as an environmental risk factor for RA (Hart et al., 2009), and in a Swedish cohort, the authors found that exposure to NO_2, but not particulate matter (based on PM_{10}), was associated with RA risk (Hart et al., 2013a). However, in a follow up analysis of the Nurses' Health Study, associations with either NO_2 or $PM_{2.5}$ were not detected (Hart et al., 2013b). More recently, one study using administrative claims (in British Columbia, Canada) for new cases of RA found no clear links between RA onset and traffic-related NO_2 levels or regional $PM_{2.5}$ (De Roos et al., 2014) levels, while another study (using administrative data from Taiwan) found an association between NO_2 and RA. Chang et al. (2016).

Since particulate matter may trigger a host of non-rheumatologic health problems (Brook, 2008), it would be intriguing to be able to confirm whether some components of air pollution trigger rheumatic disease as well. One study reported that measures of air pollution levels were associated with a 60% increased risk of juvenile idiopathic arthritis in young children (Zeft et al., 2009). Our own team has shown links between $PM_{2.5}$ levels and systemic lupus erythematosus (SLE) activity (Bernatsky et al., 2011), as well as suggesting that $PM_{2.5}$ exposures were associated with an increased risk of systemic autoimmune rheumatic diseases (those analyses included SLE but not RA). Bernatsky et al. (2015).

Serum ACPA, one of the hallmarks of RA, are often accompanied by pro-inflammatory cytokines (Kokkonen et al., 2010), even years prior to the development of RA (Quinn et al., 2003), potentially representing a 'window of opportunity' to intervene and potentially prevent the onset of disease. Van Dongen et al. (2007) Although many believe that airborne stimuli, such as tobacco smoking, may induce ACPA (Makrygiannakis et al., 2008; Anderson et al., 2016), to date, no prior published papers have linked air pollution and ACPA. One previous study presented in abstract form, suggesting that among 320 RA patients enrolled in the Veterans Affairs Rheumatoid Arthritis registry, higher levels of ACPA were seen with higher $PM_{2.5}$ ambient levels (Kunkel et al., 2011). Another study was unable to detect associations, within first degree family members of RA patients, between $PM_{2.5}$ and PM_{10}, and a combined serological outcome (anti-CCP2 and/or two or more rheumatoid factor, RF, isotypes) (Gan et al., 2013); the point estimate for $PM_{2.5}$ and RF-positive visits was actually compatible with a positive association (odds ratio 1.36, 95% CI 0.82–2.24) but the results were imprecise, precluding definitive conclusions.

There are potential limitations with respect to the exposure variables we used, which may have introduced non-differential misclassification. Recorded industrial emissions are rough estimates of concentrations of pollutants to which people are exposed to. Emissions are diluted in a volume of air, which can vary with meteorological conditions and concentrations are higher downwind of industries. Here we did not model concentrations of exposure based on emissions and meteorological conditions; we assume that the exposure is only a function of distance and quantity of pollutants emitted. We believe this non-differential misclassification of exposure would have under-estimated our observed relationships of ACPA with pollution emissions.

Also, associations reported in most papers, including our own, are based on residential exposures of subjects, and does not account for exposures that individuals may encounter at work (although the workplace of many individuals is close to their residence, and individuals still spend more time at home than at work). This may also have led to non-differential misclassification of our exposures and conservative estimates. It may in fact be one reason why the existing literature on ambient air pollution and RA risk is so inconsistent.

In summary, we provide intriguing evidence that industrial air pollution emissions, and proximity to major industrial emitters, are associated with ACPA. Our results are more precise for $PM_{2.5}$ than SO_2, and require duplication in other datasets and improved exposure estimates. If confirmed in other datasets, these results may strengthen the case for initiatives to improve air quality, in order to decrease chronic disease burden and improve the health of our nation.

Acknowledgements

This project was funded by the CIHR. The authors thank Allan Brand and Patrick Belisle for their thorough analyses of the data.

References

Anderson, R., Meyer, P.W., Ally, M.M., Tikly, M., 2016. Smoking and air pollution as pro-inflammatory triggers for the development of rheumatoid arthritis. Nicotine Tob. Res. Mar. 8 (pii: ntw030.) (Epub ahead of print).
Bernatsky, S., Fournier, M., Pineau, C.A., Clarke, A.E., Vinet, E., Smargiassi A., 2011. Associations between Ambient Fine Particulate Levels and Disease Activity in SLE Environ Health Perspect, 119, pp. 45–49.
Bernatsky, S., Smargiassi, A., Johnson, M., Kaplan, G.G., Barnabe, C., Svenson, L., Brand, A., Bertazzon, S., Hudson, M., Clarke, A.E., Fortin, P.R., Edworthy, S., Bélisle, P., Joseph, L., 2015. Fine particulate air pollution, nitrogen dioxide, and systemic autoimmune rheumatic disease in Calgary, Alberta. Environ. Res. 140, 474–478.
Brand, A., McLean, K.E., Henderson, S.B., Fournier, M., Liu, L., Kosatsky, T., Smargiassi, A., 2016. Respiratory hospital admissions in young children living near metal smelters, pulp mills and oil refineries in two Canadian provinces. Environ. Int. 94, 24–32.
Brook, R.D., 2008. Cardiovascular effects of air pollution. ClinSci 115, 175–187.
Chang, K.H., Hsu, C.C., Muo, C.H., Hsu, C.Y., Liu, H.C., Kao, C.H., Chen, C.Y., Chang, M.Y., Hsu, Y.C., 2016. Air pollution exposure increases the risk of rheumatoid arthritis: a longitudinal and nationwide study. Environ. Int. Sep. 94, 495–499.

De Roos, A.J., Koehoorn, M., Tamburic, L., Davies, H.W., Brauer, M., 2014. Proximity to traffic,ambient air pollution, and community noise in relation to incident rheumatoid arthritis. Environ. Health Perspect. Oct. 122 (10), 1075–1080.

Diaz, F.J., Rojas-Villarraga, A., Salazar, J.C., Iglesias-Gamarra, A., Mantilla, R.D., Anaya, J.M., 2011. Anti-CCP antibodies are associated with early age at onset in patients with rheumatoid arthritis. Jt. Bone Spine 78 (2), 175–178.

EPA, 2009. Final Report: Integrated Science Assessment for Particulate Matter. U.S. Environmental Protection Agency, Washington, DC, pp. 2009.

Forslind, K., Ahlmen, M., Eberhardt, K., Hafstrom, I., Svensson, 2004. Prediction of radiological outcome in early rheumatoid arthritis in clinical practice: role of antibodies to citrullinated peptides (anti-CCP). Ann. Rheum. Dis. 63, 1090–1095 (B. BARFOT Study Group).

Gan, R.W., Deane, K.D., Zerbe, G.O., Demoruelle, M.K., Weisman, M.H., Buckner, J.H., Gregersen, P.K., Mikuls, T.R., O'Dell, J.R., Keating, R.M., Holers, V.M., Norris, J.M., 2013. Relationship between air pollution and positivity of RA-related autoantibodies in individuals without established RA: a report on SERA. Ann. Rheum. Dis. Dec. 72 (12), 2002.

Hart, J.E., Laden, F., Puett, R.C., Costenbader, K.H., Karlson, E.W., 2009. Exposure to traffic pollution and increased risk of rheumatoid arthritis. Environ. Health Perspect. 117 (10659).

Hart, J.E., Källberg, H., Laden, F., Bellander, T., Costenbader, K.H., Holmqvist, M., Klareskog, L., Alfredsson, L., Karlson, E.W., 2013a. Ambient air pollution exposures and risk of rheumatoid arthritis: results from the Swedish EIRA case-control study. Ann. Rheum. Dis. Jun. 72 (6), 888–894.

Hart, J.E., Källberg, H., Laden, F., Costenbader, K.H., Yanosky, J.D., Klareskog, L., Alfredsson, L., Karlson, E.W., 2013b. Ambient air pollution exposures and risk of rheumatoid arthritis. Arthritis Care Res. Jul. 65 (7), 1190–1196.

Huizinga, T.W., Amos, C.I., van der Helm-van Mil, A.H., et al., 2005. Refining the complex rheumatoid arthritis phenotype based on specificity of the HLA-DRB1 shared epitope for antibodies to citrullinated proteins. Arthritis Rheum. 52, 3433–3438.

Kokkonen, H., Söderström, I., Rocklöv, J., et al., 2010. Up-regulation of cytokines and chemokines predates the onset of rheumatoid arthritis. Arthritis Rheum. 62, 383–391.

Kumagai, S., Hayashi, N., Kawano, S., Sugiyama, D., Nishimura, K., Kasagi, S., Saegusa, J., 2009. Prevalence of anti-cyclic citrullinated peptide antibody and its association with smoking In general population: a cross sectional study. [Abstr.]Arthritis Rheum. 60 (Suppl 10), S381. http://dx.doi.org/10.1002/art.25464.

Kunkel, G.A., Raglem, R.L., Clegg, D.O., Mikuls, T.R., Cannon, G.W., 2011. Association of Particulate Air Pollution Exposure with Anti-Citrullinated Protein Antibody Elevation in Rheumatoid Arthritis Patients Arthritis Rheum (Suppl.) S2172 https://acr.confex.com/acr/2011/webprogram/Paper22866.html.

Leffondre, K., Abrahamowicz, M., Siemiatycki, J., Rachet, B., 2002. Modeling smoking history: a comparison of different approaches. Am. J. Epidemiol. 156, 813–823.

Makrygiannakis, D., Hermansson, M., Ulfgren, A.K., et al., 2008. Smoking increases peptidylarginine deiminase 2 enzyme expression in human lungs and increases citrullination in BAL cells. Ann. Rheum. Dis. 67, 1488–1492.

Miriovsky, B.J., Michaud, K., Thiele, G.M., O'Dell, J.R., Cannon, G.W., Kerr, G., Richards, J.S., Johnson, D., Caplan, L., Reimold, A., Hooker, R., Mikuls, T.R., 2010. Anti-CCP antibody andrheumatoid factor concentrations predict greater disease activity in men with rheumatoid arthritis. Ann. Rheum. Dis. 69 (7), 1292–1297.

Quinn, M.A., Green, M.J., Marzo-Ortega, H., et al., 2003. Prognostic factors in a large cohort of patients with early undifferentiated inflammatory arthritis after application of a structured management protocol. Arthritis Rheum. 48, 3039–3045.

Rantapaa-Dahlqvist, S., de Jong, B.A., Berglin, E., Hallmans, G., Wadell, G., Stenlund, H., et al., 2003. Antibodies against cyclic citrullinated peptide and IgA rheumatoid factor predict the development of rheumatoid arthritis. ArthritisRheum 48, 2741–2749.

Sun, G., Hazlewood, G., Bernatsky, S., Kaplan, G.G., Eksteen, B., Barnabe, C., 2016. Association between air pollution and the development of rheumatic disease: a systematic review. Int J. Rheumatol. 2016, 5356307.

U.S. EPA, 2008. Final Report: integrated Science Assessment (ISA) for Sulfur Oxides – Health Criteria. U.S. Environmental Protection Agency, Washington, DC, pp. 2008.

Van Dongen, H., van Aken, J., Lard, L.R., et al., 2007. Efficacy of methotrexate treatment in patients with probable rheumatoid arthritis. Arthritis Rheum. 56, 1424–1432.

van Donkelaar, A., Martin, R.V., Brauer, M., Kahn, R., Levy, R., Verduzco, C., Villeneuve, P.J., 2010. Global estimates of ambient fine particulate matter concentrations from satellite-based aerosol optical depth: development and application. Environ. Health Perspect. 118, 847–855.

Zeft, A.S., Prahalad, S., Lefevre, S., Clifford, B., McNally, B., Bohnsack, J.F., et al., 2009. Juvenile idiopathic arthritis and exposure to fine particulate air pollution. ClinExp Rheum. 27, 877–884.