

Lumps, bumps and mysterious swellings

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Aims

- Review clinical features and mechanisms of IgE-mediated food allergy
- How to describe, report and refer food allergy
- Risk stratification in food allergy, including molecular allergology and microarrayed serology
- The basics of urticaria/ angioedema
- Advances in C1 inhibitor deficiency
- A rare allergy syndrome

Peanut allergy patient

- Patient seen in clinic following an episode of:
 - Oral itching
 - Lip swelling
 - Sensation of throat constriction, difficulty talking
- Ambulance called – settling down by arrival
- Immediately followed unroasted monkey nuts

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Symptoms,
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Possible triggers

Timecourse

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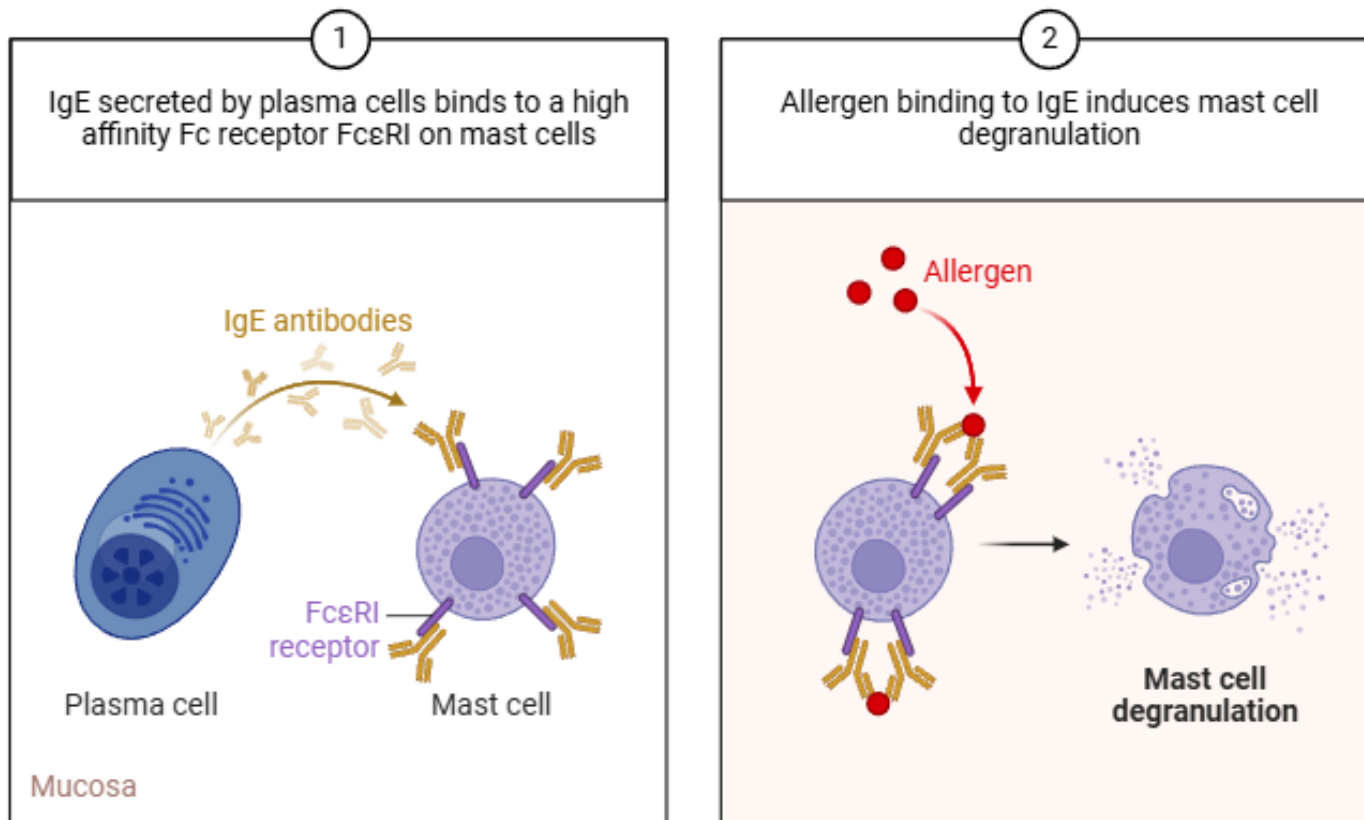
Timecourse

- Avoid diagnostic terms such as 'reaction' or 'anaphylaxis', even if it seems obvious
- High level of detail required
- Triggers at the end

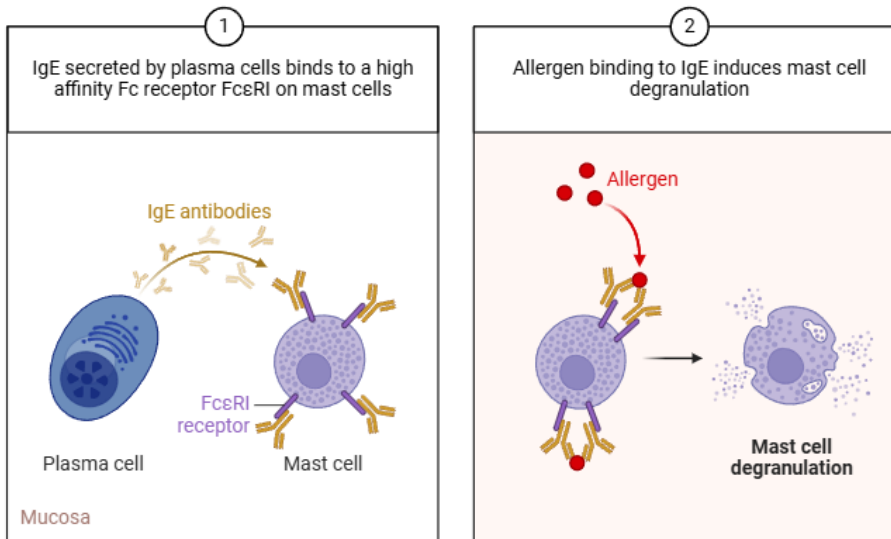
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- Ambulance called – settling down by arrival
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- Longstanding oral itching on exposure to peanut noted
- Background of seasonal hayfever, spring through summer
- Oral itching when eating applies, peaches, nectarines
- Outgrown asthma, no eczema
- Given adrenaline auto-injectors; extremely strict avoidance of all nuts and potential nut exposures
- IgE peanut (done in primary care) 1.4kU/ L (<0.35)

IgE Operates Through the Fc Receptor FCεRI on Mast Cells



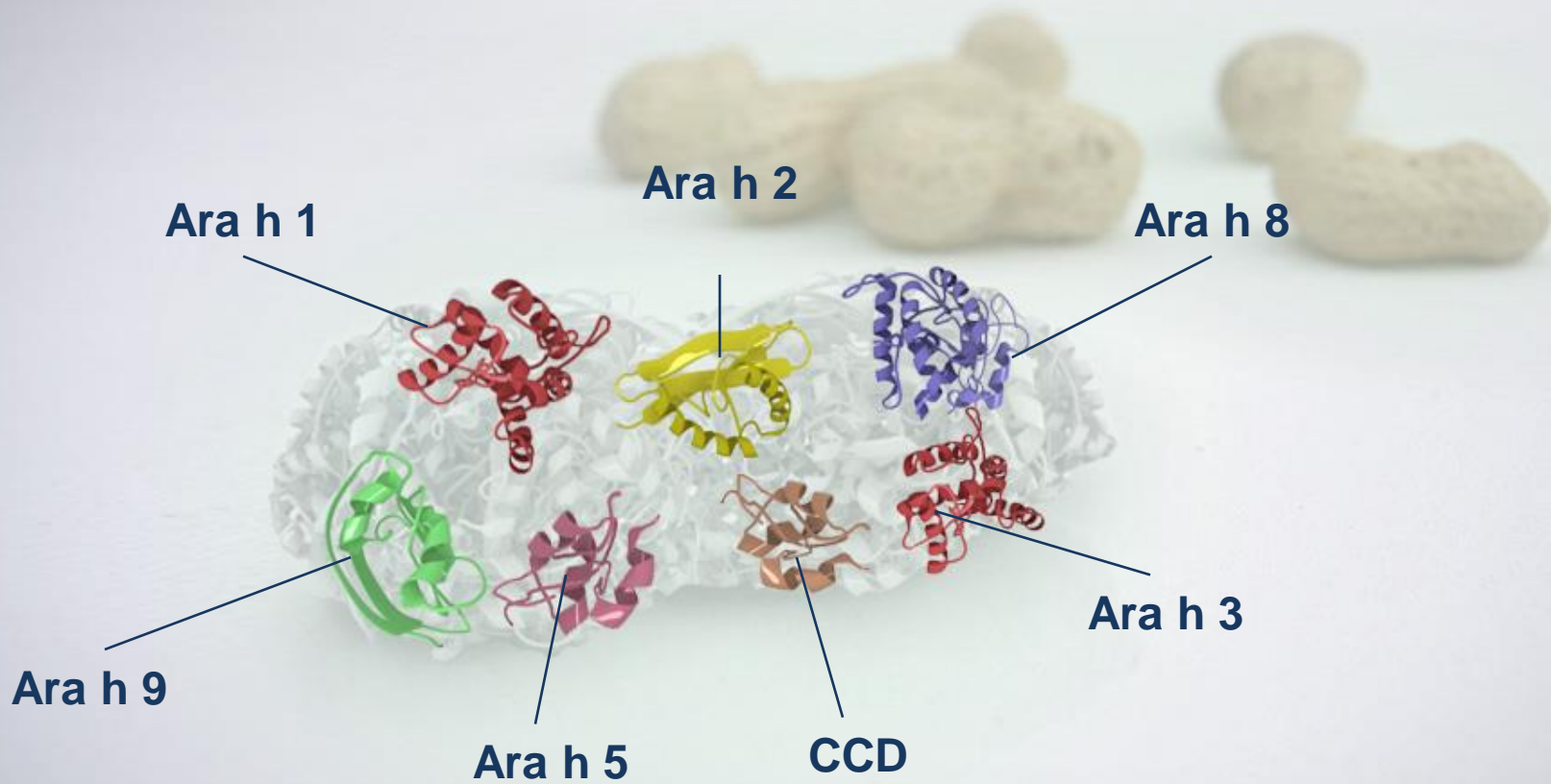
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- Rapid onset after exposure
- Symptoms compatible with the pharmacology of histamine
- Rapid resolution
- Symptoms are reproducible on repeat exposure

Peanut components



Latin name: Ara h = *Arachis hypogaea*

Peanut skin prick test 3mm,
negative control 0mm

Hazelnut skin prick test 7mm,
remainder of nuts negative

Birch skin prick test 14mm

Ara h 1, 2 and 3 all <0.35 kU/L

Cor a 9 and 14 both <0.35

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Birch skin prick test 14mm

Ara h 1, 2 and 3 all $<0.35\text{kU/L}$

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- Final diagnosis is **pollen-food syndrome**
- Sensitisation to birch pollen proteins that are also found in fruits, nuts and vegetables
- Proteins are heat-labile
- Not dangerous – avoidance doesn't need to be absolute, adrenaline pens not needed

Nuts

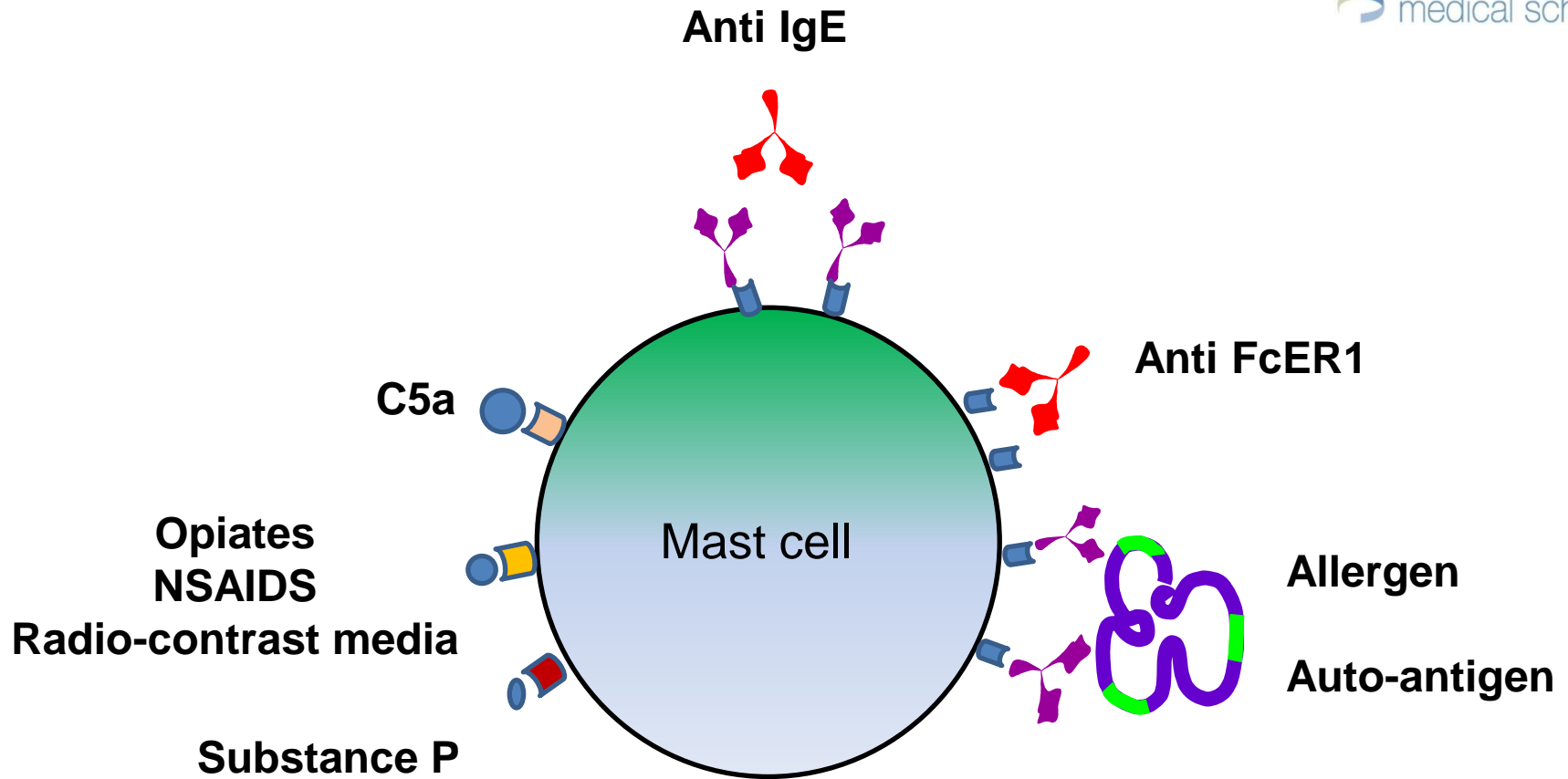
Cashew	••••	Ana o		3.53	
	⊙	Ana o 2	11S Globulin	≤ 0.10	
	⊙	Ana o 3	2S Albumin	2.43	
Brazil nut	••••	Ber e		0.48	
	⊙	Ber e 1	2S Albumin	0.15	
Pecan	••••	Car i		0.19	
Hazelnut	⊙	Cor a 1.0401	PR-10	≤ 0.10	
	⊙	Cor a 8	nsLTP	≤ 0.10	
	⊙	Cor a 9	11S Globulin	0.48	
	⊙	Cor a 11	7/8S Globulin	0.61	
	⊙	Cor a 14	2S Albumin	0.71	
Walnut	⊙	Jug r 1	2S Albumin	0.29	
	⊙	Jug r 2	7/8S Globulin	0.10	
	⊙	Jug r 3	nsLTP	0.13	
	⊙	Jug r 4	11S Globulin	0.56	
	⊙	Jug r 6	7/8S Globulin	≤ 0.10	
Macadamia	⊙	Mac i 2S Albumin	2S Albumin	≤ 0.10	
	••••	Mac inte		0.10	
Pistachio	⊙	Pis v 1	2S Albumin	5.02	
	⊙	Pis v 2	11S Globulin subunit	0.69	
	⊙	Pis v 3	7/8S Globulin	≤ 0.10	
Almond	••••	Pru du		0.39	

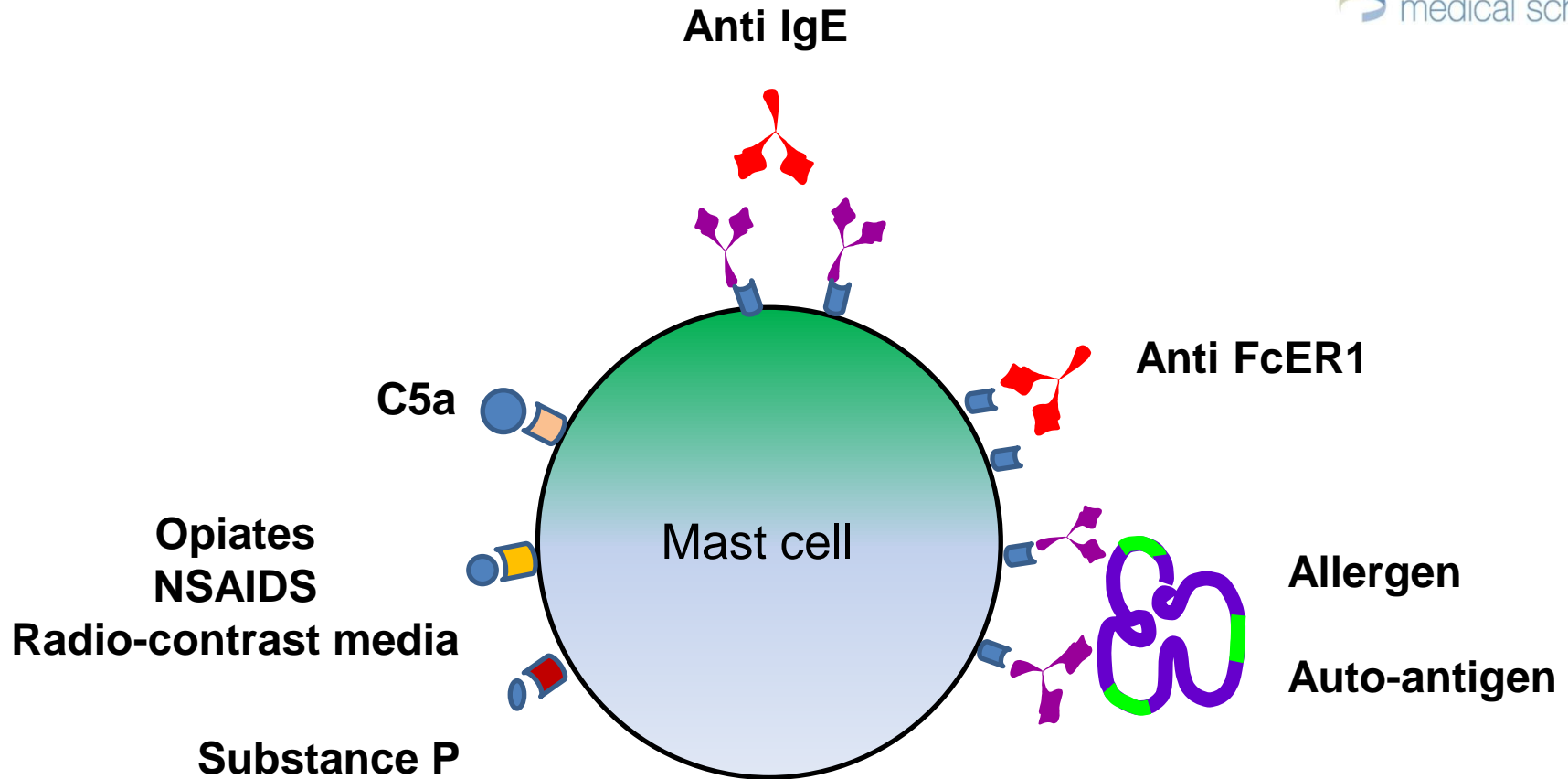
'Allergic reactions to unknown trigger'

- Some months ago, awoke with swelling around eyes, lips and tongue
 - Given adrenaline in ED
 - Discharged with adrenaline autoinjectors
 - Advised that allergic reactions worsen each time; should be 'careful about diet'
- Episodes 1-2 per week subsequently, varying severity; swelling persists for 24-48 hours regardless of on-demand treatment
- Repeated adrenaline pen use and ED visits
- Now eating only rice and chicken

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- Now eating only rice and chicken
- This is not anaphylaxis or allergy:
 - No triggers
 - Wakes up with symptoms
 - Persistent
 - Swelling-only
- A 'spontaneous' form of angioedema





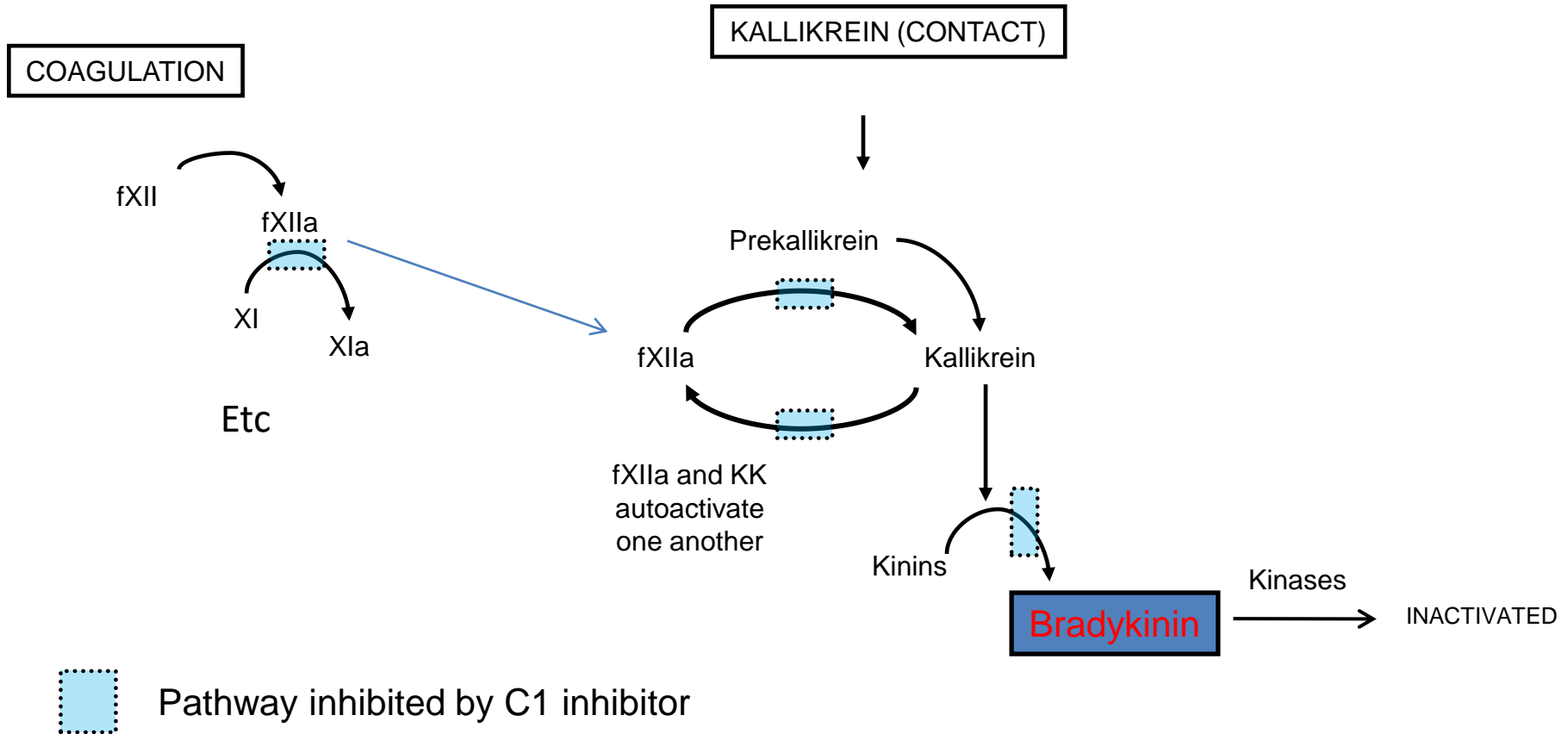
CSU = itchy hives on
most days for >6 weeks

- This is patient has a variant of CSU
 - Also has daily itching, minor whealing and minor dermographism
 - Unprovoked swelling = rash in deeper skin layers
 - Some patients even have a 'swelling only' variant of CSU
- Rendered asymptomatic with high-dose anti-histamines
- Adrenaline pens withdrawn and foods gradually re-introduced

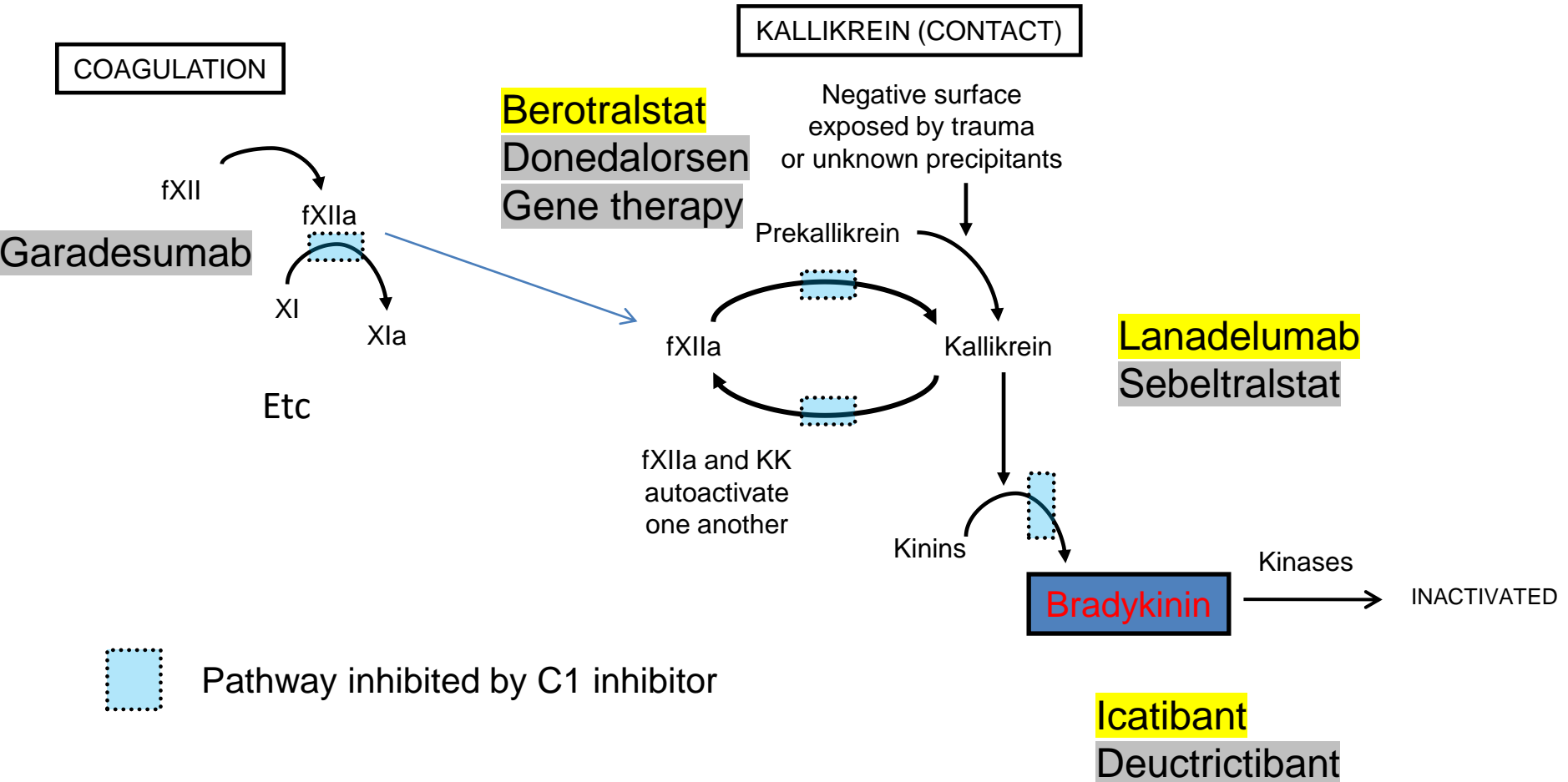
C1 inhibitor deficiency

- Unprovoked swelling attacks, without urticaria
- Most patients have autosomal dominant mutations in gene encoding C1 inhibitor protein (hereditary angioedema, HAE)
- Extremely rare acquired form (AAE) often associated with paraprotein
- Over-represented in Brighton area with several large affected families
 - Swelling may affect any body site
 - Risk of laryngeal oedema with airway compromise
 - Abdominal swelling mimicks acute abdomen

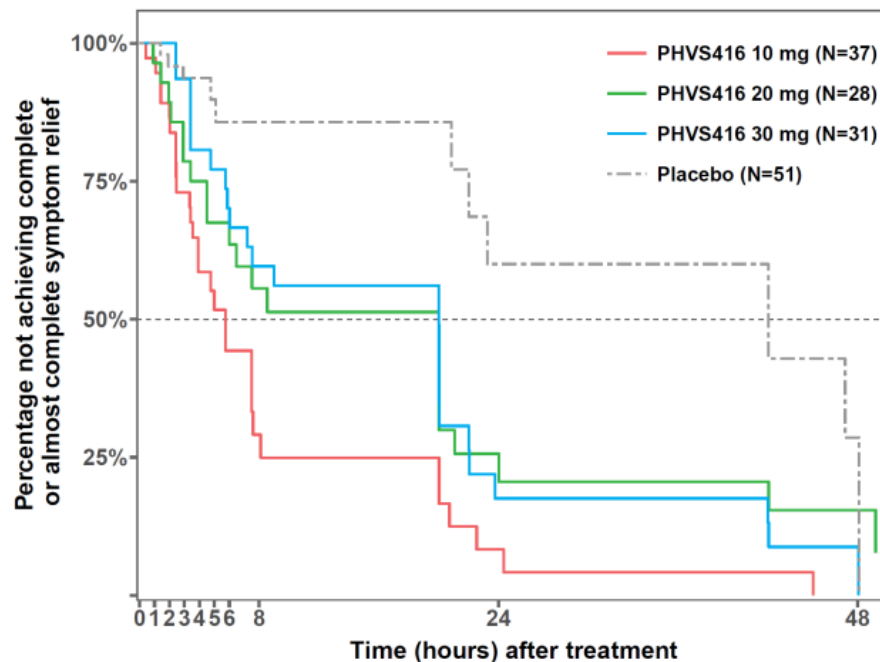
Bradykinin is the major mediator of swelling in C1 inhibitor deficiency



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PHVS416 significantly reduces time to almost complete or complete symptom relief (all individual VAS ≤ 10)



Median time in hours (95% CI)

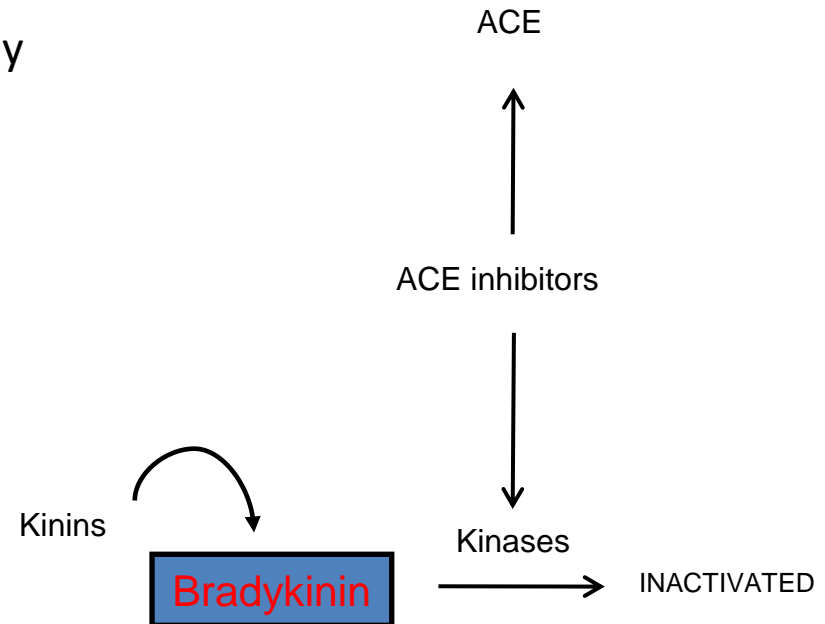
Placebo	42.0 (22.0, 48.1)	
PHVS416 10 mg	5.8 (3.6, 7.5)	$p < 0.0001^{\dagger}$
PHVS416 20 mg	20.0 (4.5, 20.0)	$p = 0.0127$
PHVS416 30 mg	20.0 (6.0, 20.1)	$p = 0.0001$
Combined PHVS416	7.5 (5.9, 20.0)	

VAS assessed every 30 minutes up to 4 hours post-treatment, then at 5, 6, 8, 24, 48 hours

[†]Nominal p -value; N = The number of attacks in the mITT Analysis Set. Median time based on Kaplan-Meier estimates. p -values based on a marginal Cox proportional hazards model. The combined PHVS416 results are based on post-hoc analyses to provide a reference of the result by pooling all three active doses.

ACE-inhibitor angioedema

- Spontaneous swelling without hives
- Incidence perhaps 0.2%, but not really known
- Tends to appear within first few weeks, but may appear at any time
- Drug class contraindicated following first swelling attack, but A2RBlockers may be used
- Said to be a 3-month washout period
 - Risk of airway compromise
 - Abdominal attacks possible
 - 'Allergy' treatments don't help
 - Management is supportive



- 39 year old woman seen in clinic
 - Rapid onset of itching, redness and hives
 - Vision distorted, transient loss of consciousness; woke up feeling very tired but improved
 - Went to bed – fine next morning
- About 60 minutes beforehand, had eaten pizza and salad, also glass of wine
- Brisk uphill walk home
- Has eaten the same pizza again without issues
- Background of what was described as ‘heat rash’
 - Generalised itchy hives, only when exercising
 - Very variable, and intensity of exercise unrelated
 - Persists around 30-60 minutes
 - No recollection of foods involved

Wheat skin prick test
3mm

Wheat IgE 0.28kU/ L
(<0.35)

Omega-5-gliadin IgE
3.56kU/ L

- Diagnosis is **wheat-dependent, exercise-induced anaphylaxis**
- A rare disorder in which the clinical expression of anaphylaxis is dependent upon co-factors: exercise, alcohol, NSAIDS and infection
- Can continue to eat wheat; avoid combination with co-factors

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- Review a couple of rare allergy syndromes