Vaccinations and allergies

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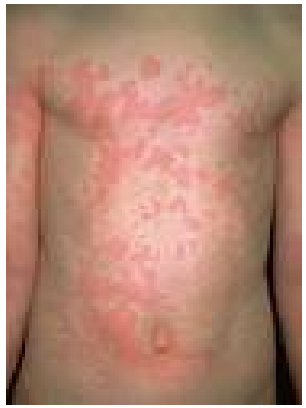

The following are true allergic (IgE-mediated) reactions?

A anaphylaxis
B serum sickness
C Arthus reaction
D urticaria
E itching nodules
F local (painfull) swelling and erythema

1. A + C + D + F
2. A + C + D + E + F
3. B + C + D + F
4. A + C + F
5. A + D

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Hypersensitivity reactions

- Immediate reactions (type 1 hypersensitive reactions)
  - → IgE-mediated
  - → minutes upto 4h after vaccine
  - → urticaria, angio-edema, resp. distress, anaphylaxis
- Delayed reactions (type 3 hypersensitive reactions)
  - → immune complexes, T-cell mediated (?)
  - → hours to days (upto 2-3 weeks) after vaccine
  - → rashes (urticaria, erythema multiforme), Arthus reaction, angio-edema, arthritis,…
- Non immunologic:
  - → hard itching nodules < adjuvans ex. Aluminium

The following symptoms are common in anaphylaxis

A itching erythema or urticaria
B pailness
C coughing
D bradycardia
E urinary loss
F unconsciousness

1. A + B + C+ F
2. A + C + D+ E + F
3. B + C + D + F
4. A + C + F
5. A + C + D + F

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Anaphylaxis <-> pseudo allergic reactions

- Anaphylaxis:
  - → acute allergic reaction (resp tract, and/or cardiovascular sympt and/or cutaneous sympt)
    - laryngeal oedema/ bronchospasme
    - shock (volume deficit due to increased vascular permeability)
    - urticaria, angio-edema
- Syncope:
  - → palor, hypotension, nausea, (vomiting), muscle weekness, bradycardia
- Hyperventilation

The following statements are correct

A A non-allergic person may go home immediately after any vaccination

B In a non-allergic person, observation for 15 min. is only necessary after vaccination with a life-attenuated vaccine

C Observation for at least 15 min. is necessary for any person following any vaccination

D An egg allergic person must be observed during 30 min. after YF-vaccination

1. A + D
2. B + D
3. C + D
4. C
5. None is correct

Risk of adverse reactions following vaccination1

Syncope

- → Incidence: unknown [1]
- → 77.4% in persons < 20y (45.5% in 10-19y) [1]
- → Morbidity related to fall [1]

- FDA: 2000-2006: 107 reports of syncope/presyncope/unintended injury on day of vaccination [2]
  - → 100/107 within 20' after vaccination
  - → 105/107 falls; 2 motor cycle collisions
  - → 83/107: 2-17y old
  - → 3/107 severe head injuries (2 fatal cases)
  - → 65/107: moderate to minor injuries of the head or extremities
  - → 39/107: falls without any injuries

[1] C. Vandermeulen Tijdschr. Voor Geneeskunde 2004; 60 (20): 1456-61
[2] E.J. Woo et al. Arch Pediatric Adolesc Med 2005; 159: 1083

Risk of adverse reactions following vaccination2

Anaphylaxis

- Anaphylaxis in children/ ado's
  → 0.65 cases/ 10^6 doses – 1.53 cases/ 10^6 doses [1]
- Estimated incidences:
  - DTP: 2/ 100.000
  - HBV: 0.16/ 100.000
  - MMR: 0.016 - 0.35/ 100.000 [2]
  - YF vaccine: 0.76/ 100.000 (40/5.236.820 doses) [3]

Other

- YF-vaccine associated neutropenic disease [4]
  → 0.4/ 100.000
- YF-vaccine associated viscerotropic disease [4]
  → 0.3/ 100.000

[1] Bohlke K. et al. Pediatrics 2003; 112 (4): 815-20)
[2] Plotkin 2008
[3] Kelso J.M. et al. J Allergy Clin Immunol 1999;103 (4): 698-701
[4] N.P. Lindsey et al. Vaccine 2008; 26: 6077-6082

Anaphylaxis

- onset
  - → minutes upto 4h after vaccination
- resp. symptoms
  - → larynx edema
  - → bronchospasm, coughing
- cutaneous symptoms
  - → urticaria
  - → pruritus
  - → angio-edema
- cardiovascular symptoms
  - → hypotension (persistent)
  - → tachycardia
- neurological symptoms
  - → unconsciousness (persistent)

Syncope

- onset
  - → before
  - → during
  - → upto 15 min after vaccination
- no resp. symptoms
- cutaneous symptoms
  - → pailness
  - → sweating
- cardiovascular symptoms
  - → hypotension (short)
  - → bradycardia
- neurological symptoms
  - → unconsciousness (short)
  - → urinary loss

Adapted from “Handboek Vaccinaties” Van Gorcum 2007

Increased risk for anaphylaxis is associated with

A Contact allergy for neomycin

B dyspnoea after ingestion of eggs

C swelling of the limb after formal vaccination (Arthus reaction)

D urticaria after formal vaccination

1. A + B + D
2. B + D
3. B + C + D
4. All of the above

Prevention of anaphylaxis

- Identification of patients at increased risk through anamnesis

  Previous reactions (edema of mouth / larynx, dyspnoe, cardiovascular signs) after contact with
  - any vaccin,
  - latex,
  - antibiotics (neomycin, polymyxine),
  - eggs,
  - yeast,
  - other
- Other evaluations if “+” anamnesis: ID test, skin test,…
- Patients with increased risk => vaccination in hospital setting with rescusitation possibilities
- Always 15 min. observation after any vaccination

HGR dec 2004 preventie en aanpak van anafylactische shock bij de vaccinatie van kinderen volgens het aanbevolen vaccinatieschema

Suspected IgE-mediated reaction: work-up

- Evaluation of IgE-mediated reaction [1]
  - → skin prick tests: 1/10 ; full strenght
  - → specific serum IgE
  - → intradermal tests: 1/ 100 ; 1/ 10
    - If '-": IgE-mediated allergy very unlikely
  - → basophil activation test (BAT)[2]
    - IgE-mediated allergy for in- and outdoor allergens, food allergies, latex allergy, hymenoptera venom allergy, some drug allergies
    - no routine analysis

} Cave false or clinically irrelevant "+" results

- IgG-level [1]
  - → if level consistent with protection from disease => consider witholding additional doses

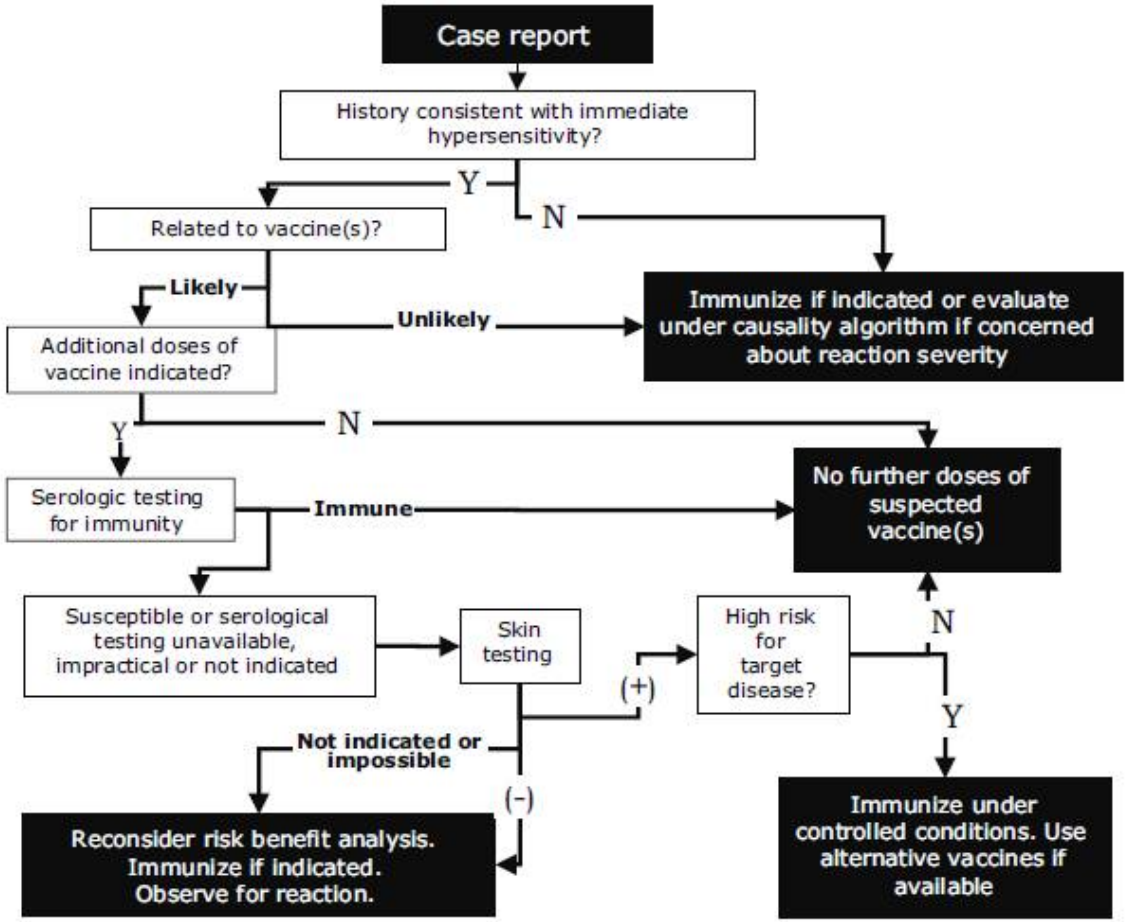
[1] Kelso J. et al. Ann Allergy Asthma Immunol 2009; 103: S1-14
[2] Ebo D. et al. Cytometry Part B 2008; 74B: 201-210

Table 1. Levels of Antibody Associated With Protection From Vaccine-Preventable Diseases

Vaccine	Protective level of IgG antibody ≥
Diphtheria	0.1 IU/mL[11]
Haemophilus influenzae type B	0.15 μg/mL[29]
Hepatitis A	10 mIU/mL[30]
Hepatitis B surface antibody	10 mIU/mL[31]
Measles (rubeola)	120 mIU/mL (PRN titer)[32]
Polio (inactivated)	1:8 neutralizing antibody titer[33]
Rabies	0.5 IU/mL (VNA titer)[34]
Rubella	10 IU/mL[80]
Tetanus	0.1 IU/mL[11]
Yellow fever	0.7 IU/mL[29]

Abbreviations: IU, international units; mIU, milli-international units; PRN, plaque reduction neutralization; VNA, virus-neutralizing antibodies.

Algorithm for management of suspected allergic reactions to vaccines



RA Wood et al. Pediatrics 2008;122;e771-e777

Treatment of anaphylaxis

- Adrenaline (epinephrine) IM (1:1000 sol.) in m. quadriceps.
- Dosis: 0.01mg/kg (= 0.01ml/kg) max. 0.5 mg

< 1year:	0.05-01ml
1-2y (~10kg):	0.1ml
2-3y (~15kg):	0.15ml
4-6y (~20kg):	0.20 ml
7-10y (~30kg):	0.30ml
11-12y (~40kg):	0.40ml
≥13y:	0.40-0.50ml

Repeat dosis after 5 min. if no clinical response

HGR dec 2004 preventie en aanpak van anafylactische shock bij de vaccinatie van kinderen volgens het aanbevolen vaccinatieschema

An egg-allergic person may be vaccinated under normal conditions with:

A YF-vaccine
B MMR
C hepatitis A vaccine
D influenza vaccine
E japanese encefalitis vaccine

1. A + B + C
2. B + C + E
3. C + D + E
4. B + C + D
5. B + C + D + E

The following statements are true

A Gelatine is a major allergen in MMR and JE-vax
B latex allergy is a contra-indication for any vaccine
C yeast allergy is associated with adverse events following hepatitis A vaccine
D contact allergy for neomycin is a contra-indication for vaccination with neomycin containing vaccines
E thiomersal is a major cause of anaphylaxis after vaccination

1. A + B + D + E
2. A + C + E
3. A + B + C
4. A + C
5. A
6. None of the above

Egg allergy

- MMR [1, 2]

  → culture on chicken embryo fibroblasts

    - no special precautions necessary

- Influenza and YF-vaccin [1, 2]

  → culture on chickeneggs

    - serious or life-treathening allergy
      - skin testing
      - desensitisation (if skintest +)
    - less severe or local manifestations of allergy
      - no skin testing
      - vaccination in 2 steps [3] (evaluated for influenza vaccines)

        1° 10% of dose SC - 30 min observation

        2° 90% of dose SC - 30 min observation

[1] Plotkin 2008; [2] Red Book 2006

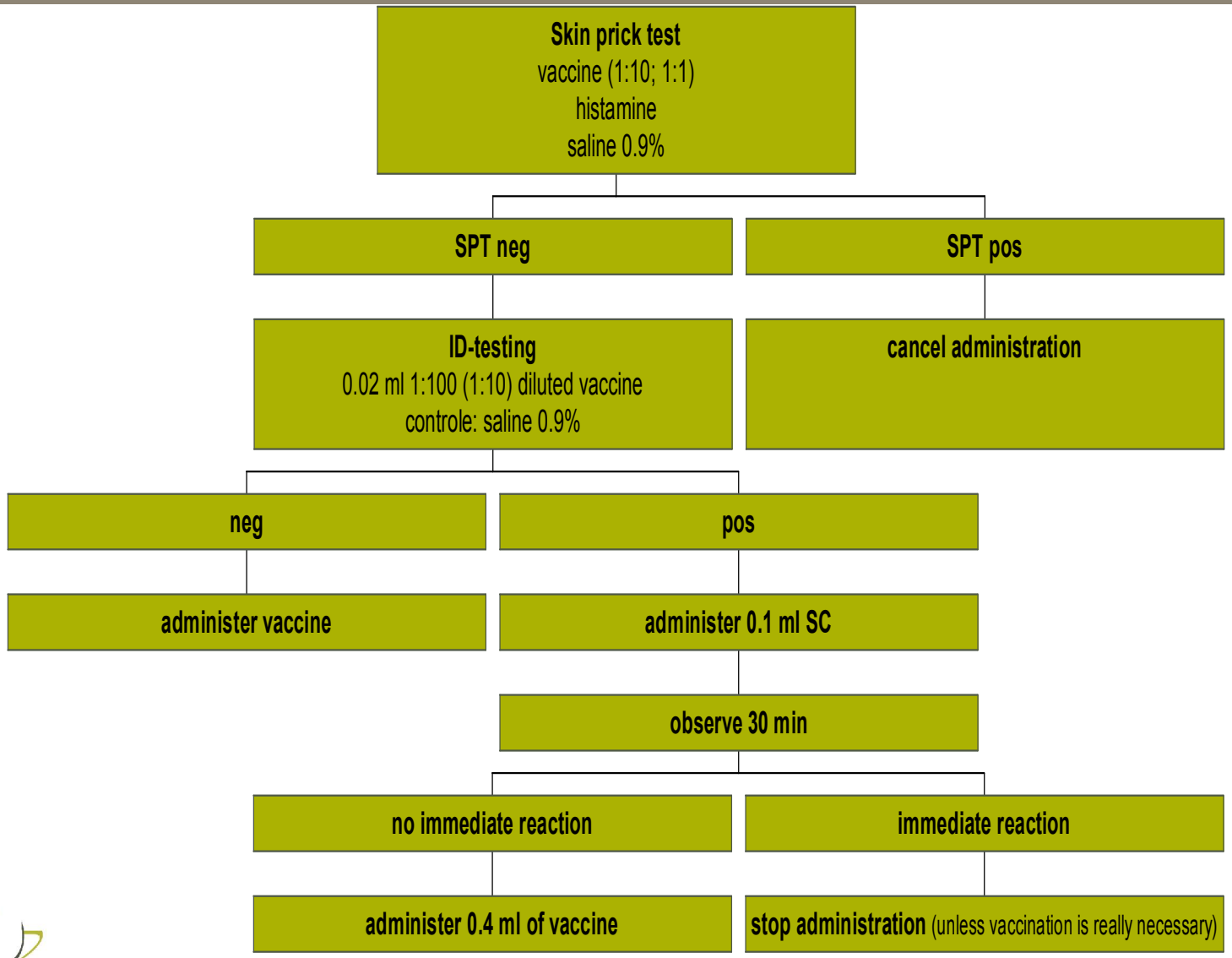
[3] Kelso J. et al. Ann Allergy Asthma Immunol 2009; 103: S1-14

Yellow fever vaccine and serious or life-treathening egg allergy

- Flow chart (3 steps)[1]
  - → Skin prick test ("+" if wheal ≥3mm larger than control + surrounding flare)
  - → ID-test ("+" if wheal ≥ 5mm or larger than control)
  - → SC administration of reduced dose vaccine
  - ⇒ no reaction: -> continue vaccination
  - ⇒ reaction: - stop vaccination
    - desensitisation if vaccine really waranted
- Protected seroimmunity after reduced dose
  - → Roukens A et al. PLoS One 2008; 3 (4): e1993
  - → Roukens A et al. Vaccine 2009; 27: 2408-09

[1] Red book 2006

Flowchart: Vaccination in patients with serious or life treathening egg allergy



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Adapted from Red book 2006

Desensitisation protocol

- Controlled setting
- interval of 30 min between doses
- next dose only when no signs of AR

a. 0.05ml of 1:10 solution
b. 0.05 ml of full strength
c. 0.10 ml of full strength
d. 0.15 ml of full strength
e. 0.20 ml of full strength
f. 0.50 ml of full strength (for 1.0 ml vaccines only)

- note: use of antihistamines or oral corticosteroids prior to vaccination has never been studied or proved effective for vaccine allergy; effectiveness? immunogenicity?

Red Book 2006, American Academy of Pediatrics

Gelatine allergy

- Often no prior known allergy to gelatine containing foods
- associated with immediate HS reactions after:
  - → JE-vaccine (not Ixiaro)
  - → YF-vaccine
  - → MMR
  - → varicella vaccines
  - → ...

Plotkin 2008

Latex allergy: ACIP recommendations

- Severe (anaphylaxis) allergy to latex
  → No administration of vaccines supplied in vials or syringes that contain natural rubber

  (unless benefit of vaccination outweighs the risk)

- Other allergic reactions than anaphylaxis (ex. contact allergy latex gloves)
  → Vaccines supplied in vials or syringes that contain natural rubber can be administered

W.L. Atkinson et al. MMWR Recomm Rep 2002;51 (2): 1-35

Yeast allergy and HBV-vaccine

- Saccharomyces cerevisae-derived vaccines
- Few patients with immediate HS-reactions [1,2]
- Bakonde et al.[3]
  - → 4 children with urticaria, angio-edema, asthma after HBV-vaccine
    - all skintest negative
    - all but 1 tolerated booster vaccination

[1] André FE. Vaccine 1990; 8(S): 74-8
[2] Brightman CA et al. Lancet 1989; 22: 903
[3] Bakonde VB et al. Rev Fr Allergol 1998; 38: 315-8

Contact allergy to formaldehyde or antibiotics present in vaccines

- Allergy diagnosed by patchtests
- If no history of systemic reaction

  ⇒ No contra-indication for vaccination

- possible adverse event:

  → exacerbation of eczema

  → Delayed type local reaction (48-96h): erythematous pruritic nodule

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Plotkin 2008
Red book 2006

Thiomersal

- Mercuric derivate – common preservative in (multi-dose) vaccines, topical medicines and cosmetics
- 1990's: association of Thiomersal and autisme spectrum disorders?
  - → no evidence for this association [1]
  - → 1999: US public health service + AAP [2]

    Recommendation to eliminate or reduce to trace amounts Thiomersal from vaccines for use in children < 24 months

    => 2002 implementation of recommendations for all childh vaccines in EU and USA[3]

[1] Parker SK et al. Pediatrics 20074; 114 (3): 793-804
[2] McMahon AW et al. Vaccine 2008; 26 (3): 427-9
[3] Hessel L. Bull Acad Nattl Med 2003; 187 (8): 1501-10

Thiomersal allergy

- Mostly delayed type[5] - Patch-tests: not clinically relevant [5,6,8]
  - → Patch-test positive adults:
    - adverse events other than occasional injection site reactions are exceedingly rare [6,8]
  - → IM Challenge of allergic adults with increasing strengths of thiomersal [9]
    - 100 µgr/ ml solution induced only mild local reaction in 9% of pts
  - → Comparison of inactivated influenza vaccine thiomersal containing and not containing in children < 2y [4]
    - no difference in rash, injection site reactions and infections
- Immediate hypersensitivity reaction
  - → Few adult case reports after influenza vaccine containing thiomersal [2,3,7]

[2] Zheng W et al. Ann Alergy Astham immunol. 2007; 99 (6): 574-5
[3] Lee-Wong M. et al. Ann Alergy Astham immunol. 2005; 94 (1): 90-4 ; [4] McMahon AW et al. Vaccine 2008; 26 (3): 427-9
[5] Hessel L. Bull Acad Nattl Med 2003; 187 (8): 1501-10 ; [6] Wattanakrai P et al. J Med Assoc Thai 2007; 90 (9): 1775-9
[7] Karsen H et al. J infect Devel countries 2007; 1 (3): 348-349 ;
[8] Rietschel et al. Antiseptics and desinfectants. Ficher's Contact Dermatitis, 5th ed. Philadelphia: Lippincott Williams & Wilkins, 2001:12:151 ; [9] Audicana et al. Am J Contact Dermat 2002: 13: 3-9

Conclusions

- SAE following vaccination are rare
- Most allergic patients can be safely vaccinated
- careful evaluation of the cause of a previous SAE is necessary to:
  → prevent another SAE
  → allow future vaccination of the patient