Advanced glycation end products and wheeze: a plausible association?

Jonathan Grigg

In 1912 the French scientist Louis Camille Maillard, while attempting to synthesise proteins in his laboratory, ended up creating a byproduct that had a meaty aroma and flavour. The eponymous Maillard reaction produces many chemical compounds depending on the type of food, cooking time, temperature and presence of air. One class of Maillard-generated compounds receiving recent research attention is advanced glycation end products (AGEs), which are generated during high-temperature cooking. Animal-derived foods high in fat and protein are generally AGE-rich and prone to new formation of AGE s during cooking. Once ingested, AGEs act via engaging with the type I receptor for advanced glycation end-products (RAGE), and increasing evidence shows a role for RAGE in asthma pathogenesis. For example, Perkins *et al*[1] reported that the RAGE knockout mouse is resistant to airway inflammation induced by intranasal type 2 cytokines, and Brandt and Lewkowich[2] in a recent review of RAGE-induced asthma concluded that understanding the mechanisms by which RAGE inhibition attenuates Th2 cytokine signalling cascades might allow for development of novel therapeutics.

Further evidence for a role of RAGE in asthma is provided by Wang *et al*[3] in this issue. In an analysis of data from the National Health and Nutrition Examination Survey (NHANES), they found an association between higher AGE intake from meat and paediatric wheeze. Of course, the usual caveats apply to this type of epidemiological study, such as the possibility of type I error from multiple analyses of this dataset which has already reported other associations between environmental toxins and wheeze, and systematic error due to confounding. Although the study of Wang *et al*[3] should be considered hypothesis-generating, it should stimulate similar analyses of other datasets, and assessment of the role of RAGE polymorphisms in asthma development, such as the T allele of 374T/A reported to be associated with vascular dysfunction in sickle cell disease.[4]

All cooks will recognise that visible fumes are generated during high-temperature cooking of foods such as red meat. These fumes are submicrometre particles of oil, combustion products, steam and condensed organic pollutants, and in some cases, carbonaceous particulate matter less than 10 micron in aerodynamic diameter (PM_{10}). To date, it is unknown whether AGEs are contained in this aerosol, but the high expression of RAGE by type 1 alveolar cells[2] raises the intriguing question—do AGEs act on RAGE not only by ingestion, but also by inhalation?

Although we are far from having enough evidence to recommend changes in meat consumption in children in order to reduce asthma, a focus on adverse respiratory effects of consuming large amounts of cooked meats resonates with wider agendas. For example, the 2020 UK Health Alliance on Climate Change report 'All consuming; Building a healthier food system for people and the planet' concludes that red meat consumption will need to be cut by half if the food system is to stay within sustainable environmental limits.[5] Irrespective of the adverse health effects of AGEs, it may therefore now be time to advocate a diet with smaller amounts of higher-quality and more sustainable cooked meat.

Correspondence to Professor Jonathan Grigg, Centre for Child Health, Queen Mary University of London, London E1 2AT, UK; j.grigg@qmul.ac.uk

Funding The author has not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Commissioned; externally peer reviewed.

Data availability statement No data are available.

To cite Grigg J. *Thorax* 2021;**76**:219.

Received 4 November 2020
Revised 6 November 2020
Accepted 9 November 2020
Published Online First 21 December 2020

Linked

► http://dx.doi.org/10.1136/thoraxjnl-2020-216109

Thorax 2021;**76**:219.
doi:10.1136/thoraxjnl-2020-216369

ORCID iD
Jonathan Grigg http://orcid.org/0000-0003-3109-6028

REFERENCES

1 Perkins TN, Oczypok EA, Dutz RE, *et al*. The receptor for advanced glycation end products is a critical mediator of type 2 cytokine signaling in the lungs. *J Allergy Clin Immunol* 2019;144:e12:796–808.
2 Brandt EB, Lewkowich IP. RAGE-induced asthma: arole for the receptor for advanced glycation end-products in promoting allergic airway disease. *J Allergy Clin Immunol* 2019;144:651–3.
3 Wang J, Liu B, Kroll F, *et al*. Increased advanced glycation end-product and meat consumption is associated with childhood wheeze: analysis of the National Health and Nutrition Examination Survey. *Thorax* 2021;76:294–6.
4 Safwat NA, ELkhamisy MM, Abdel-Wahab SEA, *et al*. Polymorphisms of the receptor for advanced glycation end products as vasculopathy predictor in sickle cell disease. *Pediatr Res* 2020. doi:10.1038/s41390-020-1014-3. [Epub ahead of print: 16 Jun 2020].
5 UK Health Alliance on Climate Change. Building a healthier food system for people and planet, 2020. Available: <http://www.ukhealthalliance.org/wp-content/uploads/2020/11/UKHACC-ALL-Consuming-Building-a-Healthier-Food-System-for-People-Planet.pdf>