

Agricultural Intensification and the Allergenic Source Term: A Hypothesis Linking Nitrogen Input to Rising Peanut Allergy Prevalence

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Abstract

The prevalence of peanut (*Arachis hypogaea*) allergy has risen markedly over the late twentieth and early twenty-first centuries, particularly in industrialized nations. Dominant explanatory models have focused on changes in human immune development, such as the hygiene hypothesis, or on post-harvest processing effects, particularly thermal modification during roasting. This paper proposes an additional, upstream variable: a change in the biochemical composition of the peanut itself, driven by modern agricultural practices. We advance a *Source Term Hypothesis*, suggesting that the transition from low-input cultivation in nitrogen-limited soils to intensive NPK fertilization regimes has increased the absolute concentration of nitrogen-rich seed storage proteins, including the major peanut allergens Ara h 1, Ara h 2, and Ara h 3. Even in the absence of altered human immune sensitivity, an increased allergenic protein density per unit mass of peanut would raise exposure flux, potentially lowering thresholds for sensitization and clinical reactivity at the population level. We outline the biochemical rationale for this hypothesis, address potential objections, propose experimental approaches for its verification, and call on agricultural scientists to test this hypothesis through controlled cultivation experiments.

Contents

1	Introduction	3
2	Agricultural Nitrogen Input and Seed Protein Expression	4
3	The Allergenic Source Term and Exposure Flux	5
4	Distinction from Stress-Induced Allergen Models	6
5	Addressing Potential Objections	6
5.1	Geographic Variation in Allergy Prevalence	6
5.2	Other Legumes and Agricultural Crops	7
5.3	Yield–Protein Trade-offs	7
6	Proposed Experimental Tests	7
7	Agricultural Research Needed: Specific Testable Predictions	8
8	Implications and Conclusion	10

1. Introduction

Peanut allergy is among the most severe and persistent food allergies, affecting approximately 1–2% of children in Western nations—a prevalence that has increased substantially since the 1990s (Sicherer & Sampson, 2018). The rise has been particularly dramatic in countries such as the United States, United Kingdom, Canada, and Australia. This trend represents a significant public health concern given the severity of reactions, the persistence of the condition into adulthood, and the substantial impact on quality of life for affected individuals and their families (Lieberman et al., 2021).

Explanatory frameworks have largely centred on host-side factors, including reduced microbial exposure during early childhood (the hygiene hypothesis) (Strachan, 1989), delayed dietary introduction of peanuts to infants (Du Toit et al., 2015), vitamin D deficiency, and immunological skewing during development. In parallel, food science research has identified post-harvest processing—particularly roasting—as a modifier of peanut allergenicity through structural and chemical alteration of allergenic proteins, with dry-roasting potentially enhancing allergenicity through Maillard reaction products (Maleki et al., 2000). A comprehensive review of peanut allergens and their chemical characterization (Montealegre et al., 2013) makes clear that the protein composition of peanut seeds is itself highly complex, with major allergens accounting for the majority of total seed protein mass (Toomer, 2018).

These approaches implicitly treat the peanut as a biochemically static object whose intrinsic allergen content is invariant across historical and agricultural contexts. This assumption may be unwarranted. Over the same period that peanut allergy prevalence has increased, global peanut cultivation has undergone profound changes, transitioning from traditional, low-input systems—often on marginal, nitrogen-depleted soils—to high-yield, fertilizer-supported monocultures optimized for maximum productivity. The potential consequences of this transition for the seed proteome, and specifically for allergenic protein abundance, have received little attention in the allergy literature.

This paper proposes that changes in agricultural nitrogen availability may have altered the *source term*

of allergenic exposure, independently of changes in human immune sensitivity or food processing practices. We frame this as an hypothesis suitable for empirical testing, outline the biochemical and agronomic rationale, and propose specific experimental approaches. We argue that this upstream, agricultural dimension of peanut allergenicity warrants systematic investigation by food scientists, agronomists, and allergy researchers working in concert.

2. Agricultural Nitrogen Input and Seed Protein Expression

Arachis hypogaea is a leguminous crop capable of biological nitrogen fixation via symbiosis with *Rhizobium* species. In nitrogen-limited soils, this symbiosis supplies nitrogen sufficient for vegetative growth and seed development. Under conditions of elevated soil nitrogen availability, however, legumes may partially or fully down-regulate fixation while still experiencing increased net nitrogen availability during seed filling, depending on cultivar, timing, and soil conditions.

Plants are known to exhibit “luxury consumption” of nutrients when availability exceeds immediate growth requirements ([Millard, 1988](#)). In such conditions, excess nitrogen is commonly partitioned into storage compounds, particularly seed storage proteins (SSPs), which serve as nitrogen reservoirs for germination. This phenomenon is well-documented in agricultural research, where protein content of legume seeds typically increases with nitrogen fertilization.

The principal peanut allergens are themselves SSPs ([Koppelman et al., 2004](#)). Ara h 1 and Ara h 3, members of the cupin superfamily (vicilin- and legumin-type globulins), account for substantial proportions of total seed protein. Ara h 2 is a 2S albumin, notable for its proteolytic and thermal stability and high allergenic potency despite representing a smaller fraction of total protein ([Lehmann et al., 2006](#)). Together, these three allergens—alongside Ara h 6—react with IgE antibodies in the serum of the large majority of peanut-allergic patients ([Montealegre et al., 2013](#); [Toomer, 2018](#)).

It is therefore plausible that increased nitrogen availability during seed development leads to an increase in the absolute abundance of these proteins within the mature seed. This hypothesis does not require preferential up-regulation of allergenic proteins relative to other SSPs; an increase in

total SSP content alone would increase the absolute allergen dose per gram of peanut consumed. Furthermore, the effects of food processing—including fermentation, which has attracted growing interest as an allergenicity-reduction strategy (Pi et al., 2022)—would operate on a larger initial substrate, potentially yielding a different final allergenic burden than in lower-input-grown peanuts.

3. The Allergenic Source Term and Exposure Flux

In physical detection systems, event probability is determined by the product of incident flux and detector cross-section. An analogous framing can be applied to food allergy. The probability of sensitization or elicitation depends both on host immune sensitivity (the “cross-section”, σ) and on the quantity and biochemical form of allergen encountered (the “flux”, Φ):

$$P_{\text{reaction}} \propto \Phi_{\text{source}} \times \sigma_{\text{host}} \quad (1)$$

Most contemporary allergy research has focused on the cross-section term: genetic predisposition, immune regulation, microbiome composition, and timing of exposure. The present hypothesis instead addresses the flux: the allergenic protein density of the food source. An increase in the absolute concentration of Ara h proteins per unit mass of peanut would have several potential consequences.

First, effective thresholds for reaction could be lowered, increasing the likelihood that low-sensitivity individuals exhibit clinical symptoms. Second, enhanced early-life sensitization could occur if higher allergen doses overwhelm mechanisms of oral tolerance during immune development. Third, processing effects could be amplified, whereby thermal or chemical modifications act upon a larger initial allergen pool, potentially producing more immunogenic products in absolute terms (Maleki et al., 2000; Pi et al., 2022).

This framework is compatible with, rather than exclusive of, existing immunological and processing-based models. The Source Term Hypothesis suggests that multiple factors may act multiplicatively:

changes in immune development, processing methods, and intrinsic allergen content could all contribute to the observed epidemiological trends.

4. Distinction from Stress-Induced Allergen Models

Previous plant-based explanations for variable allergenicity have emphasized abiotic stress, such as drought or pathogen pressure, leading to increased expression of defensive proteins (Pathogenesis-Related proteins). The present hypothesis differs fundamentally in mechanism and implication.

Rather than stress-induced defence, it proposes that agricultural optimization itself—through nutrient surplus—has unintentionally increased allergenic load by enhancing storage protein accumulation. Paradoxically, this suggests that highly “successful” agricultural systems, optimized for yield and protein content, may produce food that is immunologically more potent than their low-input predecessors.

This framing connects the hypothesis to wider debates in food science about the unintended nutritional and immunological consequences of agricultural intensification. It also invites comparison with parallel arguments advanced regarding the effects of agricultural practices on other food components—including phytochemicals, micronutrients, and antinutritional factors—that have shifted in abundance as a function of fertilization regimes.

5. Addressing Potential Objections

5.1. Geographic Variation in Allergy Prevalence

One potential objection to this hypothesis is that countries with intensive peanut agriculture (notably China and India) do not exhibit the high allergy prevalence observed in Western nations. Several factors may contribute to this discrepancy.

First, consumption patterns differ markedly: boiled peanuts are traditional in many Asian countries, whereas dry-roasted peanuts predominate in Western markets ([Beyer et al., 2001](#)). Boiling has been

shown to reduce allergenicity relative to roasting, potentially offsetting any increase in allergen content per unit weight. Second, early-life exposure patterns differ, with earlier and more consistent peanut introduction in some Asian populations potentially promoting tolerance even in the presence of higher allergen doses (Du Toit et al., 2015). Third, Western markets increasingly source peanuts internationally, and export-oriented production may employ different fertilization regimes than domestic cultivation for local consumption.

5.2. Other Legumes and Agricultural Crops

A related question is whether allergies to other legumes have risen comparably. Peanuts are botanically distinct and are consumed in larger quantities in more allergenic forms (roasted) than many other legumes. Furthermore, the specific allergenic proteins in peanuts, particularly Ara h 2, are unusually stable and potent (Lehmann et al., 2006). Nevertheless, the hypothesis would predict that if similar allergen-content increases have occurred in other intensively cultivated allergenic crops, corresponding effects should in principle be detectable at the population level.

5.3. Yield–Protein Trade-offs

Agronomic literature has documented a general negative relationship between yield and seed protein concentration in some legume species, including soybean. If such a trade-off operates strongly in peanut cultivation, yield-optimized farming might in principle *reduce* protein density. However, this trade-off is not universal: it is highly cultivar- and environment-specific, and the relationship between nitrogen fertilization and allergenic SSP accumulation in peanut has not been directly measured. Furthermore, absolute allergen yield (total allergen produced per field area and per unit of final food product reaching consumers) may increase even if concentration per seed is marginally reduced, because yield gains outpace protein dilution effects under many agronomic regimes. This empirical question is precisely what the proposed experiments would resolve.

6. Proposed Experimental Tests

The Source Term Hypothesis is experimentally tractable, and testing it lies squarely within the capabilities of agricultural research institutions. A rigorous experimental programme would involve the following elements.

Cultivation conditions: Genetically identical cultivars should be grown under controlled nitrogen regimes, ranging from reliance on biological fixation in low-nitrogen soils through escalating NPK supplementation to levels representative of intensive commercial production. Both greenhouse and field experiments would be valuable.

Proteomic analysis: Quantification of Ara h 1, Ara h 2, and Ara h 3 should be performed using liquid chromatography–mass spectrometry (LC-MS/MS) ([Koppelman et al., 2004](#)), providing absolute values (mg allergen per g protein or per g dry seed mass) rather than relative proportions.

Functional immunological assays: Protein extracts from different cultivation conditions should be tested using sera from clinically confirmed peanut-allergic patients to assess IgE binding and basophil activation, providing functional evidence of differential allergenicity.

Processing interactions: Extracts from differently fertilized peanuts should be subjected to representative commercial processing conditions (roasting, boiling, fermentation) to assess whether the magnitude of processing-induced changes in allergenicity is substrate-dependent.

Historical archive analysis: Where seed banks retain archived peanut samples spanning several decades, retrospective proteomic analysis could provide a historical record of allergen content trends, offering ecological evidence complementing the controlled experimental approach.

7. Agricultural Research Needed: Specific Testable Predictions

The Source Term Hypothesis generates a set of specific, falsifiable predictions that can be tested through controlled agronomic experiments. We outline these here to provide a concrete research agenda for agricultural scientists.

Prediction 1: Nitrogen fertilization increases absolute Ara h protein content. Peanut plants grown under progressive NPK supplementation (e.g., 0, 50, 100, 150 kg N ha⁻¹) will show a dose-dependent increase in the absolute concentration of Ara h 1, Ara h 2, and Ara h 3 per gram of dry seed mass, as measured by LC-MS/MS quantification. This prediction is the core of the hypothesis and its falsification would substantially weaken the case.

Prediction 2: Nitrogen effects on total seed storage protein precede effects on specific allergen fractions. If the mechanism is a general increase in SSP accumulation under nitrogen surplus, total seed protein content should increase before or concomitantly with individual allergen fractions, rather than showing allergen-specific up-regulation. Proteomic profiling of total and fractionated seed protein across nitrogen treatments would test this.

Prediction 3: Modern high-yield cultivars show greater nitrogen-induced protein responses than heritage varieties. If contemporary peanut breeding has selected, incidentally or deliberately, for high-protein seed phenotypes, these cultivars should show a steeper protein-accumulation response to nitrogen inputs than older or traditional varieties. A comparative trial using heritage and modern cultivars across nitrogen gradients would test this.

Prediction 4: Western commercial production conditions yield higher Ara h concentrations than traditional low-input production conditions. Side-by-side comparisons of peanuts grown under conditions representative of Western commercial agriculture and traditional low-input systems (e.g., as practised in parts of sub-Saharan Africa or South Asia) would provide ecologically relevant evidence.

Prediction 5: Allergen enrichment is positively associated with nitrogen nutrition index during seed fill. The timing and rate of nitrogen supply during the critical seed-filling period (R5–R7 growth stages) may be the key determinant of allergen accumulation. Experiments manipulating the timing as well as rate of nitrogen application, alongside measurement of the nitrogen nutrition index at reproductive stages, would allow mechanistic dissection of the relationship.

These predictions can be addressed through controlled field experiments, greenhouse trials, and

retrospective analysis of existing germplasm collections. Agricultural research stations in peanut-producing regions already possess the infrastructure necessary for such trials. We call on agronomists, plant biochemists, and food scientists to pursue this programme of investigation.

8. Implications and Conclusion

If peanut allergenicity has increased as a consequence of agricultural inputs, it would reflect a shift in the biochemical composition of the peanut itself—an overlooked consequence of agricultural intensification. This would not diminish the importance of immunological and processing-based factors in peanut allergy pathogenesis, but would add a further dimension to the causal landscape.

The implications, should the hypothesis be confirmed, extend in several directions. Mitigation strategies might include agronomic interventions such as optimised nitrogen management, timed application to reduce nitrogen surplus during seed fill, or cultivar selection for lower allergen-to-total-protein ratios. Regulatory frameworks for peanut production and labelling might need to consider the agricultural context of peanut production as a potential modifier of clinical risk. Food safety assessments that currently treat peanut allergenicity as a fixed property of the crop would need revision.

The hypothesis also raises broader questions about the extent to which other allergenic foods have been similarly affected by agricultural intensification. As food production has become more intensive globally, the biochemical composition of staple crops and commodity foods has changed in ways that are not always captured by nutritional surveillance. The question of whether these changes have immunological consequences—beyond those already recognised for micronutrient density, phytochemical content, and antinutritional factors—deserves systematic investigation.

The Source Term Hypothesis presented here is consistent with all available evidence, is mechanistically plausible on the basis of well-established plant physiology, and generates specific empirical predictions. We call on agricultural scientists, food chemists, and allergy researchers to test this hypothesis through controlled cultivation experiments. Determining whether the food itself has

changed—and whether that change has contributed to rising allergy rates—is a question of both scientific and substantial public health importance.

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