

# The Scientific Legacy of Stephen Rothman

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The year 2014 marks the centennial of events that led to the First World War (“the war to end all wars”) following the assassination of Archduke Ferdinand of the crumbling Austro-Hungarian Empire. It also marks the 120th anniversary of the birth of Stephen Rothman and the 60th anniversary of the publication of his epic textbook *The Physiology and Biochemistry of the Skin*. In this review, we document our belief that Rothman had a seismic impact on moving investigative dermatology from a medical backwater to a scientific discipline that can hold its own with any other specialty.

*Journal of Investigative Dermatology* (2015) **135**, 954–959; doi:10.1038/jid.2014.447; published online 6 November 2014

Stephen Rothman (Figure 1) was described as the “widely acknowledged grand master of modern investigative dermatology” by Allan Lorincz (1924–2010) in his forward to a 1958 Festschrift in the *Journal of Investigative Dermatology* honoring Rothman (Lorincz, 1958). Few would dispute this accolade. The year 2014 marks the 60th anniversary of the publication of Rothman’s classic textbook *Physiology and Biochemistry of the Skin* (Rothman, 1954), as well as the 120th anniversary of his birth. It seems an appropriate time to revisit Rothman’s scientific career and its decisive impact on modern investigative dermatology.

Rothman took a circuitous route to his lofty position (Rothman and Lorincz, 1995; Everett, 2013). He was born into a wealthy Jewish family on 10 September 1894 in Budapest, Hungary. After graduating from medical school at the University of Budapest in 1917, he served in the Austro-Hungarian army during the First World War and helped to manage a debilitating scabies epidemic in cavalry horses. Rothman trained in dermatology with Albert Jesionek (1870–1935), a pioneer in cutaneous photobiology at the University of Giessen, Germany, from 1920 to 1928. He also spent 6 months with Bruno Bloch (1878–1933) at the University of Zurich doing pigment cell research and crossing paths with Marion

Sulzberger (1895–1983). He returned to Budapest, opened a private practice, ran a large public outpatient clinic, and continued his research at Semmelweis University where Lajos Nékám (1868–1957) was chairman. As Secretary-General, he helped Nékám organize the 9th International Congress of Dermatology and Syphilology in Budapest in 1935, making numerous international contacts that later helped him.

In the 1930s, anti-Semitism flared in Hungary and a variety of repressive measures were instituted. Rothman traveled to the United States in 1938 ostensibly to attend a meeting in San Francisco but in fact to immigrate. Sulzberger introduced him to Samuel W Becker (1894–1964) who offered him a faculty position at the University of Chicago where he spent the rest of his academic life.

Rothman advanced rapidly at the university, immediately starting to publish on a wide variety of investigative topics. After Becker and Maximilian Obermayer (1896–1982) left the Section of Dermatology in the Department of Medicine in 1942, he was named Chief, and 3 years later promoted to Professor. He retired in 1959 but remained active in research until his death on 31 August 1963 (Lorincz, 1964).

Rothman’s impact on investigative dermatology can be tracked in several ways. He trained a cadre of superb research scientists, as well as many outstanding clinicians. Table 1 contains an abridged list of his students and their contributions. With his strong encouragement, Harvey Blank (1918–2001), then a medical student at the University of Chicago, trained in dermatology; Blank later developed a premier department at the University of Miami. In addition, Gerd Klaus Steigleder (1925–) spent time with Rothman; he later became chairman of dermatology at the University of Cologne (Burgdorf and Bickers, 2013).

Rothman also wrote and edited a remarkable textbook *Physiology and Biochemistry of the Skin* in 1954 that was unprecedented in its erudition and comprehensiveness (Rothman, 1954). To assemble this magnum opus, he enlisted an extraordinary cohort of coauthors (Table 2) but still wrote 23 of the 28 chapters himself. The book was enthusiastically reviewed by the *Archives of Dermatology* and the reviewer thanked Rothman for “having compiled such a great fund of information...” (1954), whereas the *British Journal of Dermatology* recommended it to “any dermatologist interested in his subject beyond morphological diagnosis and empirical treatment.” (1955) In the preface to his epic two-volume textbook *Biochemistry and Physiology of the Skin* published in 1983, Lowell Goldsmith commented, “Yet no single text has attempted to review all of skin biochemistry and physiology since Rothman’s *Physiology and Biochemistry of the Skin* (1954), an extraordinary benchmark for dermatology.” (Goldsmith, 1983).

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Abbreviation: PABA, para-aminobenzoic acid

Received 30 June 2014; revised 25 August 2014; accepted 1 October 2014; published online 6 November 2014

Rothman's bibliography shows that he was creative, insightful, and extraordinarily productive and that he concentrated most of his efforts in a few major areas. The epidermis was perhaps his first love and his students throughout their careers



Figure 1. Stephen Rothman (courtesy of Gerd Plewig, MD, Munich, Germany).

carried this forward, several becoming acknowledged leaders—keratinization (Flesch), epidermal fragility (Pearson), epidermal kinetics (Van Scott), and percutaneous absorption (Stoughton). His other main interests were epidermal lipids, melanogenesis, neurophysiology, endocrinology, and photobiology. Although he was a multifaceted clinician, pruritus was a special focus. In Rothman's era, research in skin biology was largely descriptive and generally considered to be vastly inferior to that occurring in most other specialties. This makes his prescient accomplishments all the more impressive. In his introduction to the Rothman Festschrift, Lorincz listed 11 seminal contributions (Lorincz, 1958). With the help of several present-day leaders, we show how these advances have helped lead the way to the current elevated status of dermatologic research in 2014.

### CUTANEOUS NEUROBIOLOGY

Rothman worked with Julius M Coon (1910–2000), a pharmacologist, to analyze the role of acetylcholine in the skin (Rothman and Coon, 1940). They identified the axon flare, which we now know is driven by a branching network of axons that also interact with sensory nerves, which may be involved in “flushing” and “blushing” (Roosterman *et al.*, 2006), as well as the pilomotor response that has been described as “gooseflesh”. They also identified cholinergic signaling as the primary mediator for parasympathetic cutaneous vasodilation, as well as for sympathetic eccrine sweating. Because acetylcholine is also released by non-neuronal cells and receptors for acetylcholine are widely

Table 1. Students of Stephen Rothman

| Name                  | Later affiliations                  | Major contributions  |
|-----------------------|-------------------------------------|--|
| Calvin B Dillaha      | Arkansas                            | Systemic corticosteroids for alopecia areata, 5-fluoruracil for actinic keratoses                    |
| Kenneth Halprin       | Miami                               | Psoriasis  |
| Allan L Lorincz       | Chicago                             | Cutaneous physiology and pharmacology  |
| Frederick D Malkinson | Rush-St Luke's                      | Percutaneous absorption, effects of ionizing radiation and chemotherapy on hair matrix, oral biology |
| Roger W Pearson       | Rush-St Luke's                      | Electron microscopy of blistering disorders  |
| Richard B Stoughton   | Case Western, Scripps, UC San Diego | Percutaneous absorption, topical corticosteroids   |
| Eugene J Van Scott    | NIH, Temple                         | Epidermal kinetics, psoriasis  |
| Dorothy Windhorst     | Minnesota, Hoffman-LaRoche          | Immunodermatology, pharmacology (isotretinoin)   |

Table 2. Contributors to *Physiology and Biochemistry of the Skin*

| Name            | Later affiliations     | Major contributions  |
|-----------------|------------------------|--|
| Zachary Felsher | Illinois, Northwestern | Collagen biochemistry  |
| Peter Flesch    | Pennsylvania           | Disorders of keratinization  |
| Aaron B Lerner  | Yale                   | Melanocyte physiology, identified both melanocyte-stimulating hormone and melatonin, described cryoglobulins |
| Allan L Lorincz | Chicago                | Cutaneous physiology and pharmacology  |
| Hermann Pinkus  | Wayne State            | Dermatopathology   |
| George C Wells  | St Thomas-London       | Histochemistry, immunodermatology, described eosinophilic cellulitis (Wells' syndrome)                       |

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