

Hymenoptera Venom Allergy

David F. Graft, M.D.

Stinging Insect Hypersensitivity: A Practice Parameter Update 2010 *

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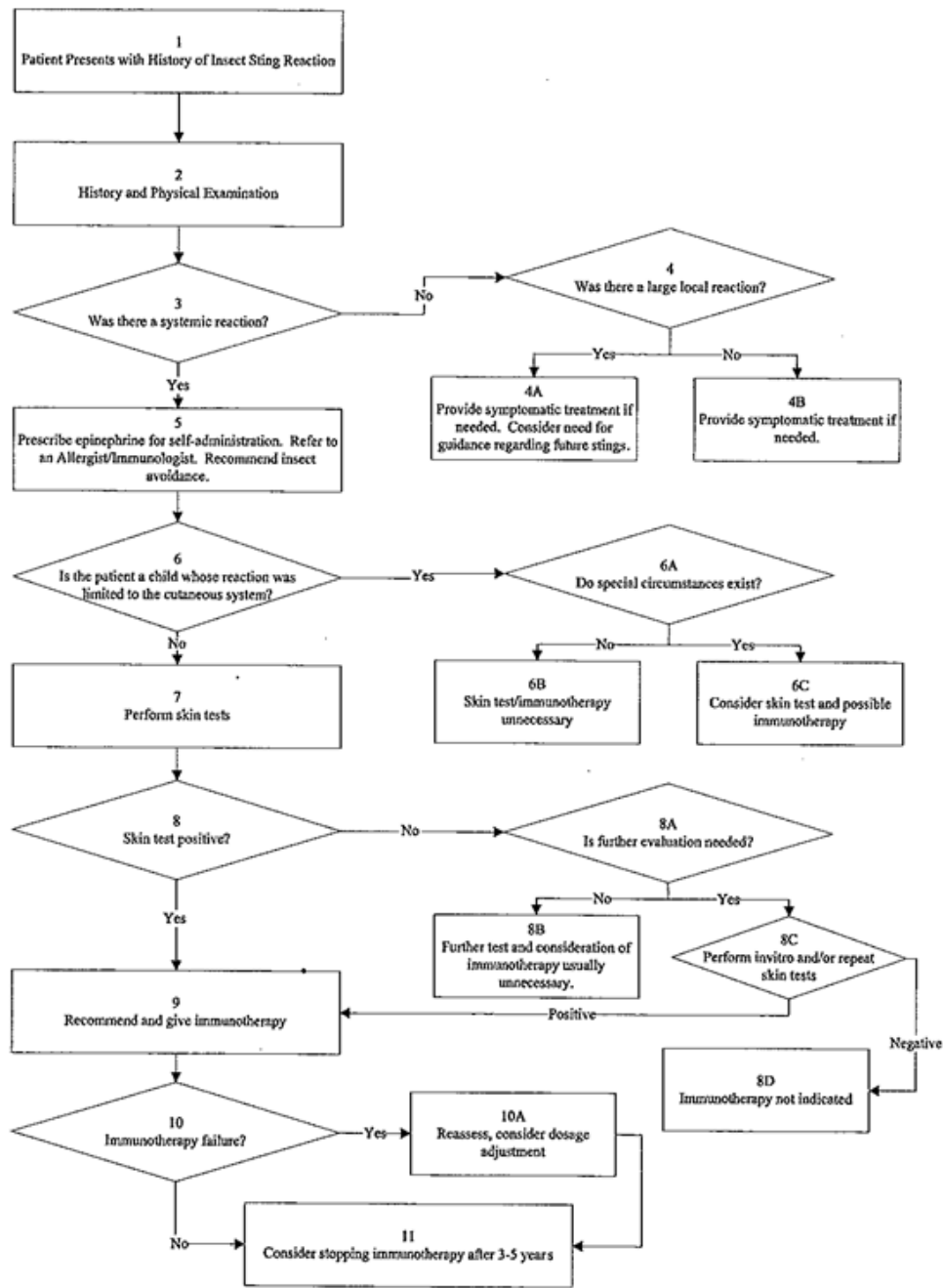


FIG 1. Algorithm: management of stinging insect reactions.

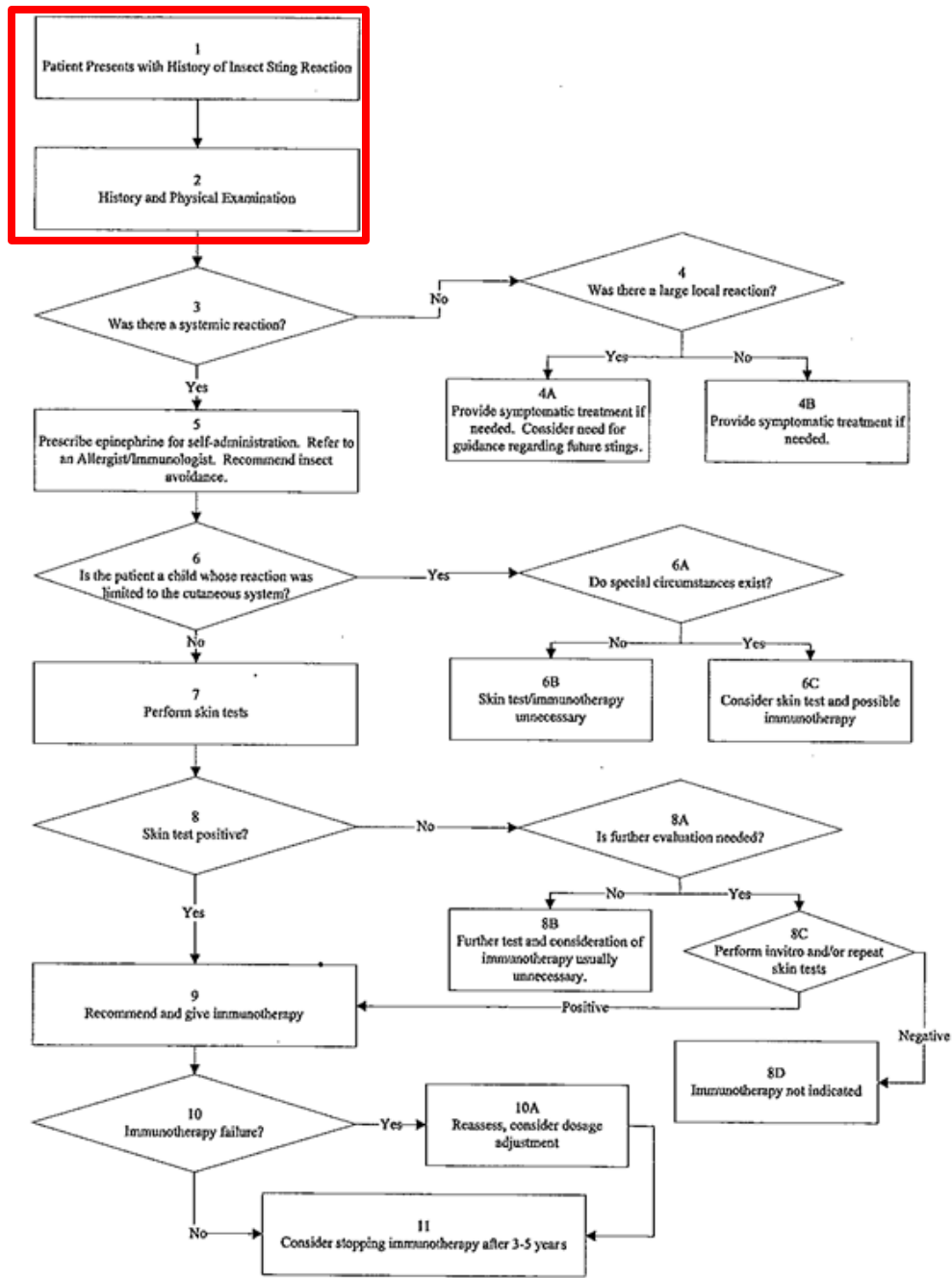
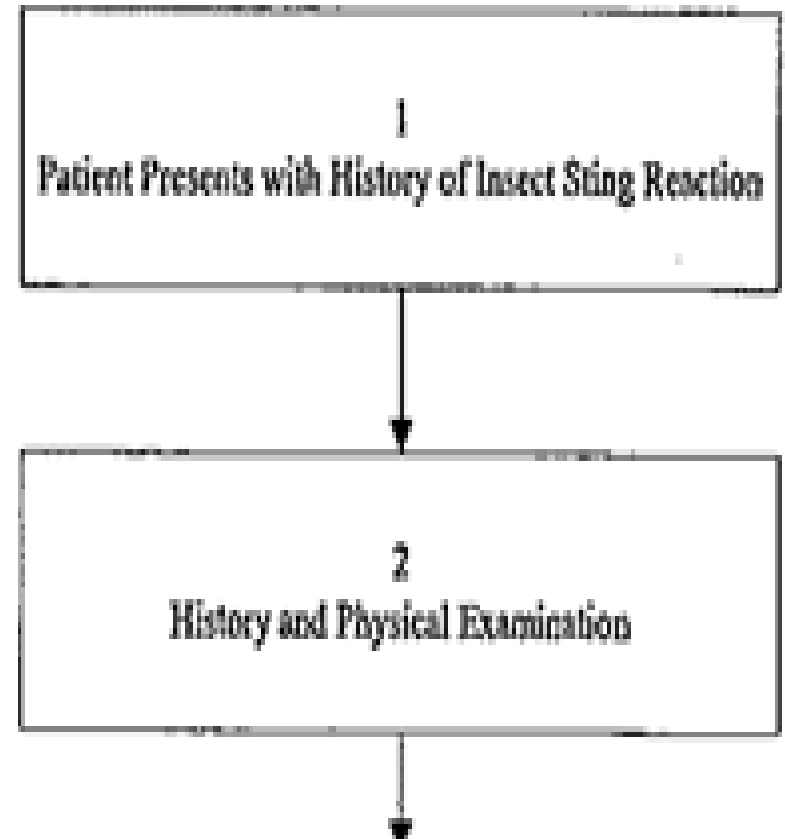


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Algorithm: Managing Sting Reactions

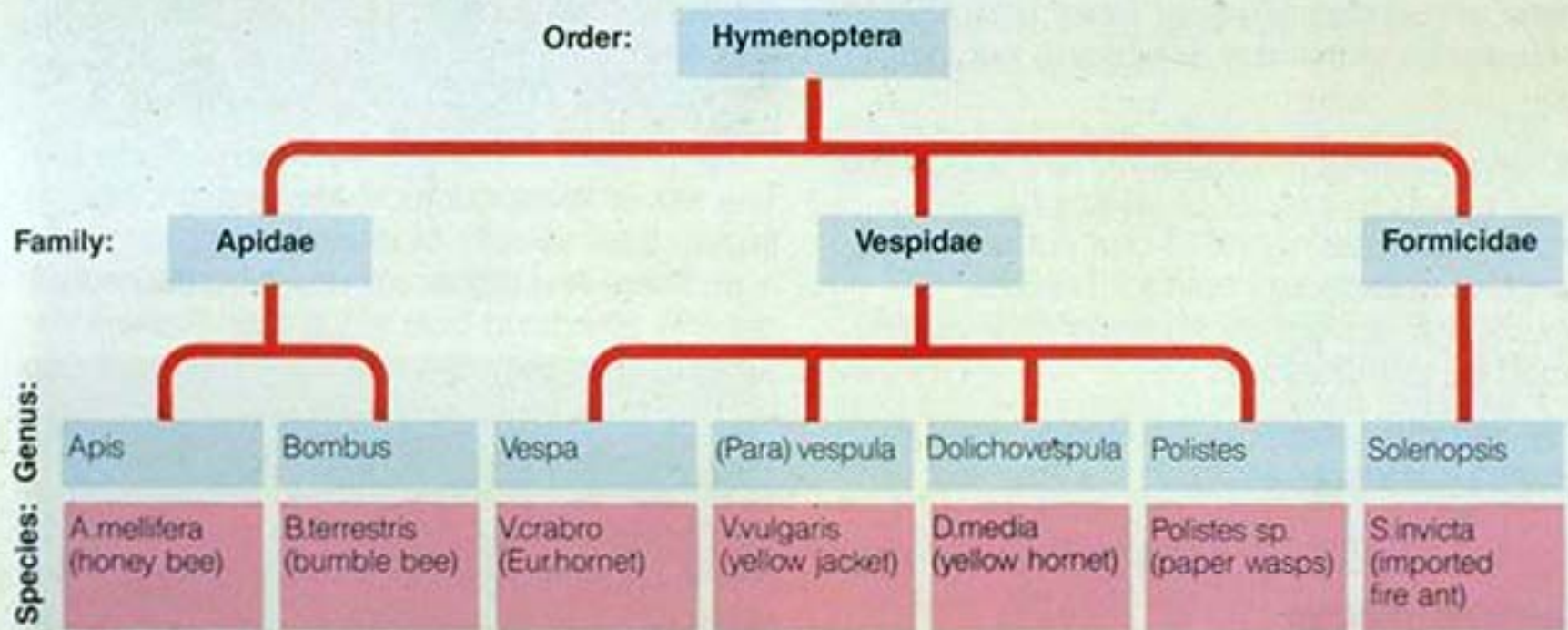
Review of important historical points

- Type of insect
- Type of reaction
 - Expected
 - Large local
 - Systemic



Biology of Hymenoptera

Figure 4. Taxonomy of Hymenoptera. Examples of common species are given below:

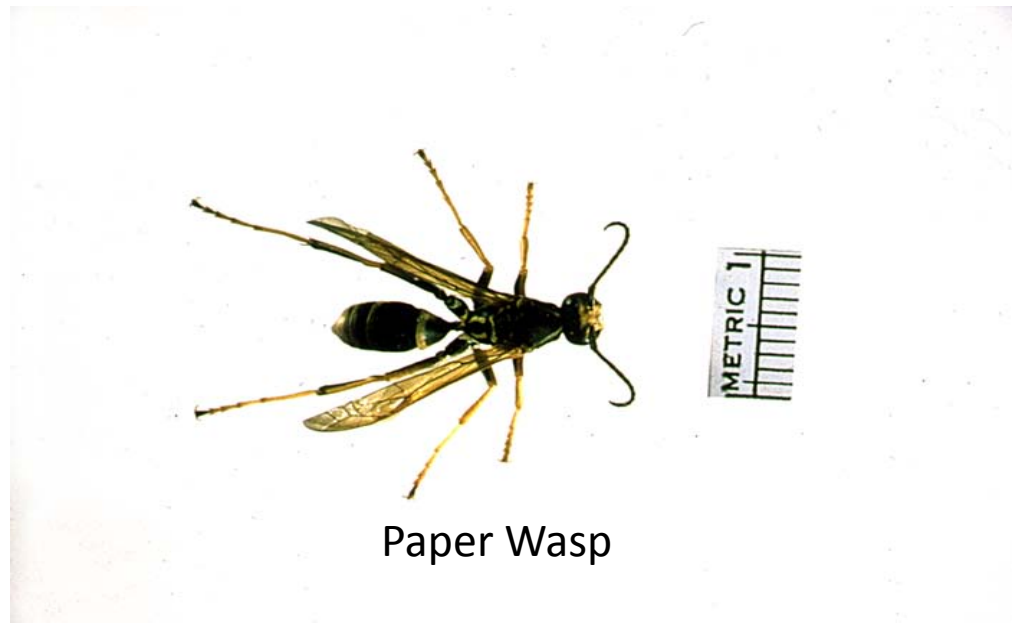












Paper Wasp



Fire Ant



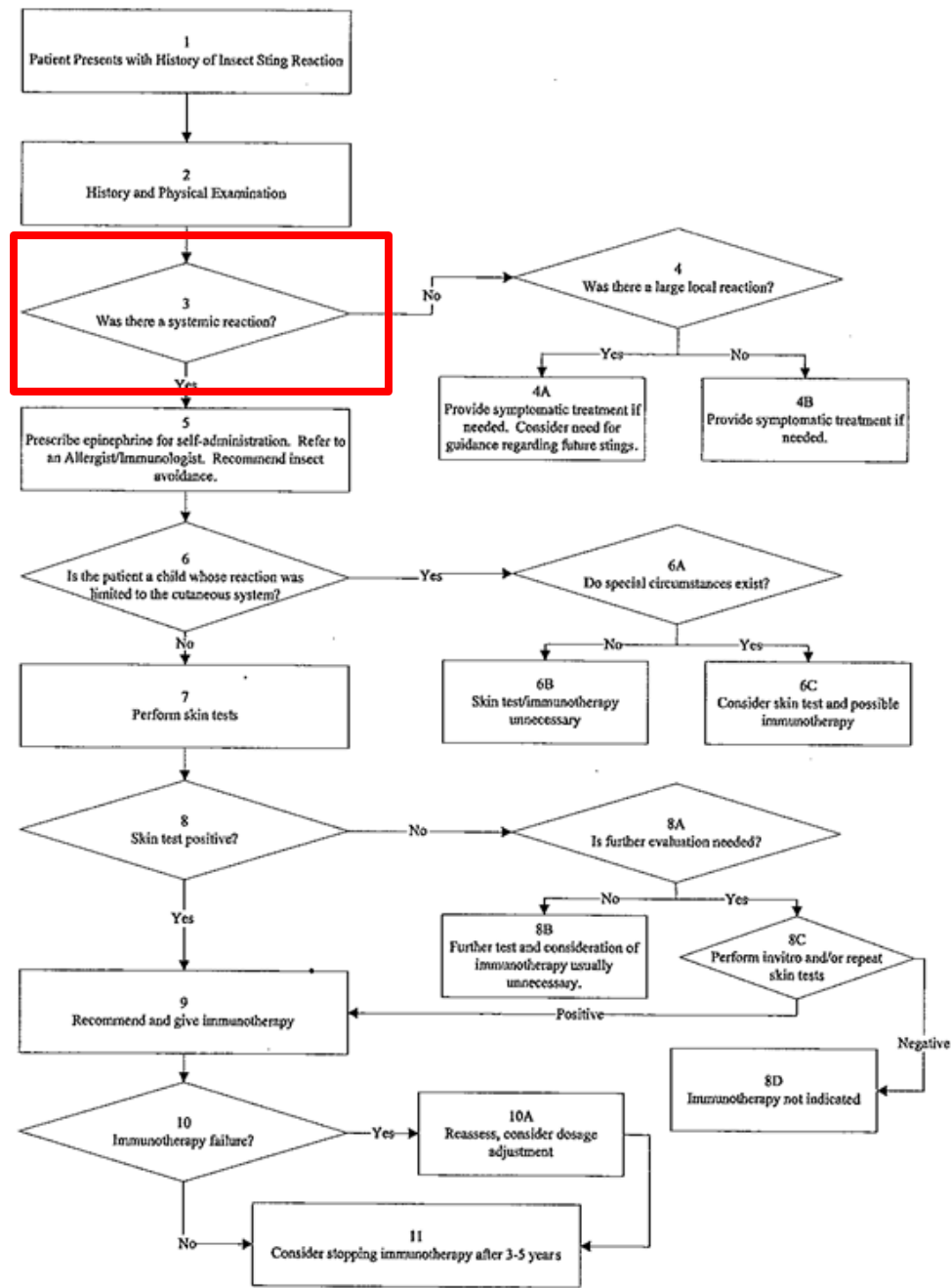


FIG 1. Algorithm: management of stinging insect reactions.

Algorithm: Managing Sting Reactions

General population risk
= ~5%

Systemic spectrum

- Cutaneous only
- Bronchospasm
- Upper airway obstruction
- Hypotension and shock
- GI

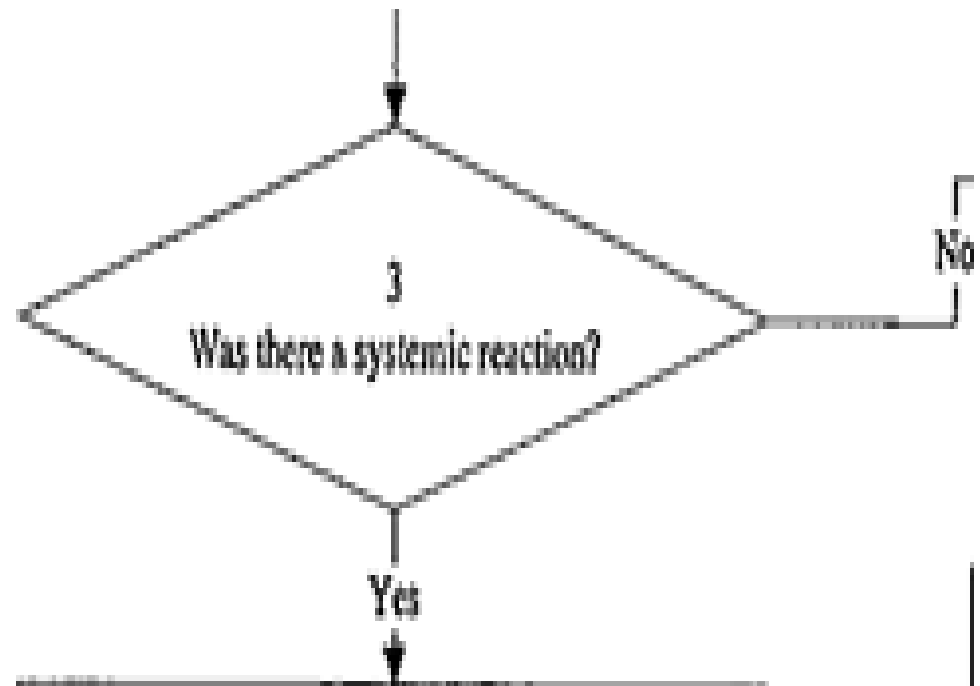




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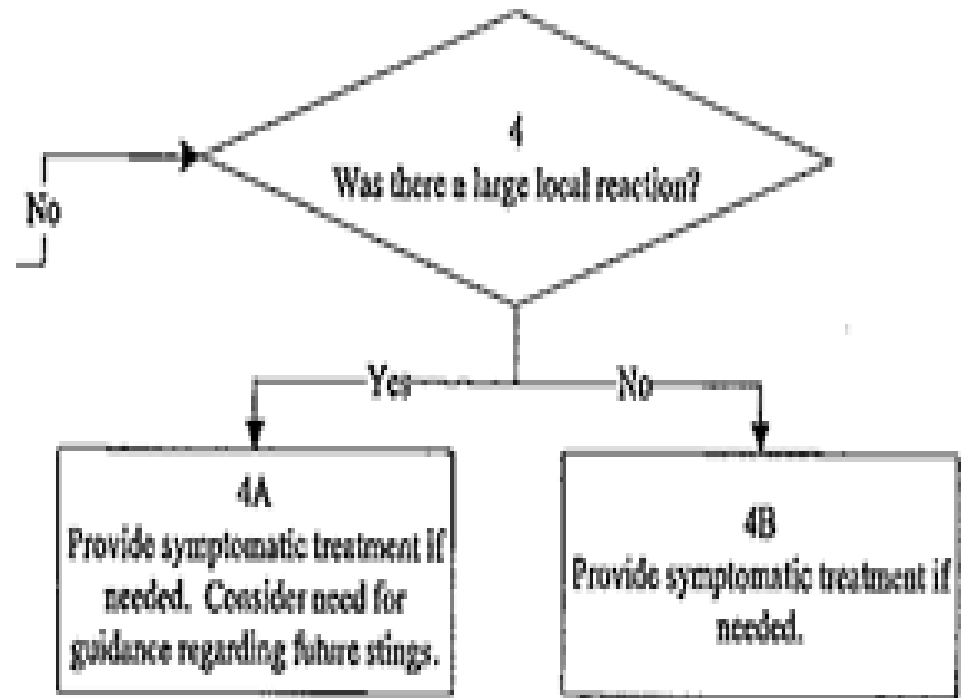
Algorithm: Managing Sting Reactions

Large local therapy

- Cold compresses
- Antihistamines
- Analgesics
- Possibly steroids

Future stings

- Up to 10% chance of future systemic
- Epi Rx - optional
- Immunotherapy may reduce reaction



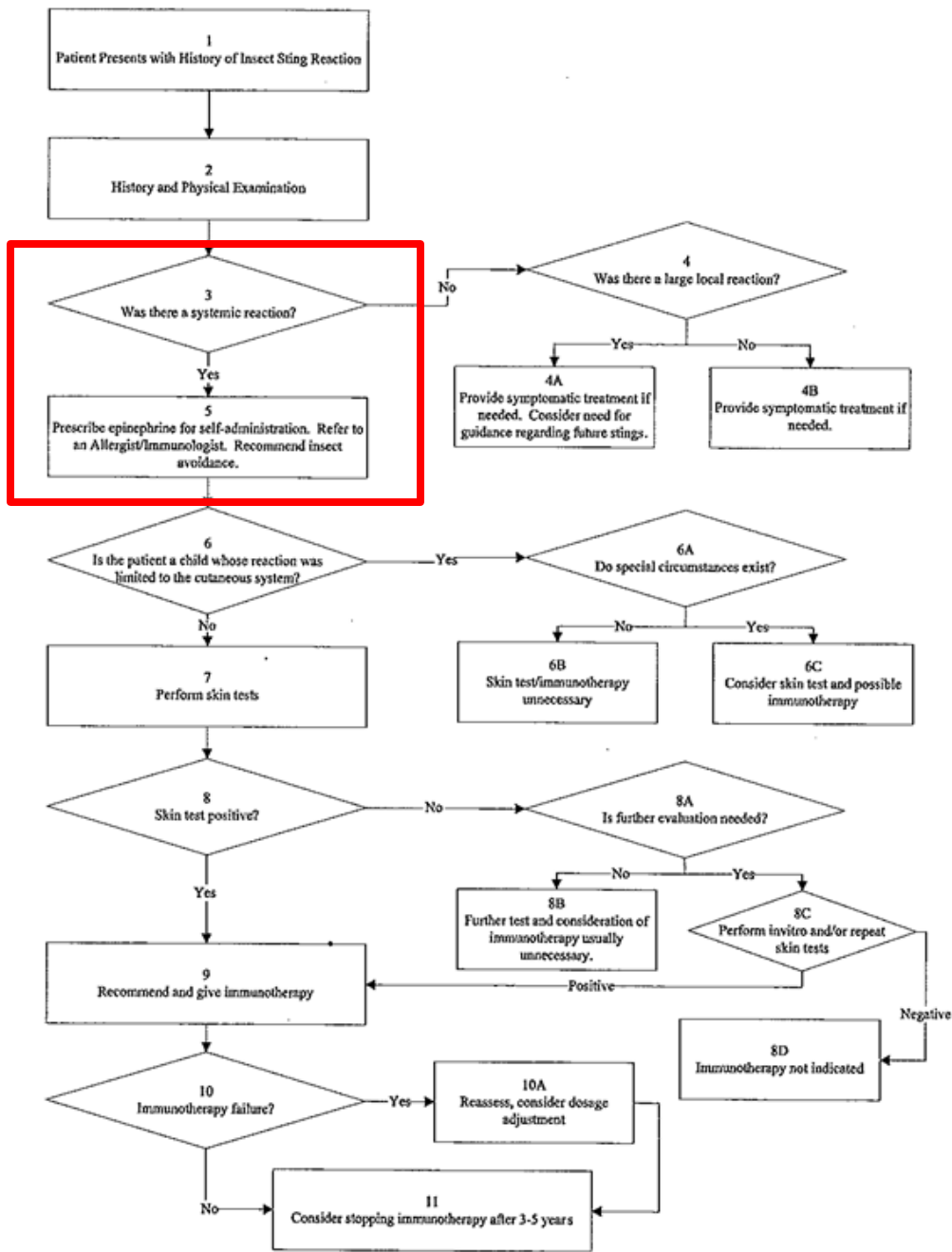


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Algorithm: Managing Sting Reactions

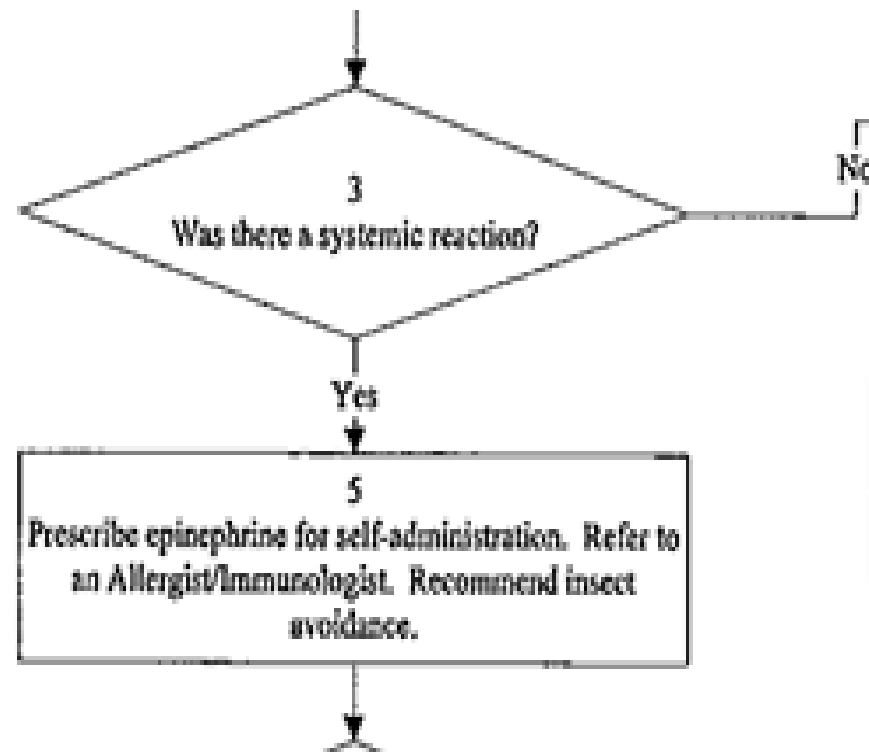
Initial plan

- Rx: Epi for self-administration
- Recommend medical alert bracelet
- Avoid insects

Future prophylaxis – Refer to an Allergist

2005: 617 pts; 15 EDs

Sys rxn: 12% epi in ED; discharge;
27% epi, 20% ref to allergist



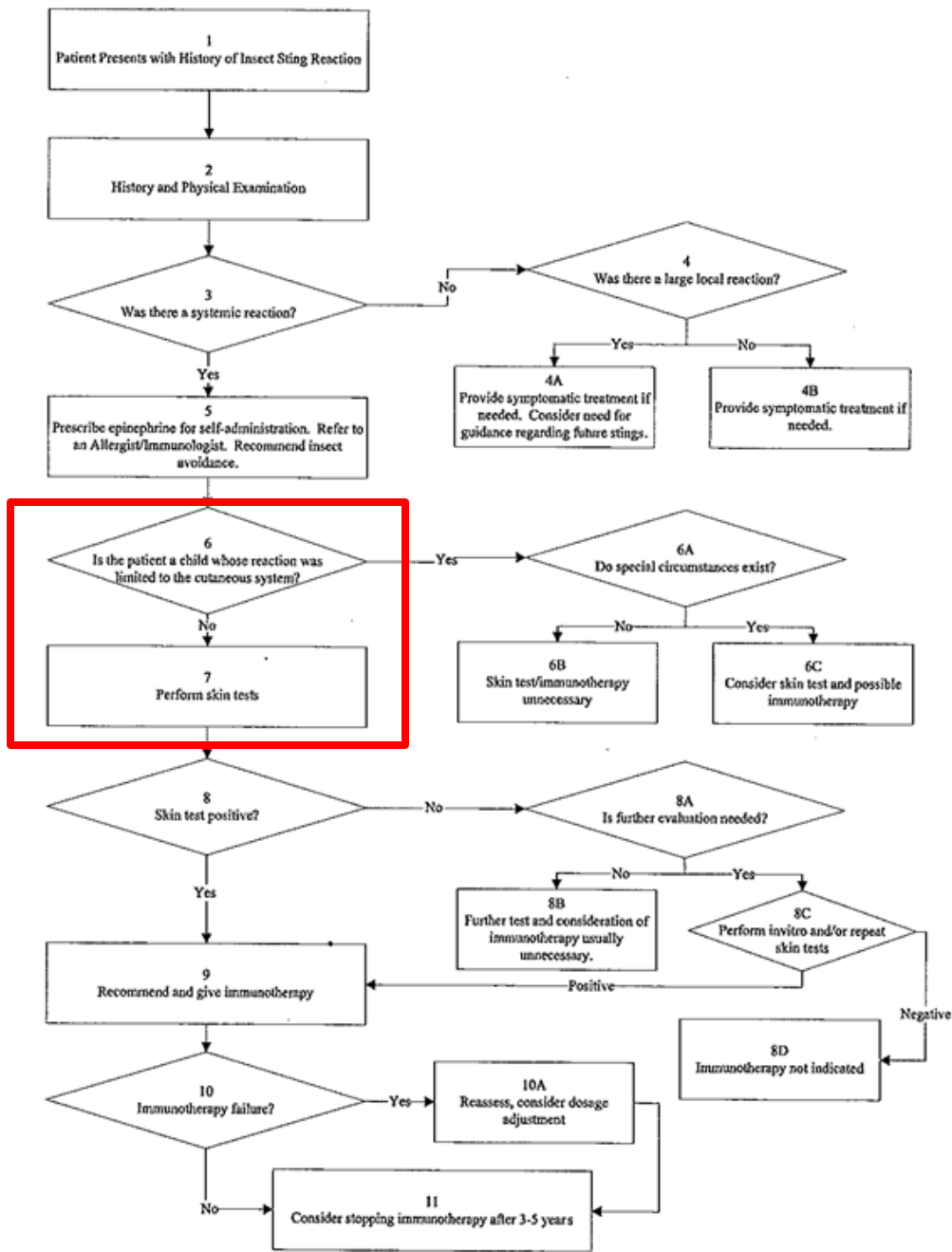


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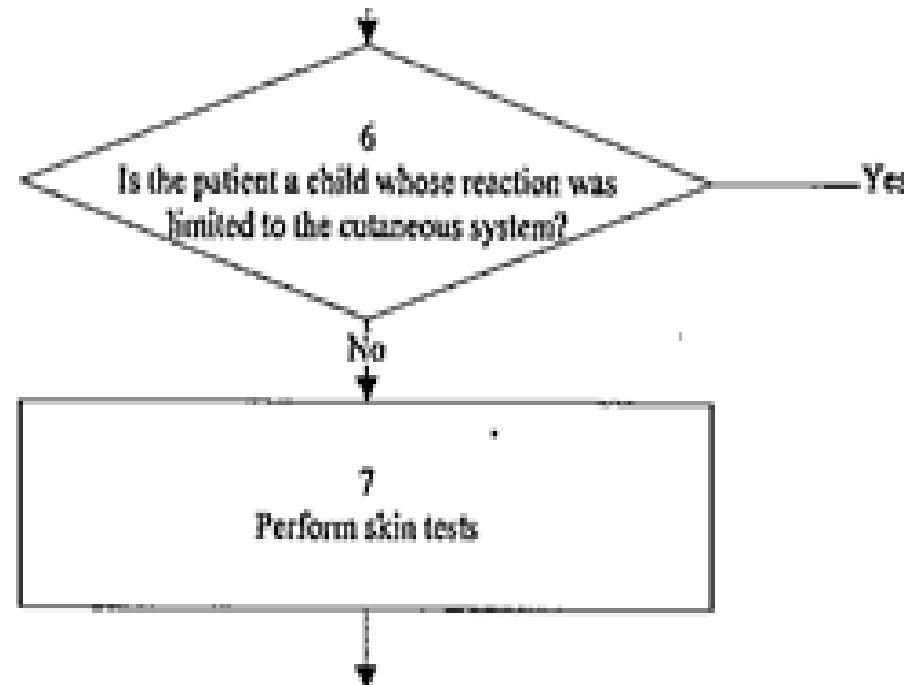
Algorithm: Managing Sting Reactions

Cutaneous in Children
(< 16 yo)

- Risk of future systemic
~ 10%

Cutaneous in Adults - Lack
evidence to withhold IT

Limited data for children
and fire ants



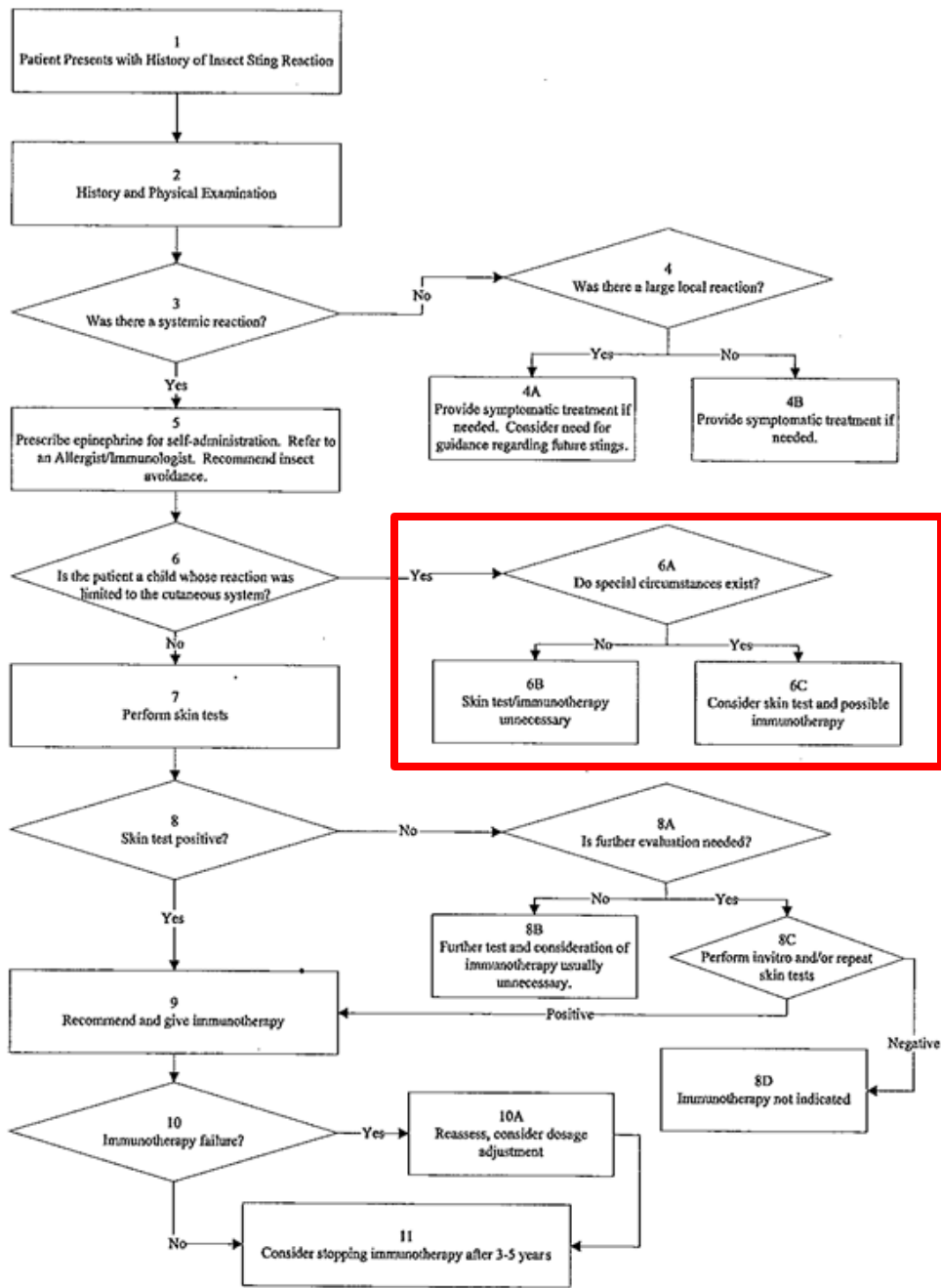


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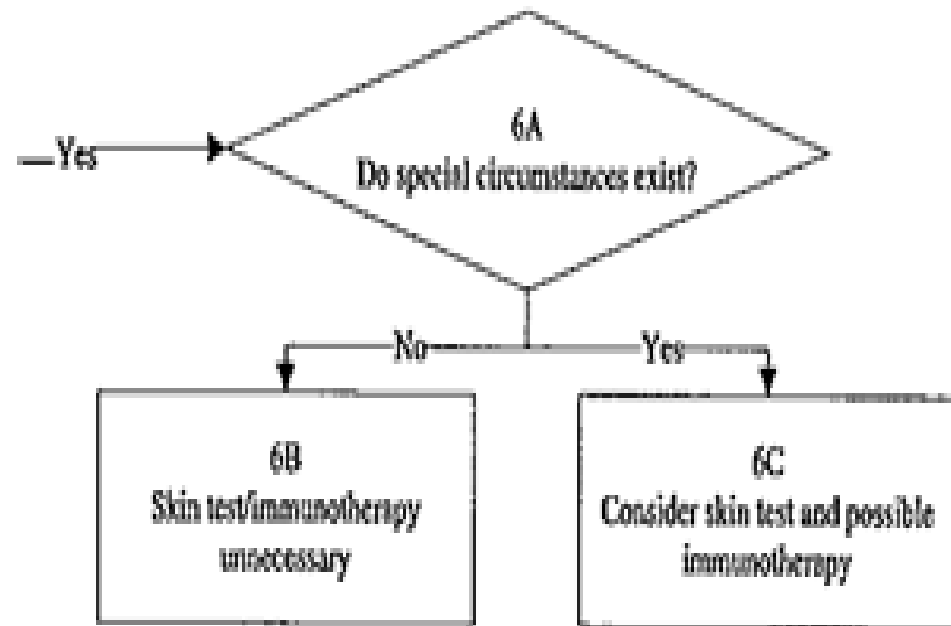
Algorithm: Managing Sting Reactions

Special considerations

- Increased risk
- Parents request IT

Need to carry Epi

- determine after discussion



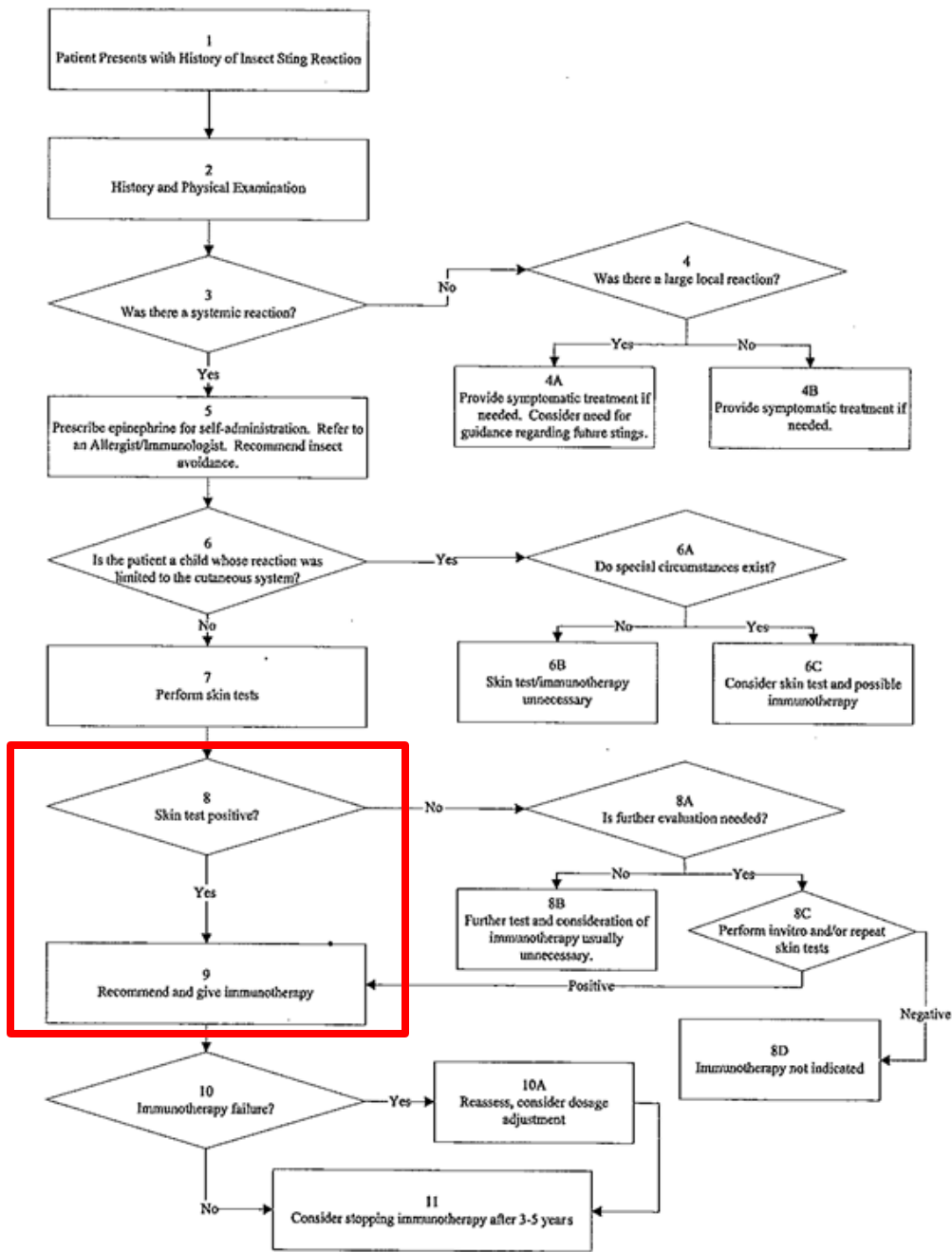


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Algorithm: Managing Sting Reactions

Prick at 1.0 - 100µg/ml

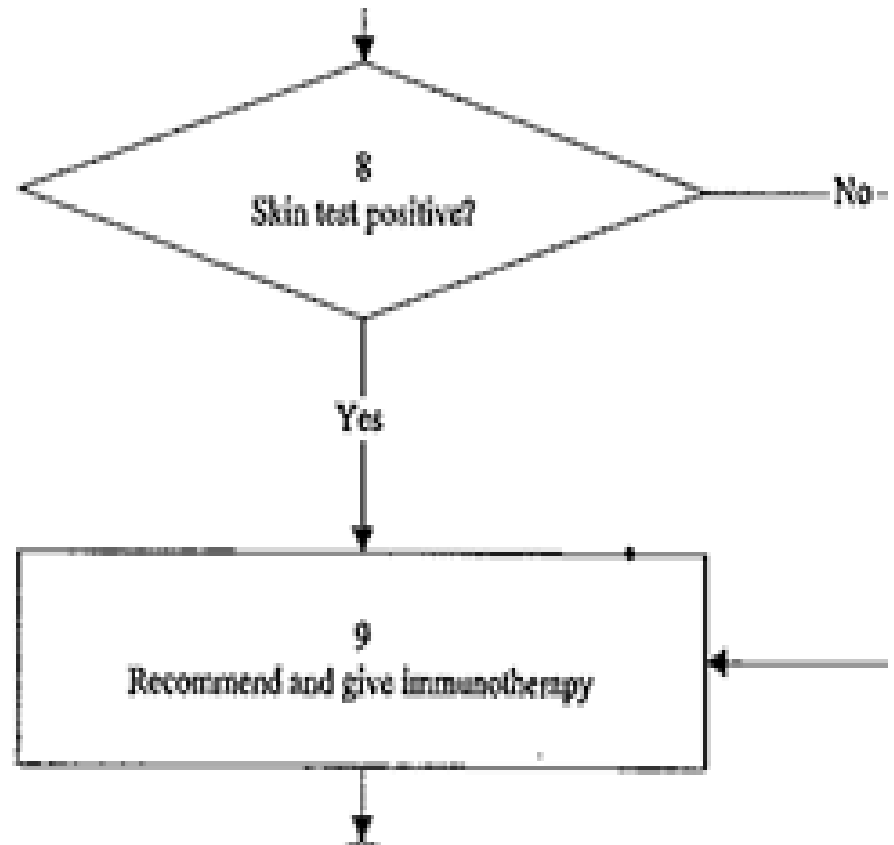
Intracutaneous

- Initial 0.001 to 0.001 µg/ml
- Then 10-fold increments
- Maximum 1.0 µg/ml

Usually all venoms tested

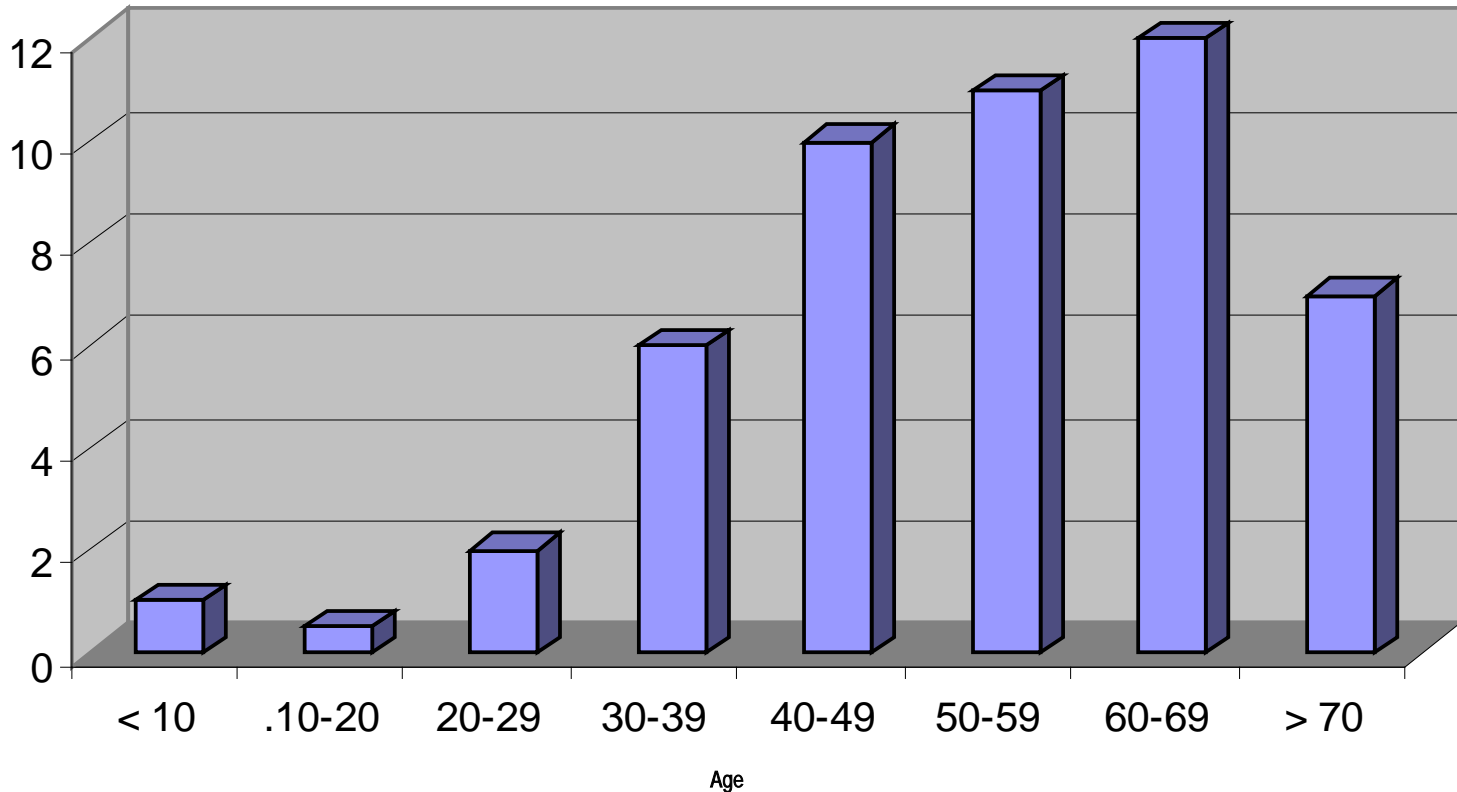
- Due to poor identification
- Except for fire ants

No correlation between level of reactivity and severity of clinical reaction



Why
Start
Venom
Immunotherapy
???

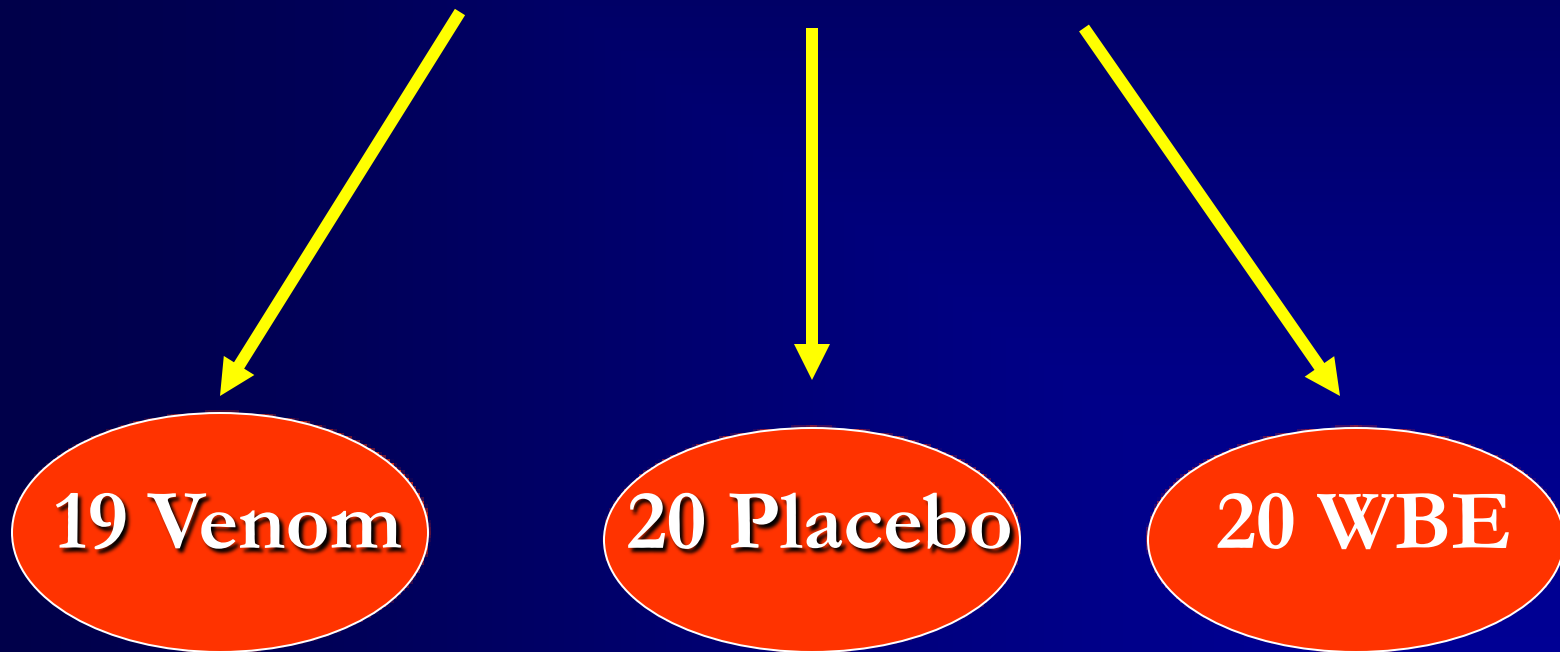
Insect Sting Deaths in USA from 1982-1991



Mean Insect Deaths in USA
Per Year

Controlled Trial of Venom Immunotherapy

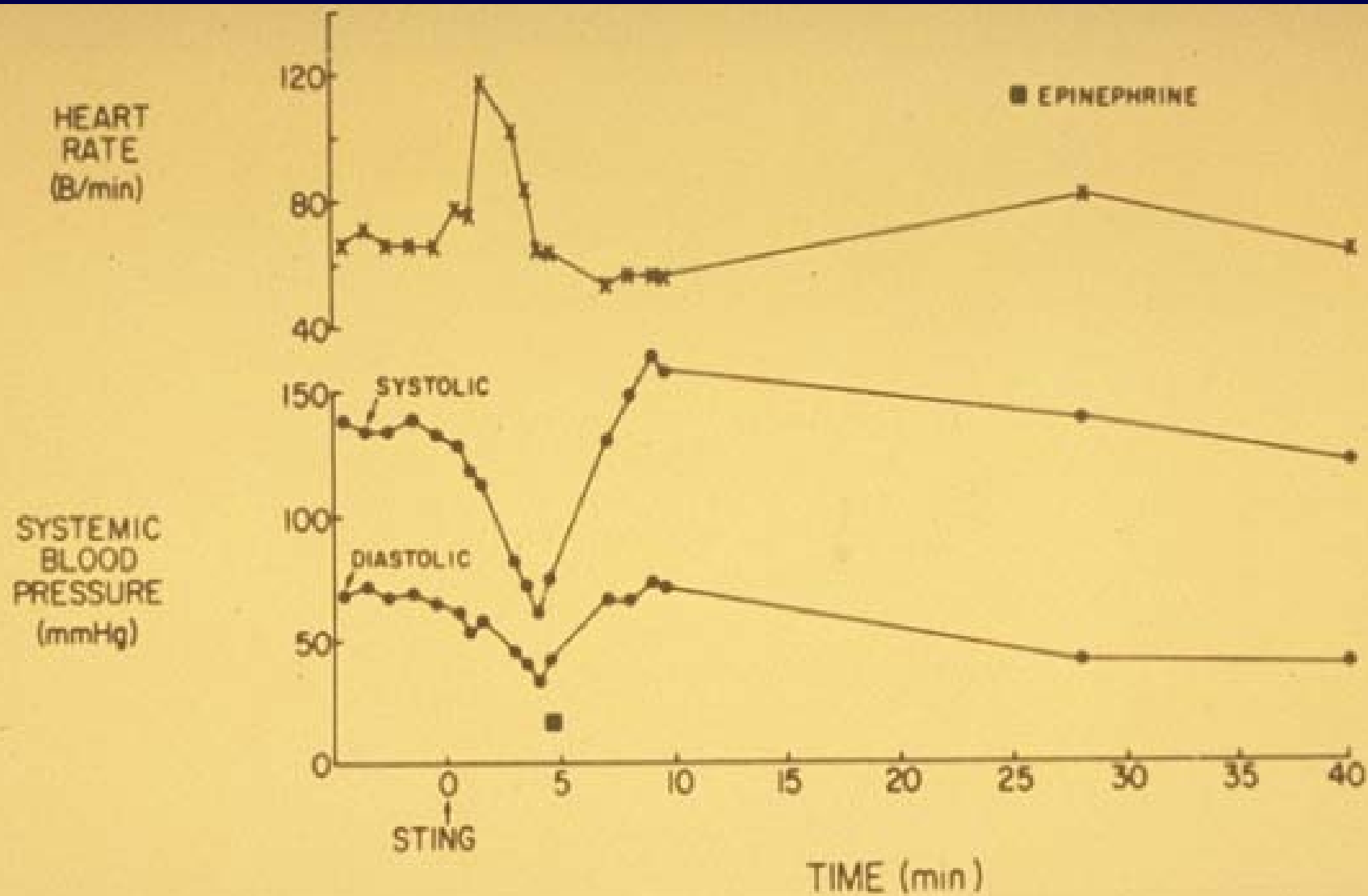
59 Insect-Allergic Patients

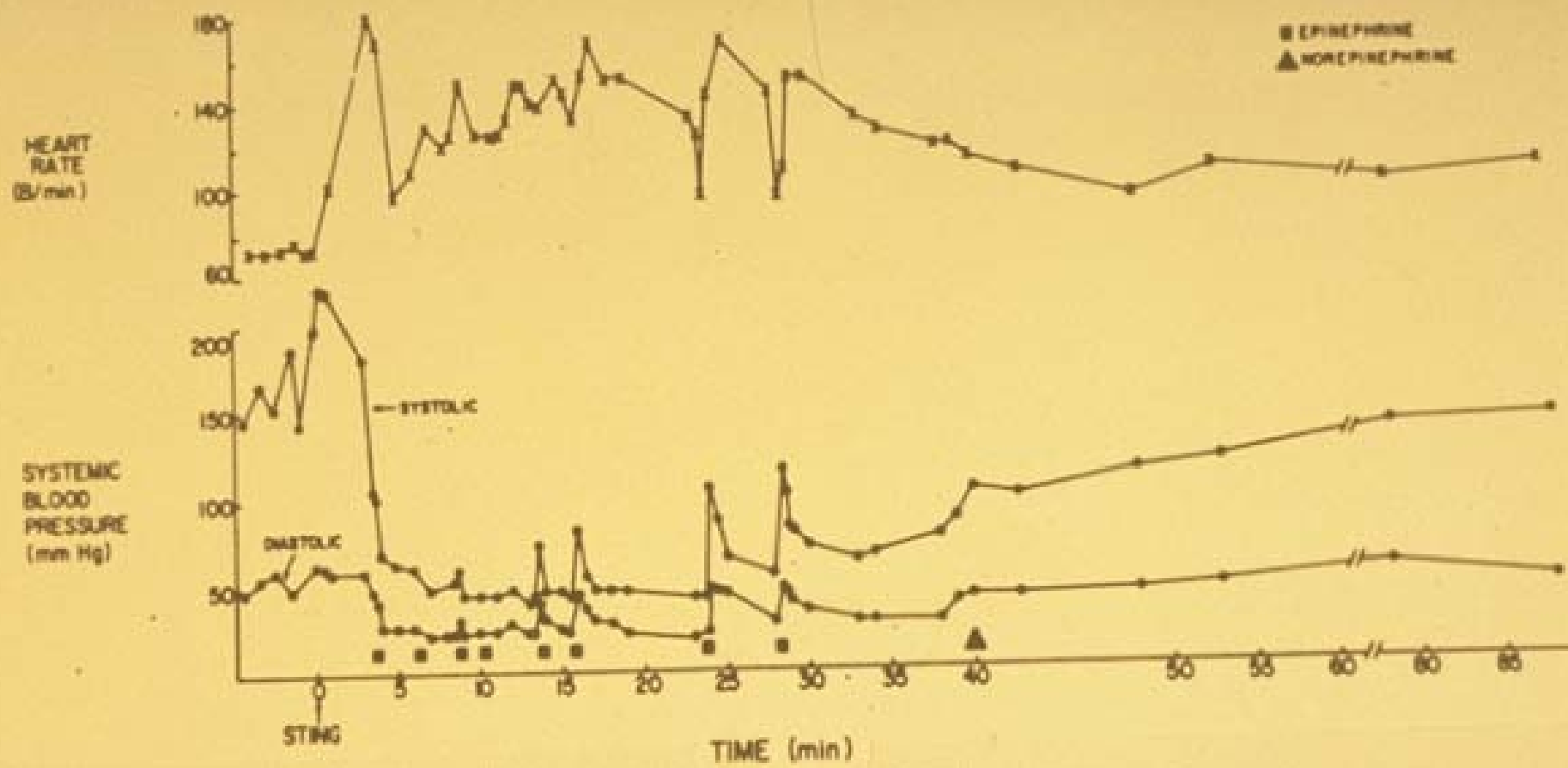


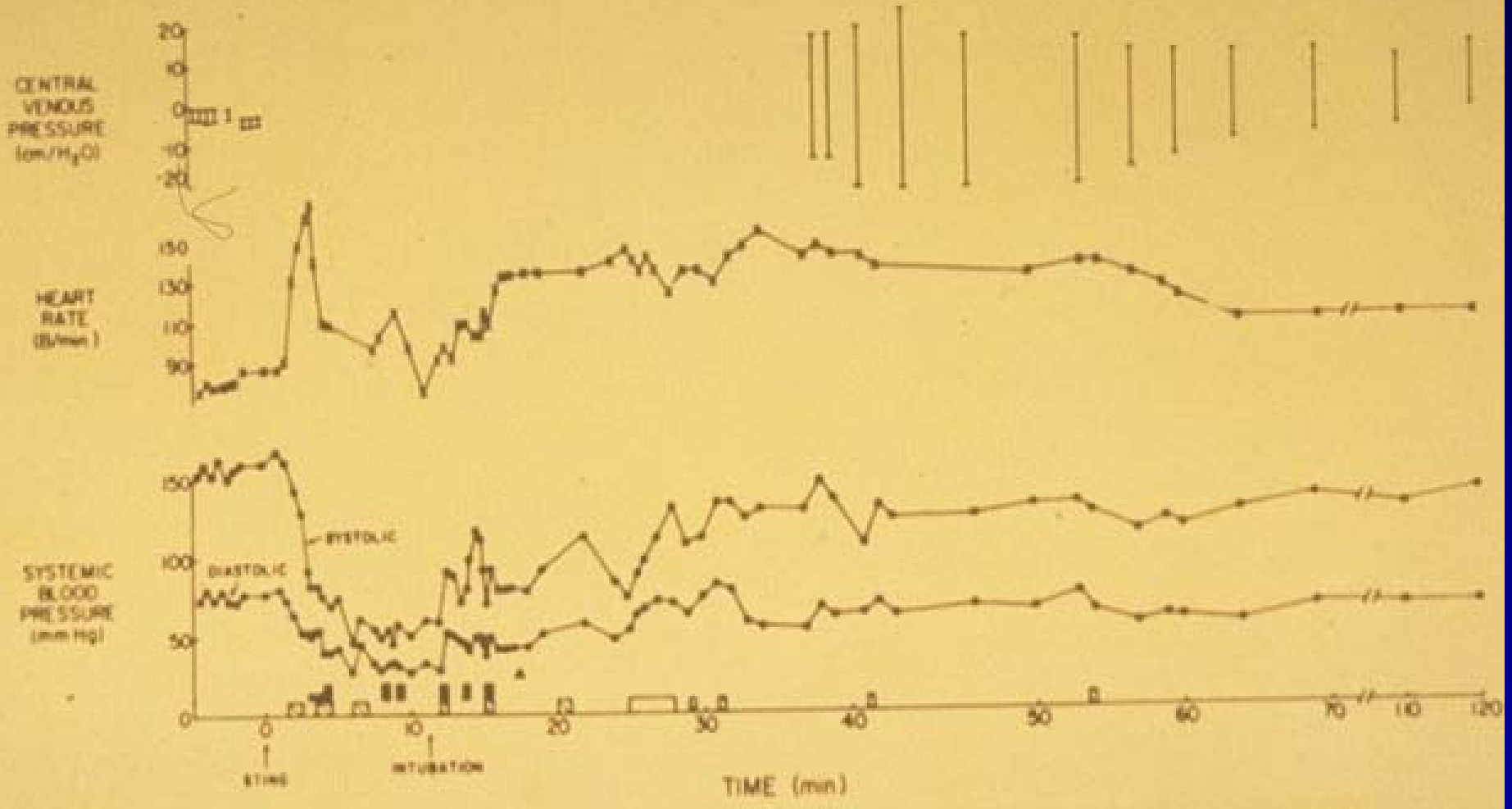


Controlled Trial of Venom Immunotherapy

	<i>Venom</i>	<i>WBE</i>	<i>Placebo</i>
Number stung	18	12	11
Number reacted	1	7	7



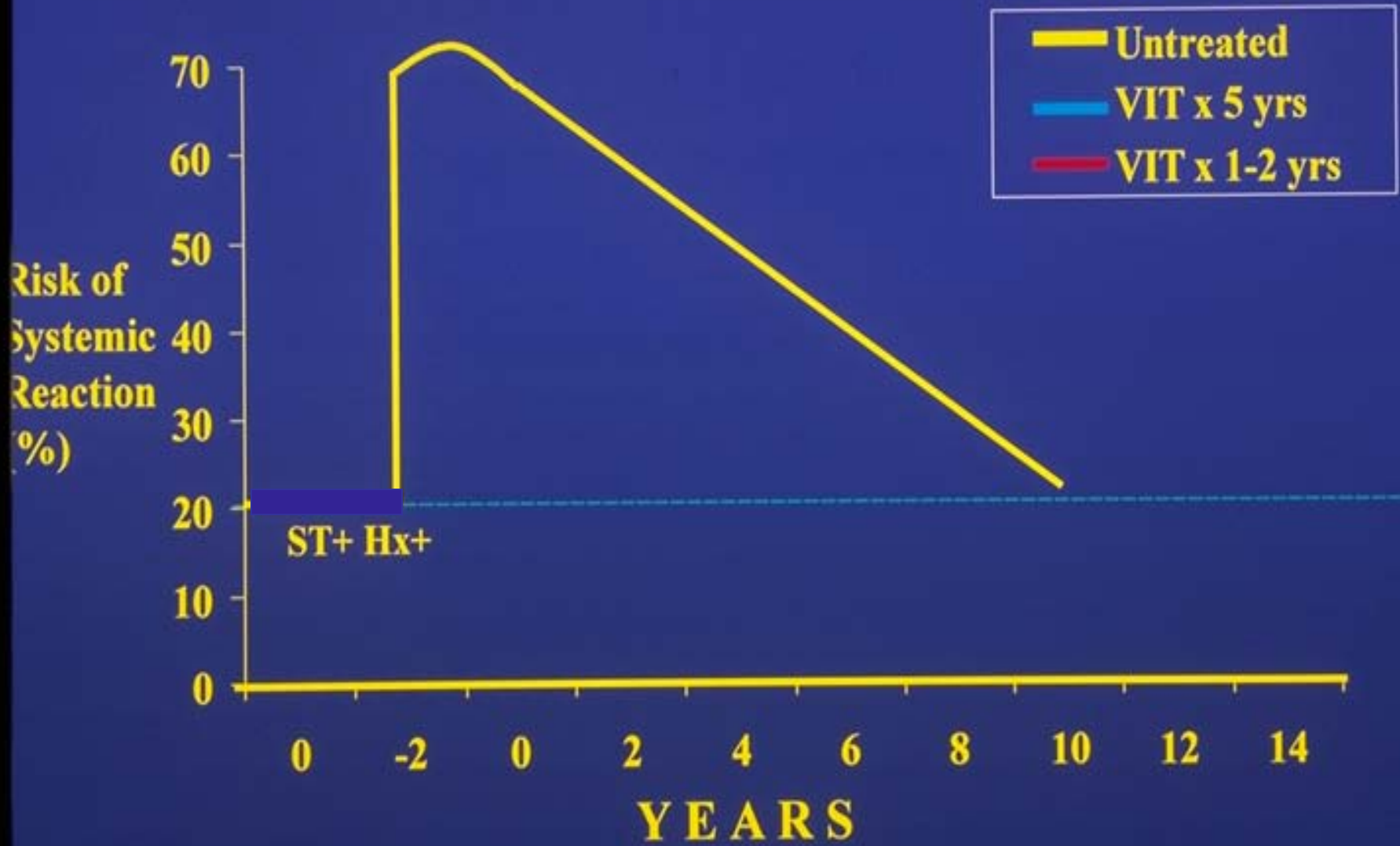




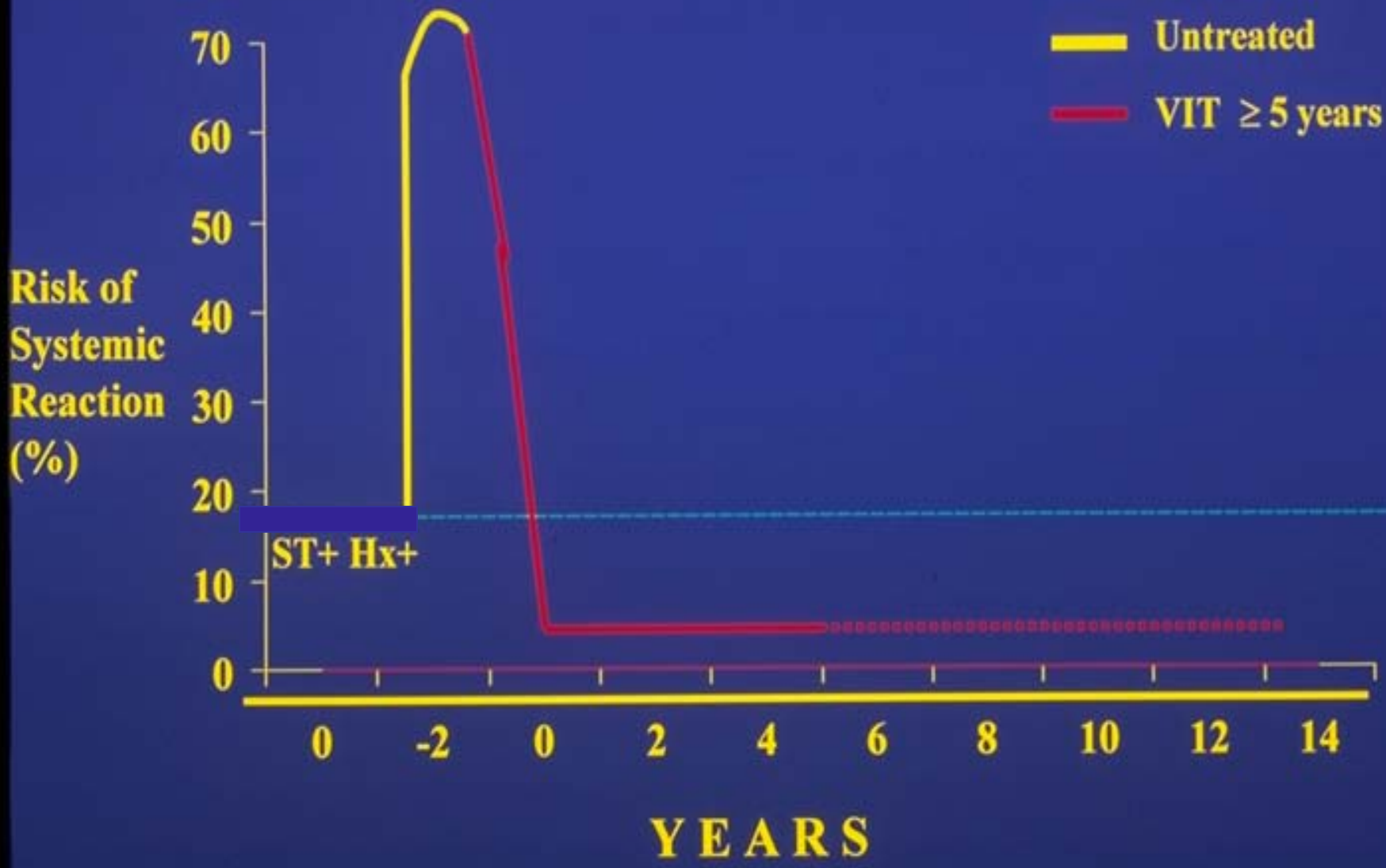
Treatment

	epi (mg)	norepi	plasm (ml)	nlsal (ml)
Patient 1	0.5	No	0	300
Patient 2	3.5	Yes	875	1500
Patient 3	7.5	Yes	1750	3000

Natural History of Insect Sting Allergy



Natural History of Insect Sting Allergy



Freeman TM, et al.
IFA Immunotherapy: Effectiveness of WBE.
JACI 1992;90:210-215.

76 patients with anaphylaxis post-IFA stings

- 11 refused immunotherapy
 - 4 re-skin tested - all positive
 - 6 field stings - all reacted
- 65 accepted WBE IT
 - 31 re-skin tested - all decreased
 - 47 field stings - 1 reaction
 - 30 challenged - no reactions

Why does WBE work?

It works because there is enough venom

- 100 ng/sting, 1µg/event
- 1.5 to 2.4 µg delivered at maintenance

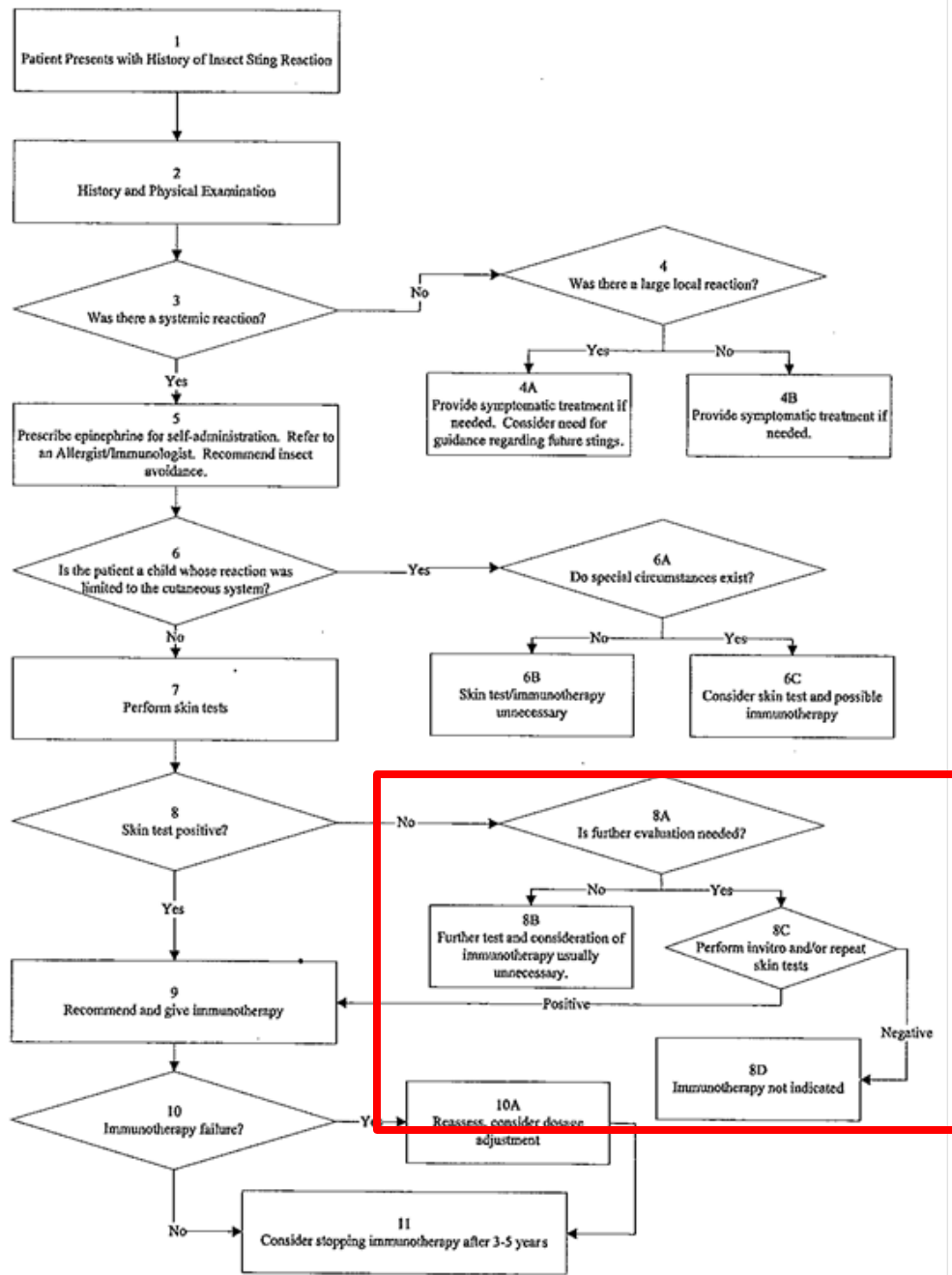
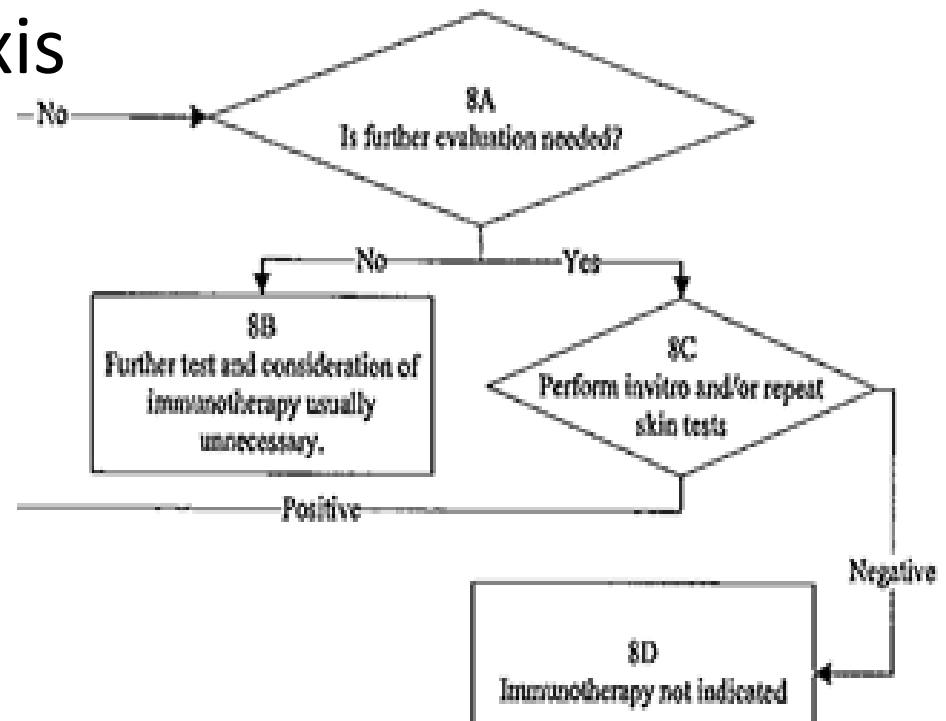


FIG 1. Algorithm: management of stinging insect reactions.

Algorithm: Managing Sting Reactions

Skin test negative patients with a hx c/w anaphylaxis

- Should have specific IgE determined *in vitro*
- Repeat determinations may be necessary
- Consider baseline tryptase



Tryptase...what's new?

- Baseline serum tryptase an important predictor
 - severity of sting rxns HaeberliG, ClinExpAll, 2003
 - freq of systemic rxns during VIT Rueff, JACI, 2010
BonadonnaP, JACI ,2009
 - chance of VIT failure
 - risk of relapse if VIT is stopped OudeElberinkJNG, JACI, 1997

Predictors of Systemic Reactions During Buildup Phase of VIT

- Observational prospective study
- 57 (8.4%) of 680 pts req emerg intervention (def: any type of measure/medication felt necessary to control systemic side effect assoc with VIT)
- Freq of interventions increased by:
 - Higher basal tryptase; 68 (10%) had >11.4 ; 18 (2.6%) >20 ; odds ratio 1.556 ($p=0.004$)

Risk to need an emergency intervention during buildup phase of immunotherapy

Variable	<i>P</i> value	Odds ratio		95% CI
Therapy with HB venom	<.001	3.60	2.36	5.50
Venom specific IgE	.013	6.243	1.435	27.159
Index sting grade III/ IV	.149	1.421	0.874	2.310
Female sex	.157	1.349	0.883	2.061
Any BP med during VIT	.032	2.144	1.051	4.374
Age at therapy (per year)	.034	0.984	0.970	0.999
Conventional dose increase during VIT	.044	0.397	0.158	0.995
Ultrarush dose increase during VIT	.008	1.787	1.153	2.770
Interval from most recent sting reaction and VIT	.039	1.199	1.006	1.429
BTC at first office visit	.004	1.556	1.149	2.108



Honeybee Sensitivity More Problematic

- Untreated: higher recurrence rate
- More SR during VIT
- VIT less effective
- More sting rxns after VIT stopped

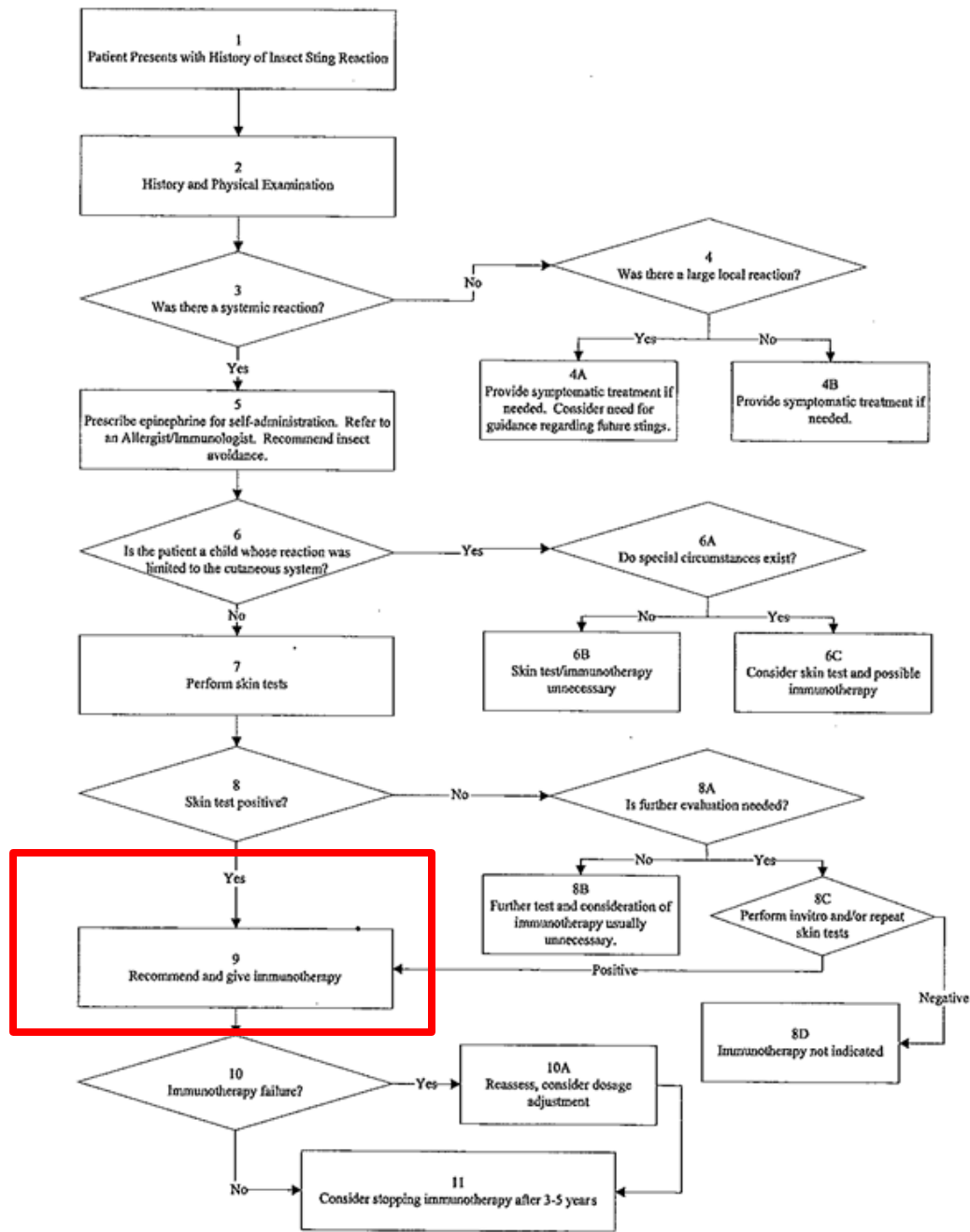


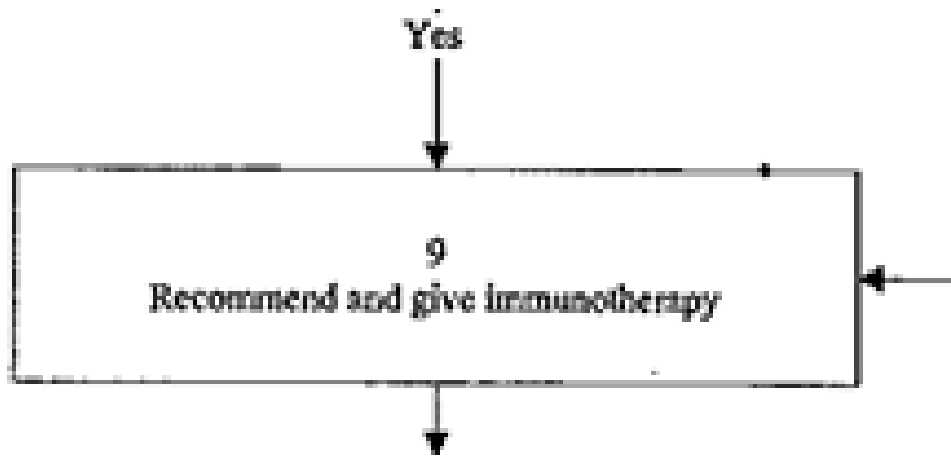
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Algorithm: Managing Sting Reactions

VIT reduces risk to as low as 2% on subsequent stings

Protocol

- 0.1 to 1.0 μg initial
- 100 μg maintenance
- Q 4 wk interval first year
- Q 6-8 wks subsequent years

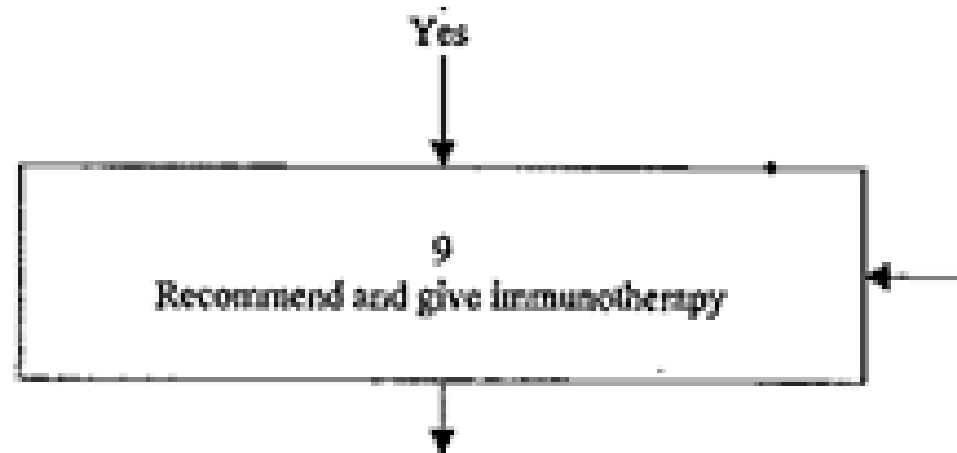


Algorithm: Managing Sting Reactions

Fire ants use WBE

- Less well defined
- Maintenance = 0.5 ml of 1:100 wt/vol

Rapid protocols have been used safely and effectively



Algorithm: Managing Sting Reactions

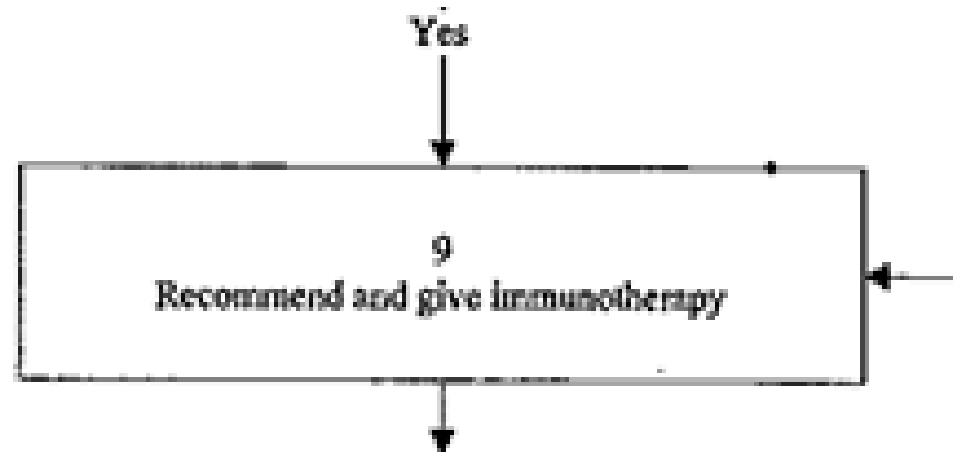
Special Considerations

β -adrenergic blockers

- Increased risk of severe reactions
- Prefer to d/c β -blockers
- Can receive VIT if must have β -blockers

Angiotensin-converting enzyme inhibitors

- One study (Rueff et al JACI 2009) showed increase risk of severe reactions



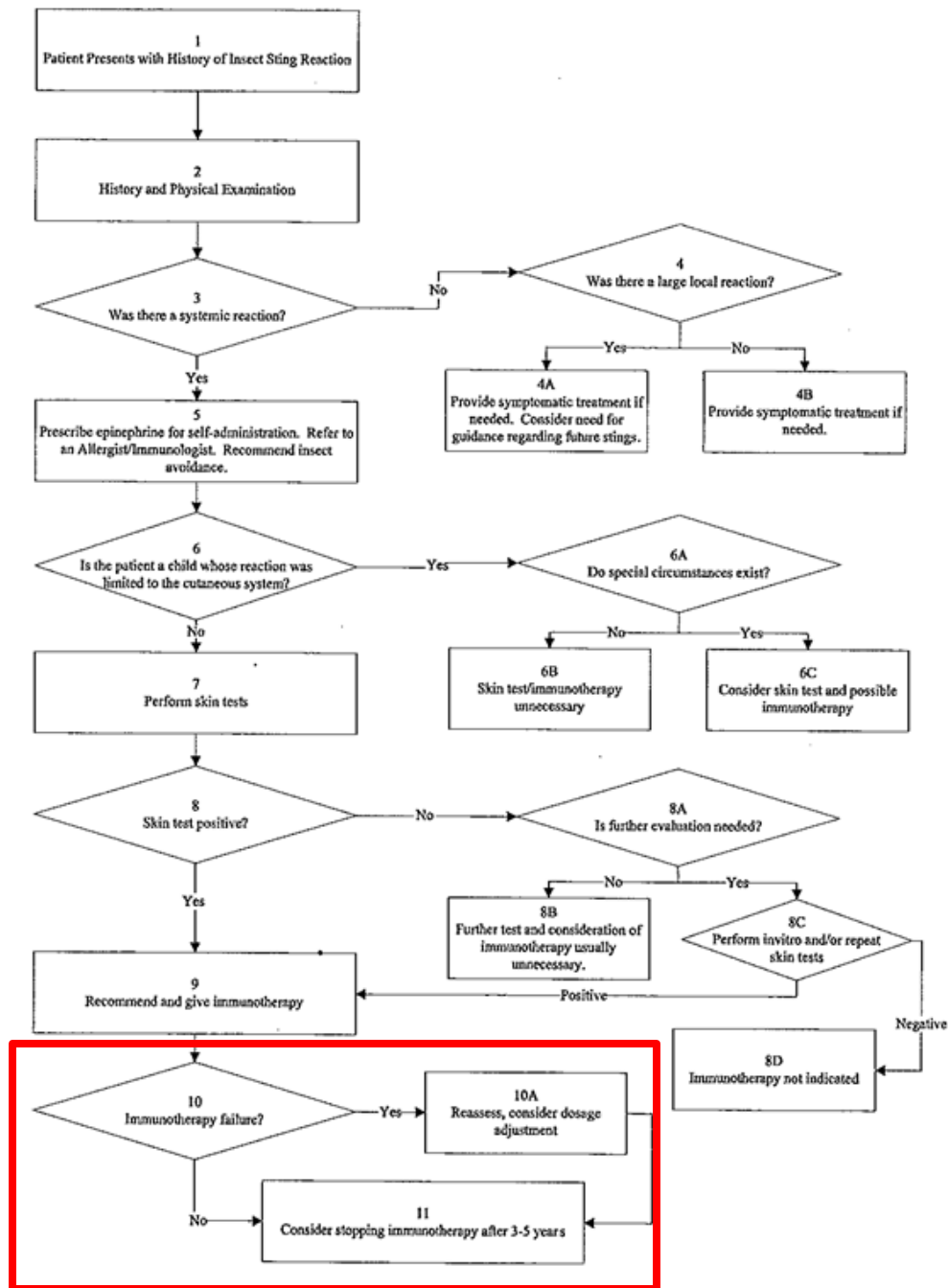
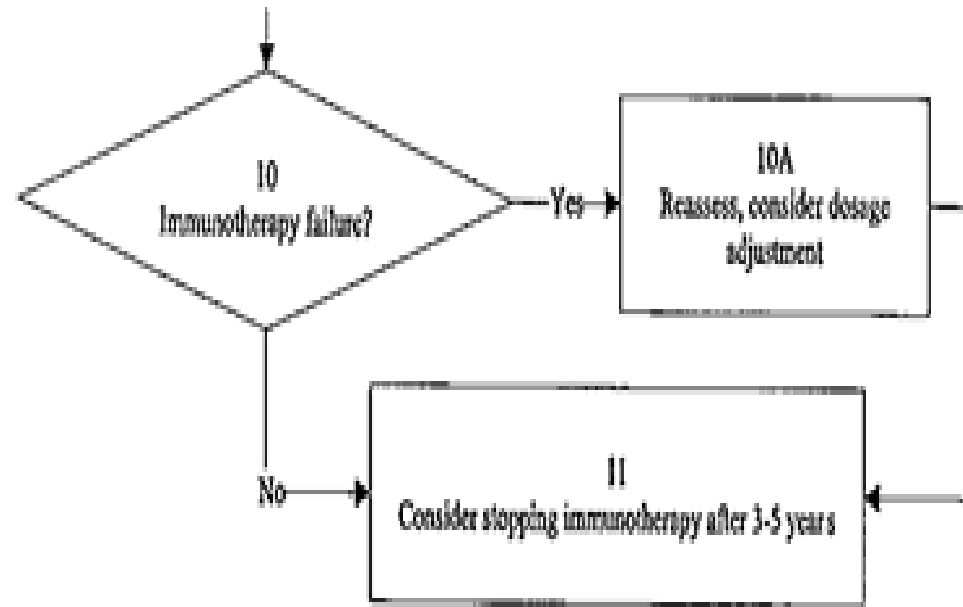


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Algorithm: Managing Sting Reactions

If has systemic reaction on maintenance VIT

- If same insect consider increased dose to 200 $\mu\text{g}/\text{ml}$
- If unknown or different check for specific IgE



Algorithm: Managing Sting Reactions

Stopping IT

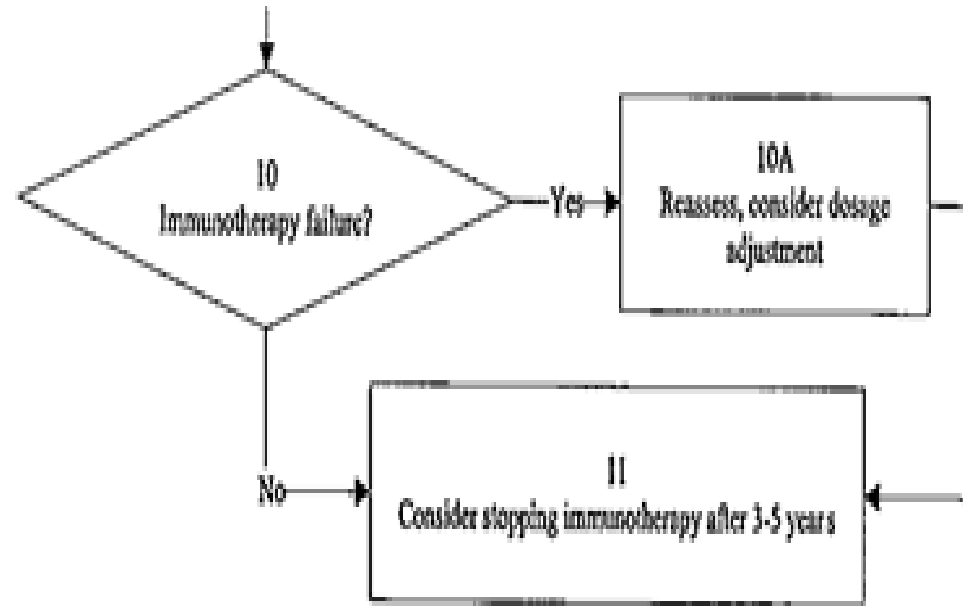
Consider after 3-5 yrs

- Esp if IgE negative
- Future risk ~ 10 %

Special considerations

- Life style, occupation
- Coexistent diseases
- Medications
- Severity of reactions

No definitive recommendation for fire ants

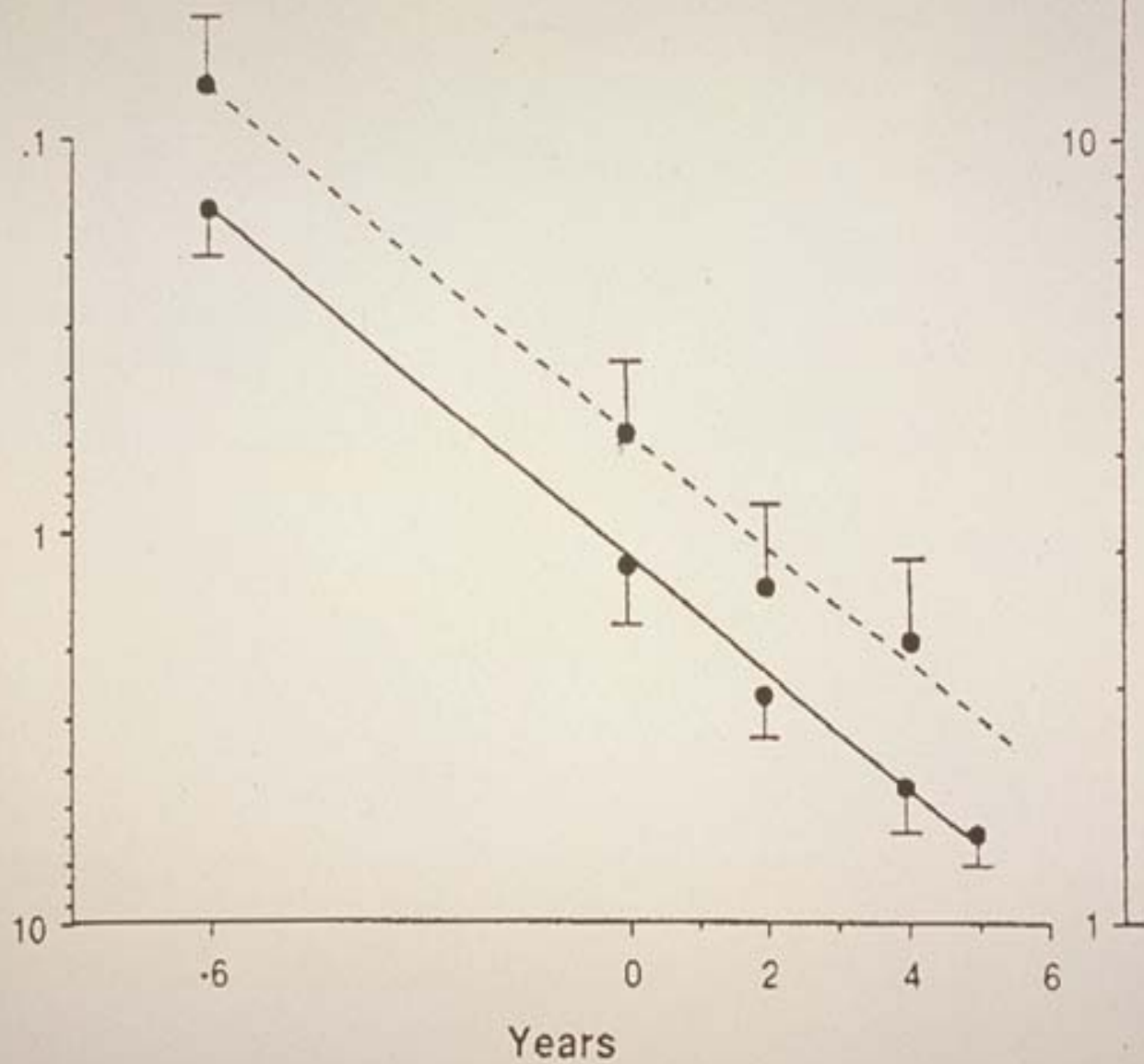


Discontinuation of VIT: Hopkins

- 74 pts: ≥ 5 yrs of VIT
- Every 1-2 yrs, VST, venom-specific IgE, sting challenge
- Usual group of VIT pts: 75% \downarrow BP
- Neg VST when VIT stopped = 26%

Change in VST and IgE level during and after VIT

VENOM CONCENTRATION FOR
2+ SKIN TEST ($\mu\text{g}/\text{ml}$)



Discontinuation of VIT: Hopkins

Year	GROUP 1		GROUP 2		GROUP 3		ALL PTS	ALL STGS
	# Pt Rxn /#Pt	# Stg Rxn/ # Stg	# Pt Rxn/ #Pt	# Stg Rxn/ # Stg	# Pt Rxn/ # Pt	# Stg Rxn/ # Stg		
1	0/29	0/29	-	-	-	-	0/29	0/29
2	1/28	1/28	2/25	2/25	1/20	1/40	4/73	4/93
3	1/26	1/26	-	-	-	-	1/26	1/26
4	0/24	0/48	3/24	3/48	-	-	3/48	3/96
5	0/26	0/26	-	-	-	-	0/26	0/26
Total	2/29	2/157	4*/25	5/73	1/20	1/40	7*/74 (10%)	8/270 (3%)

*One of pts in Group 2 reacted in both yr2 and yr 4.

Golden, JACI 1996; 97:579

Sting Reactions After Stopping VIT

Study Group/Yrs	Systemic Symptoms to Sting		
	Patients (N)	Patients (Stung)	Stings
Group 1 (Yrs 1-5)	74	7/74 (9.5%)	8/270 (3%)
Group 1 (Yrs 6-7)	74	1/11	2/14
Group 2	51	4/15	4/25
TOTAL (to date)	125	12/89 (13.5%)	14/309 (4.5%)

Sting Rxns After Stopping VIT

	Patients (N)	No Reaction	Systemic Reaction
No reaction during VIT	76	70	6 (8%)
Systemic reaction during VIT	13	7	6 (46%)

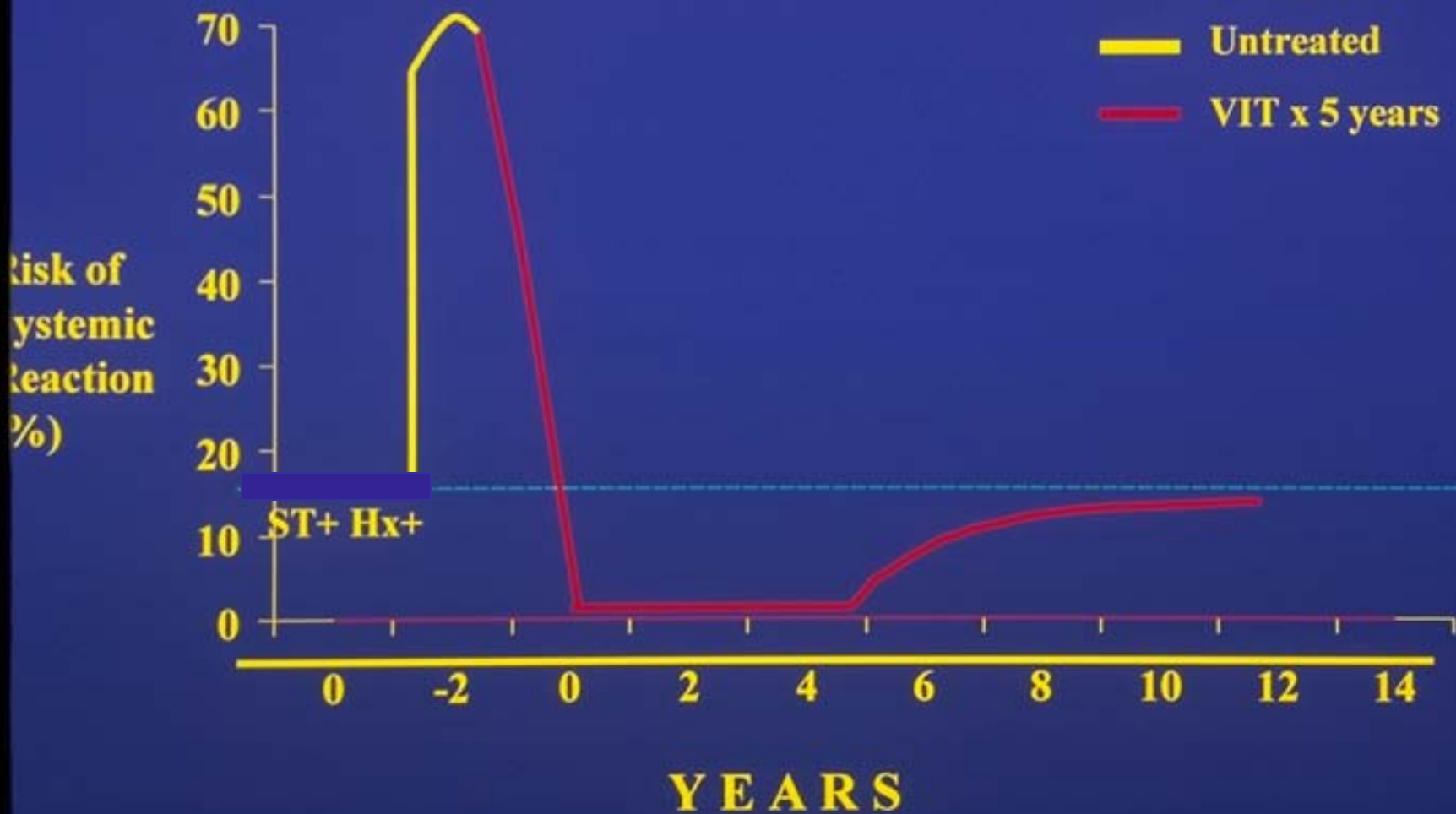
Severity of Systemic Reactions Before VIT and After VIT Stopped

Sting Reaction	Before VIT	After VIT
Minimal	0	6
Gen. Urt/angio only	13	2
Respiratory*	41	3
Hypotension [#]	35	1

* Dyspnea, throat tightness, asthma, cough

[#] Dizziness, unconscious, BP < 90/60

Natural History of Insect Sting Allergy



Considerations in Decision to Start/Stop VIT

1. VIT very effective
2. Maintenance VIT can be extended to 8-12 wk
3. Patients with most severe reactions at most risk
4. Coexistent health problems
5. Occupation and leisure exposures

Perhaps VIT Shouldn't Be Stopped If:

- Severe pre-VIT reaction
- VIT duration < 5 years
- Honeybee sensitivity
- Rxns to injections or stings on VIT
- Venom sensitivity doesn't decline

**However, the majority of even
these most-at-risk patients
tolerate discontinuation of VIT
after 5 years of treatment**

B E E S



WORKER



QUEEN



DRONE



CONSULTANT

Merriford