

100 years from the birth of Georg Rajka – atopic dermatitis over a century and more!



**G Rajka centennial
birth anniversary**



Johannes Ring & Alain Taïeb
Munich TUM, Bordeaux INSERM 1312

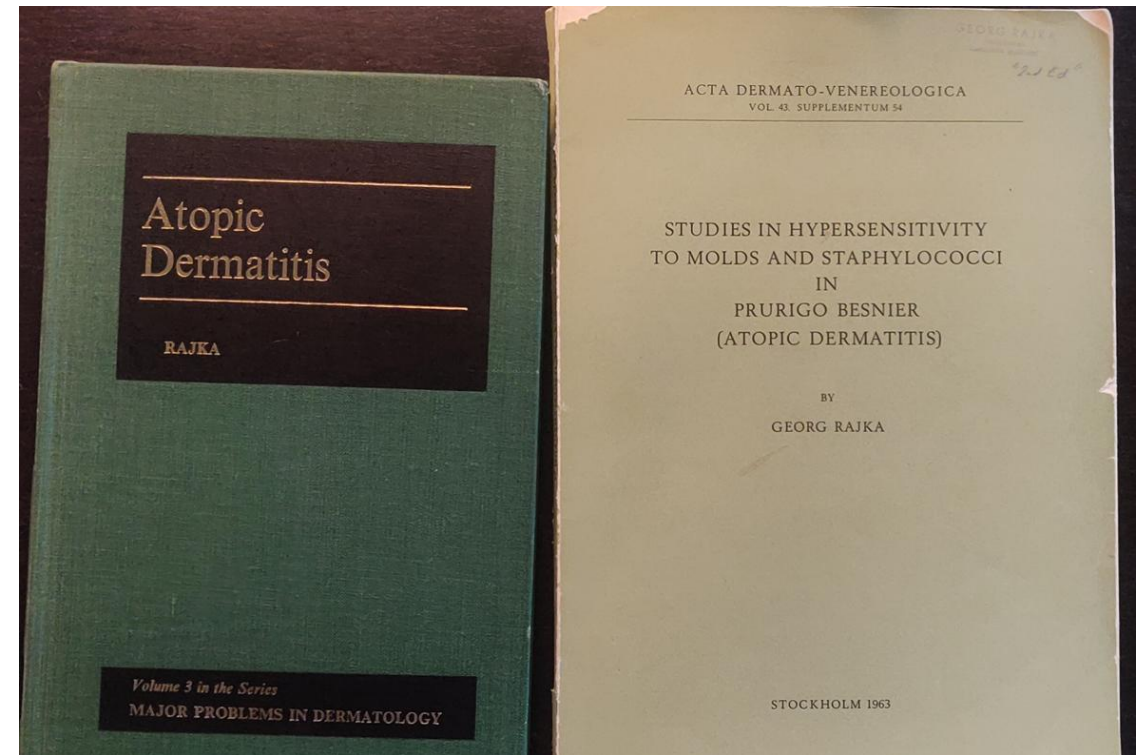
*15th Georg Rajka International Symposium on Atopic Dermatitis
Melbourne 2025*

« Memory, History and Retelling »

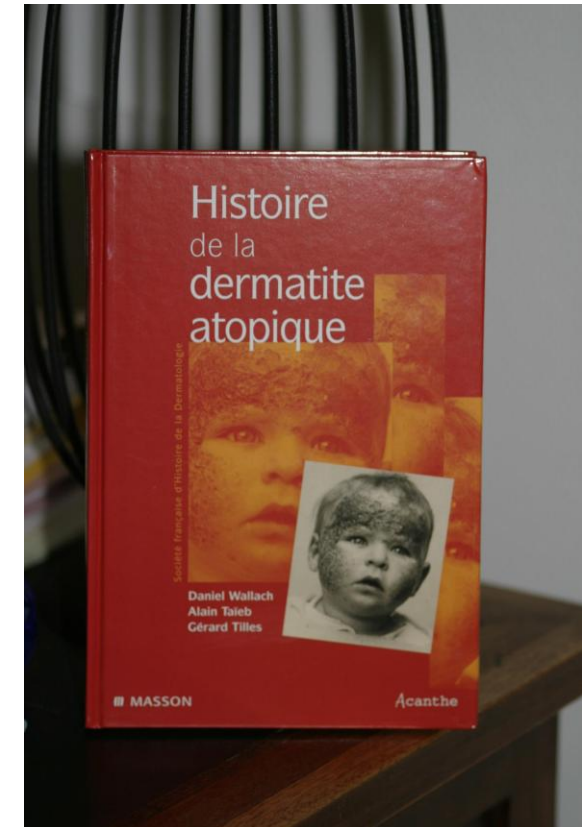


Georg Rajka

- **10 march 1925:** born in Budapest
- Medical school and dermatovenereology in Budapest (1952)
- 1956 soviet occupation, migration to Sweden, Karolinska
- 1959 marriage to Susanne Rajka (2 sons)
- **1963 PhD thesis (Prurigo Besnier)**
- 1970 Associate professor
- 1971 Head of Dermatol Dept Umea and call to Oslo
- 1971 – 1995 Director Dermatology Oslo Rigshospitalet
- **16 March 2013:** died shortly after his 88th birthday



**The Prehistory of Atopic
Dermatitis: From Eczema and
Prurigo to a Unified Concept**
The Genesis of a Clinical Entity
(1800–1933)



From (1800) Willanism to the modern period (second half of XIXth century)

The Willanist doctrine -Willan-Bateman- was based on morphology. Despite a confusing nomenclature, two groups could be progressively separated:

- **The Eczema group “The Weeping Disease”:**
 - Defined clinically in the early 1800s
 - Characterized by acute, vesicular, and weeping lesions typical of later Wilson’s infantile eczema.
 - Often reserved for conditions with identifiable external causes (contact, irritants).
- **The Prurigo group “The Itching Papule”**
 - The term derives from the Latin *prurire* (to itch).
 - **Lichen** was a term also used in this group
 - Characterized by chronic, intensely pruritic papules, often leading to secondary skin thickening (*lichenification of Brocq*).

Infantile eczema (Wilson)



Photo (top) and moulage (bottom)
Hôpital Saint Louis, Paris

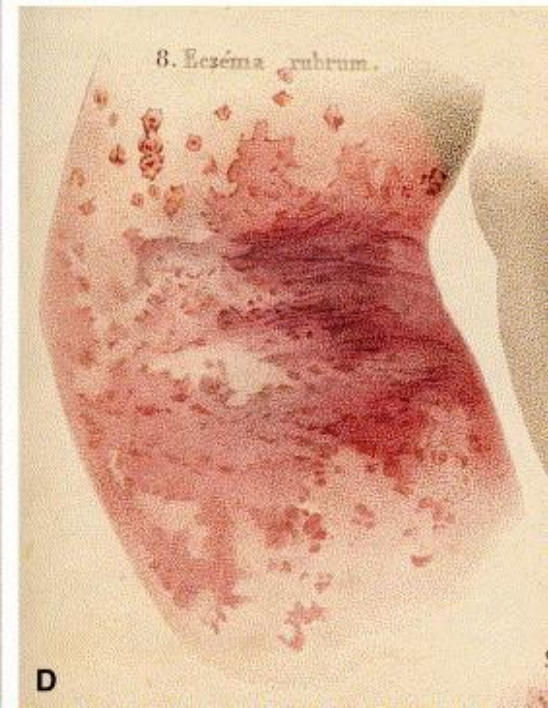


Prurigo Besnier

First representations of atopic dermatitis

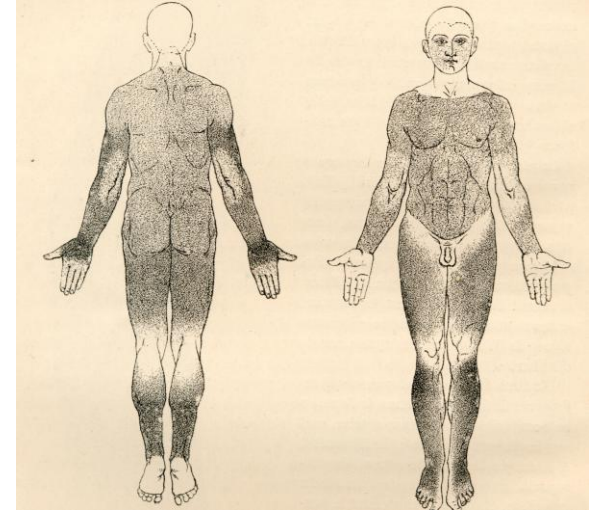
- A, *Strophulus confertus* (Willan, 1796).
- B, *Lichen agrius* (Willan, 1796).
- C, *Porrigo larvalis* (Bateman/Willan, 1816).
- D, *Eczema rubrum* (Rayer, 1835).

Wallach D, Coste J, Tilles G, Taïeb A. The first images of atopic dermatitis: an attempt at retrospective diagnosis in dermatology. *J Am Acad Dermatol*. 2005 Oct;53(4):684-9.



Hebra's Constitutional Prurigo

- **Concept:** Isolation of "Constitutional Prurigo" (also called *Prurigo Ferox*).
- **Key Contribution:** Hebra described a **chronic, recurrent, intensely pruritic disorder** beginning in infancy with urticarial-like rashes, progressing to firm papules on the trunk and limbs.
- By defining it as a "**constitutional**" (**endogenous**) **disorder**, Hebra began to separate a group of chronic itchy diseases from the vast category of simple, external eczema.



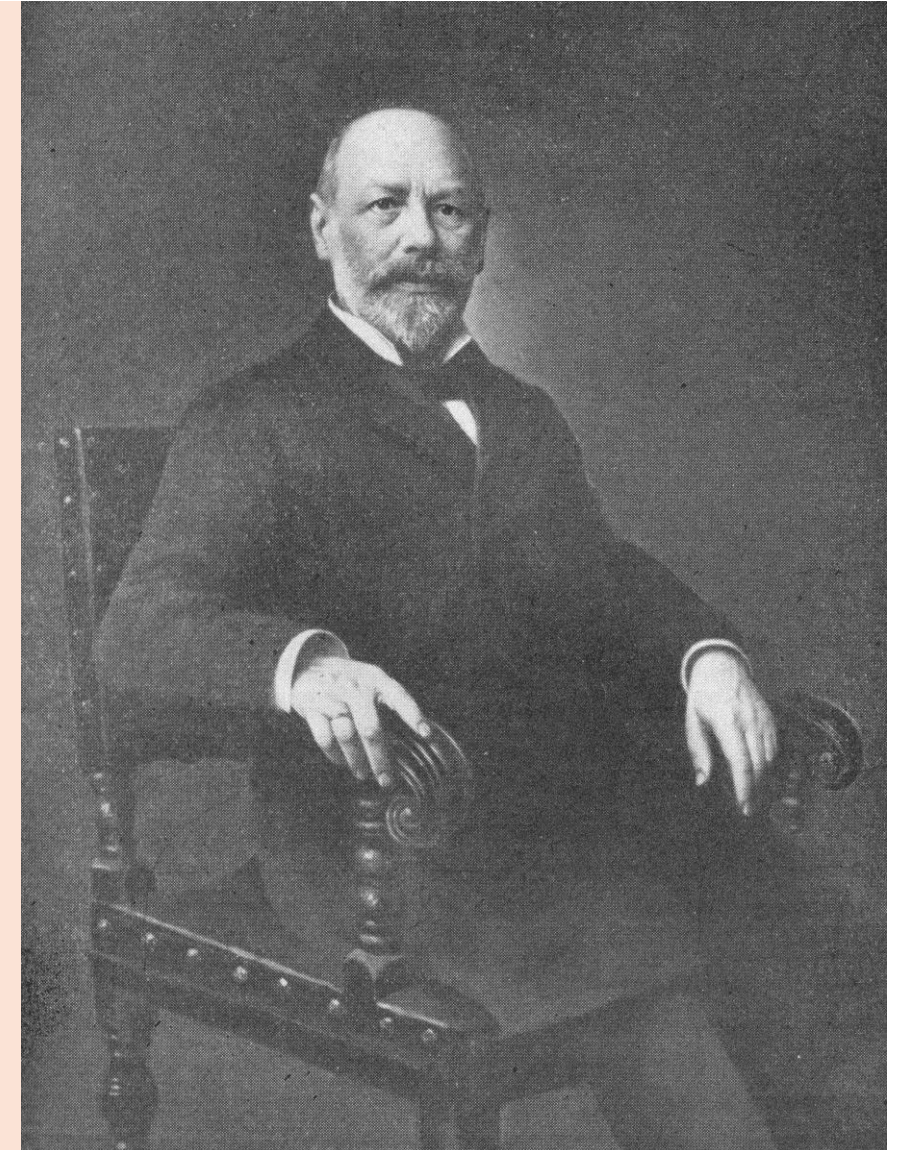
Ferdinand Hebra (1816–1880)

**« Reverse pattern » AD with
FLG LoF mutations: the
model for Hebra's prurigo?**



Kaposi Challenging Hebra

- **Hebra's description** was later criticized for its rigid extensor distribution and confusion with other forms of prurigo.
- **Moriz Kaposi** (Hebra's successor) offered a rebuttal to Hebra's theory, challenging the original definition and its relation to urticaria and distribution patterns.
- This intense late 19th-century debate focused the dermatological community on the **need for a more precise classification of chronic, relapsing, pruritic diseases.**



Moritz Kaposi (1837-1902)

QUESTIONS FOR DISCUSSION.

(1) Should Hebra's name be dropped out of the nomenclature of prurigo ?

(2) Should the term " prurigo " be limited to affections presenting the papule described by Hebra and the subsequent lichenification ?

(3) Does prurigo begin as an urticaria ?

(4) Does the itching precede the papule, or the papule the itching, or is there no invariable order ?

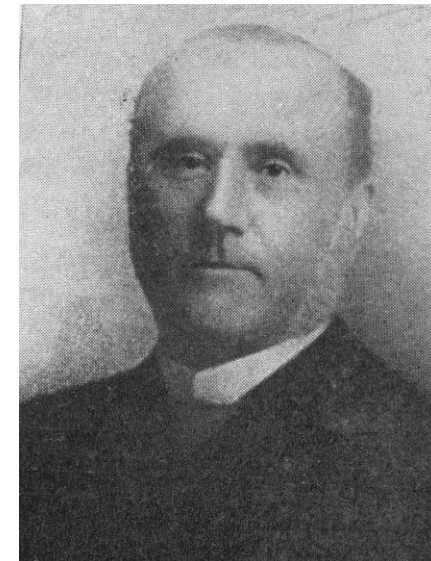
(5) Is prurigo curable ?

(6) What are the best methods of treatment ?

(7) Why is not lichenification always a sequel of much scratching?

1892: Prurigo diathésique/Diathetic prurigo

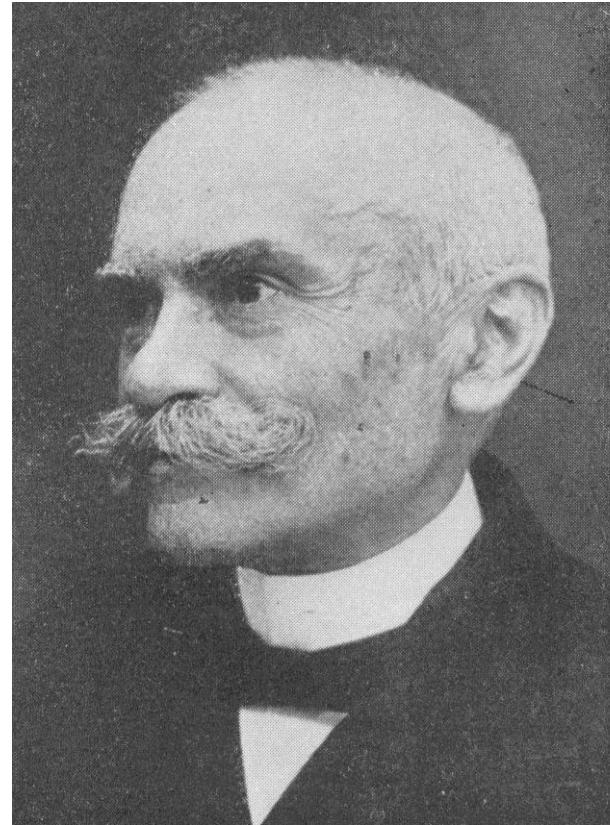
- **1892: Besnier** described *Prurigo Diathésique* (Diathetic Prurigo).
- Besnier's concept prefigures what we now call Atopic Dermatitis.
 - He describes a **spectrum** disorder that incorporates both **infantile eczema** and **chronic prurigo** and **suggests a link to asthma**
 - The term "**diathetic**" refers to a general hereditary or constitutional predisposition to disease.
- **Clinical Continuum:** Besnier saw the disease as a progressive process:
 - **Infantile Eczema** (acute, oozing phase)
 - **Prurigo Diathésique** (chronic, lichenified phase).
- **Itch as the Cardinal Symptom**



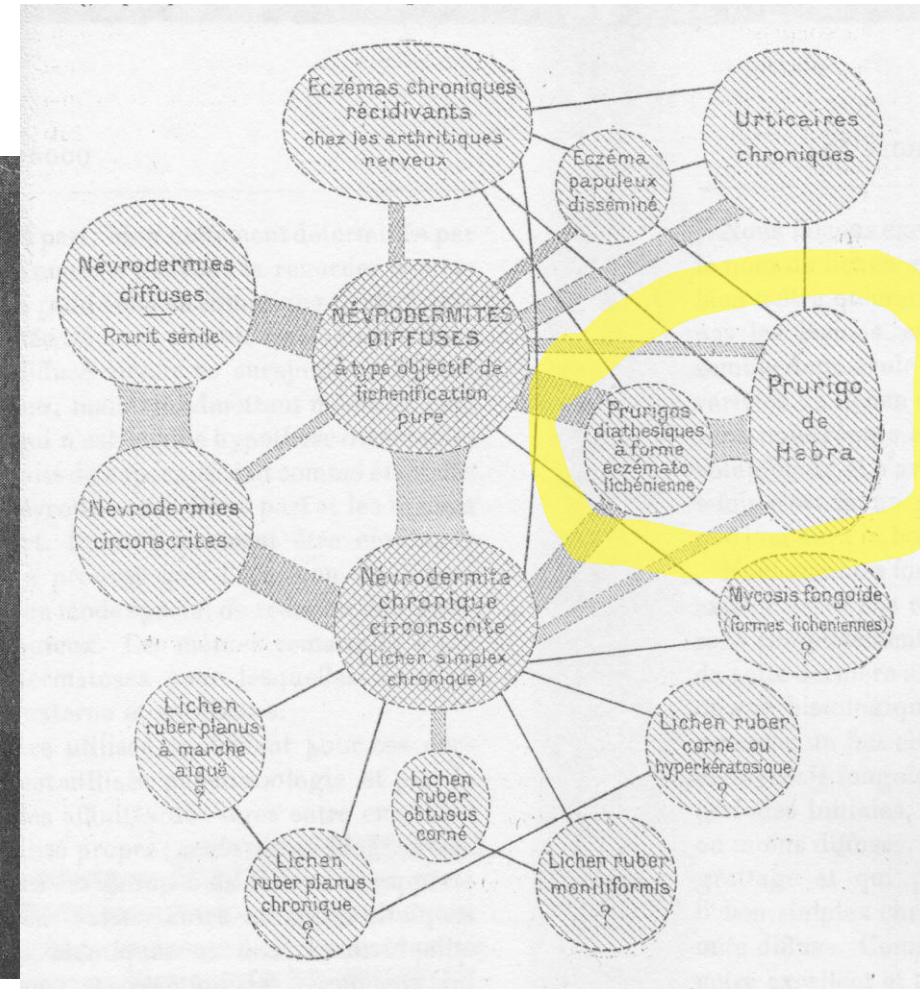
Ernest Besnier (1831-1909)

Diathetic Doctrine and Neurodermatitis

- **The French School: Besnier's** work was part of a larger effort by French dermatologists (**Vidal, Jacquet, Brocq**) to delineate a group of diseases featuring **chronic relapsing lichenified lesions**.
- **Prurigo Diathésique** incorporated the key features of modern AD:
 - **Chronic, relapsing course.**
 - **Intense pruritus.**
 - **Lichenification** (skin thickening from scratching).
- **Diathesis** moved the focus from individual lesions (vesicle = eczema; papule = prurigo) to the **patient's underlying constitutional tendency (neurodermatitis, Brocq)**



Louis Brocq 1856-1928



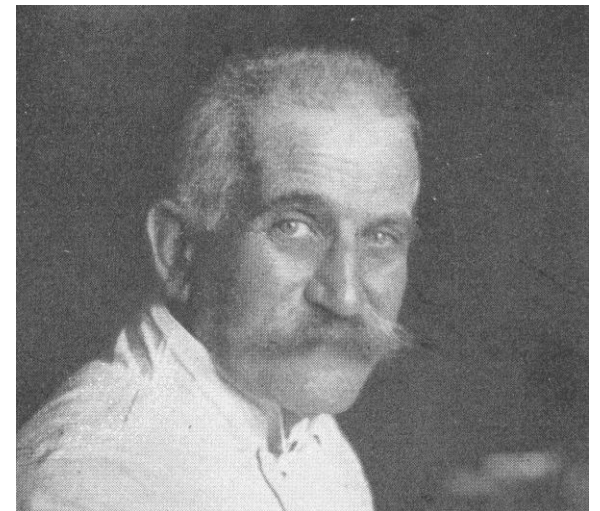
**Le graphique des
Névrodermites, 1896**

The Final Years of the Prehistory (1900–1933)

- **Nomenclature Confusion:** Even after Besnier, the condition was known by many names, including: *Prurigo Hebra*, *Prurigo Besnier*, *Disseminated Neurodermatitis*, and *Eczema*.
- **The "Neuro" Influence:** *Neurodermatitis* was popular, suggesting that emotional stress and the nervous system were primary causes (stress often worsens the itch-scratch cycle).
- By the 1920s, the condition was understood as a distinct, chronic, constitutional dermatitis, **but a unified name and clear etiology were still missing**.
- The emergence of hypersensitivity, allergy and **contact dermatitis (Jadassohn, Bloch)** was key



Bruno Bloch 1878-1933

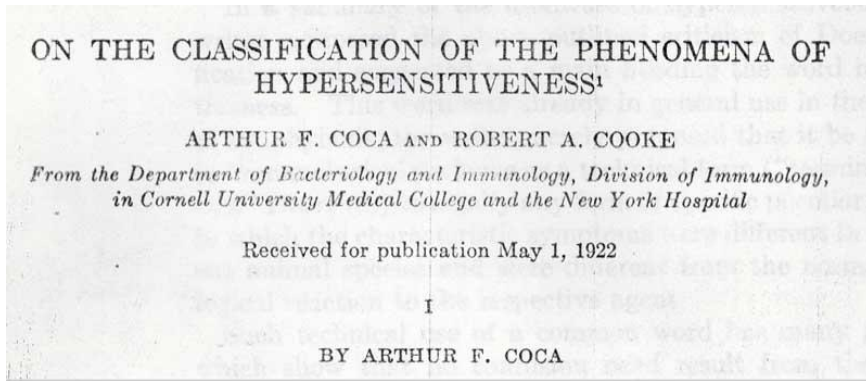


Josef Jadassohn 1863-1936

**1923: Coca and Cooke coined the term "Atopy"
(from the Greek atopos, meaning "out of place").**



Arthur F. Coca (1875–1959)



Hypersensitiveness

Normal

Dermatitis venenata
Serum sickness

Abnormal

Anaphylaxis
Infections (e.g. tuberculosis)
Atopy



Robert Cooke (1880–1960)

Atopy: applies to asthma and rhinitis.
Hereditary hypersensitiveness to common antigens

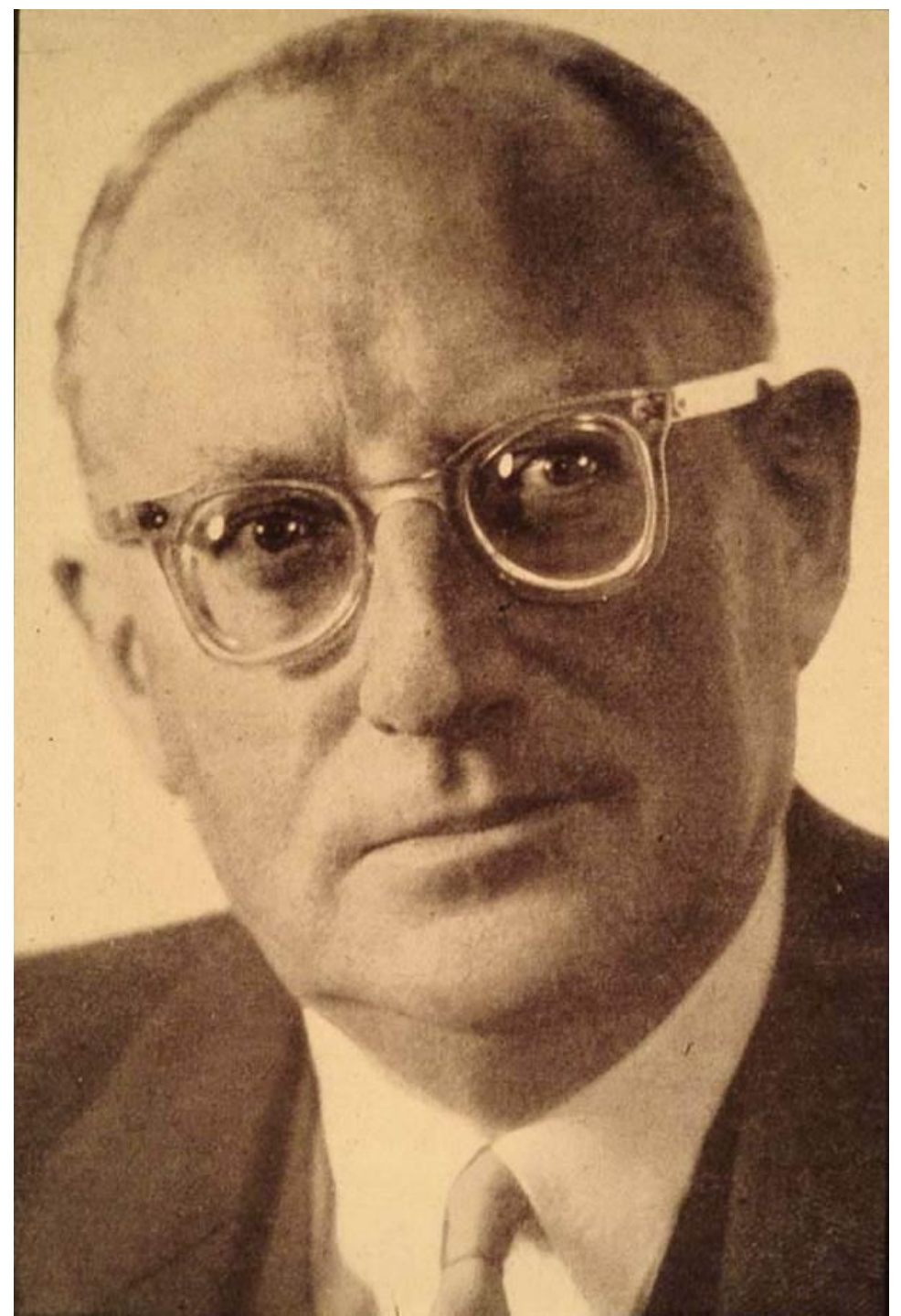
In each decade since the atopic state was conceived it has required some redefinition of its frontiers in the light of new research.... (Arthur Rook, 1974)

Alfred Marchionini 1899-1965

„Säure-Mantel....

.... The acid mantle..“

*Schade, H., Marchionini, A. Der Säuremantel der Haut
(Nach Gaskettenmessungen). Klin Wochenschr 7, 12-14 (1928).*



1933: « ...this is best called atopic dermatitis » Wise & Sulzberger 1933

Wise & Sulzberger criteria: the atopic diathesis is *first*

- 1 – family history of atopy (Coca & Cooke, 1923)
- 2 – personal history of infantile eczema
- 3 – location of lesions (elbow and popliteal folds, neck, thorax, face, eyelids)
- 4 – greyish/brownish discoloration of the skin
- 5 – no true vesicles clinically and histologically
- 6 – vasomotor instability/irritability
- 7 – negative skin patch tests to contact reactants
- 8 – numerous positive tests of immediate type (intradermal or after scratching) (Blackfan, 1916)
- 9 – presence of reagins in serum (Prausnitz & Küstner, 1921; Coca & Grove, 1925)



Marion B Sulzberger (1895-1983)

Atopic Dermatitis in the 20th century

- 1923 Coca und Cooke Atopy
- 1929 Rost Early-/late-exsudative eczematoid
- **1933 Sulzberger Wise Atopic dermatitis**
- 1962 Schnyder/Borelli Neurodermitis constitutionalis sive atopica
- 1966/67 Ishizaka/Johansson Immunoglobulin E
- 1982 Hanifin/Rajka Diagnostic criteria
- 1988 Mossman/Coffman Th1/Th2, Interleukin 4
- 1989 Wüthrich Intrinsic vs extrinsic Neurodermitis
- 1989 Platts-Mills/Ring Atopy Patch Test
- 1993 Taieb/Stalder SCORAD
- 1992 Novartis Anti-IgE (Omalizumab)
- 1999 Wahn/Ring/Gieler Neurodermitis-Schulung/“Eczema school“



Teruko and Kimishige Ishizaka



Hans Bennich and S.G.O. Johansson

1966:Discovery of Immunoglobulin E

Atopic dermatitis in the 21st century

- 2001 Fujisawa Tacrolimus ointment
- 2002 Novartis Pimecrolimus cream
- **2006 McLean/Irvine** **Filaggrin mutations IV/AD**
- 2016 Sanofi/Regeneron Dupilumab (anti-IL4R/13R)
- *Today* *>100 clinical trials*

„Brave new world“ of new substances

Biologics: *Tralokinumab, Lebrikizumab, Nemolizumab, Amlitelimab etc,*
Janus kinase (JAK) Inhibitors
Phosphodiesterase inhibitors....

Georg Rajka and AD

- Starting with itch studies
- Thesis on Prurigo Besnier 1960/1961
- **Pathophysiology of itch**
- Role of allergy
- Decreased rates of delayed type hypersensitivity
- Non-immunological vascular responses

- Organization of International Symposia on Atopic Dermatitis (1979 – 1994)

3. Itch in Atopic Dermatitis

SHORT SURVEY OF ITCH

The central role played by pruritus in atopic dermatitis was stressed in Chapter 2, and it is apposite to its importance to present a short survey of pruritus in general. Tissue injury or an immune reaction produces an initial chemical stimulus which, possibly by kinase production and proenzyme activation (Cormia, Dougherty and Unrau, 1957), liberates proteolytic enzymes; these latter either are mediators of pruritus or liberate such mediators. Thus, not only proteolytic enzymes of the endopeptidase variety but histamine which they liberate (Rocha e Silva, 1940; Craps and Inderbitzin, 1957) are all assumed to be possible itch mediators. On the other hand, the role of a peptide, which is not bradykinin (Cormia and Dougherty, 1960), has, as yet, not been confirmed. In ordinary skin inflammation, for instance, allergic reactions (Ungar and Hayashi, 1958) release proteinases from the epidermis, blood and cellular infiltrates, or from bacteria or fungi. The activity of these proteinases in tissues is complex, as it may be dependent on several factors including inhibitors (Arthur and Shelley, 1958). Itch has been induced by intra-cutaneous injection of endopeptidases in dilutions found in clinical practice; and papain, which acts without either liberating histamine or producing visible signs, and trypsin, which does act in part as an histamine liberator, are the two best-studied representative substances (Arthur and Shelley, 1955, 1958; Hägermark, Rajka and Bergqvist, 1972). Histamine produces pruritus (Cormia, 1952; Cormia and Kuykendall, 1953), as can be demonstrated by injecting it intracutaneously in concentrations as low as 10^{-4} . However, as wealing is produced by concentrations as low as 10^{-8} , it is felt that pruritus is independent of any overt vasodilatory reaction, despite a possible connection between itch and the initial phase of vasodilatation, especially in clinical situations.

ITCH IN ATOPIC DERMATITIS

39

Table 3.2. Itch duration tests in patients with atopic dermatitis, various eczematous lesions and psoriasis (involved skin)

| Itch duration | I. Atopic dermatitis | II. Various eczematous patients | III. Psoriasis |
|----------------------------|----------------------|---------------------------------|----------------|
| a. Over 2 minutes | 23 | 1 | 1 |
| b. Between 1 and 2 minutes | 2 | 20 | 17 |
| c. Less than 1 minute | — | 4 | 7 |
| Total | 25 | 25 | 25 |

χ^2 test and significance I to II for a: $P < 0.1\%$.

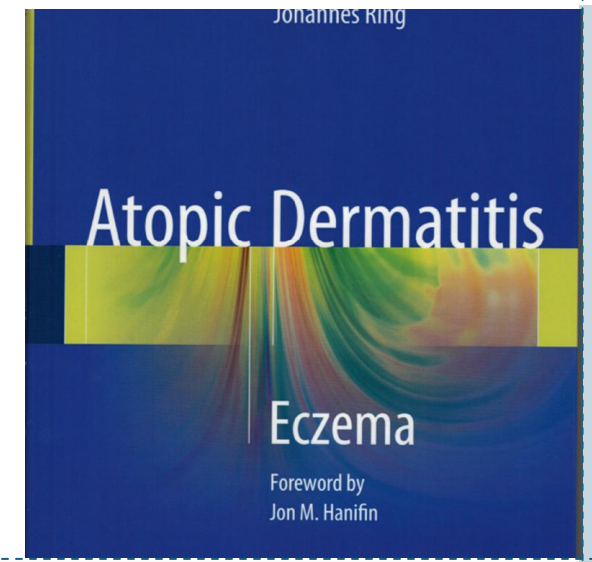
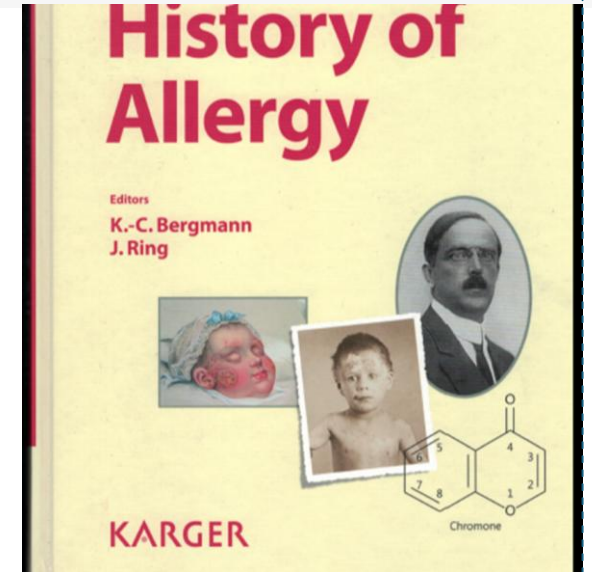
How atopic dermatitis was represented internationally 60 years ago:

Congressus Mundi Dermatologiae
World Congress Dermatology
October 1977 Mexico City (5 days)

- 1 Workshop „Atopic Dermatitis“
- Chairpersons J. Hanifin, G. Rajka

- **15 Participants**

Ebner, Juhlin, Lobitz, Öhmann, **Ring**, Saurat, Schöpf, Uehara, Wüthrich, Yoshida et al



International Symposia on Atopic Dermatitis

- 1979 Oslo G Rajka
- 1984 Loen G Rajka
- 1988 Oslo G Rajka
- 1991 Bergen G Rajka
- 1994 Lillehammer G Rajka
- 1996 Aarhus K Thesdrup-Pedersen,
G Rajka, J Ring

Atopic Dermatitis

Editor

LASSE R. BRAATHEN

Oslo 1988

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Atopy patch test (APT)



Epicutaneous patch test with allergens known to elicit IgE-mediated reactions, for the provocation of eczematous skin lesions due to these allergens

Ring J et al. JACI 1989; 82: 195

SCORAD Europäische Experten-Gruppe für Atopische Dermatitis

Patient: Name/Vorname

Geburtsdatum

Besuchsdatum

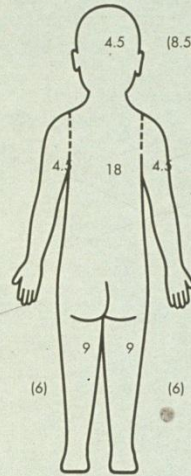
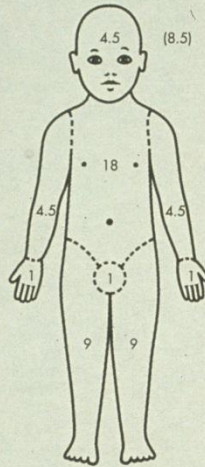
Eingesetztes topisches Steroid

(g)

Wirkstoff (Handelsname, Konzentration)

Menge/Monat

Anzahl der Erytheme/Monat



Ziffern in Klammern
für Kinder unter 2 Jahren

A: Ausmaß

Bitte geben Sie die Summe der betroffenen Hautareale an.

B: Intensität

Bemessungswerte

Angaben zur Intensität (üblicherweise typische Stellen)

0 = keine 1 = leicht 2 = mäßig 3 = stark

Kriterien

Intensität

Kriterien

Intensität

Erythem

Exkoriation

Ödem/Papelbildung

Lichenifikation

Nässen/Krustenbildung

Trockenheit

Die Hauttrockenheit wird an nicht betroffenen Stellen bewertet

C: Subjektive Symptome

Pruritus und Schlaflosigkeit

SCORAD A/5+7B/2+C

Visuelle Analog-Skala (Durchschnitt für die letzten drei Tage oder Nächte)

0 ||||| 10

Pruritus (0-10)

0 ||||| 10

Schlaflosigkeit (0-10)

Behandlung

Anmerkungen



Mexico, 2002

International Symposia on Atopic Dermatitis: „Georg Rajka Symposia“

| | | | |
|---------------|-------------|------------------|--|
| • 1th | 1999 | Davos | Ring |
| • 2nd | 2001 | Portland | Hanifin |
| • 3rd | 2003 | Rome | Giannetti |
| • 4th | 2005 | Arcachon | Taieb |
| • 5th | 2008 | Kyoto | Takigawa |
| • 6th | 2010 | Munich | Ring, Behrendt, Darsow |
| • 7th | 2012 | Moshi | Mazenga, Grossmann, Ring, Schmid-Grendelmeier |
| • 8th | 2014 | Nottingham | Williams |
| • 9th | 2016 | Sao Paulo | Takaoka |
| • 10th | 2018 | Utrecht | Bruijnzeel, Hijnen |
| • 11th | 2020 | Montreal | Marcoux, Ramien |
| • 12th | 2021 | Seoul/virtual | Kim |
| • 13th | 2023 | Gdansk | Trzeciak |
| • 14th | 2024 | Doha | Steinhoff |
| • 15th | 2025 | Melbourne | Su |



7th Georg Rajha Meeting

Int. Society for Atopic
Dermatitis (ISAD)

January, 15th - 18th 2012
Moshi, Tanzania.



*Karibu
Sana*

Moshi + Verona
2012:
Official birth of
ISAD



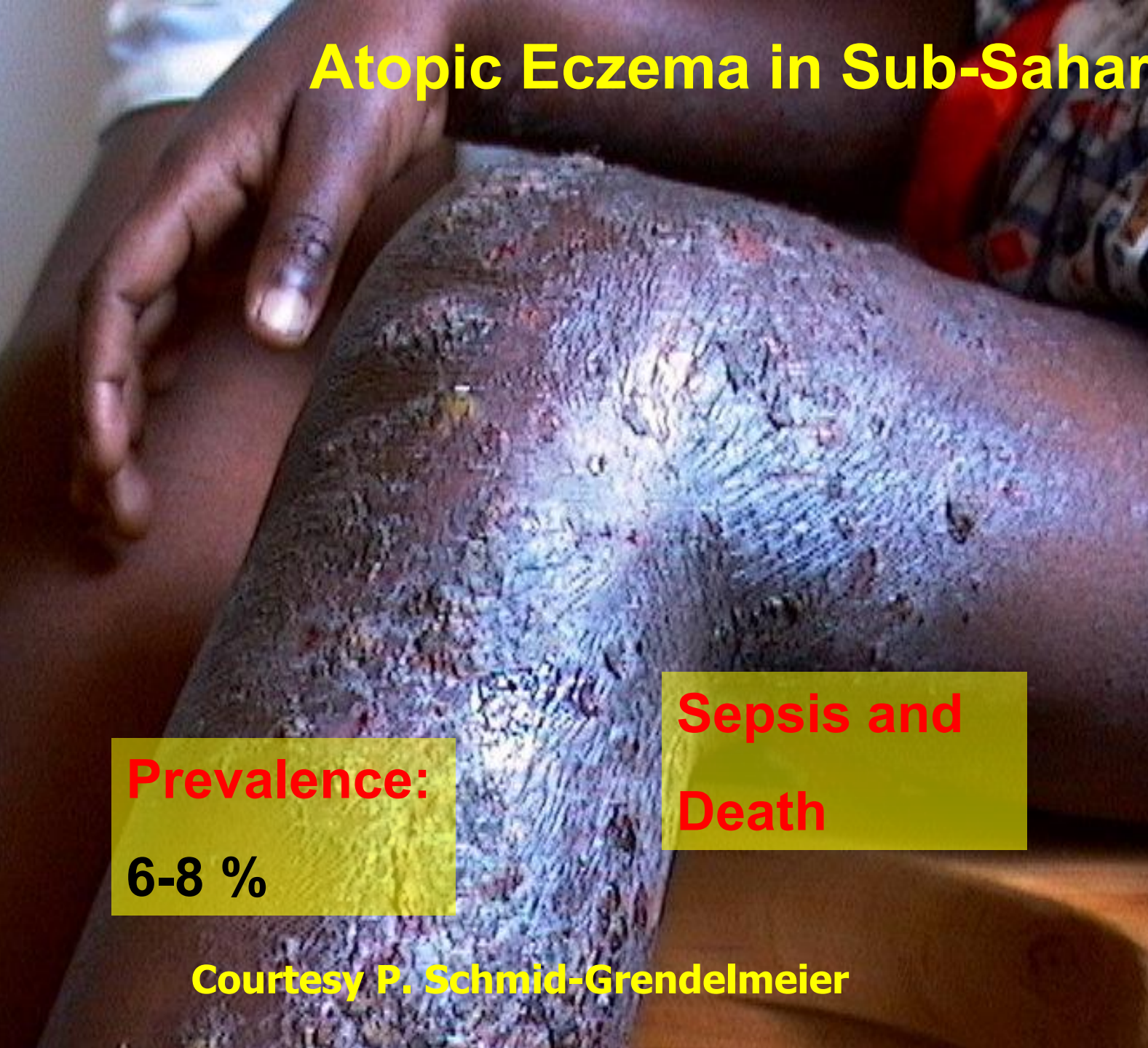
Atopic Eczema in Sub-Saharan Africa

Prevalence:

6-8 %

**Sepsis and
Death**

Courtesy P. Schmid-Grendelmeier



First Georg Rajka Medal for
Jonathan Silverberg
Nottingham 2014





Georg Rajka Medalists

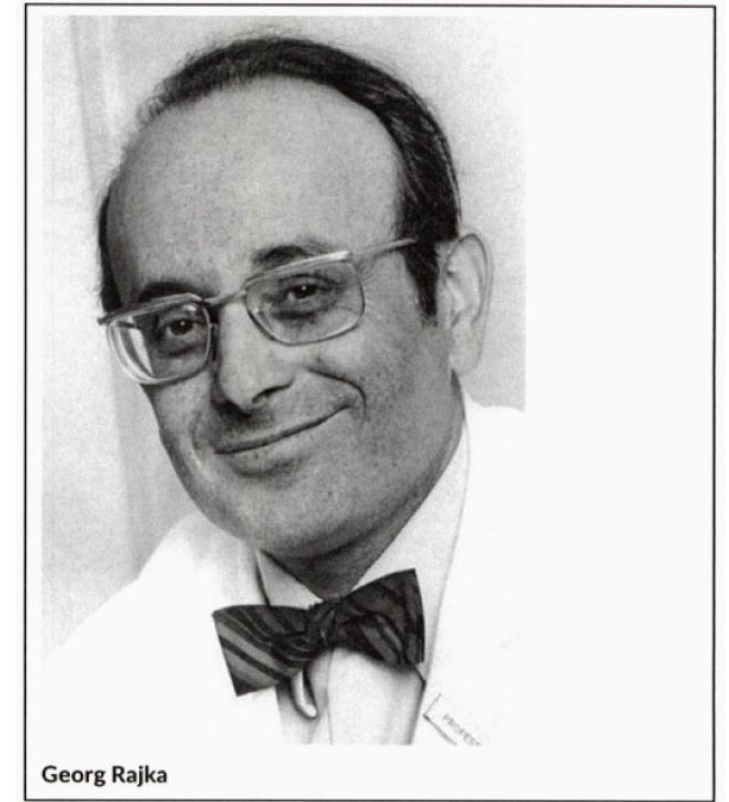
- 2014 Jonathan Silverberg
- 2016 Kilian Eyerich
- 2018 Judith Thijs
- 2020 Lennart Rösner
- 2022 Aaron Drucker
- 2024 Fang Wang
- 2026?? Applications to be sent!

Summary

- Atopic dermatitis was **not compatible with Willanism** and **challenged dermatological classifications**
- Atopic dermatitis was a rather **rare condition around world war II**
- A major breakthrough in pathophysiology was the **discovery of IgE** as reagenic antibodies by Ishizaka (1966) and Johansson (1967)
- There was a **steep increase in prevalence** between 1960 and 2000 leading to enhanced interest in this condition, supported also by **International Symposia** in Norway between 1979 and 1994 organized by **Georg Rajka**
- There the „**diagnostic features of AD**“ (Hanifin and Rajka) were defined.
- Treatment consisted in **topical steroids** (Sulzberger 1952) followed by topical **calcineurin inhibitors** (TCI) around 2000. Then also **AD school** programs were developed
- For severe cases systemic immunosuppression was used like **Cyclosporin A**, or Methotrexate, azathioprin or mycophenolate off label.
- With the development of new specifically targeted **biologics** against mediators of the Th2 response – as **IL 4, IL 13, IL 31** – and of **JAK inhibitors** treatment of AD has been revolutionized since the late 2010s

Literature

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*Ring J. Legends of Allergy and Immunology:
Georg Rajka.
Allergy (2020) 75:2709-2710*



**Thank you George from
the AD community!**