

Immunotherapy for Uncommon Foods (with a side of AI for 2025)

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Goals

- Review published data for immunotherapy to (relatively) uncommon / unusual foods, including fish/shellfish, seeds, and spices
- Discuss how to approach these foods on a practical basis from both the patient and provider sides
- Try to answer the “Is it worth it?” question using a shared-decision making model
- Review how AI can actually be helpful, but still needs to be approached with caution



Fish and Shellfish Challenges

- Cross-reactivity patterns are uncertain
 - Finned fish: major allergenic protein is parvalbumin, but there are clearly others (enolases, aldolases)
 - Shellfish: major allergenic protein is tropomyosin, but there are clearly others (arginine kinase, myosin light chain allergen)
- It is unclear whether desensitization to one canonical finned fish allergen (cod) or one canonical shellfish allergen (shrimp) will confer adequate desensitization to other class members.
- In at least one pediatric case report, a child with clinically allergies to both cod and salmon was desensitized using a cod substrate and tolerated both cod and salmon after completing OIT



Fish and Shellfish, yet more challenges!

- Taste Aversion / smell - Can be very hard to overcome.
- Masking agents such as orange juice, yogurt, and ketchup have been tried
- Source stability
 - Obviously an issue with fresh fish /shellfish (days)
- Portability issues - hard to travel with fresh fish
- Solutions can include:
 - Dried extracts / powders (cod, hake, shrimp)
 - Fish jerky
 - Glycerinated extracts



Possible sources for fish/SF OIT



Precision probably more important than accuracy for source material



Sample fish OIT protocol

TABLE 2. INDUCTION PHASE WITH DILUTED COD EXTRACT (A) AND BAKED COD (B)

<i>(a)</i>				
<i>Days/weeks</i>	<i>Drops^a</i>	<i>mL</i>	<i>Capsules (65 mg)</i>	<i>mg</i>
1/1	1	—	—	0.072
07/2	2	—	—	0.144
14/3	4	—	—	0.288
21/4	8	—	—	0.576
28/5	16	—	—	1.152
35/6	32	1.8	—	2.304
42/7	64	3.5	—	4.608
49/8	128	7.1	—	9.216
56/9	256	14.2	—	18.432
63/10	—	28.4	—	36.864
70/11	—	—	1	65
77/12	—	—	2	130
84/13	—	—	3	195
91/14	—	—	4	260
98/15	—	—	6	390
105/16	—	—	9	585
<i>(b)</i>				
<i>Days/weeks</i>	<i>G</i>			
112/17	1			
119/18	2			
126/19	4			
133/20	8			
140/21	16			
147/22	32			
154/23	64			
161/24	100			

- Achieved 100g codfish (ca. 20 g protein) in 6 months
- Continued consuming cod and salmon 2-3x/week as maintenance
- Used commercial dehydrated codfish extract until 1g
- Report did not comment on allergy to other finned fish species

^aSolution of 65 mg dehydrated cod extract in 50 mL water.



Shrimp SLIT

RESEARCH

Open Access

Sublingual immunotherapy for allergy to shrimp: the nine-year clinical experience of a Midwest Allergy-Immunology practice



Lydia M. Theodoropoulou^{1*}  and Niamh A. Cullen²



Shrimp SLIT

- 66 pts over nine years
- 64 ng start if shrimp IgE >100 kU/L; 320 ng if shrimp IgE < 10 kU/L
- Maintenance 0.5 mg three times daily for average 51 months
- Challenge results:
 - 18 pts challenged to 42 g shrimp
 - 11/18 outright passed -> freely consuming shrimp
 - 7/18 local reactions -> 5/7 rescued with high dose OIT, 2/7 declined further consumption
- Ultra-low/ultra-slow can work but long duration and frequency of exposure likely important



OIT Advisors - A great source of information!

- Learn to search within the Google group

The screenshot shows a Google Groups search results page. The browser address bar displays the URL: `groups.google.com/g/oitadvisors/search?q=shrimp%20OIT`. The search bar contains the text "shrimp OIT". The results are sorted by date and show 1-8 of 8 results. The left sidebar contains navigation options: "New conversation", "My groups", "Recent groups", "Favorite groups", "Starred conversations", "advisors", "Conversations 99+", "Members", "About", and "My membership settings".

Profile	Participants	Topic
	weymanlam, ... Dave Fitzhugh 11	Dupilumab vs Omalizumab adjunct for OIT – can make OIT safer/easier for a select group of highly sensitized...
	bnovick	Shellfish OIT – Hi All, Does shrimp OIT provide cross protection to crab and lobster? Thanks. Best, Brian
	drcm...@gmail.com, ... myassin 6	Meat OIT Protocols – pre cooked shrimp bites. Yum shrimp popsicles! I've done salmon in the same way for a ...
	Lisa Martora..., ... Mack MD Do... 3	Cashew PB2 protocol – label peanut OIT product. It truly is amazing to witness children > be able to consume ...
	tdominguez..., ... Dareen Siri ... 5	Dosing idea – scit for shrimp allergy, anyone start with odactra? It has the tropomysin in it. > > > Sent from ...
	jparismd, ... tdominguez.pa 4	Shrimp OIT – patients do shrimp and fish OIT and I can tell you there is only one pt that is still eating fish regul...
	drrichw...@gmail.c..., ... myas... 3	FDA – OIT Colleagues, As many of you know, I was invited to meet with regulators from FDA at the AAAAI mee...
	drkarabus, ... David Paull 20	FISH OIT – : Fish OIT Follow-up Hi Dr Paull, Here is my response: On Tue, Feb 25, 2020, 11:50 AM Keith Paull > ...

Seed immunotherapy

- Sesame has by far the most published literature
- Two very helpful reports (2017 - high dose; 2024 - low dose)
- Many of use have done sesame OIT in the real world
- Just like fish, taste aversion for sesame (particularly tahini) tends to be a major issue



Sesame - High dose OIT

- 53/60 pts successfully desensitized to 4000 mg sesame protein challenge
- Remaining 7/60 partially desensitized > 240 mg but < 4000 mg sesame protein
- Used maintenance dose of 1200 mg sesame protein (5g of tahini)
- Fairly intensive regimen with 2 day initial escalation and monthly dose increases, which could be 12+ months (variable, based on initial eliciting dose)

Elizur, 2019



Sesame - Low dose OIT

- 21 toddlers desensitized with very straightforward 9 step protocol
- Maintenance dose 200 mg sesame protein (1 mL tahini)
- At 1 year on maintenance, 18/21 patients passed a 2000 mg sesame challenge
- 2000 mg felt to be more consistent with “real-world exposure” for a toddler (this is about 90 mL of hummus)

Erdle, 2024



Low-dose Sesame protocol

TABLE I. Protocol for sesame OIT with 200 mg maintenance dose

Visit no.	Food protein (mg)	Absolute quantity of food measured*
1†	3	7 mg sesame flour
2	6	15 mg sesame flour
3	12	30 mg sesame flour
4	25	62 mg sesame flour
5	50	124 mg sesame flour
6	80	0.4 mL tahini
7	120	0.6 mL tahini
8	160	0.8 mL tahini
9	200	1 mL tahini

Exact allergen content may vary according to brand; it is crucial to confirm dose calculations of protein content for brand or form of food before providing dosing suggestions. Dose increases are performed every 2-4 weeks using this protocol.

*Sesame flour (Kevela Organic Sesame Flour, Dallas, Tex) contained 40.32 g sesame protein per 100 g sesame flour. Tahini (Organic Fair Trade Sesame Tahini, Nuts to You Nut Butter, Brantford, Ontario, Canada) contained 200 mg sesame protein/mL tahini.

†Optional.

Erdle, 2024



Consider chocolate tahini for taste aversion



Other seeds

- Very little published data for other seeds (sunflower, flax, mustard, etc)
- Be practical:
 - Find a reasonable source (sunbutter, Lattini milk, mustard powder)
 - Create a protocol aligned with well-known OIT protocols (dairy, peanut)
 - Assign a reasonable maintenance dose (1000 mg, perhaps higher if free consumption desired)
 - Consider challenging to full serving after 6-12 months on maintenance
- Remember, OIT Advisors is your friend here! Please use the search function within Google Groups.



Spices

- Can you do OIT to cumin, coriander, garlic, red pepper, etc?
- There is zero published literature here
- There is a good chance that much of this may related to Mugwort-Spice syndrome, which often can present less as OAS and more as systemic reactions
- Fairly common to see systemic reactions with cofactors (exercise, NSAIDs, etc) as a variant of Mugwort-Spice syndrome
- Might consider SCIT to sage/mugwort



Another pitch for OIT Advisors



4 of 4



red pepper allergy 40 views



Sugerman MD Robert

Mar 9, 2020, 11:02:49 AM



Colleagues: I recently saw a young woman with a convincing history of allergic reactions to cayenne



jeffreynugent

Mar 9, 2020, 6:22:25 PM



to Sugerman MD Robert, oitad...@googlegroups.com

Dr Sugerman,

Our practice in the Great Basin biome (Northern Nevada) has several patients with similar histories, who ultimately prove to be a variant of PFAS (Pollen-Food-Allergy-Syndrome) to sagebrush (AKA mugwort). "Mugwort-spice" patients often do not have classic oral itching, but rather can have anaphylaxis-spectrum symptoms as you describe, particularly in association with "co-factors" eg: exercise within 2 hrs after ingestion, NSAIDS within 48 hrs prior, alcohol ingestion (common), or concomitant illness, menses, but interestingly also increased when they "stack" cross reactive spices/ foods together (eg paprika and onion w/ bell pepper or broccoli, or mustard and cabbage w/ bratwurst). Unlike typical OAS where the proteins are heat-labile, several of our patients have reacted to cooked foods as well as fairly small amounts in marinades & dressings.



Spices blends on complicated!!

Spice blend	Components
Bay seafood seasoning blend	Bay leaves, black pepper, cardamom, celery, cloves, ginger, mustard, nutmeg, paprika, pepper, salt
Cajun seasoning	Black pepper, chili powder, garlic powder, nutmeg, onion powder, parsley flakes, red pepper (cayenne), salt
California style garlic blend	Cottonseed, garlic, parsley, soybean oil
Creole seasoning blend	Bay leaves, black pepper, chili powder, garlic, onion, oregano, paprika, red pepper, salt, thyme
Curry powder, general	Cinnamon, cloves, coriander, cumin, nutmeg, onion, peppercorns, turmeric,
Curry powder, Indian	Red chili, coriander, cumin, mustard seeds, black peppercorns, fenugreek, curry leaves, ginger, turmeric
Curry powder, Japanese	Turmeric, coriander, cumin, cardamom, black pepper, chili (cayenne) pepper, clove, fennel, cinnamon, star anise, allspice, nutmeg, fenugreek, bay leaf, sage, oregano, cocoa powder, coffee powder
Curry powder, Thai	Chili pepper, garlic, lime peel, galangal, coriander, lemon grass, black pepper, cumin, fennel, mace, shallots
Five-spice powder blend	Allspice, anise seed, cinnamon, cloves, fennel seed, ginger, pepper
Greek seasoning	Cinnamon, cornstarch, garlic, nutmeg, onion, oregano, parsley, pepper, salt
Ground seasoning blend	Celery seeds, onion powder, salt
Italian seasoning	Basil, coriander, marjoram, oregano, parsley, rosemary, sage, thyme
Ketchup	Allspice, cinnamon, cloves, garlic, onion powder, sugar, tomatoes, vinegar
Ketchup, hot	Cider vinegar, garlic, jalapeno chili, onions, oregano, salt, tomato paste, tomatoes
Lemon pepper	Black pepper, celery seed, citric acid, cornstarch, garlic powder, lemon oil, onion, salt, sugar
Masala powder	Coriander, cumin, garlic powder, paprika, ginger, mango powder, mint, chili powder
Poultry seasoning	Black pepper, cloves, marjoram, nutmeg, rosemary sage, thyme
Season-all	Black pepper, celery seed, chili pepper, coriander, garlic, nutmeg, onion, paprika, salt
Taco seasoning	Chili powder, cornstarch, cumin, garlic, onion, oregano, red pepper, salt
Thai seasoning	Basil, chili peppers, cinnamon, coriander, cumin, garlic, ginger, lemon peel, lime oil, paprika, red pepper, star anise, tomato, white pepper



ChatGPT 2024

The literature on OIT for spice allergies, though limited, suggests that it can be an effective approach for desensitizing patients to specific spice allergens such as mustard, black pepper, coriander, and cumin. Successful cases have shown that patients can achieve increased tolerance and improved quality of life. However, more research is needed to develop standardized protocols and to understand the long-term efficacy and safety of OIT for spices.

References

1. **Kruizinga, A. G., et al. (2018).** "Oral Immunotherapy for Mustard Allergy: A Pilot Study." *Allergy*, 73(3), 695-698.
2. **Lebecque, P., et al. (2020).** "Case Study of Oral Immunotherapy for Mustard Allergy in a Child." *Pediatric Allergy and Immunology*, 31(5), 518-520.
3. **Cubero-Mora, J. R., et al. (2019).** "Oral Immunotherapy for Cumin Allergy: A Case Report." *Clinical and Experimental Allergy*, 49(10), 1440-1442.
4. **Pérez-Calderón, R., et al. (2021).** "Successful Oral Immunotherapy for Coriander Allergy." *Allergy and Asthma Proceedings*, 42(1), 56-58.
5. **Sharma, R., et al. (2022).** "Oral Immunotherapy for Black Pepper Allergy: Case Study." *Annals of Allergy, Asthma & Immunology*, 129(2), 215-217.
6. **Bernstein, J. A., et al. (2023).** "Pilot Study of Combined Oral Immunotherapy for Multiple Spice Allergies." *Journal of Allergy and Clinical Immunology*, 151(4), 1122-1125.

- Journals and Authors are real
- Literally none of these “cited” articles are real!
- Generative AI is significantly hallucinatory. Be really careful here.



ChatGPT 2025

Summary Table

Context	Findings
Direct spice-OIT studies	None found; only case reports exist
OIT for similar rare foods (sesame, seeds)	Demonstrated safe desensitization (e.g., sesame OIT with omalizumab) pmc.ncbi.nlm.nih.gov +9 clinmedres.org +2
Multi-food OIT evidence	Supports applying protocols to uncommon allergens
General pediatric OIT reviews	Include tree nuts, wheat, sesame—but not spices

- No hallucinations now
- Reasonable and practical advice

Conclusion

- No formal spice-specific OIT protocols exist yet.
- However, **case diagnoses affirm spices can be allergenic and hidden.**
- **Adapting sesame/multi-food OIT methods** is the most practical pathway at this time.
- Consider using **purified spice preparations**, very gradual dosing, and possibly **omalizumab** for safety.



Other LLMs: Claude (Anthropic)

Claude 3.7 Sonnet ▾

Spices

Medical Oversight Considerations

Important Note : Food oral immunotherapy (OIT) should only be conducted under the supervision of qualified allergists, as even with common allergens it carries risks of adverse reactions including anaphylaxis.

Potential Protocols for Spice OIT

1. Modified Rush Protocol Adaptation :

- Begin with sub-threshold doses (often micrograms)
- Gradually increase by 25-50% increments every 1-2 weeks
- Consider extended maintenance phase (6-12 months) due to limited research

2. Ultra-Slow Escalation :

- Start with diluted extracts (1:1,000,000 dilution)
- Extend build-up phase to 12-18 months
- Implement more gradual dose increases (10-25%)

- Pretty reasonable
- Generic but would work



Other LLMs: Llama (Meta)

LLama 3.1 70B ▾

Phase 1: Initial Dose Escalation (Days 1-7)

1. **Initial Dose:** Start with a small dose of 1/8 teaspoon of spice mixed with a small amount of food (e.g., applesauce or yogurt).
2. **Dose Escalation:** Gradually increase the dose every 2-3 days, as tolerated, to the following amounts:
 - Day 3: 1/4 teaspoon
 - Day 5: 1/2 teaspoon
 - Day 7: 3/4 teaspoon
3. **Monitoring:** Monitor the patient for signs of an allergic reaction, such as hives, itching, swelling, stomach cramps, diarrhea, or difficulty breathing.

Phase 2: Dose Escalation and Maintenance (Days 8-28)

1. **Dose Escalation:** Continue to increase the dose every 2-3 days, as tolerated, to the following amounts:
 - Day 10: 1 teaspoon
 - Day 14: 1 1/2 teaspoons
 - Day 21: 2 teaspoons
 - Day 28: 2 1/2 teaspoons
2. **Maintenance Dose:** Once the patient reaches the maximum dose (2 1/2 teaspoons), maintain this dose for 2-3 weeks to ensure tolerance.

- Uh, I probably wouldn't do this
- Sort of a rush protocol, which wasn't in my prompt
- Quality of prompt dictates quality of result
- Zuckerberg really likes spices?



DeepSeek FTW?

DeepSeek V3 ▾

Oral Immunotherapy (OIT) Protocol for Spice Allergy

Goal: To safely desensitize the patient to the allergenic spice while minimizing adverse reactions.

Pre-OIT Requirements:

1. **Confirmation of Allergy:**
 - Positive SPT (wheal ≥ 3 mm larger than control) or sIgE to the target spice.
 - History of clinical reactivity (e.g., oral itching, anaphylaxis) or failed OFC.
2. **Baseline Assessments:**
 - Spirometry (if asthma is present).
 - Epinephrine auto-injector prescribed and training provided.
3. **Exclusion Criteria:**
 - Uncontrolled asthma, eosinophilic esophagitis (EoE), or other contraindications.

• Agreed with all of this!



DeepSeek FTW?

DeepSeek V3 ▾

OIT Phases

1. Initial Dose Escalation (Day 1 – Clinic-Based)

- Conducted under **supervision in an allergist's office** with emergency medications available.
- Start with a tiny, sub-threshold dose (e.g., 0.1–1 mg of spice protein).
- **Example Progression (Mustard Seed Powder):**
 - Dose 1: 0.1 mg
 - Dose 2: 0.5 mg
 - Dose 3: 1 mg
 - Dose 4: 5 mg
 - Dose 5: 10 mg
 - **Stop at highest tolerated dose (target: ~10–50 mg for Day 1).**

- **Completely reasonable**
- **Much more detailed than other LLMs**
- **Perhaps a little aggressive on day 1**



DeepSeek FTW?

DeepSeek V3 ▾

2. Build-Up Phase (Weeks 2–24 – Home Dosing)

- Patient takes **daily doses at home** , increasing every 1–2 weeks under allergist guidance.
- **Example Escalation Schedule:**
 - Week 1: 20 mg
 - Week 2: 50 mg
 - Week 4: 100 mg
 - Week 6: 200 mg
 - Week 8: 500 mg (~1/8 tsp)
 - Week 12: 1000 mg (~1/4 tsp)
 - Week 24: 2000–4000 mg (~1/2–1 tsp, maintenance dose)
- Pretty typical to reflect what we often do
- Probably higher than you need to go for spice
- Still, detailed and reasonable plan

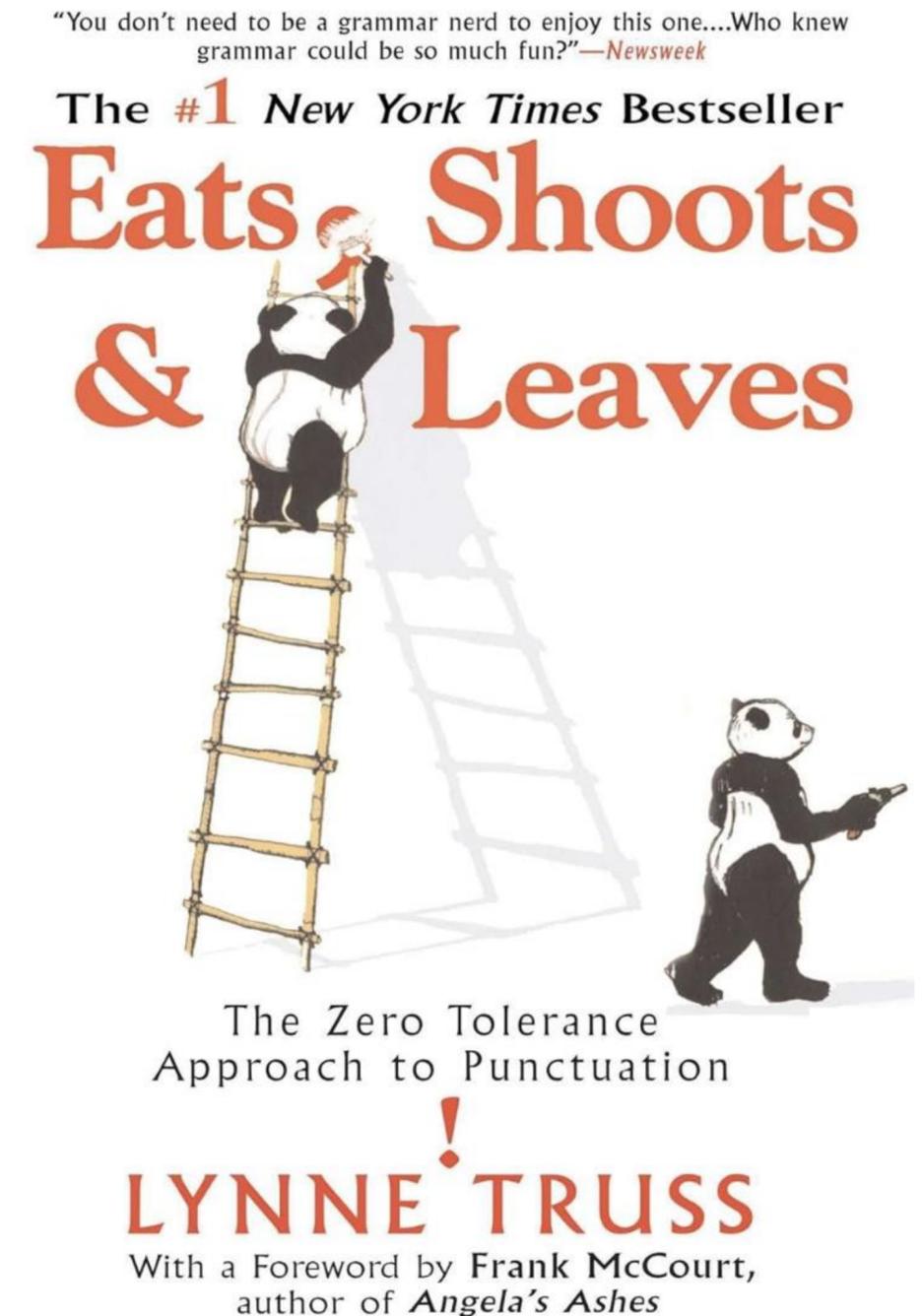
3. Maintenance Phase (Ongoing)

- Daily intake of target dose (e.g., 1 tsp of spice).
- Regular follow-ups (every 3–6 months) to monitor tolerance.



Using AI

- Everyone needs to learn to use AI capably
- GIGO = garbage in / garbage out -> quality of prompt is essential
- You're not likely to understand the relevance and quality of results if you have no baseline subject matter knowledge
- Like grammar auto-correct: if you have no clue what a gerund, appositive, or Oxford comma is, you probably don't even know if grammar correction is accurate



“Is it worth it?” - Amplified with uncommon foods

- Time / effort burden of OIT (and even SLIT):
 - Side effects, taste aversion, burden of daily dosing weighed against avoidance / fear of reaction
 - Practice-side effort to research protocol, find source material, prepare doses for low-volume patients
- Parental motivation vs. child / adolescent motivation (highly differential)
- This is not always an easy or obvious decision: cultural considerations, desire to eat the food, nutrition concerns, etc
- Goal setting: Cross-contamination vs. accidental protection vs. freely eating



Take-home nuggies

- OIT for uncommon foods is possible but many not be practical in many instances
- Taste aversion is a significant issue, particularly for fish and sesame (consider SLIT here)
- Cross-reactivity patterns in fish and shellfish desensitization are unclear
- Spice “allergy” may often represent mugwort-spice syndrome variants
- AI can help significantly but you need to ensure you have baseline knowledge and apply common sense to outputs



References

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Prom 2025



If you think AI and food immunotherapy are complicated, wait until your daughters start dating !

