

## Teofil Simchowicz (1879–1957): the scientist who coined senile plaques in neuropathology

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### Abstract

Teofil Simchowicz (1879–1957) was a Polish-Jewish neurologist who studied medicine at the Warsaw University, and worked under the founder of modern Polish school of neurology, Edward Flatau (1868–1932). It was Flatau who encouraged him to join Alois Alzheimer (1864–1915) in Munich. Simchowicz focused his research on the neuropathological changes in dementia. He emigrated with his wife to Palestine, where he continued to work as a consulting neurologist. Simchowicz coined the terms senile plaques, senile index, and granulovacuolar degeneration – discovered in the hippocampus in patients with Alzheimer's disease, and described the nasomental reflex. Simchowicz was a prolific researcher in the field of neuropathology, especially neurodegeneration but also in clinical neurology.

**Keywords:** Teofil Simchowicz, senile plaques, granulovacuolar degeneration, nasal reflexes.

### Biographical note

Dr. Teofil (Tuvia) Simchowicz was born on 8/6/1879, near Warsaw (Ciechanowicz) and died in Tel Aviv, on 31/12/1957 (Figure 1). In the obituary, which that appeared in Hebrew [1], Simchowicz is named as 'the oldest living neuro-psychiatrist in Israel'. He was described as modest person, a distinguished scholar, music and painting lover, and good hearted. In 1898, he finished his matriculation while dedicating his intellectual passion to read Schopenhauer's writings and general literature.

In 1904, he got his MD degree from Warsaw University, and started to work at Edward Flatau's Department of Neurology at 'Czyste' Jewish Hospital, *Szpitala Starozakonnych* [2]. In 1907, he replaced Adam Wizel (1864–1928), as the Head of the Department of Psychiatry while Wizel was drafted to take part in the Russo–Japanese War (1904–1905) [3]. When his grandfather died in 1907, Teofil inherited a small sum of money, which enabled him to travel to Munich and to work with Alois Alzheimer (1864–1915). After six months of laboratory work in the Munich 'Kraepelin' Psychiatric Clinic, Simchowicz won his position as an 'independent researcher' [4].

Simchowicz focused his research in Munich on *dementia senilis*. In 1911, in a chapter on this subject, *Histologische Studien über senile Demenz*, he coined the fundamental term *senile plaques* and established a quantitative method in evaluating the pathological changes in dementia. His book contribution won the Romuald Plaskowski Prize [5]. Plaskowski (1821–1896) was a Polish psychiatrist and philosopher, professor at Warsaw University.

After this publication, he was invited to the United States but he declined the offer. As a senior-assistant, he joined Edward Flatau (1868–1932) (Figure 2) and Samuel Goldflam (1852–1932) in the clinical work as well to the *Institute of Neurology of the Warsaw Scientific Association*. In Warsaw, he worked at the 'Marceli Nencki Laboratory for Experimental Biology'. Wilhelm Marceli Nencki (1847–

1901) was a Polish chemist and physician known for his contributions on urea synthesis, chemistry of purines, enzymes, and biological oxidation of aromatic compounds and especially the chemical structure of hemoglobin.



**Figure 1 – Teofil Simchowicz (1879–1957).** **Figure 2 – Edward Flatau (1868–1932).**

Simchowicz broadened the spectrum of his neuropathological studies and published a paper on the pathological findings in brain of patients who suffered from hypo- or hyperthyroidism [6]. During 1919–1921, the captain doctor Teofil Simchowicz, served in the Polish Army. After the war, he returned to Warsaw to the Flatau's Institute (*Warszawskiego Instytutu Neurobiologicznego* at ul. Puławskiej 41). He directed the anatomical pathological department until 1939. He worked for the Jewish charity organization: *Przychodnia Żydowskiego Towarzystwa Dobroczynności 'Pomoc Lekarska'* (Jewish Medical Assistance). He found time, however, to run a private practice, and clinical work, together with Drs. Rubin, Fejgin and Mész, at a diagnostic and therapy centre located in Warsaw at ul. Jerozolimski 41. He was a member of various medical, psychological and neurological organizations. He edited the Polish medical journal *Neurologia*

*i Neurochirurgia Polska*, which laid down the basis of modern neurological research in Poland.

Simchowicz was one of the founders of *Zrzeszenia Lekarzy Rzeczypospolitej Polskiej* [7]. This Association of Jewish Physicians in Poland was founded in 1923 by a group of prominent doctors, many from the renowned Jewish Hospital in Warsaw, under the name of the 'Association of Physicians of the Polish Republic'. And Simchowicz was one of them. The organization was founded because applications from Jews willing to join the general Polish medical societies were increasingly rejected after Poland achieved independence following the First World War.

Teofil married Dr. Tauba Mendelsburg, a pediatrician and internist, who studied in Vienna, Zürich and Berlin. She had finished her studies in 1912 and returned to Warsaw to work at a 'Mother and Child' Clinic, situated in ul. Złota 27. In 1940, the couple managed to escape Poland and arrived in Palestine. He worked at the clinics of the Polish Delegation and the Red Cross, and published regularly articles in the '*The Polish Doctor*' journal. Later on, he joined Drs. Kurt Lewenstein (1883–1956) and Julius Zelmeyer (1910–2004) in their neuro-psychiatric clinic of '*Kupat-Holim*' (an Israeli Workmen's Sick-Fund), and published two papers in Hebrew in *Harefuah* [8]. In Israel, he became a close friend of the neurologically disabled poet and prose writer, born in Zürich, Leo Lipski-Lipschütz (1917–1997).

Simchowicz contracted Parkinson's disease, and died in near poverty at Hadassah Hospital, on Balfour Street, in Tel Aviv. He is buried near his wife in a Tel Aviv cemetery. Most of his publications were published in Polish, German and French, and were devoted mainly to Alzheimer's disease (AD), but also to other neurological diseases including as Parkinson's disease, epilepsy, various aspects of geriatric patients, meningo-encephalitis, and on presenting the contributions of his mentor and friend, the founder of modern Polish school of neurology, Edward Flatau [9, 14].

### ☞ Simchowicz' almost forgotten descriptions of two reflexes

In two papers, published in Polish and German journals, he had described two clinically relevant reflexes (Figure 3) [15, 16].



Figure 3 – The original study in Polish on the two reflexes (left) and the German print (right), 1922.

### The nasal–ocular reflex

When we tap with a reflex hammer on the tip of the nose or along the nose, orbicularis oculi muscle contractions occur. Sometimes the contraction is weak resulting in slight elevation of the lower eyelid, and sometimes we observe a vigorous contraction resulting in a complete closure of the eyelids. After repeated tapping, the reflex slowly subsides. This is a normal reflex which appears, according to Simchowicz, during the third year of life, and disappears unilaterally in facial palsy or after electric shock treatment in psychiatry. After an epileptic attack, the reflex disappears for half an hour. During a 'hysterical' fits (conversion reaction), the reflex is elicited.

### The nasomental reflex

The same tapping produces movement of the mentalis, which reminds the palmomental reflex described in 1920, by the Romanian born neurologist Georges Marinesco – the contraction of the muscles of the chin, in response to stimulation of the thumb indicates damage to the corticobulbar tract in a variety of brain diseases, including vascular dementia, lateral amyotrophic sclerosis or pyramidal lesions [17]. The nasomental reflex, closely connected associated with the previous naso-ocular one, is a reflex elicited by tapping the side of the nose, thereby causing contraction of the mentalis muscle with elevation of the lower lip and wrinkling of the skin of the chin. In Dorland's medical dictionary [18], Simchowicz is not explicitly mentioned, but rather as: *Nasal reflex, 1. Irritation of the Schneiderian membrane provokes sneezing. 2. See Bechterev's reflex. Nasomental reflex = contraction of the mentalis muscle on tapping the side of the nose with a reflex hammer. Bechterev's reflex is tickling of the mucosa of the nasal cavity with a feather or piece of paper produces contraction of the facial muscles on the same side of the face. Called also 'the nasal reflex'*. Contraction of the mentalis muscle after a tap on the side of the nose is also to be found in other source.

Simchowicz mentioned Vladimir Bechterev (1857–1927) in his article, but it is difficult to conclude today, who was the first to describe this reflex. Many different names had been used to describe reflex contractions of the facial musculature – depending on the area tapped, the muscles responding and the mechanisms considered being involved [19]. Today we are more aware of the neuro-anatomic background of these facial reflexes: the neural supply to the nose is sensory and autonomic, from the trigeminal nerve and the efferent autonomic neural supply, both by the parasympathetic and sympathetic nerves.

For both reflexes described, Simchowicz established the term *perichondreal reflex*, in 1922, which and under this name that finally appeared in other old and new reference works [20]. Similarly, these reflexes are called: skin, periosteal, bony or myotatic reflexes. It happens, that novel treatments, neurological signs, procedures, maneuvers or reflexes, that were first published in European languages (Eastern European, German or Italian), remained less known in the West [21].

### ☞ Kraepelin, Alzheimer, Simchowicz *et al.*

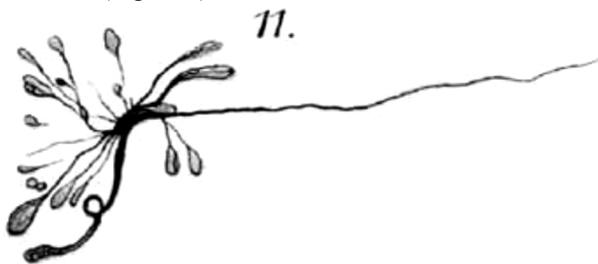
By all means, it was Emil Kraepelin (1856–1926), the psychiatrist who coined the term: '*Alzheimer's disease*'

[22], but other prominent neuroscientists, were closely associated with Alzheimer himself, and contributed to our understanding of the clinical and pathological aspects of this disease: Franz Nissl (1860–1919), Georges Marinesco (1863–1938), Paul Oscar Blocq (1860–1896), Oskar Fischer (1876–1942), Walther Spielmeier (1879–1935), Alfons Maria Jakob (1884–1931), Otto Binswanger (1852–1929), Arnold Pick (1851–1924), Gaetano Perusini (1879–1915), Ugo Cerletti (1877–1963), or Gonzalo Rodriguez Lafora (1887–1971). Max Bielschowsky (1869–1940) is known for the histological silver stain for impregnation of nerve fibers; the eponymous ‘Bielschowsky silver stain’ technique was an improvement on the method developed earlier by Ramon y Cajal (1852–1934).

It was no other than Alois Alzheimer in Munich who suggested 1908 that Simchowicz should concentrate on dementia senilis. Three years were devoted to this investigation, which resulted, whose in 1911, in a work entitled *Histologische Studien über senile Demenz*, published in a book edited by Franz Nissl and Alois Alzheimer. He examined 108 brains of patients who died with senile dementia. He found that plaques, which were described by Emil Redlich (1866–1930) and Oskar Fischer, appeared also in brain of non-senile people, but essentially, these plaques are to be found more substantially in dementia patients. Therefore, he coined these plaques *senile plaques*.

The first reference in the literature to the existence of senile plaques was made as early as 1892, by Blocq and Marinesco [23, 24] but the origin and development of such plaques were at the beginning a matter of controversy. No less than 20 different concepts regarding their origin have appeared in the literature soon after 1907. Senile plaques may be described as small, spherical, thickened, argyrophilic bodies scattered throughout the cerebral cortex. They are not uniform in structure, but consist of various components, which are different in type and situation [25].

Simchowicz furnished many illustrations and descriptive details on the process of neuritic sprouting within senile plaques. He underlined that axis cylinders in the periphery of the plaque undergo partly degenerative, partly regenerative changes. Simchowicz also described the division of the axis cylinders and observed newly formed shoots forming buds at their ends, so that sometimes numerous shoots are formed, giving the picture of a tree with many branches (Figure 4).



**Figure 4 – Simchowicz’ depiction of plaque-associated sprouting in senile dementia. The picture is taken from Simchowicz, 1911, plate XVII, Fig. 11. One can read in German [5]: *Zahlreiche Sprossbildungen aus einem Achsenzylinder, welcher einer senilen Plaque anliegt. Der Achsenzylinder sieht wie ein verzweigtes Bäumchen aus. (Numerous sprouts emanating from an axon cylinder, immediately adjacent to a senile plaque. The axon cylinder has the appearance of a ramified tree).***

Similar to Simchowicz’ research, Fischer expressed the opinion that the plaque-positive cases represented a definite clinical entity which he termed ‘presbyophrenic dementia’; in cases of simple senile dementia no plaques occurred [26] Also, Simchowicz, who in 1911 emphasized the Ammon’s horn as the area of predilection for neurofibrillary changes, clearly recognized that the distribution of neuropathological lesions in AD favors specific cortical regions, an observation that since has been corroborated in a variety of studies.

According to Critchley, Simchowicz’ contributions are of particular interest, because he regarded plaques as typical of the normal senium but believes that they increase with advancing years [27]. Simchowicz pointed out that it is not sufficient only to record the presence of plaques, but that their number, size and arrangement must also be considered. He therefore suggested that a so-called ‘*senile index*’ should be taken; the maximum number of plaques in a microscopic field (with Leitz objective 3, eyepiece 3, magnification 80) is noted. Examinations were made of different cortical regions, taking sections cut at a thickness of 20  $\mu\text{m}$  and stained by the techniques of Bielschowsky or Mann–Alzheimer. Then, the actual number of plaques in each piece was by Simchowicz assembled as ‘*senile index*’ and tabulated accordingly: Index of frontal lobe – I.F.; temporal lobe – I.T.; cornu Ammonis – I.A.; parietal lobe – I.P.; motor cortex – I.M.; occipital lobe – I.Occ.

The senile formula, which is quantitative concept, was then recorded thus: I.F./I.A./I.T./I.P./I.M./I.Occ. = 52/26/26/17/8/5 (in a case of senile dementia). In a normal old man aged 104, the formula was: I.F./I.A./I.T./I.M./I.Occ. = 8/5/3/0/0. Simchowicz stated that in Alzheimer’s disease, the maximum plaque incidence was found to be in the visual cortex: I.F./I.A./I.T./I.P./I.M./I.Occ. = 45/42/44/62/30/74. The ratio I.F./I.Occ. is, therefore, important, in Simchowicz’ opinion, in differentiating Alzheimer’s disease from senile dementia on pathological grounds (like vascular origin). According to these results, the differences between healthy old age and senile dementia are purely quantitative, and depend entirely on the actual number of plaques [28].

In cases of Alzheimer’s disease, senile plaques are present in the cortex, but in conjunction with the characteristic intracellular neurofibrillary alterations (tangles). And it was Paul Divry (1889–1967), from Liège, Belgium, who demonstrated in 1927, the presence of amyloid at the center of these senile plaques, by means of Congo red staining [29].

Simchowicz reported in 1911, important changes in hippocampal large pyramidal cells in form of granulo-vacuolar degeneration, which involves the accumulation of large, double membrane-bound bodies within certain neurons during the course of AD and other adult-onset dementias, a two-layer membrane morphology [30].

Both Simchowicz and Bielschowsky also came in 1911 to the conclusion that the old dogma on the failure of nervous fibers in the mammalian central nervous system to regenerate needed to be revised, a conclusion shared by authors who at the turn of the 19<sup>th</sup> century gave descriptions of regenerative phenomena in the nervous system under various pathological conditions [25].

The evolution of the concept and knowledge about dementia is a fascinating story [31], and our today’s challenge is to minimize, alleviate and perhaps prevent the high burden of senile dementias.

### Conflict of interests

The authors declare that they have no conflict of interests.

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