

Sublingual Immunotherapy



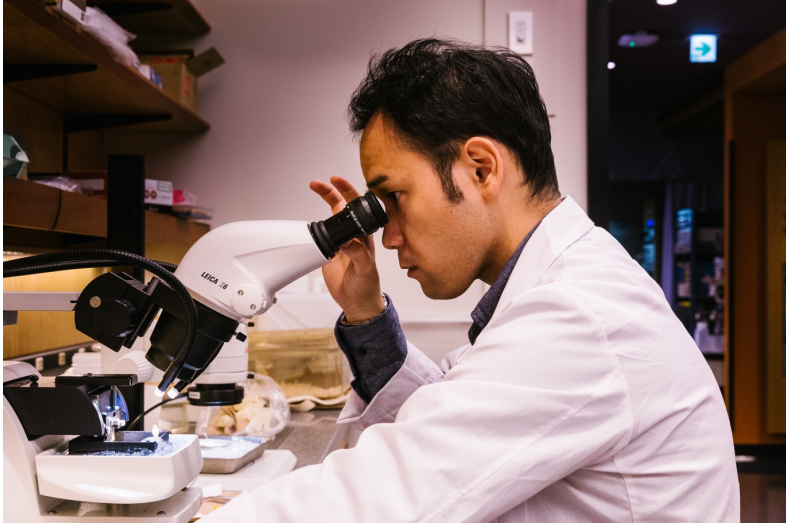
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Early SLIT – Designed to Fail



- Tested in older patients
- Asked to pass 5 gm peanut protein OFC ≤ 1 year
- Final doomsday endpoint ---- remission



Literature review

The science behind SLIT

- 11 kids peanut SLIT + 7 placebo
 - 6 mo. buildup, 6 mo. maintenance (**2 mg** pp)
[extract 5 mg/ml, 8 drops]
 - No epi use
 - 1 yr. OFC: 1700 mg pp median cumulative dose
vs 85 mg placebo
[~7 peanuts]
- Kim EH. J Allergy Clin Immunol 2011;127:640-6

Milk SLIT vs OIT



- 6-16 y.o. 10 SLIT (**7 mg**), 20 OIT (1 gm or 2 gm)
- OFC at 60 weeks to 8 gm milk protein
- 1/10 SLIT passed, 14/20 OIT passed
- Median increase OFC threshold 40-fold for SLIT (3 ml to 120 ml)





Peanut SLIT

- 20 SLIT vs 20 placebo, 12-40 yo., median 15 yo
- 42 wks buildup, 2 wks M **1.4 mg** pp, then OFC
- Epi used once
- OFC 2.5 gm (10 nuts), none passed

Yet, median dose went from 3.5 to 496 mg pp

CoFAR 3 Year F/U



- placebo pts. (20) x-over to **3.7 mg** pp SLIT, active 20 stayed on 1.4 mg pp (Greer extract 3.3 mg/ml pp)
- high drop rate (annual OFC's?), 14/40 remained, no Epi
- 3rd year OFC 5 gm peanut protein
- 2/5 high dose passed, 2/9 1.4 mg dose passed



Peanut SLIT vs OIT

- n=21, 7-13 y.o. (5 d/c 1st year, 4 in OIT group)
- SLIT **3.7 mg** pp (n=10), OIT 2 gm/day (n=11)^[13 visit buildup]
- Epi in 4 OIT pts (36%), none in SLIT
- OFC 1 yr on M: 141-fold ↑ threshold OIT, 22-fold SLIT (21 mg pp to 496)

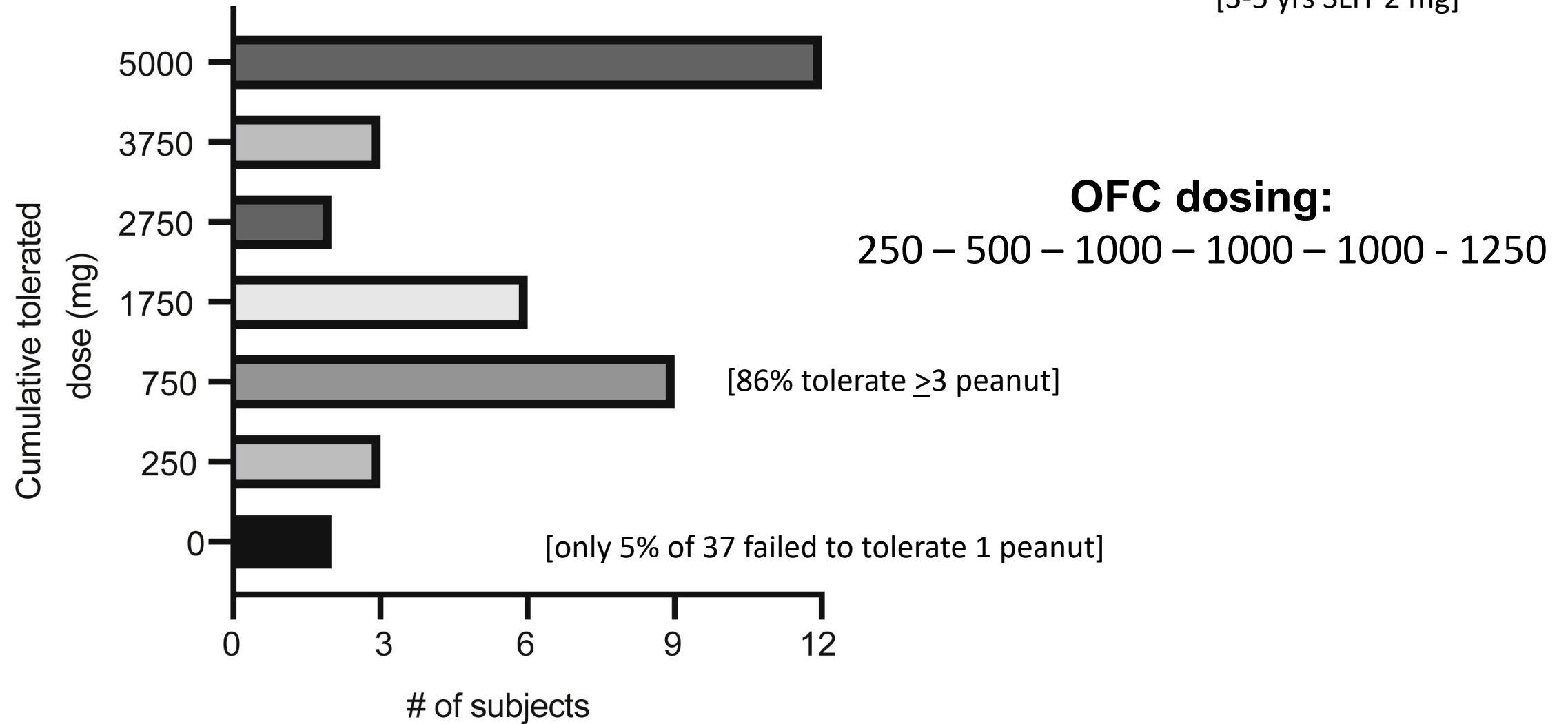
Long Term Peanut SLIT



- 3-5 years of **2 mg** pp SLIT (original 11 pts + 7 placebo in 2011 study + new cohort)
- 37/47 completed (79%), 1-11 y.o., 2 dropped GI sx.
- No epi
- OFC to 5 gm pp, 32% passed, median 1750 mg, 86% tolerated ≥ 750 mg

Robust Peanut Protection

[3-5 yrs SLIT 2 mg]



More Peanut, Please

- 54 pts. 2-11 y.o. (mean 7) peanut allergy (+ OFC, mean 66 mg pp, range 0-425)
- 4 mg peanut protein open label SLIT x 4 years (16 pumps 5 mg/ml extract) [buildup 20 wks]
- At 4 yrs: OFC to 5 gm pp, d/c SLIT, rechallenge at 1-17 weeks

Peanut 4 mg SLIT - Results

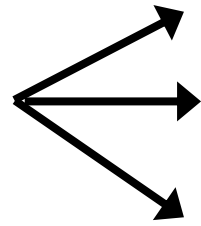
- 4 dropped in 20-week buildup; 3 later due to abd. side effects, 47/54 (87%) completed 4 years
- 44 of 47 (94%) tolerated ≥ 300 mg pp (minimal clinically relevant threshold, MCRT) [81% of original 54]
- 17 (36%) passed 5 gm OFC [31% by ITT]
- mean OFC 48 mg baseline to 2723 mg pp, no Epi

Peanut 4 mg – Missed Doses

- After 4 yrs. d/c dosing, n=37 were block randomized to OFC within 6 wks, 7-12 wks, or 13-17 wks
- OFC: 100 mg – 200 – 500 – 800 – 1300 – 2100^[5 gm]
- 49% dropped a step in the OFC threshold
- None dropped below 300 mg between 1-17 wks

In Case You've Been Napping

2 mg peanut
protein (pp)

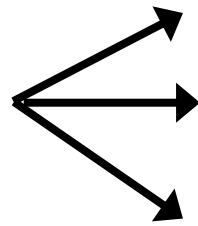


1/3 can eat 5 gm pp

5% won't tolerate 1 peanut

86% will tolerate ≥ 750 mg pp

4 mg pp



87% completed 4 years

[11 peanuts]

mean OFC SCD from 48 mg to 2723

miss dose x 4 mo., still tolerate a peanut

6 mg pp



???

SLIT: where's it fit?



- A waste of time, too weak
- Salvage treatment after failed OIT
- A 'ladder' to OIT
- Stand alone desensitization

WRONG

FOR SURE

YEAH, BUT WHY

ABSOLUTELY

SLIT ROCKS



- Safety - what's Epi?
- Lifestyle – minimal rest period, 3-4 week buildup
- Ease of administration – draw and squirt
- Missed doses – who cares
- Enjoy “your daily vitamin”



Can I Switch to OIT?

Yes, but...

- Safety – go find your Epi
- Lifestyle – slow down, 2 hour rest period
- Ease of administration – weigh, hate the taste
- Missed doses – camp, trips; call the office
- Enjoy “your daily chore”

SLIT: Finding the right place

(2022)

6 months to 5 years old → NA, + OIT works

5 to 12 years old → Maybe here

Teens and beyond → Definitely here

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(2023)

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Evolution of OIT/SLIT



Prior 21st century - avoid

2000-2020

- Avoid – unburdened, risk averse
- OIT – a beacon of light, transformative

Now

- Avoid
- OIT – still awesome, but has warts
- SLIT – couldn't be easier

SLIT Unanswered Questions



- Will adherence beat OIT?
- Build up, can we go faster?
- Extracts now, will real food work?
- Post-dose rest period, why?