Immunotherapy for Uncommon Foods

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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 resources for proceeding with immunotherapy to such foods (hint: don’t trust ChatGPT)

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)

(a)

Days/weeks	*Drops*[a]	*mL*	*Capsules (65 mg)*	*mg*
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

(b)

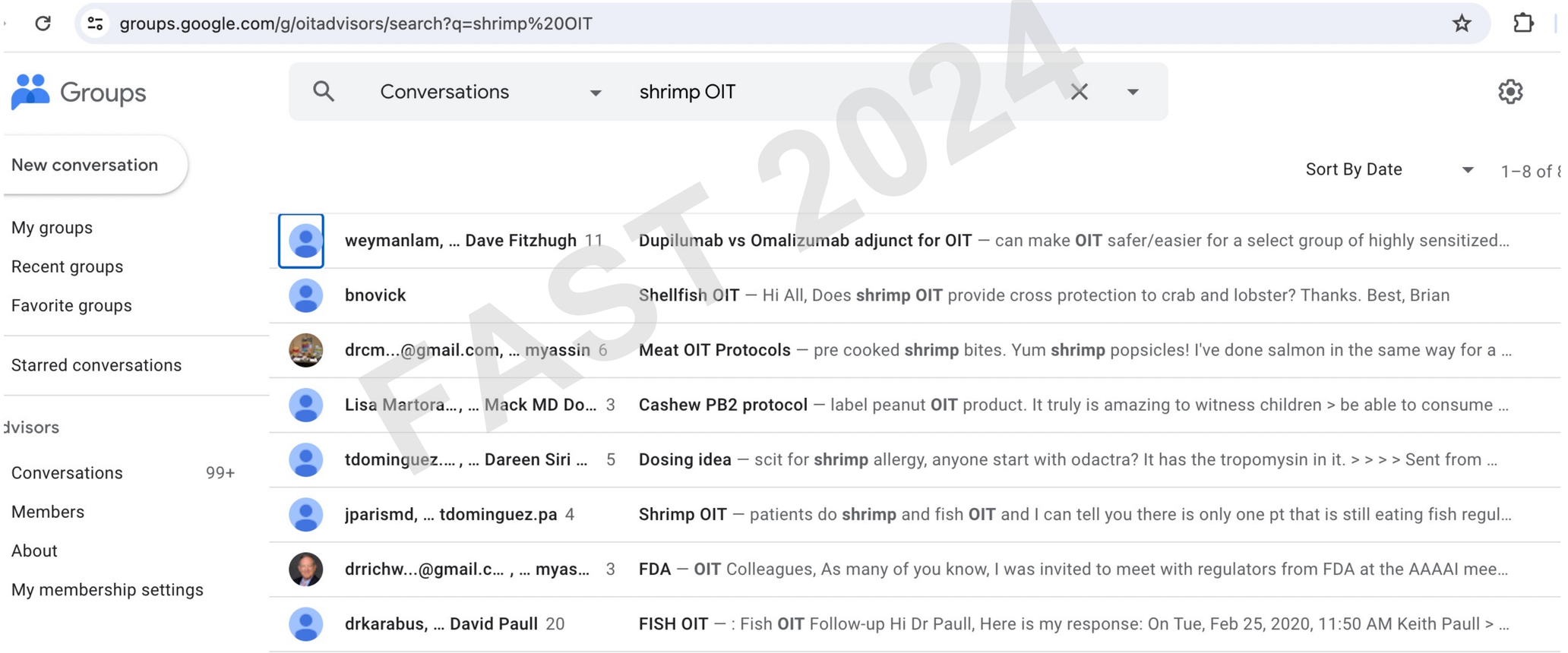
Days/weeks	*G*
112/17	1
119/18	2
126/19	4
133/20	8
140/21	16
147/22	32
154/23	64
161/24	100

[a]Solution of 65 mg dehydrated cod extract in 50 mL water.

- 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

OIT Advisors - A great source of information!

- Learn to search within the Google group



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

Bahna, 2011

Be wary of ChatGPT!

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

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

“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
- Be very wary of generative AI for evaluating the medical literature

References

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13. Have you ever done fish or shellfish immunotherapy (OIT or SLIT)?

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14. For any "uncommon" food OIT, what has been your biggest challenge?

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