

Caterpillars, Chemists and Contact Dermatitis

A Brief History of Patch Testing

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A Timeline of Key Events

1847

Georg Städel –

The Blotting paper strip technique

The first full description of an irritant being applied to the skin in an investigation.

1895

Josef Jadassohn – ‘The father of patch testing’

Taught by Neisser; practical applications of knowledge, the recognition of both a local reaction and delayed hypersensitivity to simple chemicals when applied to skin.

1897

Jean Henri Fabre – Entomologist, France

Studied the effects of caterpillar hairs on the skin. The first person to identify the individual noxious parts of a whole component.

1911-1937

Bruno Bloch – Switzerland

The first detailed description of methodology and grading skin reactions. The synthesis of Primin, the major allergen in Primula dermatitis. The definition of cross-reactivity. The development of a formative standard series.

1938

Poul Bonnevie

The proto-type for the standard series.

1940s

The spread of the standard series worldwide. Pioneered and spread by Bloch, the concept of the standard series and specific methodology of patch testing was adopted in various cities.

1940s -1950s

Marion Sulzberger

The spread of patch testing across North America.

1940 - 1950s

Conflicts in Europe

As use of the standard series was established in the USA, the concept was less well received in Europe. Hans Stauffer and Werner Jadassohn (son of Josef) were advocates of ‘selected epicutaneous tests’ rather than a restricted series of allergens. Foussereau defended similar opinions in France.

1967

The formation of the International Contact Dermatitis Research Group (ICDRG)

Led by Niels Hjørth

1974

The first Contact Dermatitis Symposium – Denmark

Developing worldwide interest in contact dermatitis

1980s

Identifying allergens

The work of international groups focussed on identifying the potential ‘allergenicity’ of individual chemicals.

1997

The first international standard series was published by the ICDRG.

Regularly updated

Introduction Patch testing is an essential part of current dermatological practice but the development of modern techniques has been slow. First reports of contact dermatitis date back to 7th century BC China ¹, where the sap from Toxicodendron Verniciflum (‘Chinese Lacquer Tree’) was noted to cause significant skin irritation in those handling it. Similar cases appear in Greek and Egyptian literature. Even the Roman author, Pliny the Younger, documents the rash suffered by those cutting pine trees ². By the early 19th century, cases were termed ‘Dermatitis Venenata’ but no understanding of the underlying causes had been determined. This changed in 1847 when the chemist Georg Städel started using his blotting-strip method to look at cutaneous reactions to various irritants ^{1, 3}. However, his work went largely unnoticed and it was nearly half a century before the next milestone in the development of the modern day patch test.

Josef Jadassohn In 1895 in Breslau, Josef Jadassohn was experimenting with the effects of the topical application of mercury ointment, as part of a treatment for pediculosis pubis. During his experiments, Jadassohn was the first to interpret his results as delayed hypersensitivity reactions. Jadassohn recognised the importance of his findings and subsequently invented his ‘Funktionelle Hautprüfung’ (‘functional skin test’), the forerunner of modern patch tests. For this he is often known as the ‘father of patch testing’ ².

Jadassohn’s success may have been significantly more taxing without the contributions of his predecessor and teacher – Albert Neisser. 11-years prior to Jadassohn’s publication, Neisser reviewed 8 cases on dermatitis reactions caused by Iodoform, a chemical containing mercury ¹. Neisser’s lifetime commitment to the study of leprosy, syphilis and gonorrhoea resulted in a staggering 22 nominations for the Nobel Prize in Medicine or Physiology, however he never won it. He died in 1916 from sepsis after an operation ⁴.

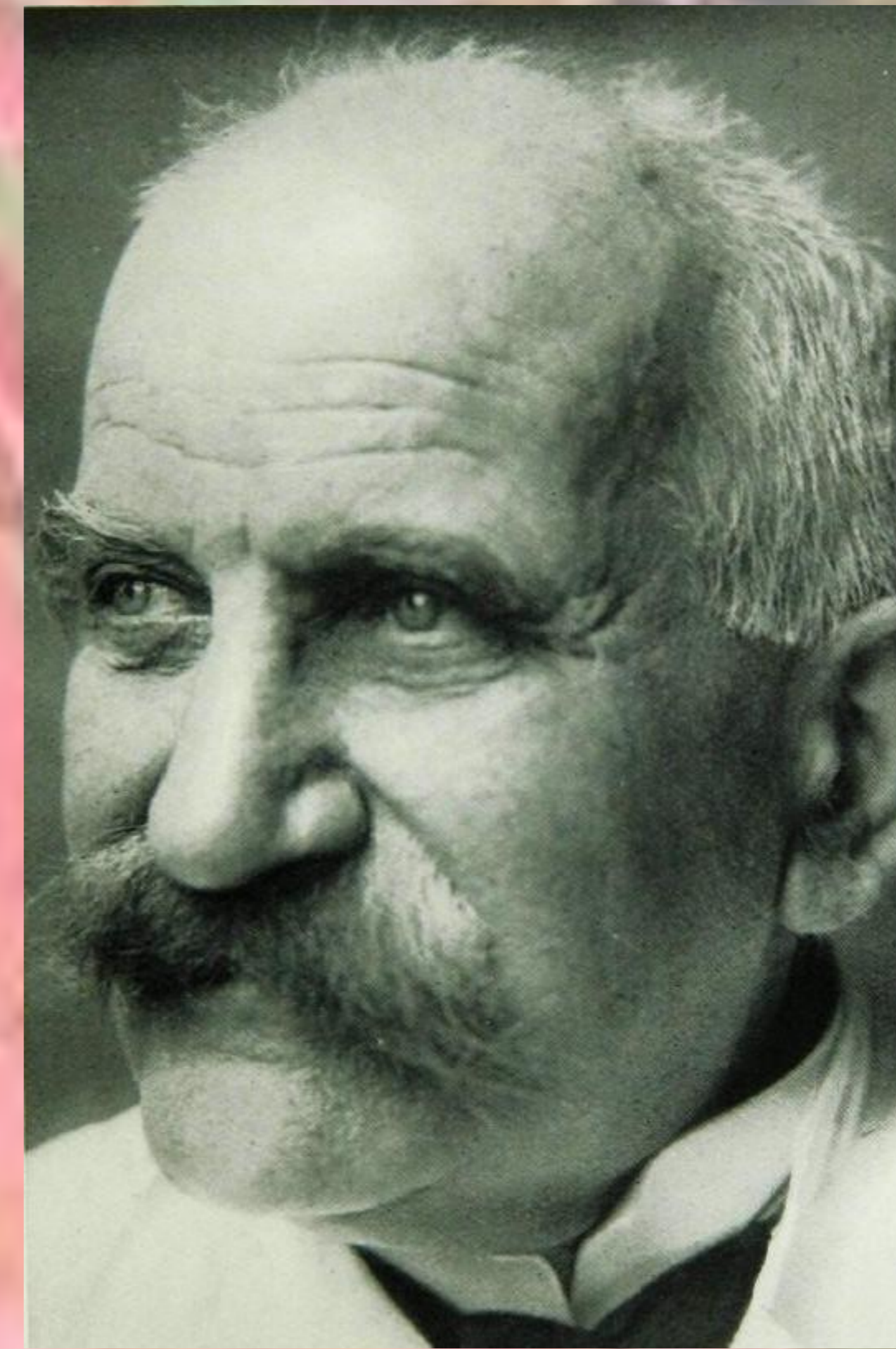


Fig. 1 – Josef Jadassohn; British Journal of Dermatology vol. XLVIII, 1937 (Public Domain)



Jean-Henri Fabre Almost 100 miles away in Provence, a French entomologist with an unrivalled passion for insects was busy making discoveries of his own ⁵. Jean-Henri Fabre worked concurrently and entirely independently to Jadassohn, spending 37 years working in solitude conducting meticulous experiments on insects. His scrupulous efforts culminated in his magnum opus ‘Les Souvenirs Entomologiques’, a 10-volume entomological encyclopaedia.

During his work with the processionary caterpillar, Fabre suffered an itch ‘even more painful and persistent than that of a nettle’ ⁵. His infallible curiosity led him to conduct a series of methodical experiments, with himself as the subject. In his initial experiments, Fabre rubbed his skin with the caterpillar hairs and observed the reaction. On further inspection he inferred that the irritation was caused by a substance coating the hairs, rather than the hairs themselves, as no part of the hair penetrated his skin. Consequently, Fabre designed a thorough, reproducible and scientific method to test his theory – he designed a patch test. He used solvent to isolate and concentrate the noxious agent that coated the hairs, which once applied topically produced a reaction ‘so conclusive in its painful effects that one hardly likes to try it a second time’.

Working in solitude from the scientific community, Fabre demonstrated pioneering insight to split a compound into its individual noxious parts. His specific documentation of application, dose used and duration of the test was one of the first methodical examples of patch testing, despite going un-noticed by dermatologists of the day.

Fig 2. Jean Henri Fabre; Original photo by Nadar; (Public Domain)

Bruno Bloch Despite the fundamental principles of patch testing having been established, the early 20th Century was a time of confusion for those practicing this new method. Definitive guidelines for patch testing had yet to be clarified, with no agreement on allergen concentrations, the duration of the patch test, the materials to be used and many other variable factors. A former student of Jadassohn, Bruno Bloch worked to correct this. His commitment to patch testing is unrivalled in the advancement of the science ². First, he defined a clear, reproducible technique:

“The allergen should be applied to a linen strip which is put on the back, covered with a slightly larger piece of gutta-percha and fixed in place with zinc oxide adhesive plaster; the test should then be left for 24 hours.”

In addition, Bloch was the first to create a visual grading system to classify the reactions of the patch test, using descriptive terms of erythema, necrosis and ulceration. This was a significant hallmark in the development of patch testing.

Finally, Bloch carried out extensive work to develop the first formative standard series of allergens. He was supported by Werner Jadassohn (son of Josef) and Hans Stauffer, who focussed on identifying suitable concentrations of each allergen to use.

Bruno Bloch’s Standard Series:

Formaldehyde
Mercury
Turpentine
Naphthalene
Arnica
P. Obonica (leaf)
Adhesive plaster
Iodoform
Quinine



Fig 3. Bruno Bloch; The Alumni Association, Medical Faculty of University of Basel. (Public Domain)

Marion Sulzberger Sulzberger, originally from New York, trained in Switzerland and on qualifying became Bloch’s assistant before working with Josef Jaddasohn in Breslau. By the time he returned to the USA in 1929, he was a highly trained clinician and it is mainly due to his drive and enthusiasm that patch testing became an established method of investigation throughout North America. In addition to this work he was an outstanding academic dermatologist, one of the founders of the Society of Investigative Dermatology and the first Editor-in-Chief of its Journal.

The Modern Era of Patch Testing Poul Bonnevie, a previous assistant of Bloch, expanded Bloch’s preliminary allergen series to produce a set of 21 allergens that are officially recognised as the first standard series. An impressive 6 of Bonnevie’s 21 allergens are still used in the British Society for Cutaneous Allergy (BSCA) standard series today. Bloch’s close contacts with key dermatologists of the era helped to spread this new standardised method of patch testing internationally. Despite some initial resistance in Europe to this more ‘restrictive’ practice, the inherent practical advantages of standardisation fuelled the development and use of patch testing far and wide. In 1940, the use of glass squares and plastic chambers by Guild and Rokstad respectively helped to modify and improve the application method even further ⁶. Throughout the decades, various methods were created and trade-marked, the most successful of which being Finn chambers[®]. In 1944, improvements were made to the visual grading system by Schwartz and Peck, who created a 4-point standardised scale ⁶. Continued world-wide interest in the field led to the formation of the International Contact Dermatitis Research Group (ICDRG) in 1967, which drove the movement of evidence based contact dermatology forward. The first volume of *Contact Dermatitis* was published in 1975, and the first international standard series for patch testing was released in 1997 ⁷. Today, patch testing remains a crucial diagnostic tool. Research continues to refine patch testing further and to maximise the efficiency of this valuable investigation in modern dermatological practice.

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