HelmholtzZentrum münchen
German Research Center for Environmental Health

VitaminD AND HUMAN HEALTH

Vitamin D supplementation of newborns and risk of allergic sensitization

Matthias Wjst

London 23rd April 2014

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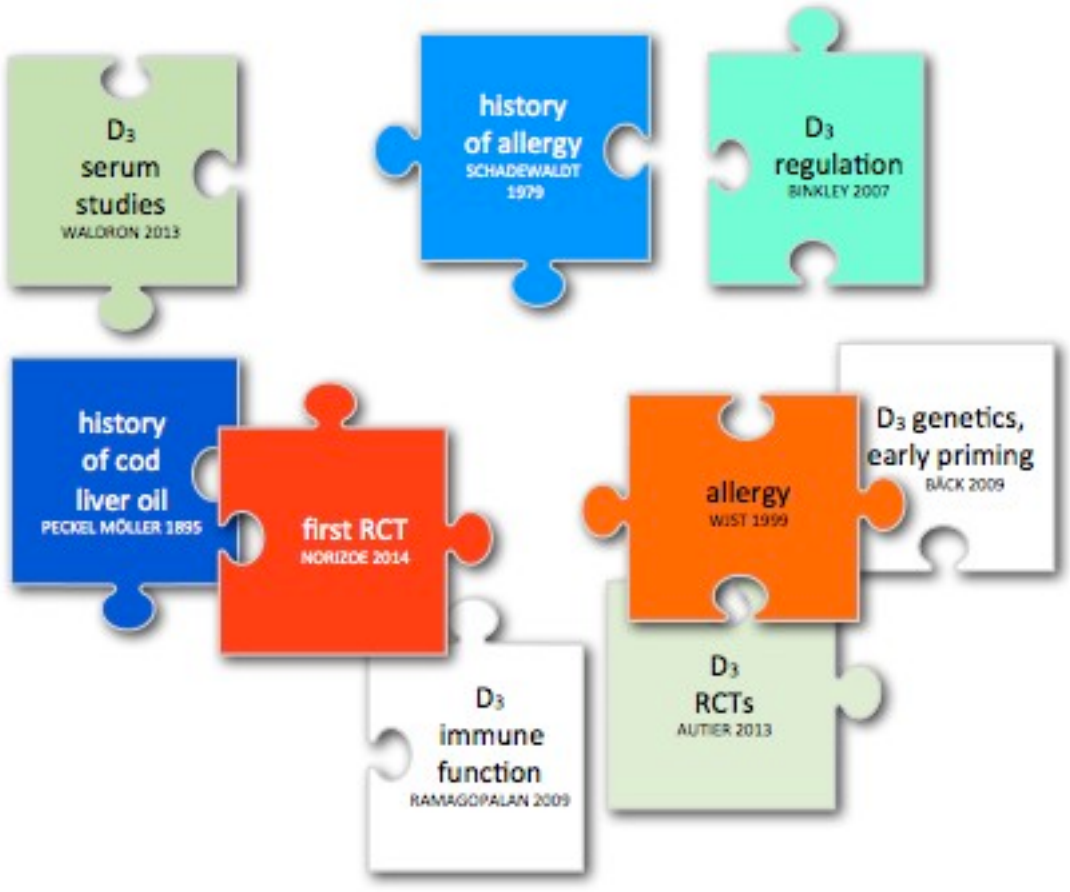

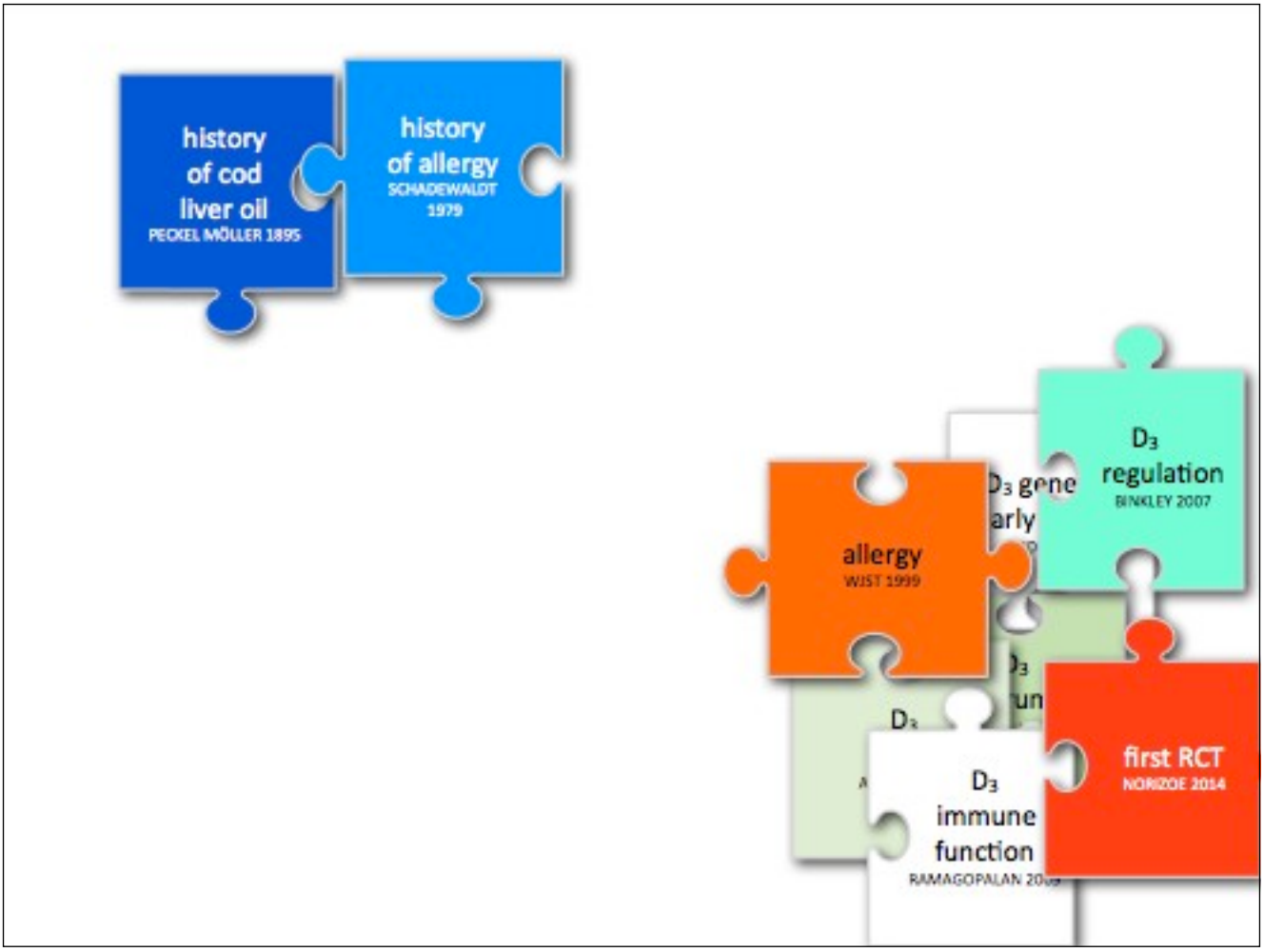
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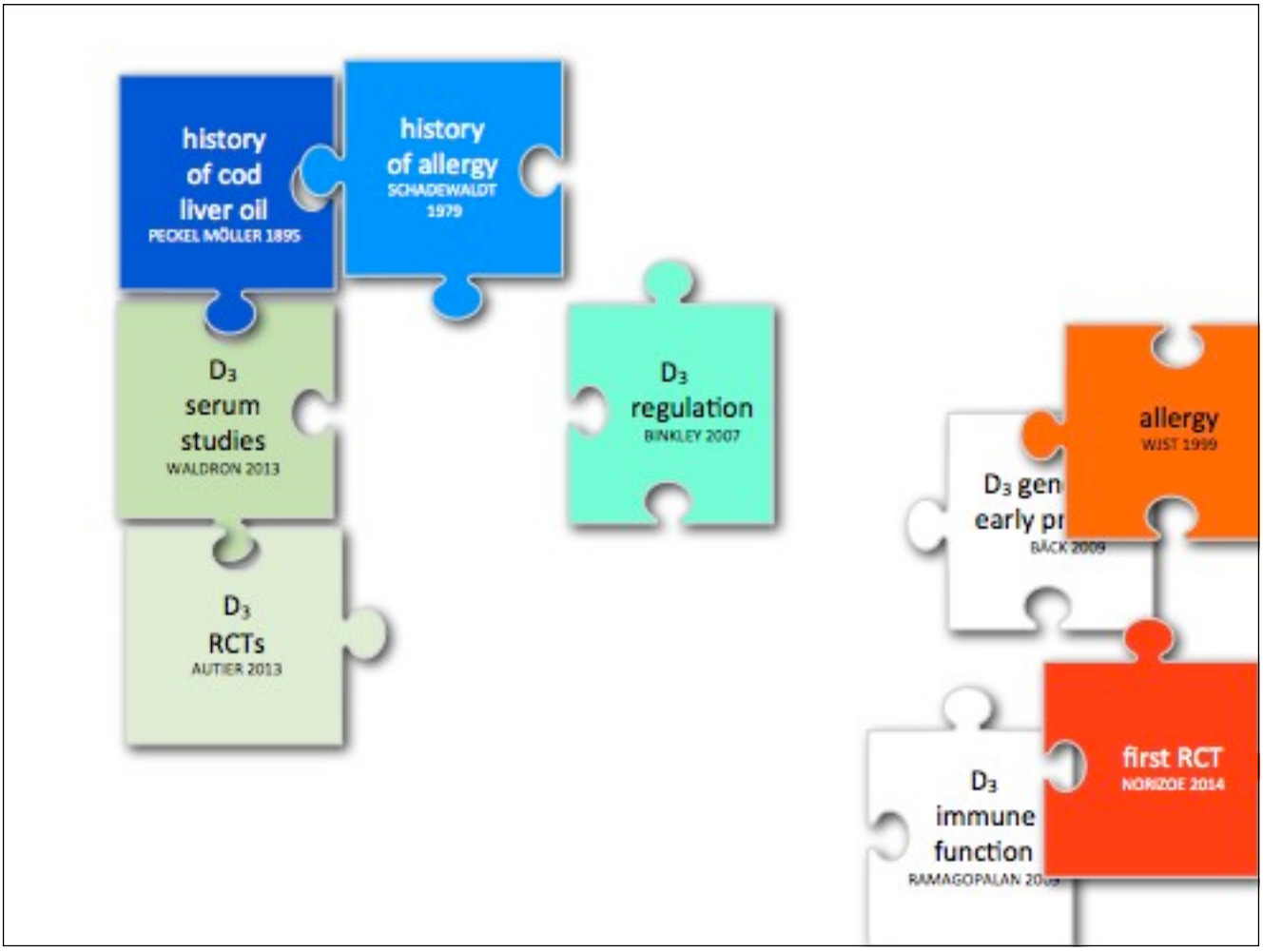
D3 immune function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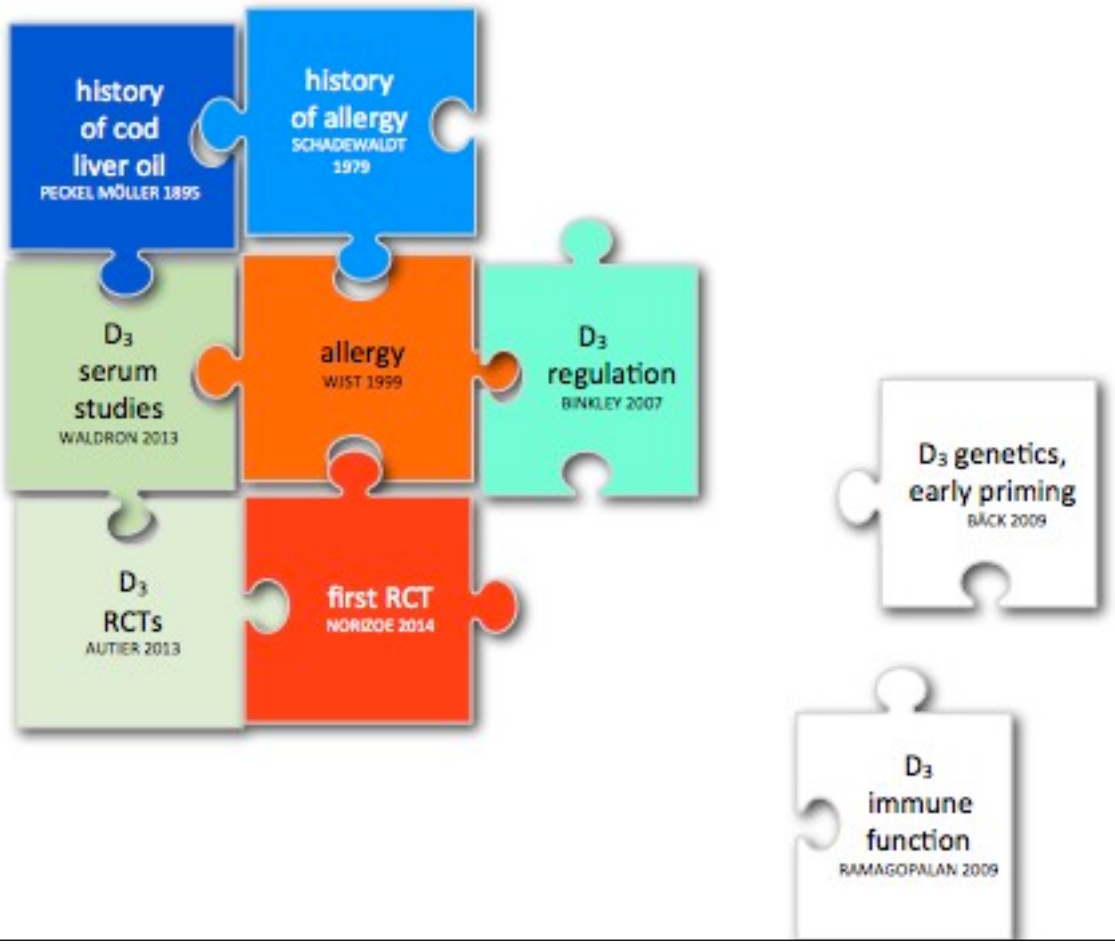
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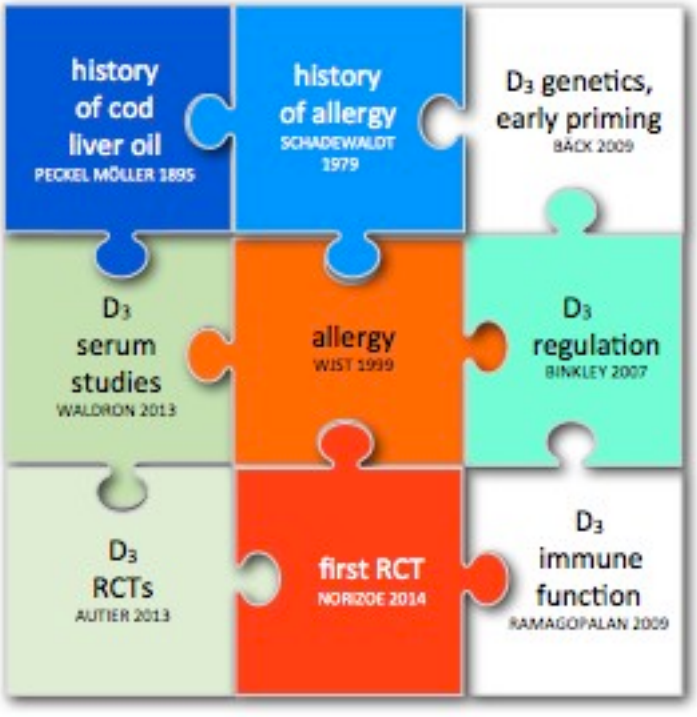
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Rickets Symptoms

	2-3 mo	4-6 mo	7-12 mo
ponderal defect >2 sd	87	62	36
hypotonia	93	100	100
bone pain	-	75	73
rachitic rosary	40	87	91
swollen wrists, knees, ankles	60	62	64
craniotabes	53	62	36
fractures	20	12	9
convulsions	20	12	27
upper respiratory tract infections	74	74	63

Holick, Vitamin D 1999, p 275

OF

THE CATARRHUS ÆSTIVUS,

OR

SUMMER CATARRH.

By J. BOSTOCK, M.D. F.R.S. Etc.

Read 22d April, 1828.

IN the tenth volume of the Society's Transactions there is an account of a disease which I conceive to be of a specific nature, and which from its symptoms, and from its occurring only at a certain period of the year, I propose to name the catarrhus æstivus. In my former communication, I detailed the symptoms as they occurred in my own person; my present object is to extend my remarks to the affection as it occurs in other individuals, to inquire into its cause, and to make some observations on the mode of treatment.

The number of cases which I have either seen or of which I have received a distinct account, amounts to eighteen, besides about ten others, which are less correctly ascertained. They all agree in the complaint making its appearance at

cod liver oil timeline

1766 First documented use in Manchester
(1721 canal, 1830 railway to Liverpool)

1771 Entered into British Pharmacopoeia
(in place since 1618)

1773* John Bostock in Liverpool, a city of 50,000
(buried at Kensal Green Cemetery)

1781 disease onset

1781 Samuel Bulley from Liverpool is operating bank fishery in Newfoundland
(importing cod fish for oil production)

MMW 1906 / reprint 1910

Aus der k. k. Universitäts-Kinderklinik in Wien (Vorst.: Hofrat Escherich).

Allergie.

Von C. v. Pirquet.

In den letzten Jahren ist eine Reihe von Tatsachen gesammelt worden, welche in das Bereich der Immunitätslehre gehören, aber unter diesen Namen schlecht passen: die Befunde von Ueberempfindlichkeit am immunisierten Organismus.[*])

Diese beiden Ausdrücke schreien gegeneinander; unter immun stellen wir uns doch einen Organismus vor, welcher gegen eine Krankheit geschützt ist, von ihr nicht mehr angegriffen wird; und der soll gleichzeitig gegenüber derselben Krankheit überempfindlich sein?

Diesen Widerspruch hat schon v. Behring gefühlt, als er den Tod von gegen Tetanus hoch immunisierten Tieren an kleinen Mengen desselben Toxins als „paradoxe Reaktion" bezeichnete.

(Aus der Universitäts-Kinderklinik in Wien [Vorstand: Prof. Dr. Cl. Pirquet].)

Über die Ätiologie der Rachitis im Säuglingsalter[1]).

Beobachtungen über Prophylaxe und Heilung.

Von
Harriette Chick, D. Sc., **Elsie J. Dalyell**, M. B., **Margaret Hume**, **Helen M. M. Mackay**, M. R. C. P., M. D. (Beit Memorial Fellow) und **H. Henderson Smith**, R. R. C.

Unter Mitarbeit von
Dr. **Hans Wimberger**, Röntgenologen der Universitäts-Kinderklinik.

Vorläufige Mitteilung an das *„Accessory Food Factors Committee"* des *Lister Institute* und des *Medical Research Council*.

Mit 2 Abbildungen im Text.

(Eingegangen am 14. Juli 1922.)

Untersuchungen über den Einfluß des Phosphorlebertrans auf den Stoffwechsel eines rachitischen Säuglings.

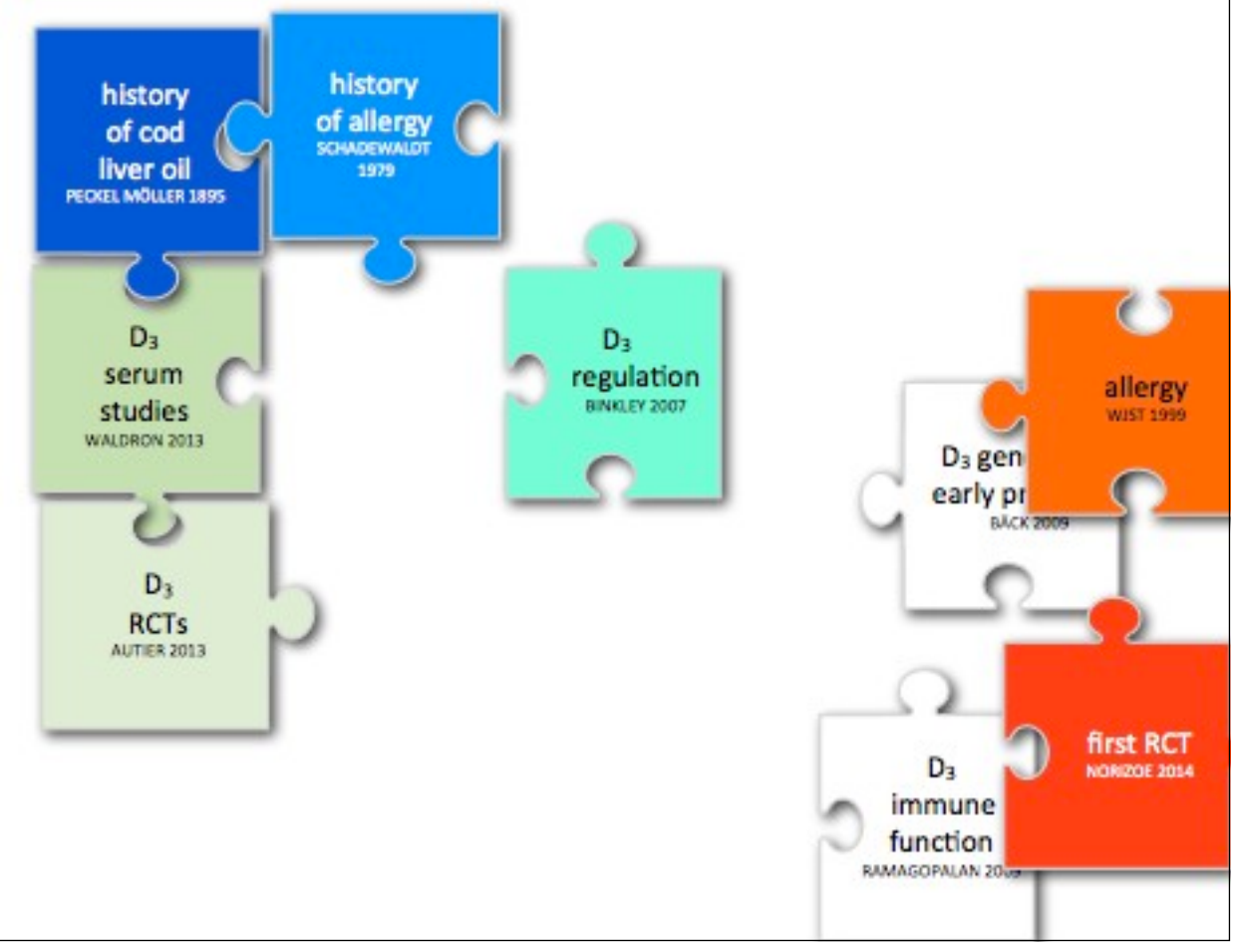
Von
Dr. **Caroline Towles.**

(Aus der Universitätskinderklinik in Breslau [Direktor: C. v. Pirquet]).

(Eingegangen am 11. Dezember 1916).

Obwohl die Literatur über Rachitis eine Anzahl von Stoffwechseluntersuchungen enthält, so bringen doch nur wenige unter ihnen eine vollständige Analyse der Nahrung, des Urins und der Faeces.

Birk[2]) machte auf diese Tatsache aufmerksam und veröffentlichte die Resultate von vier Versuchen. Zwei seiner Kinder waren gesund, zwei zeigten deutliche Rachitis. Er verfolgte den Stoffwechsel bei allen Kindern zuerst in einer 3tägigen Periode ohne Behandlung, und dann in einer ebenfalls 3tägigen Periode bei Zufuhr von Phosphorlebertran. Er fand, daß die Stickstoffretention bei beiden rachitischen Kindern in der Lebertranperiode etwas geringer war als in der Vorperiode, während die Calciumretention deutlich, die Magnesiumreten-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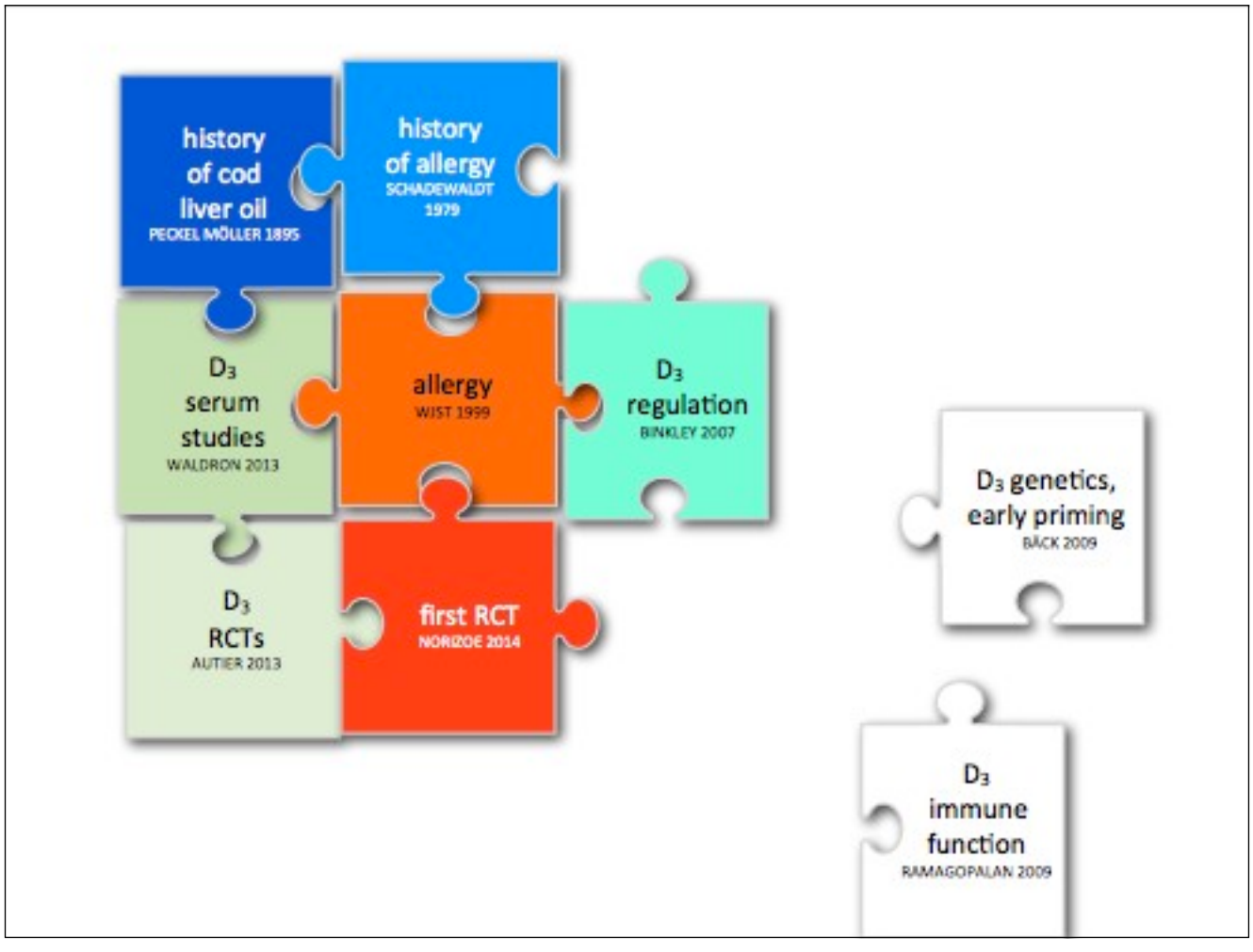
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Hypothesis paper

M. Wjst
S. Dold

Genes, factor X, and allergens: what causes allergic diseases?

Authors' affiliations:
M. Wjst, S. Dold, GSF National Research Center for Environment and Health, Oberschleissheim, Germany

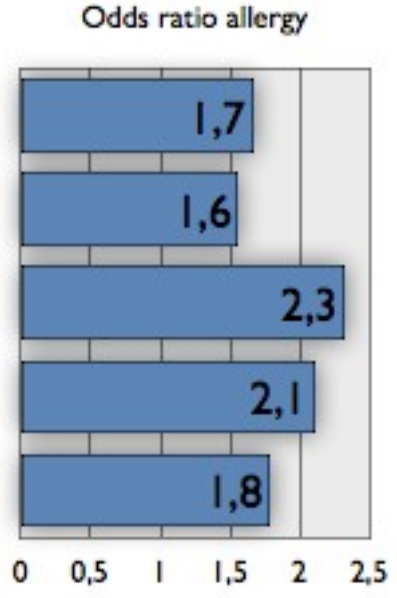
Key words: allergy; asthma; cholecalc

Genetic disposition and allergen
the development of allergic d
be involved is the nutritio

newborn gut
+ vitamin D
+ allergen
= sensitization

Birth cohorts find an association of D3 supplements and allergy

author	N exposure	outcome
Hyppönen 2003	12,058 D3 regular/irreg	atopy 31 y
Milner 2004	8,073 multivit y/n	food allergy
Kull 2006	4,089 water/oil D3	allergic rhinitis 4 y
Chatzi 2007	690 margarine y/n	allergic rhinitis 7-18 y
Nja 2005	502 cod liver oil y/n	sensitization 6-16 y



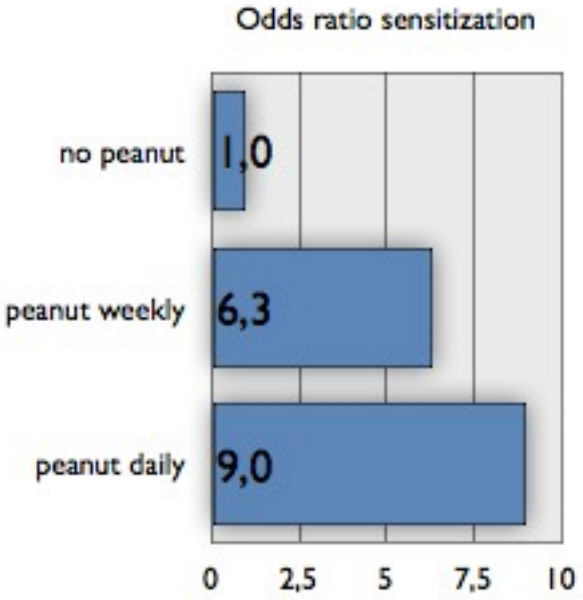
Guy des Montis 1993
(Vautrin-Moneret 1991)

open trial: identification of allergen source

methods: 122 babies received D3 either with or without peanut oil (allergen)

outcome:
peanut RAST sensitization at month 7-60

no peanut N=2 (5%)
weekly N=11 (25%)
daily N=9 (32%)



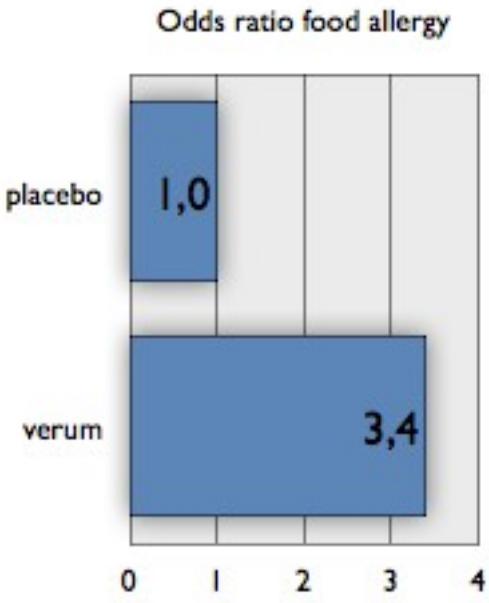
Norizoe 2014
A first RCT

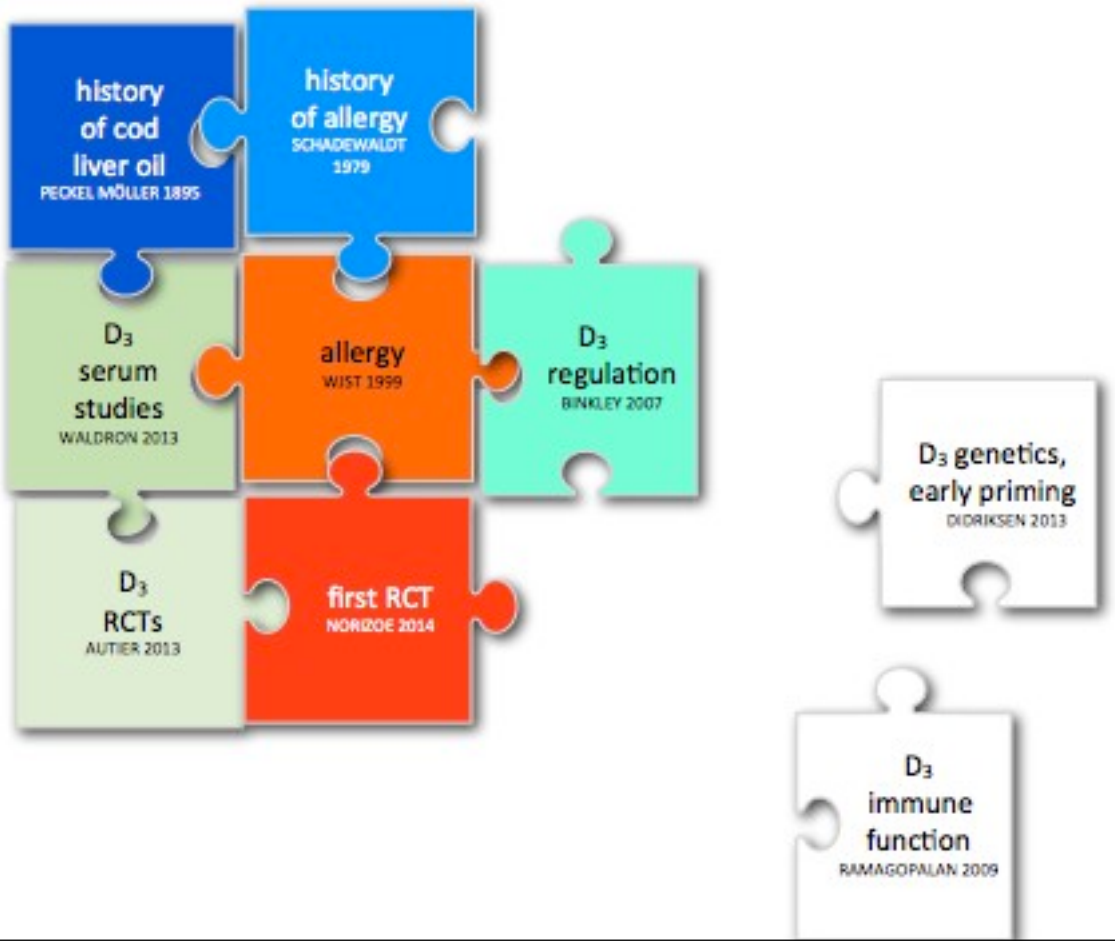
triple blind: eczema severity SCORAD index

methods: 82 of 164 eczema babies received 800 IU/d D3 for 20 month

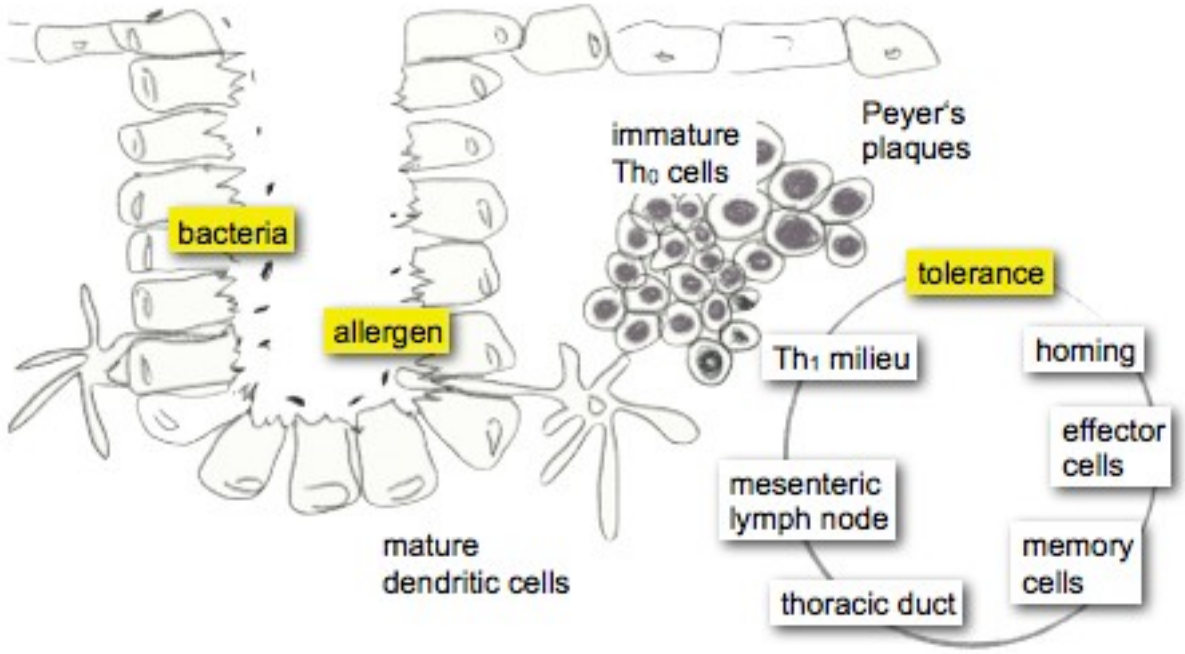
secondary outcome:
doctor diagnosed food allergy
placebo 3/40 (7.5%)
verum 10/39 (25.7%, $p<0.03$)

con: dropout>20%!
borderline significance

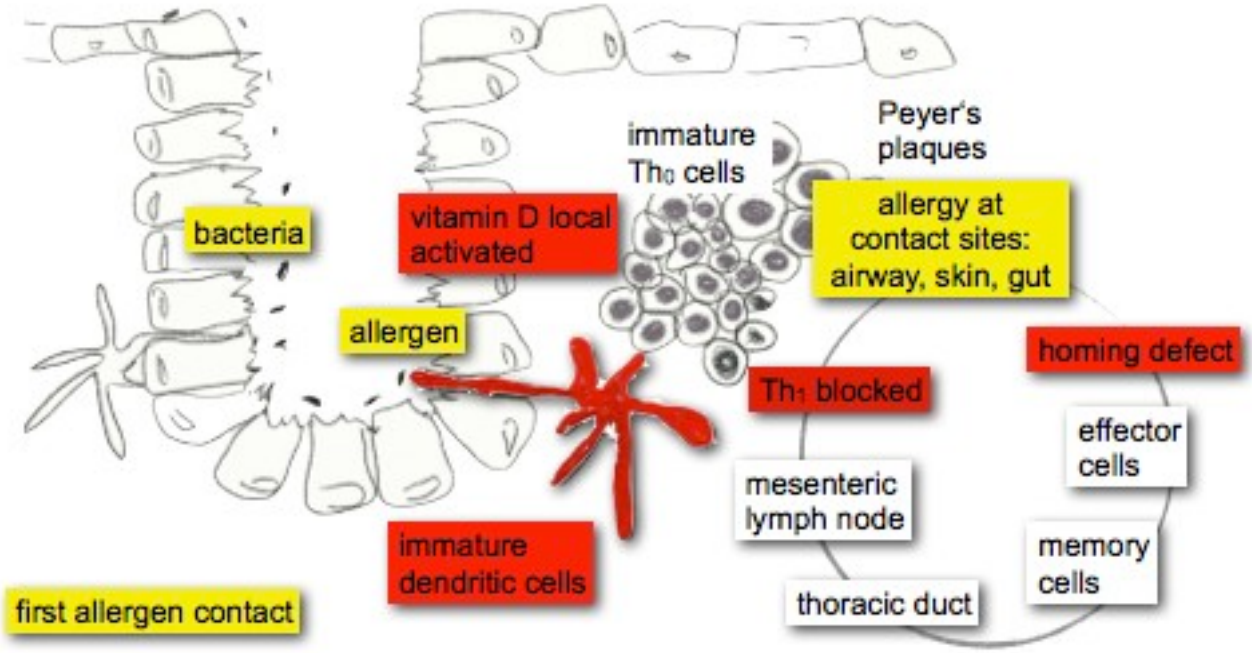




First ever allergen contact: NORMAL



First ever allergen contact: COMPROMISED



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Eur. J. Immunol. 2009. 39: 469–480 DOI 10.1002/ejl.200838367 Immunomodulation

Immunology

Imprinted DC mediate the immune-educating effect of early-life microbial exposure

Lei J... ang, Yijun Fan, Megan Yang, Hongyu Qiu and ...

DC

Immunology

IMMUNOLOGY ORIGINAL ARTI...

1,25-Dihydroxyvitamin D_3 inhibits proliferation but not the suppressive function of regulatory T cells in the absence of antigen-presenting cells

Treg

Summary

Vitamin D_3 is known to induce regulatory T (Treg) cells by rendering antigen-presenting cells tolerogenic, its direct effect on human naturally occurring Treg cells is unclear. Here, we investigated if and how 1,25-dihydroxyvitamin D_3 [1,25(OH)$_2$$D_3$] can directly affect the proliferation and function of human naturally occurring Treg cells in vitro. First, we

Th1

OPEN ACCESS Freely available online PLoS Genetics

Expression of the Multiple Sclerosis-Associated MHC Class II Allele *HLA-DRB1*1501* Is Regulated by Vitamin D

Sreeram V. Ramagopalan[1,2*], Marelle J. Maugeri[1*], Lahiru Handunnetthi[1,2], Matthew R. Lincoln[1,2], Sarah-Michelle Orton[1,2], David A. Dymont[1,2], Gabriele C. DeLuca[1,2], Bianca M. Herrera[1,2], Michael J. Chao[1,2], A. Des... ...ghe[1*]

HLA

microbiome

Vitamin D Regulates the Gut Microbiome and Protects Mice from Dextran Sodium Sulfate–Induced Colitis[1–3]

Jie Hui Ooi,[4,5] Yanfei Li,[5] Connie J. Rogers,[6,7] and Margherita T. Cantorna[6,7*]

[4]Department of Veterinary and Biomedical Sciences, [5]Department of Biochemistry and Molecular Biology, [6]Department of Nutritional Sciences, [7]Center for Molecular Immunology and Infectious Disease, and [8]Pathobiology Graduate Program, Pennsylvania State University, University Park, PA

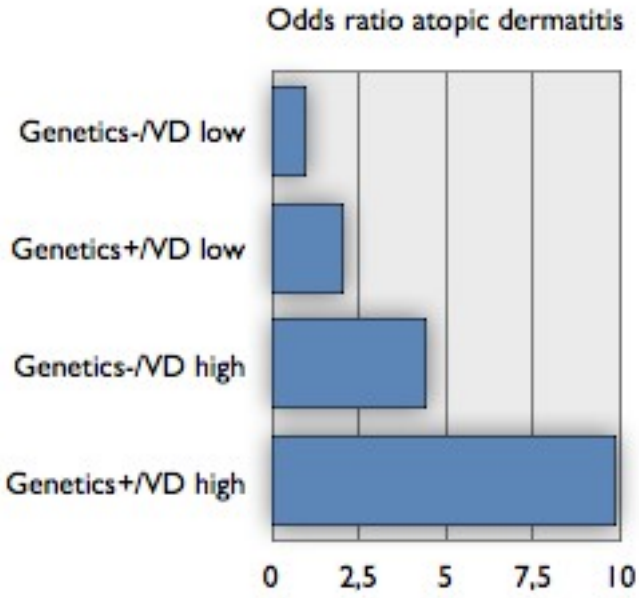
Bäck 2009
The importance of genetics

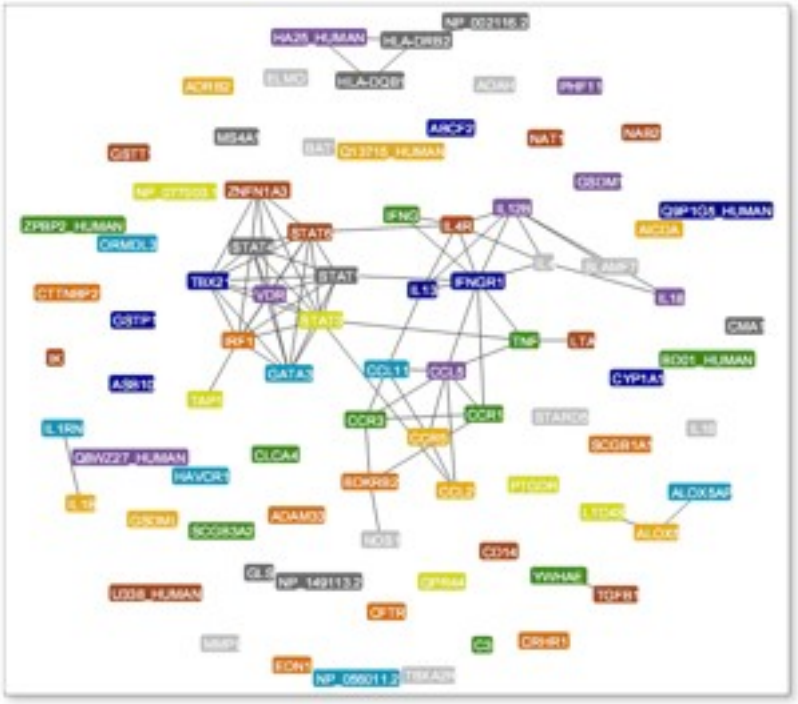
206 babies

56 questions
breastfeeding

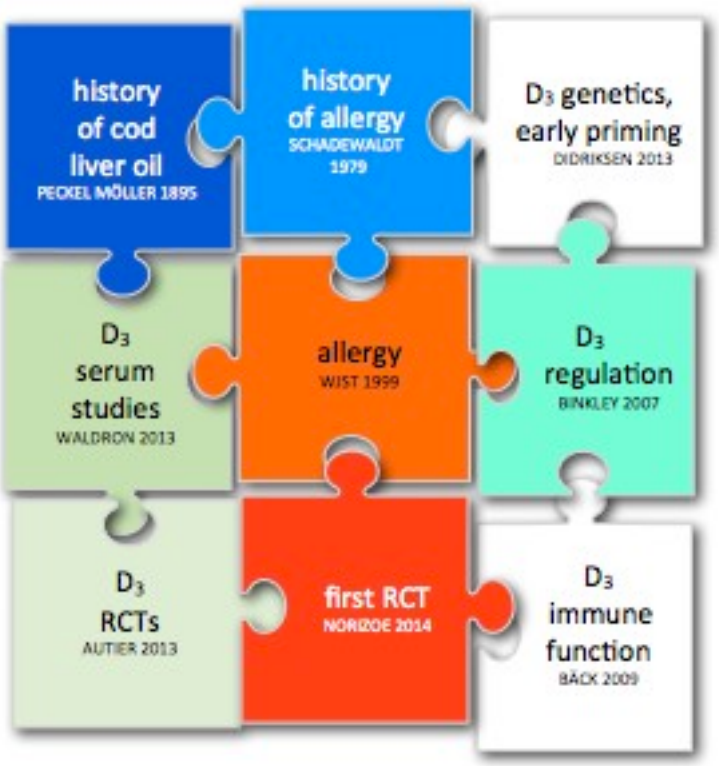
400 IU D3 daily
6 w - 24 m

re-examined
at age 6





IL12B
OPN
ADAM33
IFNγ
ADRB2
CARD15
IL4R
FLG
SOCS3
VDR
GC
TNF
IL8
IL1RN
ALOX5
[ZNFN1A3]
CD14
S100A7
CD14



Peter Granser. Sun City, 1993. „Paar im Pool"