



ThermoFisher
SCIENTIFIC

stehen

Allergologie in de



Paul Scheidegg

doctor.ch

Allergologie in der Dermatologie




255'000

PubMed.gov

dermatology

Advanced Create alert Create RSS

Save Email Send to

MY NCBI FILTERS  255,154 results

32'000

allergy dermatology

Search

Advanced Create alert Create RSS User Guide

Save Email Send to Sorted by: Best match Display options

32,964 results

3'300

PubMed.gov

IgE dermatology

Advanced Create alert Create RSS

Save Email Send to

MY NCBI FILTERS  3,308 results

Zielorgan Haut



AME – my daily business

Angioödem only – my red flag

CSU – no, it is NOT an allergy

AD/ND – my unmet needs



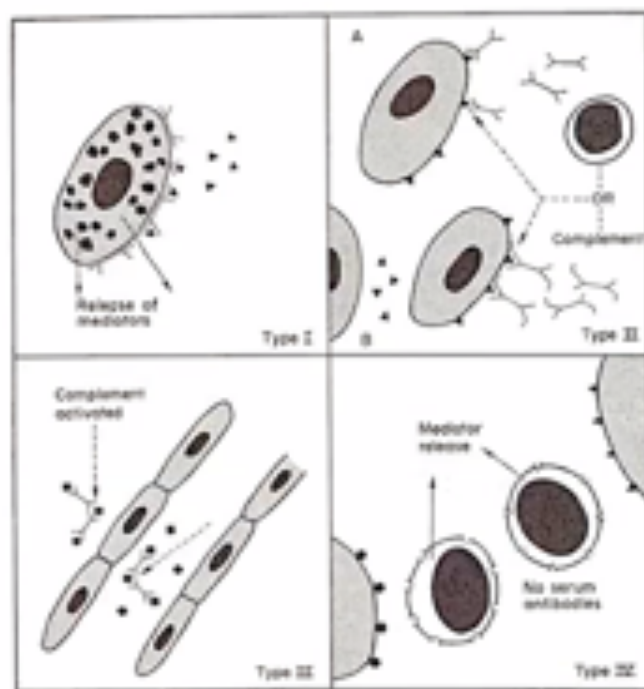
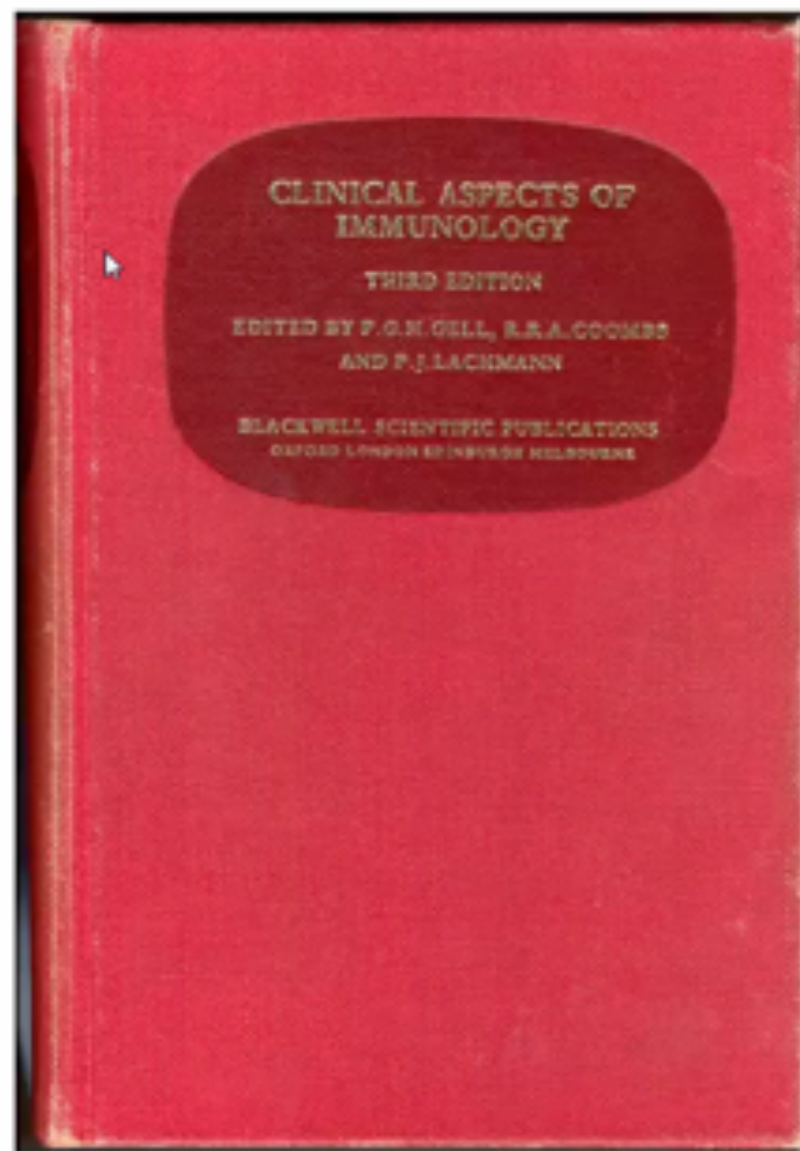
AME

80% – Spättyp

2% – echte Soforttyp

18% – «pseudo»- allergische

1963 Description of the four types of hypersensitivity reactions by Coombs & Gell

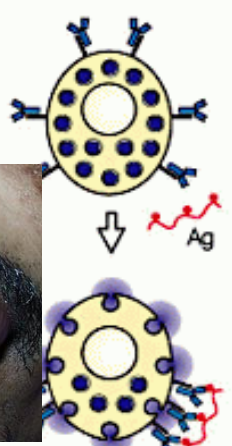
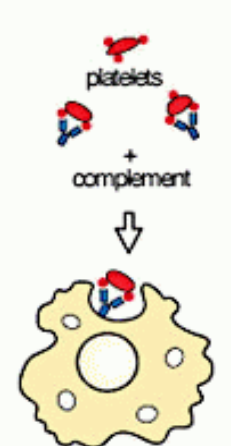
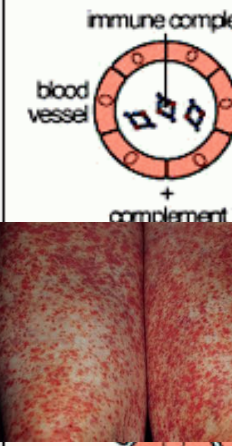
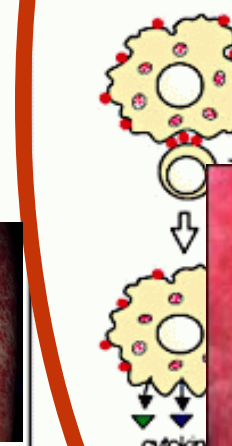


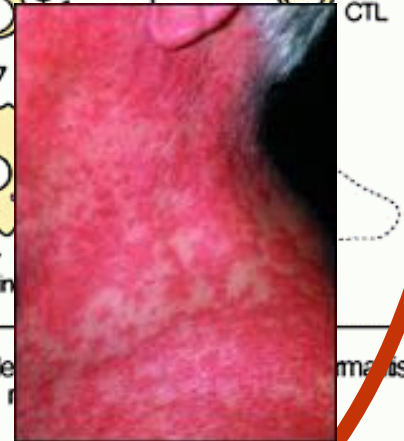
Key:

- • • Antigen
- Liberation of histamine and other pharmacologically active substances
- Y Y Antibody
- Sites of involvement of complement or non-antigenized lymphocytes
- ▷ ◁ Specific antigen-combining receptors on membrane of specifically sensitized lymphocytes

FIG. 25. The four types of allergic reaction.

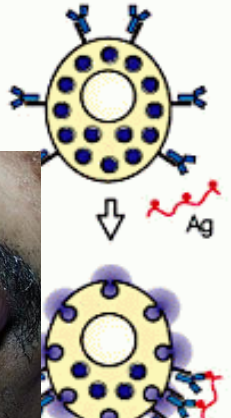
Coombs and Gell's Klassifikation der Hypersensitivität

	Type I	Type II	Type III	Type IV
Immune reactant	IgE antibody, T _H 2 cells	IgG antibody	IgG antibody	T cells
Antigen	Soluble antigen	Cell- or matrix-associated antigen	Soluble antigen	Soluble antigen Cell-associated antigen
Effector mechanism	Mast-cell activation	Complement, FcγR cells (phagocytes, NK cells)	Complement Phagocytes	Macrophage activation Cytotoxicity
				
Example of hypersensitivity reaction	Allergic rhinitis, asthma, systemic anaphylaxis	Some drug allergies (eg penicillin)	Serum sickness, Arthus reaction	Contact dermatitis, Tuberculin reaction, Hemolytic anemia



Aktuell brauchbare Labortests– Typ I

	Type I
Immune reactant	IgE antibody, T _H 2 cells
Antigen	Soluble antigen
Effector mechanism	Mast-cell activation



The diagram illustrates the process of mast cell activation. It shows a mast cell with IgE receptors on its surface. An allergen (Ag) binds to the IgE antibodies, which are already bound to the receptors. This cross-linking triggers the activation of the mast cell, leading to the release of mediators. An inset photograph shows a person's lips that are significantly swollen, a clinical sign of an allergic reaction.

Anamnese
Prick – (ic)
(Spezifische IgE)
BAT
(CASTs, LTT)
(Provokation)

Basophilen-Aktivierungstest (BAT)
Medikamenten Allergie | anti-CCR3/anti-CD63 bzw. CD203c

Basophils are easily isolated from venous blood and present good “indicator cells” of an IgE-mediated allergic response. In the BAT, a patient’s basophils are exposed to various allergens in vitro, including drugs. If the patient is allergic to an allergen, the allergen will cross-link allergen-specific IgE antibodies bound to the IgE receptor (FcεRI) on basophils, resulting in upregulation of basophil activation markers, including CD63 and CD203c, which are measured by flow cytometry.

Anamnese – Typ I



	Type I
Immune	IgE antibody, T _H 2 cells

So funktioniert der Penicillinallergie-Test PEN

PEN: Patient gibt eine Penicillinallergie an.

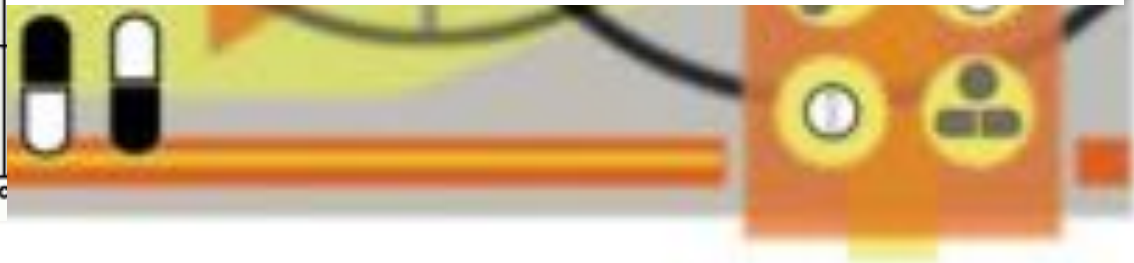
Tabelle 3: Kreuzreaktivität von Penicillinen.

Penicilline zu Cephalosporinen	<10% (meist Seitenkette)
Penicilline zu Carbapenemen	<1%
Penicilline zu Monobactamen	Keine Kreuzreaktivität, einzig zwischen Ceftazidim und Monobactamen möglich

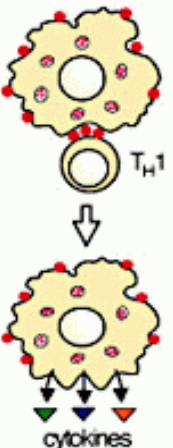
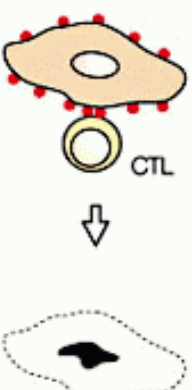
	
Example of hypersensitivity reaction	Allergic rhinitis, asthma, systemic anaphylaxis

© 1997 Current Biology Ltd. / Garland Publishing, Inc

drei Punkten kann den Studienautoren zufolge ein geringes Allergierisiko angenommen werden.



Aktuell brauchbare Labortests Typ IV

Type IV	
T cells	
Soluble antigen	Cell-associated antigen
Macrophage activation	Cytotoxicity
	
Contact dermatitis, tuberculin reaction	Contact dermatitis



Anamnese
Biopsie
(Epikutan)
LTT
Provokation

Zytokin Lymphozyten Transformationstest (Zyto - LTT)
Bei Spättyp-Medikamenten Allergien

Coombs and Gell's Klassifikation extended

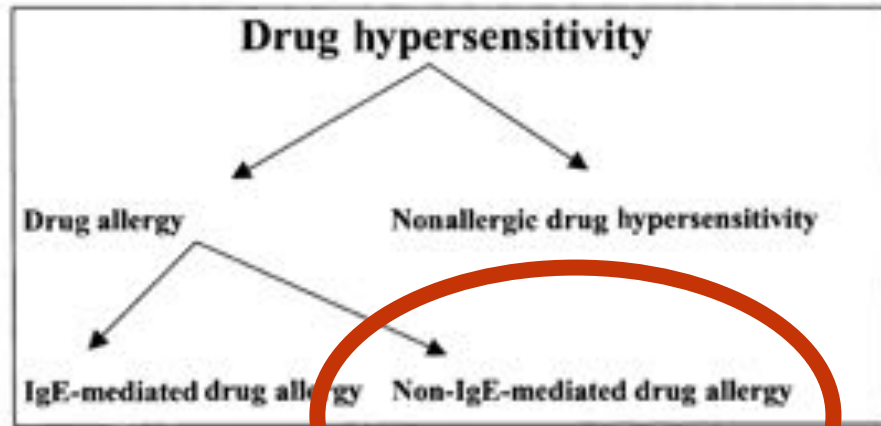


Figure 9.



Table 1. Pathogenic mechanisms and clinical symptoms of nonimmediate reactions to β -lactams [adapted from Ref. [17]]

Extended Coombs and Gell classification	Type of immune response†	Pathologic characteristics	Clinical symptoms†
Type II	IgG and FcR*‡	FcR-dependent cell destruction	Blood cell dyscrasia
Type III	IgG and complement or FcR*‡	Immunocomplex deposition	Vasculitis
Type IVa	Th1(FN- γ)*	Monocyte activation	Eczema
Type IVb	Th2 (IL-5 and IL-4)*	Eosinophilic inflammation	Maculopapular exanthema, bullous exanthema
Type IVc	CTL (perforin and granzyme B; FasL)*	CD4- or CD8-mediated killing of cells (i.e. keratinocytes)	Maculopapular exanthema, bullous exanthema, pustular exanthema
Type IVd	T cells (IL-8/CXCL8)*	Neutrophil recruitment and activation	Pustular exanthema

TESTS OF T CELL MEDIATED

Zytokin Lymphozyten Transformationstest (Zyto – LTT)

Bei Spättyp-Medikamenten Allergien



PR

LTT

ICITY

CD107

release
ay

ne B

In the Cyto-LTT, a patient's T cells are cultured with several drug dilutions for 7-days. If the T cells are specific for the drug allergens, the cells will respond to the stimuli by proliferating and secreting cytokines (IL-3, IL-13, IFN γ) and cytotoxicity markers (granzyme B, granulysin), which are read out by multiplex technology. The multiplex cytokine panel covers different T cell phenotypes and allows us to increase the sensitivity of the test.

CD71

IVc

Blasenbildung

wir berichten ihnen über oben genannten Patienten, welcher vom 08.02.2016 - 05.03.2016 in unserer Klinik zur Rehabilitation hospitalisiert war.

Diagnosen

1. Residuen eines Stevens-Johnson-Syndrom (ED 22.01.2016)
 - anfangs hoch dosiert mit Solumerdol i.v. behandelt
 - am ehesten Allopurinol-induziert DD Novalgin
 - bekannte Allergien auf Novalgin, Bactrim, Morphin und Iod
2. Neurokognitive Störung (amnesic, multidomain) offener Genese DD im Rahmen der 1. Diagnose DD mögliche Anpassungsstörung (ICD-10: F43.2) mit depressiver Symptomatik DD: Frontalhirnbetonte vaskuläre Enzephalopathie
 - neuropsychologische Testung (CERAD) aarReha vom 16.02.2016
 - MMS/Uhrentest vom 16.02.2016: 22/30 Punkte, 3/7 Punkte



Dermatologic Reactions to Immune Checkpoint Inhibitors : Skin Toxicities and Immunotherapy

Vincent Sibaud ¹

Affiliations

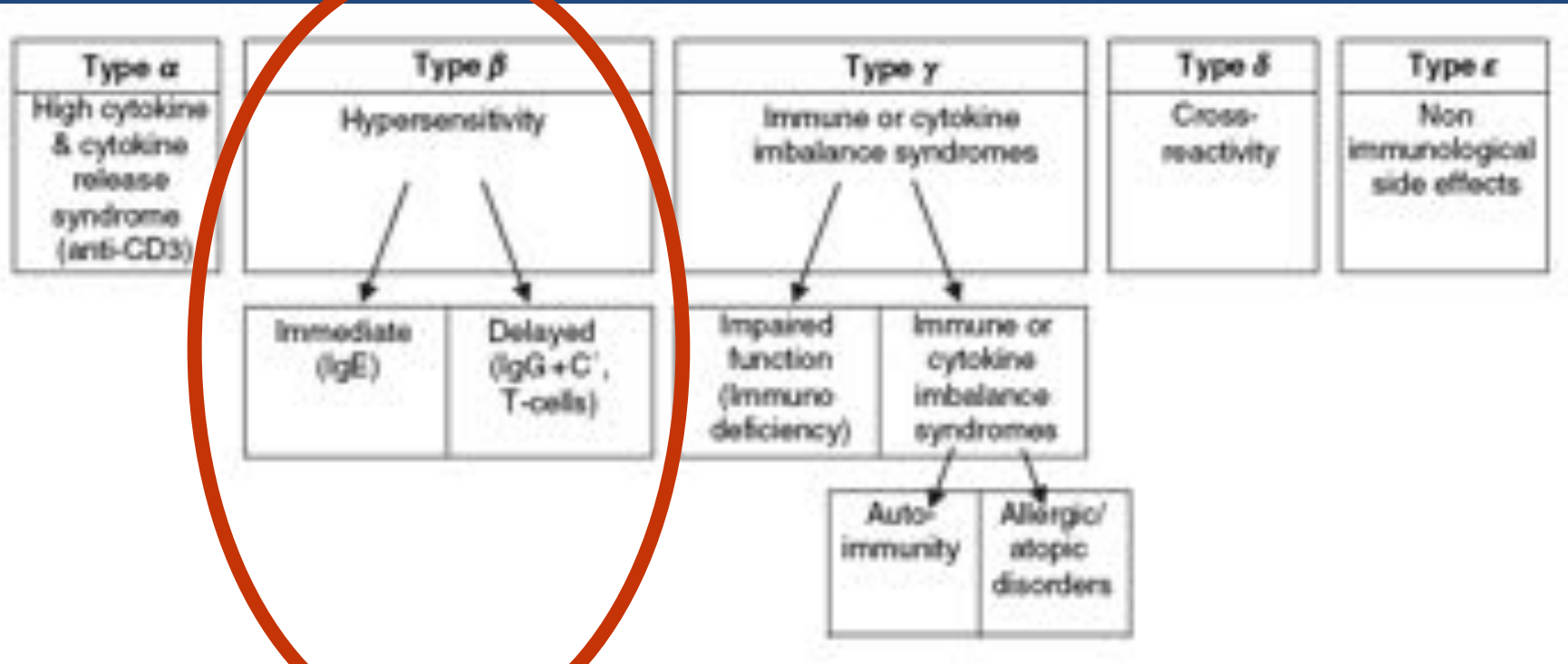
PMID: 29256113 DOI: [10.1007/s40257-017-0336-3](https://doi.org/10.1007/s40257-017-0336-3)

adverse events that are mostly immune related [immune-related adverse events (irAEs)], notably mediated by the triggering of cytotoxic CD4+/CD8+ T cell activation. Cutaneous toxicities appear to be one of the most prevalent irAEs, both with anti-PD-1 and anti-CTLA-4 agents or with the newly developed anti-PD-L1 agents, which corresponds to a class effect. They are observed in more than one-third of the treated patients, mainly in the form of a maculopapular rash (eczema-like spongiotic dermatitis) and pruritus. A wide range of other dermatologic manifestations can also occur, including lichenoid reactions, psoriasis, acneiform rashes, vitiligo-like lesions, autoimmune oral mucosal changes. In addition, the use of anti-CTLA-4 and anti-PD-1 therapies in combination is associated with the development of more frequent, more severe and earlier cutaneous irAEs compared to single agents. In most cases, these dysimmune dermatologic adverse events remain self-limiting and readily manageable. Early recognition and adequate management, however, are critical to prevent exacerbation of the lesions, to limit treatment interruption and to minimize quality of life impairment. This review describes the variable clinical and histopathologic aspects of

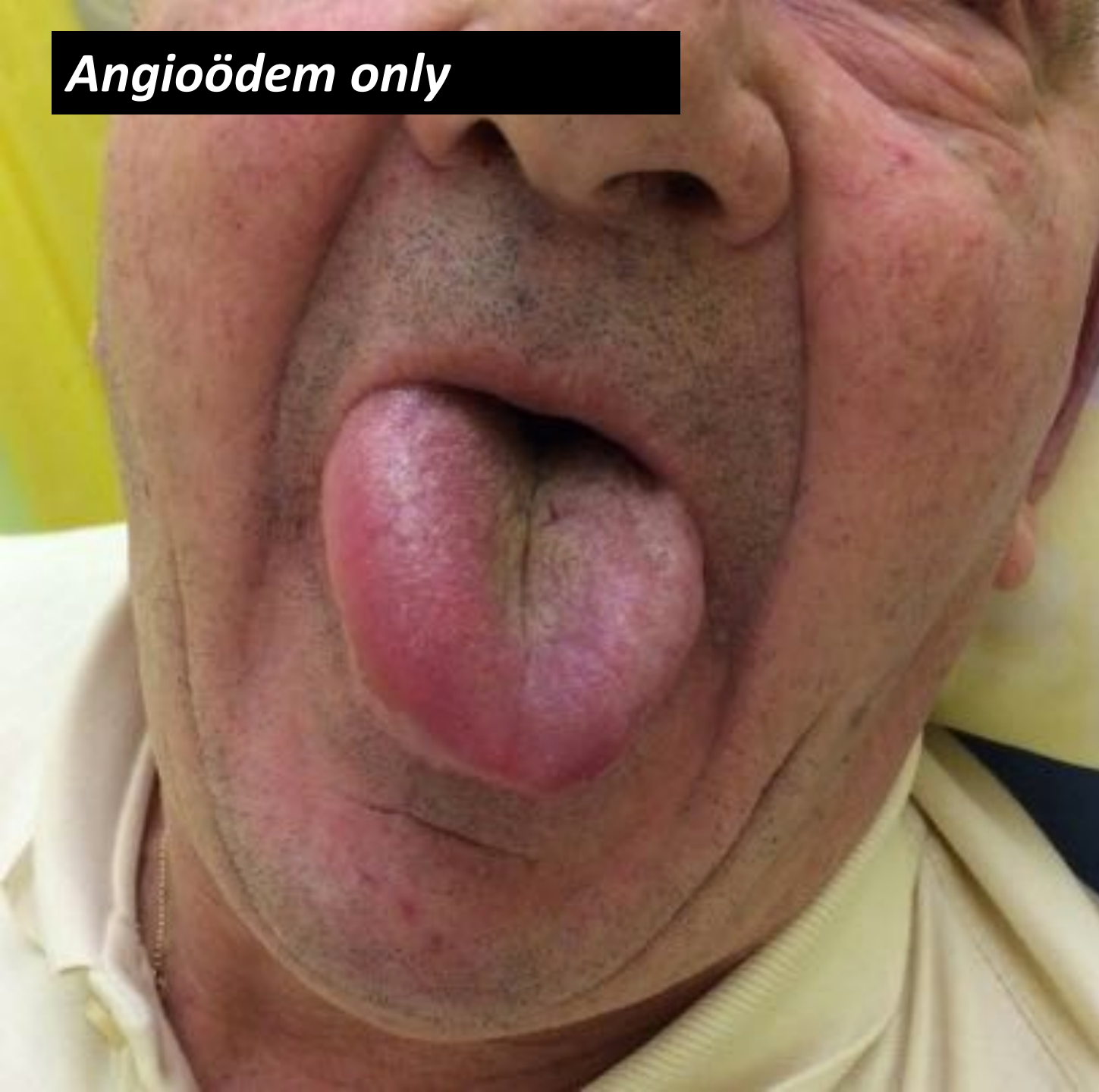
Pichler's Klassifikation

Review article

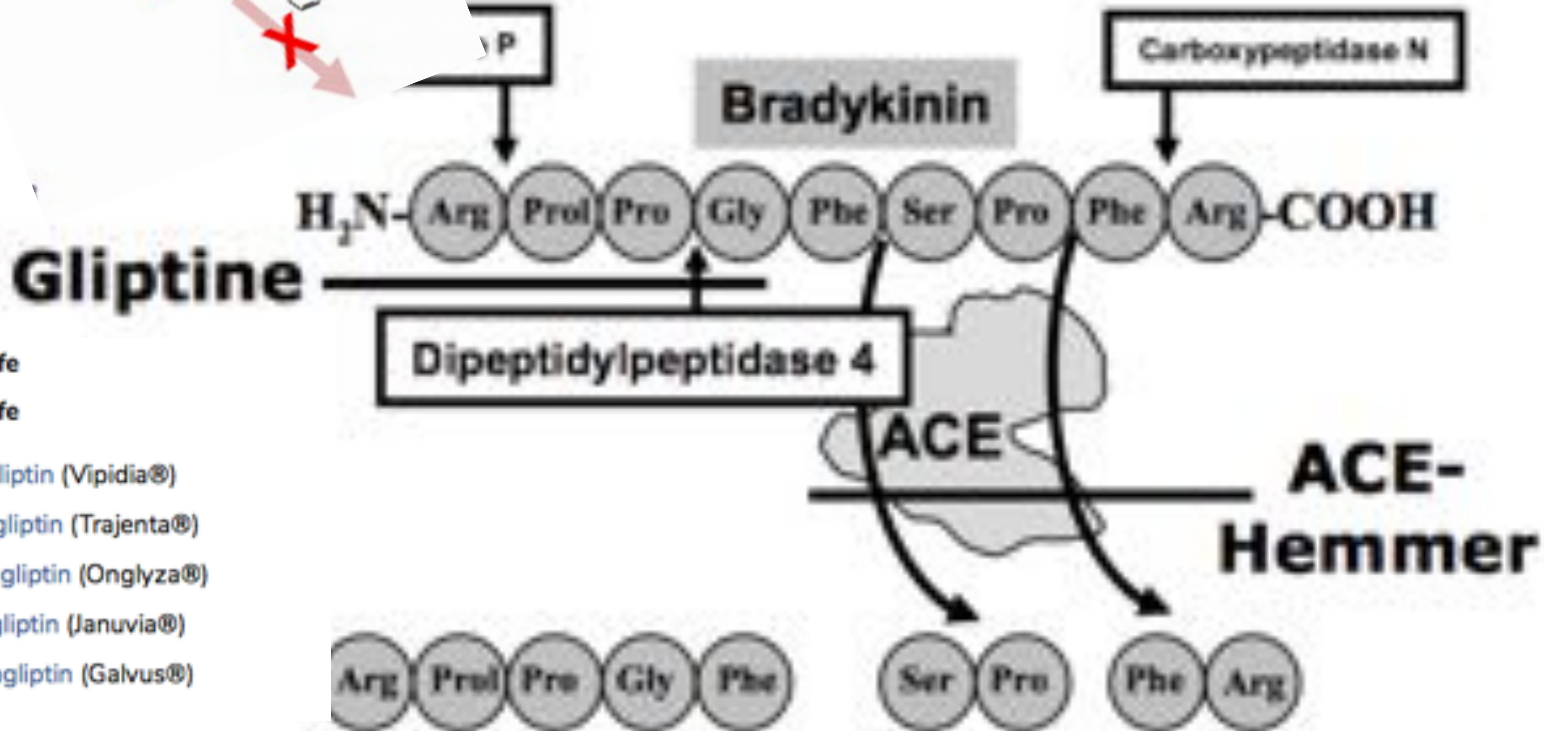
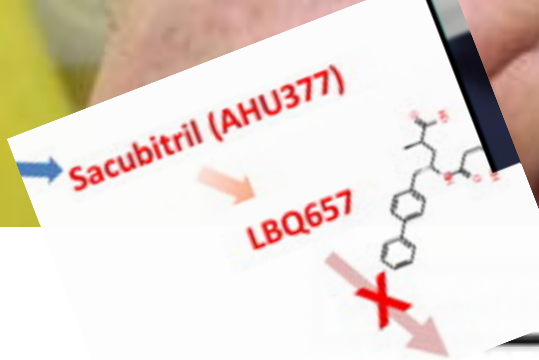
Adverse side-effects to biological agents



Angioödem only



Bradykinin-Junkies



Wirkstoffe

Wirkstoffe

- Alogliptin (Vipidia®)
- Linagliptin (Trajenta®)
- Saxagliptin (Onglyza®)
- Sitagliptin (Januvia®)
- Vildagliptin (Galvus®)

Bradykinin und Kallidin (Lys¹-Bradykinin) werden bevorzugt durch ACE abgebaut!

„Summationsanaphylaxie“

Simons et al., J Allergy Clin Immunol 2011;127:587-93

**Diabetiker nimmt ASS,
Betablocker, ACE-
Hemmer, Gliptine und
NSAR...Sacubitril**

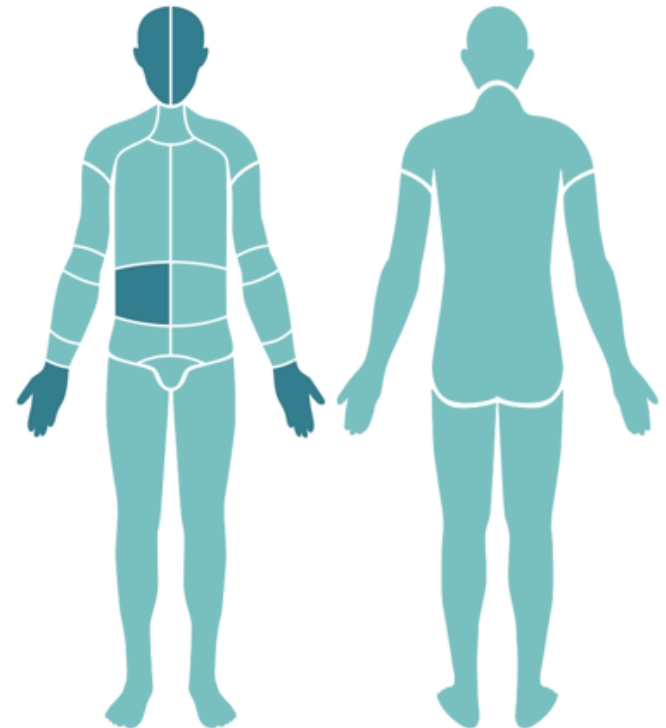
Urticaria und Angioödem



Anmerkungen

Lieber Paul. Die Patientin stellt sich notfallmässig vor bei geschwollener Zunge. Sie habe am 03.12. bereits eine Pizza (Thunfisch, Zwiebel) gegessen und 30 Minuten darauf eine juckende Rötung an beiden Handflächen palmar gehabt, welche nach ca. 30 Minuten selbstlimitierend war. Am 04.12. habe sie um 12:00 Uhr nun die restliche Pizza erneut aufgewärmt und gegessen. Initial sei nichts passiert, um 18:00 Uhr jedoch

Wo tritt Ihr Hautproblem auf?



Angioödem mit Urticaria

„echte“ allergischer Reaktionen

Diagnosen

1. Anaphylaktische Reaktion Grad II mit Angioödem der Zunge am 04.12.2020
 - Allergen am ehesten Gluten (Pizza gegessen aus Griessmehl) oder Soja
 - Klinik: Zungenschwellung, Urtikaria Rumpf und Unterarme
 - Therapie:

Semaglutid ist ein langwirksames Analogon von GLP-1 (Glucagon-like peptide-1) mit einer Sequenzhomologie von 94%. GLP-1 ist ein Peptidhormon, das aus [Aminosäuren](#) besteht und von enteroendokrinen L-Zellen im Verdauungstrakt gebildet wird. **Aufgrund des Abbaus durch die Enzyme Dipeptidylpeptidase-4 (DPP-4) und neutrale Endopeptidase (NEP) hat es eine Halbwertszeit im Bereich von lediglich zwei Minuten.**

Marker
Wirkstoff
Bemerkung
OZEMER
mi Fert
Semaglu
Wochen
mg, jew
bei uns
PLAVIX
Clopidog

und inhalativ) am 04.12.2020

ne von Pizza

li	Ab	Na

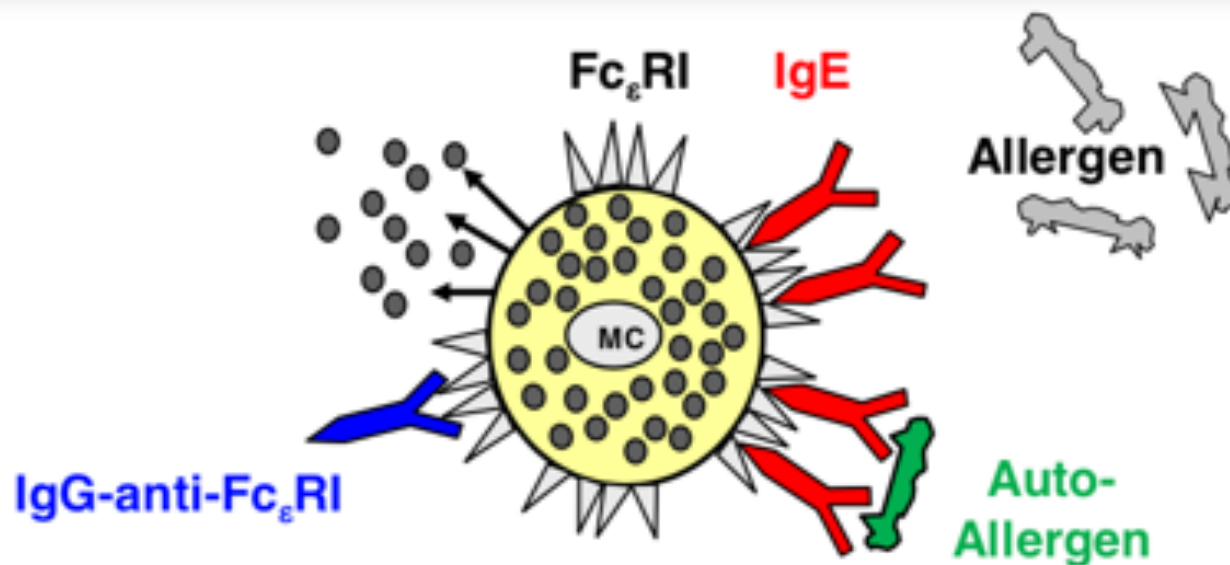
e und / oder
medierten
noch nicht schon
inhibitor Inhibitor

ir die Testungen

Chronische spontane Urtikaria

Die chronische spontane Urtikaria hat zwei Endotypen

Kolchir et al., *J. Allergy Clin. Immunol.* 2017; 139; 1772-1781

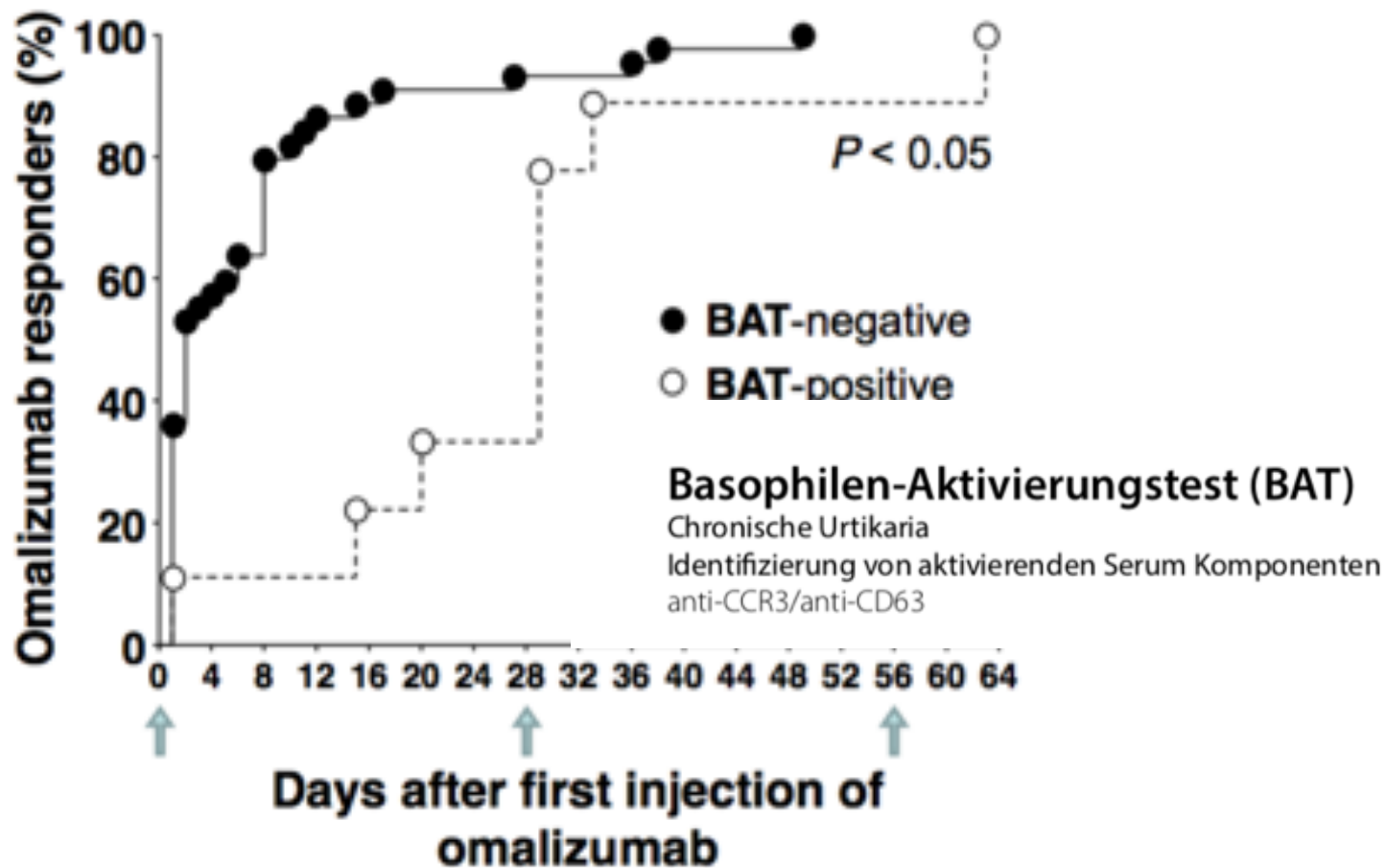


Autoimmun

Autoallergisch

autoimmun CSU poor response to anti-IgE

Gericke et al., J. Allergy Clin. Immunol. 2017: in press.



Autoimmun vs autoallergische CSU

Wenig IgE ist schlecht.

Deza et al., Acta Derm Venereol 2017; 97: 698-704



Kalibration von sIgE Assays



- Kalibration von Gesamt-IgE Assay erfolgt mittels WHO Standard (Probe mit bekannter Konzentration von IgE)

▪ Für sIgE Assays bisher keine Standards zur Kalibration verfügbar

Gesamt IgE	107 (0-4)	116 (42-277)	151 kU/l	20 kU/l	0.0034
	36 (32-39)				0.843
UCT at the start of omalizumab therapy	1 (0-4)		0 (0-0)	1 (0-2)	0.904

Autoimmun vs autoallergische CSU

Gesamt IgE vor, während, nach anti-IgE Tx

BAT Bestimmung (?)

Anti-TPO IgG Bestimmung (?)

ANA Screening (?)

Basophilen-Aktivierungstest (BAT)

Chronische Urtikaria

Identifizierung von aktivierenden Serum Komponenten

anti-CCR3/anti-CD63

In patients with chronic urticaria (CU), serum factors, including autoantibodies against IgE (anti-IgE) and/or the IgE receptor (anti-FcεRI), activate basophils, which can be measured with CU-BAT. CU-BAT tests whether serum from patients with CU can activate basophils from healthy donors, as demonstrated by the upregulation of activation markers (CD63 and/or CD203c).

„episodische“, intermittierende Urticaria

Urtikaria und Weizenallergie

Xu et al, World Allergy Organ J 2019;12:100013

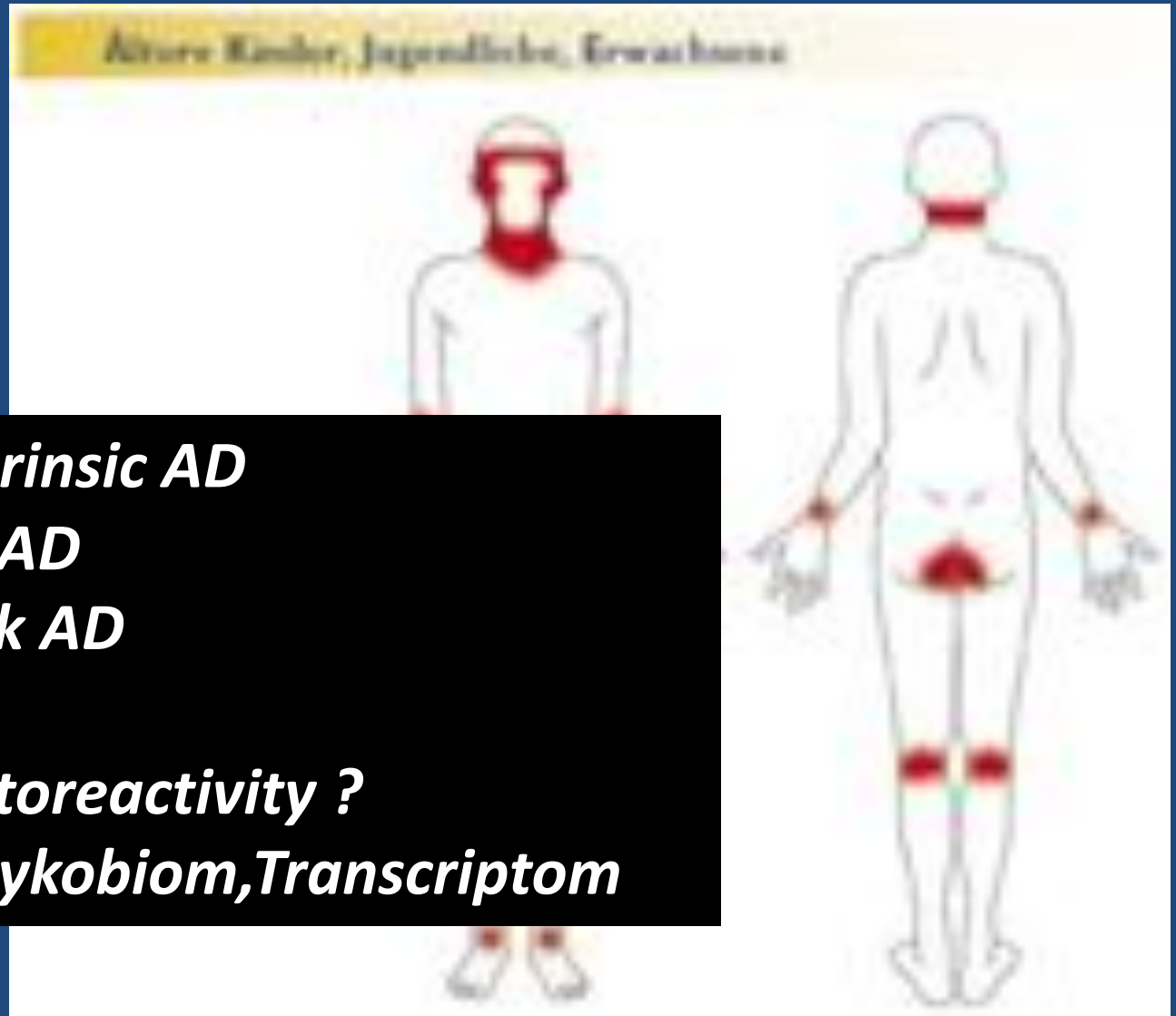
- 164 von 193 Weizenallergikern, (darunter 104 mit WDEIA) hatten anamnestisch Urtikariaepisoden.
- Patienten mit Urtikaria hatten in 13.1% (23/175) s.-IgE gegen Weizen / Gluten und in 4.4% (7/159) gegen Tri a 19.

Fazit

Weizenallergiker haben vor Diagnose der Weizenallergie häufig episodische Urtikaria (vermutlich durch die Allergie).

Allergiediagnostik zumindest bei episodischer Urtikaria!

Neurodermitis – eine sehr heterogene Angelegenheit



Intrinsic vs extrinsic AD

Child vs Adult AD

Head-and-neck AD

biomarkers ?

Markers of autoreactivity ?

Microbiom, Mykobiom, Transcriptom

Neurodermitis – candidate biomarkers ?

TABLE I. Subtypes of candidate biomarkers in AD

Biomarker	Screening	Diagnostic	Severity	Sensitization	Predictive therapeutic response	Prognostic fate of AD/comorbidities
Total/specific IgE				+++	Potential for prevention	?
TARC/CCL17	+		+++			
MDC/CCL22			+			
CTACK/CCL27			+			
FLG1/2	++				Potential for prevention	?
SPINK5/LEKTI	+					?
TSLP	+			?		Risk for viral complication
IL-31			+			
IL-33			+			Risk for viral complication
IL-22			+			
FcεRI/FcγRII		+				
IDO						Risk for EH
LL-37			+			
IL-18			+			
IL-16			+			
Soluble IL-2 receptor			+			
PARC/CCL18			+			
TEWL	++			?	Potential for prevention	?
Periostin			+			
BDNF			+			
IgE against <i>Malassezia</i> species			+			+

BDNF, Brain-derived neurotrophic factor; CTACK, cutaneous T-cell-attracting chemokine; EH, eczema herpeticum; FLG, filaggrin; IDO, indolamine-2,3-dioxygenase; MDC, macrophage-derived chemokine; PARC, pulmonary and activation-regulated chemokine; SPINK5/LEKTI, serine protease inhibitor Kazal-type 5/lympho-epithelial Kazal-type-related inhibitor; TARC, thymus and activation-regulated chemokine; TEWL, transepidermal water loss; TSLP, Thymic stromal lymphopoietin.

The missing link ? – Malassezia

Malassezia-Spezies als Trigger der Neurodermitis

Darabi et al., J Am Acad Dermatol 2009;60:125-136



Vor Itraconazol Nach Itraconazol

100 mg Itraconazol über 4-8 Wochen täglich,
danach 100 mg Itraconazol 2 x pro Woche

german shepherd
with atopic dermatitis

Heavy colonization
with
M. pachydermatis



After treatment with
Itraconazol

Sensitization to the Yeast *Malassezia Sympodialis* Is Specific for Extrinsic and Intrinsic Atopic Eczema

Barbra Fischer Casagrande¹, Sabine Flückiger², Maria T. Linder³, Catharina Johansson³, Annika Scheynius³, Reto Cramer² and Peter Schmid-Grendelmeier¹

Journal of Investigative Dermatology (2006)

BF Casagrande et al.
Extrinsic and Intrinsic Atopic Eczema

IgE- and T-cell-mediated reactivity against *M. sympodialis* was also found in patients with the intrinsic form of AE. Thus, sensitization to *M. sympodialis* is specific for AE patients and occurs in both the extrinsic and intrinsic variant of eczema.

IgE-mediated and T cell-mediated autoimmunity against manganese superoxide dismutase in atopic dermatitis

Peter Schmid-Grendelmeier, MD,^{a,b} Sabine Flückiger, PhD,^c Rainer Disch, MD,^d Axel Trautmann, MD,^e Brunello Wüthrich, MD,^b Kurt Blaser, PhD,^e Annika Scheynius, MD,^e and Reto Cramer, PhD^e Davos and Zürich, Switzerland, and Stockholm, Sweden

IgE-mediated and T cell-mediated autoimmunity against manganese superoxide dismutase in atopic dermatitis

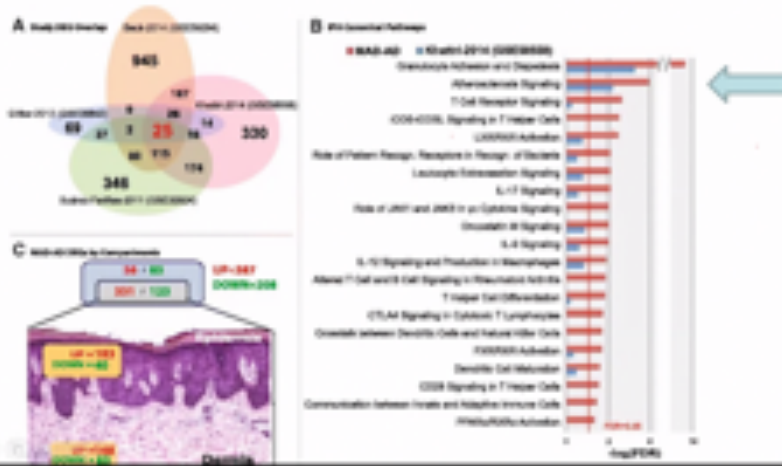
Peter Schmid-Grendelmeier, MD, Sabine Flückiger, PhD, Rainer Disch, MD, Axel Trautmann, MD, Brunello Wüthrich, MD, Kurt Blaser, PhD, Annika Scheynius, MD, Reto Cramer, PhD

Journal of Allergy and Clinical Immunology
Volume 115, Issue 5, Pages 1068-1075 (May 2005)
DOI: 10.1016/j.jaci.2005.01.065

Conclusion: Human MnSOD may play a role as an autoallergen in a subset of patients with AD, including nonatopic eczema. By molecular mimicry leading to cross-reactivity such sensitization might be induced primarily by exposure to environmental fungal MnSOD of *M. sympodialis*

Micro-dys-biom, Myko-dys-biom, Dys-Transcriptom HLA-Haplotyp, Exposome?

AD Transcriptome = Atherosclerosis



HHS Public Access

Author manuscript

Immunity. Author manuscript; available in PMC 2016 April 21.

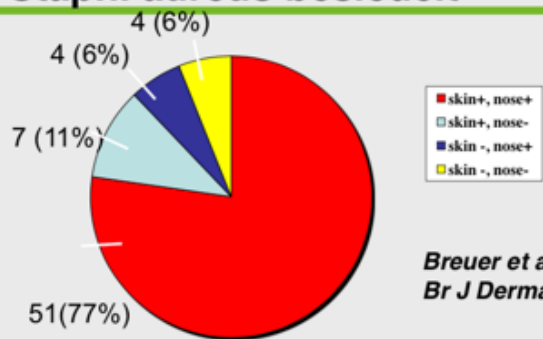
Published in final edited form as:

Immunity. 2015 April 21; 42(4): 756-766. doi:10.1016/j.immuni.2015.03.014.

Dysbiosis and *Staphylococcus aureus* colonization drives inflammation in atopic dermatitis

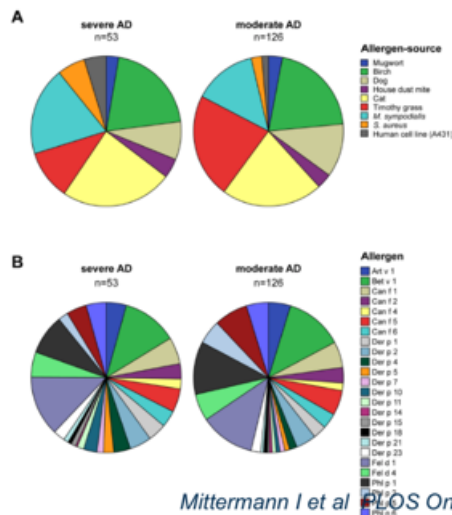
Tetsuro Kobayashi^{1,2}, Martin Glatz², Keisuke Horiuchi³, Hiroshi Kawasaki¹, Haruhiko Akiyama⁴, Daniel H. Kaplan⁵, Heidi H. Kong², Masayuki Amagai¹, and Keisuke Nagao^{1,2,†}

State of the Art:
Die Mehrheit der Patienten mit AD ist
mit Staph. aureus besiedelt



Breuer et al.,
Br J Dermatol 2002

In severe AD sensitization to *S. aureus* and *Malassezia* is more common



Mittermann I et al. PLOS One 2016

Isolierung von befallener/nicht befallener Haut
Isolierung von akuten/chronischen Läsionen
Isolierung von gesunden Partnern

The missing link ? – Atopic patch

Non-IgE-reactive rBet v 1 fragment mix induce a positive eczematous reaction in almost

Frequent occurrence of T cell-mediated late reactions revealed by atopy patch testing with hypoallergenic rBet v 1 fragments



Raffaella Campana, PhD,^a Katharina Moritz, MD,^b Katharina Marth, MD,^a Angela Neubauer, PhD,^c Hans Huber, PhD,^c Rainer Henning, PhD,^c Katharina Blatt, PhD,^d Gregor Hoermann, MD, PhD,^e Tess M. Brodie, PhD,^f Alexandra Kaider, MSc,^g Peter Valent, MD,^h Federica Sallusto, PhD,ⁱ Stefan Wöhrl, MD, MSc,^g and Rudolf Valenta, MD^a
 Vienna, Austria, and Bellinzona, Switzerland
 (J Allergy Clin Immunol 2016;137:601-9.)

www.nature.com/scientificreports

SCIENTIFIC REPORTS

OPEN | Epicutaneous allergen application preferentially boosts specific T cell responses in sensitized patients

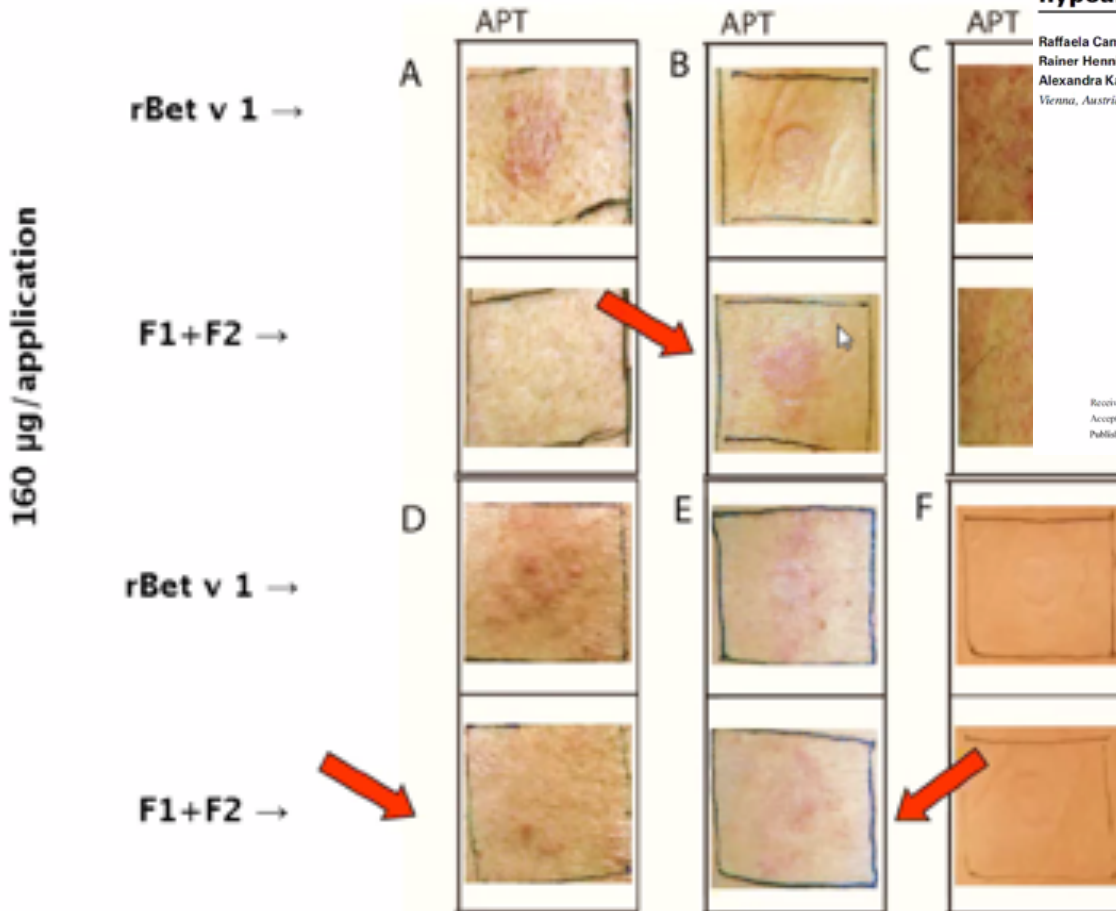
Received: 5 April 2017
 Accepted: 7 August 2017
 Published online: 14 September 2017

Raffaella Campana¹, Katharina Moritz², Angela Neubauer³, Hans Huber³, Rainer Henning³, Tess M. Brodie⁴, Alexandra Kaider⁵, Federica Sallusto^{6,7}, Stefan Wöhrl¹ & Rudolf Valenta¹

SCIENTIFIC REPORTS 17: 11657 | DOI:10.1038/s41598-017-10278-1

allergic patients suffering from AD

F: birch pollen allergic patient without AD



Quo vadis ?

Examples of chip diagnosis in real life

Pediatr Allergy Immunol. 2016 Mar 31. doi: 10.1111/pai.12572. [Epub ahead of print]

Microarray-based IgE-serology improves management of severe atopic dermatitis in two children.

Fedenko E, Elisyutina O, Shtyrbul O, Pampura A, Valenta R, Lupinek C, Khaitov M.



- Asp f 6
- Bos d 8
- Der p 11
- Gal d 1
- Mala s 11
- Tri a 19

Autoreactivity

Severity in adult AD

Food Sens in child AD

Autoreactivity

EIA/Urticaria



Molecular allergology applied to skin diseases

Prof Peter Schmid-Grendelmeier

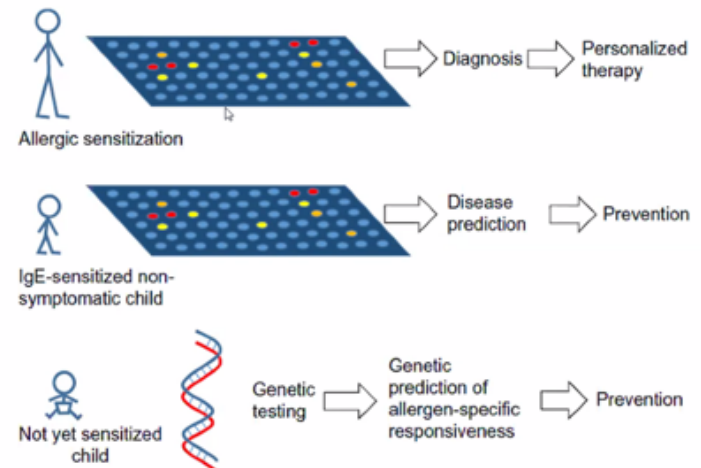
Head of Allergy Unit, Department of Dermatology, University Hospital of Zurich, Switzerland

Neurodermitis – was mir noch bleibt ... Sx1/ Phadiatop

CODE	Nom français	Deutsche Bezeichnung	Nome italiano	NO ART.	Q
	Dépistages	Screening	Screening		
pha	Allergènes d'inhalation	Phadiatop (Inhalation Screen)	Phadiatop (Inhalation Screen)	14-4405-35	48
sx1	Allergènes d'inhalation (d1, e1, e5, g6, a12, m2, t3, w6)	Inhal. screen (g6, g12, t3, w6, d1, e1, e5, m2)	g6, g12, t3, w6, d1, e1, e5, m2	14-4332-35	48
	Médicaments	Arzneimittel	Farmaci		
pc1	Penicilline G	Penicillou G	Penicillou G	14-4164-01	16

ImmunoCAP Phadiatop	
Allergen	Extract
House dust mite	d1, d2
Cat	e1
Dog	e5
Birch pollen	t3
Mugwort	w6
Timothy grass	g6
Cladsporium	m2
Horse	e3
Olive pollen	t9
Wall pellitory	w19

From the diagnosis to the prediction of allergic sensitization: What comes next?



54 **FORSCHUNG**

Das Mik

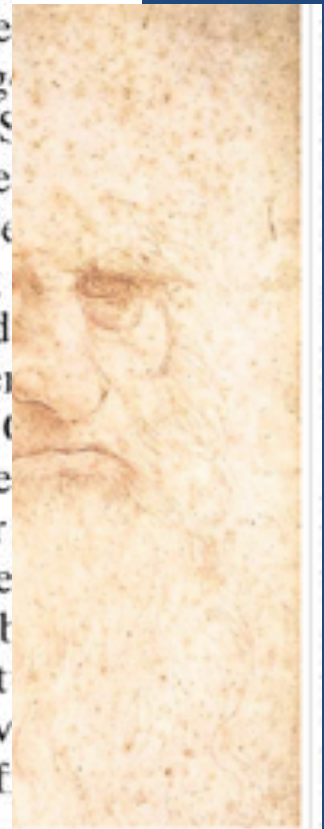
Auf alten Zeichnung
Gemeinschaft von M
um Neues über die

ratoren in Kom Probenmaterial und schickten dieses zur Analyse nach Wien. Jede Zeichnung besitzt ein einzigartiges Mikrobiom, wie Piñar und ihre Kollegen jetzt in einem Fachartikel berichten.² Zu ihrer Überraschung befinden sich auf den Werken mehr Bakterien als Pilze, darunter so allgemein bekannte Darmkeime wie Kolibakterien und Salmonellen. Die meisten Bakterien stammten aus dem Mikrobiom von Menschen, vermutet Piñar. Auch Insekten haben ihre Spuren hinterlassen. Trotz der bakteriellen Überzahl unterstreicht die Wiener Mikrobiologin: «Am gefährlichsten sind die Pilze.» Denn sie bilden Sporen, die selbst Trockenheit extrem lange überdauern. Wird es feuchter und wärmer, können sie ihre zerstörerische Aktivität schnell entfalten. Zudem entdeckten die Forscher einen Schimmelpilz, der Allergien auslösen und bei Nässe gefährlich werden kann.

Die Spur der Restauratoren

Wie viele der winzigen Organismen tat-

meisi
Resta
stoffs
rieru
huma
organ
Ev
vielfa
Wahl
grunc
Pferd
Papie
Indig
war. S
bielle
Ge
zung
von d
läuten
dere
Papie
mehr
bielle
dem b
perat
das M
veröf



Mein Fazit.....

AME – BAT, LTT (prick, ic, OPT)

*Angioödem only – Medis, Medis, Medis, new kids
on the block*

CSU – IgE (?), (BAT), TSH, (ANA)

*AD/ND – sx1, Phadiatop, antiseptische Basispflege,
ISAC ??*

Liebe Grüsse nach Wien

