

Historical Review

Giuseppe Gradenigo: Much more than a syndrome! Historical vignette

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Abstract

Background: Giuseppe Gradenigo (1859–1926), a legendary figure of Otology, was born in Venice, Italy. He soon became a pupil to Adam Politzer and Samuel Leopold Schenk in Vienna, demonstrating genuine interest in the embryology, morphology, physiopathology, as well as the clinical manifestations of ear diseases. In this paper, the authors attempt to highlight the major landmarks during Gradenigo's career and outline his contributions to neurosciences, which have been viewed as looking forward to the 20th century rather than awkward missteps at the end of the 19th.

Methods: Several rare photographs along with many non-English, more than a century old articles have been meticulously selected to enrich this historical journey in time.

Results: It was after Gradenigo that the well-known syndrome consisting of diplopia and facial pain due to a middle ear infection was named. However, Gradenigo was much more than a syndrome. Surprisingly, despite the fact that he is considered a pioneer of the Italian Otology of the late 19th and early 20th century, little is written of his life and his notable achievements in the English literature.

Conclusions: Even though his name lives on nowadays only in the eponym "Gradenigo's syndrome," his accomplishments are much wider and cast him among the emblematic figures of science. His inherent tendency for discovering the underlying mechanisms of diseases and his vision of guaranteeing quality of services, professional proficiency, respect, and dedication toward the patients is in fact what constitutes his true legacy to the next generations.

Key Words: Audiology, Giacomo Puccini, Giuseppe Gradenigo, Otology, Primo Dorello, syndrome

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THE BEGINNING

On Thursday, September 29th, 1859, Giuseppe Gradenigo (1859–1926) [Figure 1] was born in Venice (Italy).^[4,7,8,37,40]

Gradenigo descended from a long line of powerful Venetians, numbering 14 procurators, 3 Doges, 2 cardinals, and several diplomats.^[8,37] In fact, Pietro Gradenigo (1251–1311) was a Doge (1289–1311)

when Marco Polo returned from the Orient in 1294.^[37] Giuseppe Gradenigo's family roots can be traced back to the 7th century with the most acceptable region of origin being the area between Grado and Aquileia in the northwestern Italy.^[37]

He was the eldest child of Ernesta Conto and Pietro Gradenigo (1831–1904) who was an influential Professor of Clinical Ophthalmology at the University of Padova.^[4,8,37] Pietro Gradenigo had served in the rebellion against the Austrian-ruled kingdom of Lombardy-Venice, during which his brother (Giuseppe) had died.^[37]

MEDICAL TRAINING

At the age of 18 (1877), Gradenigo was admitted to the University of Padova, from where he graduated in 1883.^[4,7] Considering his father's advice, he turned to Otology, working in Vienna under Adam Politzer (1835–1920),^[35,40] and Samuel Leopold Schenk (1840–1902) on the embryology of the ear.^[40] Actually, his very first research was devoted to this topic.^[2,37] While in Vienna, Gradenigo met the Hungarian-Austrian anatomist Emil Zuckerkandl (1849–1910) who at that time was appointed assistant professor at the local university, and maintained correspondence with him for more than 20 years.^[7]

APPOINTMENTS

After his studies in Vienna, Gradenigo returned to Padova where in 1888 he was nominated *Libero Docente* (private professor).^[4,35,37] One year later, on 1 June 1889, he became Head of the Department of Otolaryngology of the Turin's Polyclinic and subsequently (1890)^[4,40]

founded the University Clinic in the same town. It was in that clinic that Gradenigo established a training program, one of the firsts in Italy, in Otolaryngology and insisted on integrating this program in the formal university curriculum. In 1908, he wrote: "*Diseases of organs as important as ears, nose and throat are still not included in the compulsory teaching program... continuing to consider the study of a Specialty as an optional, is the equivalent of recognizing that it is of limited value.*"^[7] Yet, only in 1929, Otorhinolaryngology (ORL) was finally assigned to the 4th year of medical studies as an obligatory course.^[35]

During this period, for his clinical practice, 10 beds for hospitalization and surgery in a General Surgery Clinic directed by A. Carle were at his disposal.^[4]

On 13 February 1896, Gradenigo was nominated *Professore Straordinario* (newly appointed professor) of Otology in Turin [Figure 2].^[4,5,35] In 1902, he was ranked first for the Chair of ORL in the University of Rome, but he chose to refuse the new position.^[4] On 24 March 1910, Gradenigo was appointed *Professore Ordinario* (full professor) in Turin.^[4,7,37] The next year (1911) he declined an invitation extended by the Medical School of Naples to succeed Professor Vincenzo Cozzolino (1853–1911), another student of Politzer.^[4] However, 6 years later (1917), he was appointed Professor of Clinical Otolaryngology in Naples after the death of Ferdinando Massei (1847–1917).^[4,7,37,40]

With the support of 20 Italian colleagues, Gradenigo founded in 1891 the Italian Society of Laryngology, Otology and Rhinology (*La Società Italiana di Laringologia, Otologia e Rinologia – SILOR*) [Figure 3].^[7,35] He served as President of this society twice but not in consecutive terms (1897–1900 and 1925-1926).^[7,37] In



Figure 1: Photographs of Count Giuseppe Gradenigo, MD (1859–1926). (a) Gradenigo in his middle age (Reprinted with permission from Felisati D, Sperati G: Italian ORL Society. Past and Present. Genova:Tipografia Mengotti Carlo & c. snc, 2005).^[7] (b) Gradenigo in his later years (Reprinted with permission from Felisati D, Sperati G: Gradenigo's syndrome and Dorello's canal. Acta Otorhinolaryngol Ital 29:169-172, 2009)^[8]

Professori straordinari				
N. d'ordine progressivo	COGNOME E NOME	Facoltà	DATA del decreto di nomina a straordinario	anno di istituzione della cattedra
1	Bjardi Daniele	M	25 settembre 1883	3
2	Broni Vittorio	G	9 dicembre 1885	7
3	Carusa Mario	M	26 novembre 1888	10
4	Castellari Giovanni	G	29 ottobre 1895	6
5	Elinaudi Luigi	G	14 luglio 1912	14
6	Fano Gino	S	7 novembre 1899	11
7	Ferroglio Gustavo	G	25 novembre 1885	4
8	Germano Michele	G	6 marzo 1872	1
9	Gradenigo Giuseppe	M	13 febbraio 1896	8
10	Hugues Luigi	L	30 novembre 1897	9
11	Perronchio Edoardo	M	24 giugno 1889	5
12	Rossi Francesco	L	3 ottobre 1891	9
13	Valzaghi Luigi	L	23 ottobre 1901	12
14	Trojano Paolo Raffaele	L	30 dicembre 1901	13

(1) A Firenze; trasferito a Torino il 17 agosto 1902.
(2) A Pisa; trasferito a Torino il 31 luglio 1902.

Professori incaricati				
N. d'ordine progressivo	COGNOME E NOME	Facoltà	DATA del decreto di nomina al incaricato	anno di istituzione della cattedra
1	Amar Moise	G	31 dicembre 1912	4
2	Risnow Federico	M	29 gennaio 1912	3
3	Sarelli Alessandro	G	25 gennaio 1893	2
4	Sacco Federico	S	31 dicembre 1896	1
5	Vicarelli Giuseppe	M	...	5
6	Strano Paolo	S	...	6

Figure 2: Photograph of an extract (page 63) from Chironi's Annuario Della R. Università di Torino 1903–1904. Anno 500o dalla fondazione (Yearbook of the R. University of Turin 1903–1904. 500th year from establishment), printed in Turin, 1904. In the first table (number 9), Giuseppe Gradenigo is demonstrated as "Professore Straordinario"^[5]

1893, Gradenigo together with Professor Emilio De Rossi (1844–1902) launched the journal *Italian Archives of Otolaryngology, Rhinology and Laryngology* (*Archivio Italiano di Otolologia, Rinologia e Laringologia*) [Figure 4],^[4,7,35,40] and in 1902, he founded together with Oskar Brieger (1914†) from Breslau (Germany) the *Central Journal for Otolaryngology* (*Zentralblatt für Ohrenheilkunde*) in which they were co-editors until the beginning of the First World War.^[4,37,40]

During this war, he founded together with C. Biaggi and A. Stefanini the Italian Society of Experimental Phonetics (*Società Italiana di Fonetica Sperimentale*).^[4,37] Gradenigo was actively involved in numerous associations [Table 1] and received several prestigious awards [Table 2].^[4,7,8,37]

THE GRADENIGO HOSPITAL

In 1899, the limited resources of the public hospitals forced Giuseppe Gradenigo to establish in Turin a private Clinic (*Ospedale Gradenigo*) with 70 beds to provide treatment to the poor ear, nose, and throat (ENT) patients.^[4,35] The official inauguration was held on 29 January 1900.^[4,37] During the First World War, he granted the clinic as well as his villa in Lancenigo (Treviso, Italy)



Figure 3: Photograph of Count Giuseppe Gradenigo, taken during the 5th Congress of the Italian Society of Laryngology, Rhinology and Otolaryngology (SILOR), Naples, April 1900 (front row, the second from the right) (Reprinted with permission from Felisati D, Sperati G: Italian ORL Society. Past and Present. Genova:Tipografia Mengotti Carlo & c. snc, 2005)^[7]

Table 1: Gradenigo's membership in medical associations^[4,7,8,37]

Italian Society of Laryngology, Otolaryngology and Rhinology
Italian Society of Experimental Phonetics
Royal Academy of Medicine of Turin
Medico-Chirurgical Academy of Naples
Medico-Chirurgical Society of Bologna
Venetian Institute of Sciences, Arts and Letters
Medical Society of Budapest
Royal Society of Medicine of London

to the Italian army. Along with this clinic, a post-graduate school was also established at that time.^[4,6]

Since then, the Sisters of Charity (*Figlie della Carità*) of San Vincenzo de' Paoli have been the cornerstone of the hospital management “with generosity, passion, and far-sightedness.” It was for this reason that Gradenigo wanted them to inherit the hospital after his death.^[6,37]

Nowadays, the Gradenigo Hospital has become much larger. Over the course of time, a unit of general medicine, a surgical unit, and an emergency ward have been added to the initial ENT unit.^[6]

GRADENIGO AND GIACOMO PUCCINI

Gradenigo had the unfortunate privilege to meet Giacomo Puccini (1858–1924), the Italian composer of various famous operas such as *La bohème* (1896), *Tosca* (1900), and *Turandot* (1924).^[30] In February 1924, the composer began suffering from hoarseness, difficulty in swallowing, persistent cough, and cervical swelling. After having consulted many famous professors of his time at Florence, among whom were Camillo Torrigiani (1881–1946) and Addeo Toti (1861–1935), he finally

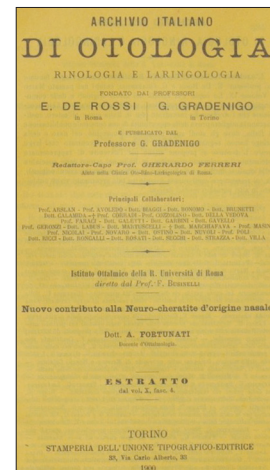


Figure 4: Photograph of the title page of Archivio Italiano di Otolologia, Rinologia e Laringologia (Italian Archives of Otolaryngology, Rhinology and Laryngology) (Reprinted with permission from the website “Maremagnum.com”)

Table 2: Gradenigo's awards^[4]

Superior Consultant of the Navy
Superior Consultant of the State Railways
Inspector of the Psycho-physiological Institutes of Aviation
Director of the Medical Committee of the International Aeronautical Federation
Commander of the Crown of Italy
Commander of the Crown of Romania
Commander of the Order of Saint Thomas Aquinas
Knight of Saints Maurice and Lazarus

turned to Gradenigo who was then a professor at the University of Naples.^[30] Puccini wrote to his good friend and also general director of his publisher (BMG Ricordi) Carlo Clausetti: “*il mio male è papilloma, non grave, ma bisogna levarselo e presto; è situato sotto l’epiglottide. Ho telegrafato al Prof. Gradenigo... vedremo il responso del Gradenigo*” (my bad papilloma is not serious, but we must get rid of it and immediately as it is located below the epiglottis. I telegraphed to Professor Gradenigo... we will see the response of Gradenigo).^[31]

Indeed, on 2 November 1924, Professors Gradenigo, Torrigiani, and Toti visited Puccini and performed a laryngeal biopsy. Gradenigo promptly suggested that he should go to Dr. Louis Ledoux’s Clinic in Brussels, where laryngeal cancer was treated by radium therapy. In the words of Gradenigo: “...*macché Firenze! Vada a Bruxelles. Lì il radium fa miracoli. Le darò io una lettera per il Prof. Ledoux. Un tumoretto... Andrà via tutto*” (...not in Florence! Go to Brussels. There, radium makes miracles. I’ll give you a letter for Professor Ledoux. A little tumor... It will all go away).^[31]

Unfortunately, Puccini prophetically anticipated the end; just a few days before leaving for Brussels, in a discussion with the conductor Arturo Toscanini (1867–1957), he stated concerning his unfinished opera *Turandot*: “*L’opera verrà rappresentata incompleta, e poi qualcuno uscirà alla ribalta e dirà al pubblico: A questo punto il maestro è morto*” (the opera will be presented incompletely, and then somebody will come before the audience and say: ‘at this point the maestro is dead’).^[31] At 11:30 a.m. of 29 November, Puccini passed away.

SCIENTIFIC CONTRIBUTIONS

Gradenigo occupies a unique position in the world of medicine and his work reflects a wide spectrum of physiological and clinical research.^[7,8,37] Besides History of Medicine,^[4,27] his publications concern the microbiology,^[4] embryology,^[4,9,28,38] morphology,^[4,9,28] physiopathology,^[4,11] as well as the clinical entities of the ear and pharynx.^[3,4,15,18-21,23,40] He studied tinnitus, abnormal adaptation (tone decay) in patients with retrocochlear lesions, hysterical hearing loss [Figure 5], genetic hearing impairment, experimental phonetics, and audiological rehabilitation.^[2,3,12,36,37] He devoted much of his time on Acoumetry, working with Aristide Stefanini (1846–1925).^[3] Among others, he developed a variety of audiometers including the first bone conduction device and performed several vestibular tests.^[37]

Gradenigo’s publications exceed 400 (with 9 books included).^[3,4,40] Four of the books and 87 articles were focused on Audiology.^[3,37] He made substantial contributions to this scientific domain.^[4,7,10-14,16,17,22,24-27,34,37,39] For example,

in 1899, he presented a device to vary the oscillations of the tuning fork. It was composed of two metal bands inserted in the tips of the prongs of the instrument. This invention instantly met with success.^[7,37] In the next century, many series of tuning forks were used among which the most popular were the series of Gradenigo and Hartmann composed of seven elements with a frequency varying from 64 to 4096 Hz.^[7,37] In 1904, during an Otology Congress, Professors Gradenigo, Deleaux, and Politzer classified the acoumetric tests by integrating them to an *Acoustic Schema* in order to achieve uniform diagnostic criteria for hypoacusia.^[7,13,34,37]

However, his favorite topic was by far otitis media;^[1,17] the study of its complications led to the description of the so-called “Gradenigo’s syndrome,”^[17,18,23,37,40] which will be presented more thoroughly later in this vignette. Moreover, he exhibited special interest in the embryology of the ear.^[4,9,28,38] Concerning the double origin of stapes, he wrote: “*The human and mammalian stapes arises from two elements, which are embryologically and morphologically completely different. First from the annulus stapedis, which is formed by the second gill arch. Secondly, by the lamina stapedis stemming from the wall of the labyrinth capsule.*”^[28] In his study Gradenigo used cat, dog, pig, and rabbit embryos for the earlier stages and human embryos for the later stages, studying them histologically.^[37]

During the First World War, he held the rank of lieutenant colonel.^[2,4] He had the opportunity to focus on the pathology of war and, in collaboration with the physiologist Amedeo Herlitzka (1872–1949), created a psycho-physiological laboratory to study several methods for selecting air pilots.^[2,4,40]

As already mentioned, Gradenigo wrote many monographs and books. One of his most influential ones, perhaps the epitome of his accumulated experience, was *Patologia e Terapia Dell’ Orecchio e Delle Prime Vie Aeree (Otologia, Rinologia, Laringologia)* (Pathology and Therapeutics of the Ear and Upper Respiratory Passages (Otology, Rhinology, Laryngology) which instantly attracted the attention of the readership in 1903 [Figure 6].^[17,40] One year after its publication, an anonymous book critic wrote: “*The general textbook of diseases of the ear and upper air passages which he has now published ought to command the attention of a large circle of readers. It combines many of the excellences both of the German and of the French schools, and it will be found clear and thorough without being laboured.*”^[1] It is in this book that a very touching dedication to his father can be found: “*a mio padre Conte Piero Gradenigo temprà geniale di scienziato e di artista nelle discipline optalmologiche versatissimo clinico ed operatore mirabile con affetto e riconoscenza perenni questo libro dedico*” (to my father, Conte Pietro

Gradenigo, a brilliant scientist and artist of clinical ophthalmology and wonderful surgeon, with affection and everlasting gratitude I dedicate this book).^[17]

Of more limited interest, yet of great value for the field of Audiology, was the book entitled *Sulla Acumetria. Proposta di Nuovi Metodi Acumetrici* (On Acoumetry. Proposal for New Acoumetric Methods) [Figure 7].^[4,25,37]

Some of the numerous publications of Gradenigo are summarized in Table 3.^[3,4,9-28,34,37-40]

GIUSEPPE GRADENIGO'S SYNDROME AND PRIMO DORELLO

In a communication made to the Royal Academy of Medicine in Turin in the sessions of 29 January, 22 April, and 17 June of 1904, Gradenigo presented for the very

first time some cases of paralysis of the abducens nerve of post-otitic origin [Figure 8].^[21,32] These cases formed the basis for the description of a syndrome currently known as *Gradenigo's syndrome*. In the same year, he published his findings in many journals in Italy,^[20] France [Figure 9],^[18] and Germany [Figure 10].^[3,19,23]

The syndrome consists of homolateral trigeminal neuralgia and paresis or paralysis of the homolateral abducens nerve in the context of chronic or acute suppuration of the ear after involvement of the apex of the petrous part of the temporal bone.^[8,17,18,23,33,41]

Although everybody agreed with the syndrome's description, the pathogenesis of the sixth cranial nerve involvement was under great debate. Many explanations

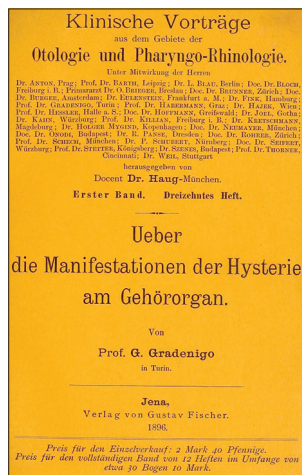


Figure 5: Photograph of the title page of *Ueber die Manifestationen der Hysterie am Gehörorgan* (On the manifestations of hysteria on the hearing organ) by Giuseppe Gradenigo



Figure 7: Photograph of the title page of *Sulla Acumetria. Proposta di Nuovi Metodi Acumetrici* (On Acoumetry. Proposal for New Acoumetric Methods) by Giuseppe Gradenigo, printed in Siena, Italy, 1908^[25]



Figure 6: Photograph of the title page of *Patologia e Terapia Dell' Orecchio e Delle Prime Vie Aeree* (Pathology and Therapeutics of the Ear and Upper Respiratory Passages) printed in Firenze, Italy, 1903^[17]

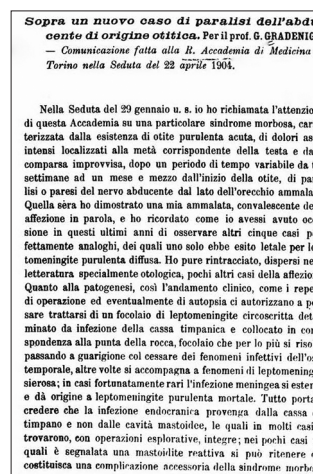


Figure 8: Photograph of an extract (first page) from Gradenigo's *Sopra un nuovo caso di paralisi dell' abducente di origine otitica: Comunicazione fatta alla R. academia di medicina di Torino nella seduta dei 22 aprile 1904* (On a new case of paralysis of the abducens nerve of post-otitic origin: Communication made to the R. Academy of Medicine in Torino in the session of 22 April 1904), printed in Turin, 1904^[21]

Table 3: Some publications of Giuseppe Gradenigo in chronological order (title, year, and type of publication)^[3,4,9-28,34,37-39]

Embryology		
<i>Die Anlage des Embryonal Mittelohres: Die morphologische Bedeutung der Gehörknöchelchen</i> (The structure of the embryonic middle ear: The morphological significance of the ossicles) ^[9]	1887	B
<i>Sulla derivazione embrionale della staffa: La omologia delle ossicina dell' udito nei vertebrates</i> (On the derivation of embryonic stapedius: The homology of auditory ossicles in vertebrates) ^[28]	1923	A
<i>Lo sviluppo embrionale dell' orecchio medio ed esterno e della capsula periotica</i> (The embryonic development of the middle and external ear and periotic capsule)	1924	M
Microbiology		
<i>Osservazioni batteriologiche sul contenuto della cavità timpanica nei cadaveri di neonati e bambini lattanti</i> (Observations on the bacteriological content of the tympanic cavity in cadavers of newborns and infants)	1890	A
<i>Le complicazioni auricolari nell' influenza; contributo clinico e batteriologico</i> (The auricular complications of influenza: Clinical and bacteriological contribution)	1890	A
<i>Über die rationelle Therapie der acuten Mittelohrentzündung: Klinische und bakteriologische Studien</i> (About the rational therapy of acute otitis media: Clinical and bacteriological studies)	1894	A
<i>Contributo allo studio delle otiti medie acute da bacillus pyocianeus</i> (Contribution to the study of acute otitis media by <i>Bacillus pyocyanus</i>)	1894	A
Physiology – Pathophysiology		
<i>Sull' eccitabilità elettrica dell' acustico</i> (On the electrical excitability of the acoustic nerve)	1889	A
<i>Les lésions anatomiques de l' organe de l' ouïe, dans les affections endocraniennes en général, et dans les diverses formes de méningite</i> (The anatomical lesions of the organ of hearing in intracranial diseases in general and in the various forms of meningitis) [‡]	1889	A
On the clinical signs of the affections of the auditory nerve ^{‡[11]}	1893	A
<i>Ascesso cerebrale otitico; trapanazione del cranio e svuotamento dell' ascesso; guarigione</i> (Brain abscesses, otitis, trepanation of the skull and draining of the abscess; healing) [‡]	1895	A
<i>Notes bacteriologiques sur l' ozène</i> (Bacteriological notes on ozena)	1896	A
<i>Sulla terapia dell' ozena</i> (On the therapy of ozena)	1897	A
<i>Sulla tecnica operativa dell' ascesso cerebrale otitico</i> (On the technical operation of cerebral abscesses of otic origin) [‡]	1897	A
<i>Sopra due casi di ascesso cerebrale otitico</i> (About two cases of brain abscess of otic origin) [‡]	1900	A
<i>Die Hypertrophie der Rachentonsille</i> (The hypertrophy of the pharyngeal tonsil) ^[15]	1901	M
<i>Sur un syndrome particulier des complications endocraniennes otitiques: Paralysie de l' abducteur d' origine otitique</i> (On a particular syndrome of intracranial complications concerning the ear: Paralysis of the abducens of post-otitic origin) ^{‡[18]}	1904	A
<i>Über circumscribte Leptomeningitis mit spinalen Symptomen und über Paralyse des N. abducens otitischen Ursprungs</i> (On circumscribed leptomeningitis with spinal symptoms and on paralysis of the abducens nerve of post-otitic origin) ^{‡[19]}	1904	A
<i>Sulla leptomeningite circoscritta e sulla paralisi dell' abducente di origine otitica</i> (On circumscribed leptomeningitis and on abducens paralysis of post-otitic origin) ^{‡[20]}	1904	A
<i>Sopra un novo caso di paralisi dell' abducente di origine otitica</i> (On a new case of paralysis of the abducens nerve of post-otitic origin) ^{‡[21]}	1904	M
A special syndrome of endocranial otitic complications (paralysis of the motor oculi externus of otitic origin) [‡]	1904	A
The surgical treatment of otitic facial paralysis [‡]	1906	A
<i>Über die Paralyse des Nervus abducens bei Otitis</i> (Abducens nerve palsy originated from otitis) ^{‡[23]}	1907	A
<i>Sulla fisiologia dell' organo dell' udito</i> (On the physiology of the organ of hearing)	1915	A
<i>Mastoidite acuta e paralisi facciale</i> (Acute mastoiditis and facial paralysis) [‡]	1916	A
<i>Sulla patogenesi dell' ozena; l' ozena come malattia ereditaria a tipo recessivo</i> (On the pathogenesis of ozena; the ozena as a recessive hereditary disease)	1925	A
Audiology		
<i>Über ein neues elektrisches Akumetermodell</i> (On a new electric acoumetric model) ^[10]	1890	A
<i>Sulle manifestazioni auricolari dell' isterismo</i> (On the auricular manifestations of hysteria) ^[12]	1895	B
<i>Metodo per la notazione uniforme dei risultati dell' esame uditivo</i> (A method for the uniform notation of results of the auditory examination) ^[13]	1899	A
<i>Nuovo metodo ottico di acumetria</i> (New optical methods of Acoumetry) ^[14]	1899	A

(Contd...)

Table 3: Contd...

<i>Patologia e Terapia Dell' Orecchio e Delle Prime Vie Aeree</i> (Pathology and Therapeutics of the Ear and Upper Respiratory Passages) ^[17]	1903	B
<i>Sopra la misurazione dell' udito col mezzo dei diapason</i> (On the measurement of hearing by means of diapason) ^[22]	1905	A
<i>Sui criteri diagnostici nelle malattie del labirinto auricolare</i> (On the diagnostic criteria for the diseases of the auricular labyrinth) ^[24]	1907	B
<i>Sulla Acumetria. Proposta di Nuovi Metodi Acumetrici</i> (On Acoumetry. Proposal for New Acoumetric Methods) ^[25]	1908	B
Suggestions in Acoumetry	1913	A
<i>Dispositivo Semplice per ottenere Suoni di intensita costante e graduabili colla elettricità</i> (Simple device to obtain constant and scalable intensity with electricity) ^[26]	1916	A
<i>Guida pratica di acumetria clinica</i> (Practical guide of Clinical Acoumetry)*	1934	B
History of Medicine		
<i>Fu Helmholtz veramente l' ideatore della teoria sulla audizione che porta il suo nome?</i> (Was Helmholtz really the creator of the hearing theory that bears his name?) ^[27]	1917	A
<i>Una grave epistassi di Ugo Foscolo</i> (Severe epistaxis by Ugo Foscolo)	1920	A

A: Article, B: Book, M: Monograph, †Subject of neurosurgical interest, *in collaboration with A. Stefanini, published in Milan by U. Calamida^[3]

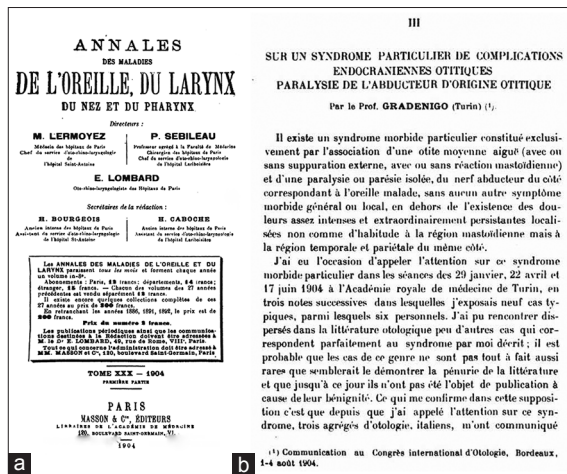


Figure 9: Photograph of Gradenigo's *Sur un syndrome particulier des complications endocraniennes otitiques: paralysie de l' abducteur d' origine otitique* (On a particular syndrome of intracranial complications concerning the ear: Paralysis of the abductors of post-otitic origin).^[18] (a) Title page of the journal *Annales des maladies de l' oreille, du larynx, du nez et du pharynx* (Annals of diseases of the ear, larynx, nose and pharynx), published in Paris, 1904. (b) An extract (first page) from the article

were formulated. Gradenigo assumed that it was the result of the limited areas of serous and purulent leptomenigitis initiated by the inflammatory process of the tympanic cavity.^[8]

At the age of 33 (1905), Primo Dorello (1872–1963), a young assistant at the University of Rome (Department of Anatomy), postulated that the abducens nerve could only be compressed by the post-otitic edema in a non-extensible canal through which this cranial nerve and inferior petrous sinus pass.^[41] According to Dorello, this canal was formed from a narrowing of the inferior petrous foramen located at the tip of the petrous bone.^[29] This foramen measured 6–12 mm in length and 1–3

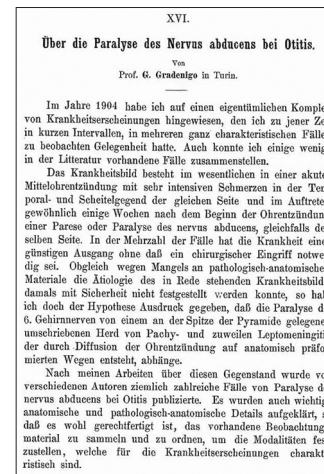


Figure 10: Photograph of an extract (first page) from *Über die Paralyse des Nervus abducens bei Otitis* (Abducens nerve palsy originated from otitis) by Giuseppe Gradenigo, published in 1907.^[23]

mm in width.^[41] He also stated that a thickening of Grüber's petrosphenoidal ligament bordered the superior wall of the canal (since then known as the *Dorello's canal*).^[29,41] Gradenigo argued this thesis by saying that the veins of the tympanic cavity had no direct relationship with the inferior petrous sinus. This argument in turn was not found persuasive by Dorello who invoked the work of other researchers suggesting that "*the inferior petrous sinus receives,*" among others, "*the internal auditory veins.*" It was through these veins, Dorello believed, that the infection was transmitted. On the contrary, Gradenigo thought that "*the infectious process through peritubaric pneumatic cells or through those of the carotid canal extends as far as the tip of the pyramid.*"^[17,18,23] Yet, this route, according to Dorello would "*have given rise to more severe consequences and have required a long period before returning to normal.*"^[8]

THE END

Giuseppe Gradenigo died on 15 March 1926, in Treviso, Italy, and was buried with exceptional honors and respect.^[2,7,37,41] Italians and foreigners sent many telegrams, among whom was Benito Mussolini, the Italian Air Force, and the University of Turin.^[37]

According to an obituary of that time, Gradenigo was “the ‘Master’ in the true sense of the word. His words were for the pupils an invitation for pursuit of truth. They stimulated them during their patient and scrupulous researches, which could contribute, in a significant way, to the enrichment of our scientific knowledge.”^[40]

CONCLUSIONS

Giuseppe Gradenigo made notable contributions to Audiology^[37] and Neurosciences^[41] in general. Even though his name lives on nowadays only in the eponym “Gradenigo’s syndrome,” his accomplishments are much wider and cast him among the emblematic figures of science. His inherent tendency for discovering the underlying mechanisms of diseases and his vision of guaranteeing quality of services, professional proficiency, respect, and dedication toward the patients^[6] is in fact what constitutes his true legacy to the next generations. After all, Gradenigo was in complete agreement with Professor De Rossi’s statement (1892) that “the scientist should not shrink his brain, by limiting it to a special study, but should continue to cultivate it, and not separate it from the rest of the scientific world which is the basis of medical and surgical culture.”^[7]

REFERENCES

1. Anonymous: Laryngology, rhinology, and otology. *Br Med J* 1904;2:605.
2. Anonymous: The death of giuseppe gradenigo. *JAMA* 1926;86:1710.
3. Calamida U. [Bibliographic essay on the scientific publications of Count Prof. Giuseppe Gradenigo – Saggio bibliografico delle pubblicazioni scientifiche del conte Prof. Giuseppe Gradenigo.] *Arch Ital Otol Rinol Laringol* 1930;41:41-75.
4. Celestino D. Gradenigo Giuseppe. In: Romanelli R, editor. [Dizionario Biografico degli Italiani – Biographical Dictionary of the Italians.] Vol. 58. Rome: Istituto della Enciclopedia Italiana; 2002.p. 323-8.
5. Chironi GP. [1903-1904 Yearbook of the R. University of Turin. 500th year from establishment – Annuario Della R. Università di Torino 1903-1904. Anno 500o dalla fondazione.] Torino: Stamperia Reale di Torino; 1904.p.63-75.
6. Congregation of the Sisters of Charity of St. Vincent De’Paoli: Introducing Gradenigo, In: Presidio Sanitario Gradenigo. 2007. Available from: http://www.gradenigo.it/Gradenigo_eng/index.php?pid=14 [Last accessed 2012 Aug 16].
7. Felisati D, Sperati G. Italian ORL Society. Past and Present. Genova: Tipografia Mengotti Carlo & c. snc; 2005.p.23, 25-26, 33-37, 47, 55, 65, 67, 109.
8. Felisati D, Sperati G. Gradenigo’s syndrome and Dorello’s canal. *Acta Otorhinolaryngol Ital* 2009;29:169-72.
9. Gradenigo G. [The structure of the embryonic middle ear: The morphological significance of the ossicles – Die embryonale Anlage des Mittelohres: Die morphologische Bedeutung der gehörknöchelchen.] *Med Jahrb* 1887;83:257.
10. Gradenigo G. [Über ein neues elektrisches Akumetermodell – On a new electric acoumetric model.] *Arch Ohrenheilk* 1890;30:240-5.
11. Gradenigo G. On the clinical signs of the affections of the auditory nerve. *Arch Otol* 1893;22:213-5.
12. Gradenigo G. [On the auricular manifestations of hysteria – Sulle manifestazioni auricolari dell’ isterismo.] Turin: Unione Tipografico-editrice; 1895.
13. Gradenigo G. [A method for the uniform notation of results of the auditory examination – Metodo per la notazione uniforme dei risultati dell’ esame uditivo]. *Arch Ital Otol Rinol Laringol* 1899;8:317-9.
14. Gradenigo G. [New optical methods of Acoumetry – Nuovo metodo ottico di acumetria.] *Arch Ital Otol Rinol Laringol* 1899;9:46-8.
15. Gradenigo G. [The hypertrophy of the pharyngeal tonsil. One Monography – Die Hypertrophie der Rachentonsille. Eine Monographie.] *Klin Vortr Otol* 1901;4:181-392.
16. Gradenigo G. [On the decrease in the intensity of the sound of the tuning fork in relation to the duration of vibration – Sul decremento dell’ intensità del suono del diapason in rapporto alla durata di vibrazione.] *G Accad Med Torino* 1903;9:622.
17. Gradenigo G. [Pathology and Therapeutics of the Ear and Upper Respiratory Passages (Otology, Rhinology, Laryngology) – Patologia e Terapia Dell’ Orecchio e Delle Prime Vie Aeree (Otologia, Rinologia, Laringologia).] Firenze, Italy: S. Lattes & C., Librai-Editori; 1903.
18. Gradenigo G. [On a particular syndrome of intracranial complications concerning the ear: Paralysis of the abducens of post-otic origin – Sur un syndrome particulier des complications endocraniennes otitiques: Paralyse de l’ abducteur d’ origine otitique.] *Annales des Maladies de l’ Oreille, du Larynx du nez et du pharynx* 1904;30:120-52.
19. Gradenigo G. [On circumscribed leptomeningitis with spinal symptoms and on paralysis of the abducens nerve of post-otic origin – Über circumscriphte Leptomeningitis mit spinalen Symptomen und über Paralyse des N. abducens otitischen Ursprungs.] *Arch Ohrenheilk* 1904;62:255-70.
20. Gradenigo G. [On circumscribed leptomeningitis and on abducens paralysis of post-otic origin – Sulla leptomeningite circoscritta e sulla paralisi dell’ abducente di origine otitica.] *G Accad Med Torino* 1904;10:59-64, 361-7.
21. Gradenigo G. [On a new case of paralysis of the abducens nerve of post-otic origin: Communication made to the R. academy of medicine in Torino in the session of April 22, 1904 – Sopra un novo caso di paralisi dell’ abducente di origine otitica: Comunicazione fatta alla R. academia di medicina di Torino nella seduta dei 22 aprile 1904.] Turin: Stamperia dell’ unione tip. Editrice Torinese; 1904.p.1-4.
22. Gradenigo D. [On the measurement of hearing by means of diapason – Sopra la misurazione dell’ udito col mezzo dei diapason.] *Arch Ital Otol Rinol Laringol* 1905;16:265-78.
23. Gradenigo G. [Abducens nerve palsy originated from otitis – Über die Paralyse des Nervus abducens bei Otitis.] *Arch Ohrenheilk* 1907;74:149-87.
24. Gradenigo G. [On the diagnostic criteria for the diseases of the auricular labyrinth – Sui criteri diagnostici nelle malattie del labirinto auricolare]. In: Clerici A, editor. *Il Morgagni*. Milano: Società Editrice Libreria; 1907.p.593-624, 696-709.
25. Gradenigo G. [On Acoumetry. Proposal for New Acoumetric Methods – Sulla Acumetria. Proposta di Nuovi Metodi Acumetrici.] Siena: Tip. Editrice S. Bernardino; 1908.
26. Gradenigo G. [Simple device to obtain constant and scalable intensity with electricity – Dispositivo Semplice per ottenere Suoni di intensita costante e graduabili colla elettricità.] *Arch Ital Otol Rinol Laringol* 1916;27:1-4.
27. Gradenigo G. [Was Helmholtz really the creator of the hearing theory that bears his name? – Fu Helmholtz veramente l’ ideatore della teoria sulla audizione che porta il suo nome?]. *Arch Ital Otol Rinol Laringol* 1917;64:10-2.
28. Gradenigo G. [On the derivation of embryonic stapedius: The homology of auditory ossicles in vertebrates – Sulla derivazione embrionale della staffa: La omologia delle ossicina dell’ udito nei vertebrati.] Turin: Vincenzo Bona; 1923.
29. Iaconetta G, Fusco M, Cavallo LM, Cappabianca P, Samii M, Tschabitscher M. The abducens nerve: microanatomic and endoscopic study. *Neurosurgery* 2007;61(3 Suppl):7-14; discussion 14.
30. Marchese-Ragona R, Marioni G, Staffieri A. The unfinished Turandot and Puccini’s laryngeal cancer. *Laryngoscope* 2004;114:911-4.
31. Marchese-Ragona R, Staffieri A. [The last days of a great composer – Gli ultimi giorni di un grande compositore]. In: Felisati D, Sperati G, editors. *Pazienti Celebri – Malati O.R.L. nella storia e nell’ arte*. Rome: Società Italiana de Otorinolaringologia e Chirurgia Cervico-Facciale; 2008.p.247-58.
32. Montelucci R. [On limited leptomeningitis and on abducens paralysis of post-

- otic origin – Sulla leptomeningite circoscritta e sulla paralisi dell' abducente di origine otitica.] *Bollettino delle Malattie dell' Orecchio, dela Gola e del Naso* 1904;8:184.
33. Nathan H, Ouaknine G, Kosary IZ. The abducens nerve. Anatomical variations in its course. *J Neurosurg* 1974;41:561-6.
 34. Politzer A, Gradenigo G, Delsaux V. The choice of a simple and practical acumetric formula. *J Laryngol* 1904;19:525-32.
 35. Sperati G, Felisati D: Birth and development of otorhinolaryngology (ORL) in Italy. *J Laryngol Otol Suppl* 2005;119:60-3.
 36. Stephens D. A History of Tinnitus. In: Tyler RS, editor. *Tinnitus handbook*. San Diego, CA: Singular Thomson Learning; 2000. p.437-48.
 37. Stephens D, Orzan E, Galletti Di San Cataldo F: Giuseppe Gradenigo and his contributions to audiology. *J Laryngol Otol* 1997;111:418-23.
 38. Strickland EM, Hanson JR, Wis M, Anson BJ. Branchial Sources of Auditory Ossicles in Man. I. Literature. *Arch Otolaryngol* 1962;76:100-22.
 39. Stuffer A. [On the decrease in the intensity of the sound of the tuning fork in relation to the duration of vibration – Sul decremente dell' intensità del suono del diapason in rapporto alla durata di vibrazione. *Bollettino delle Malattie dell' Orecchio, dela Gola e del Naso* 1904;1:21.
 40. Torrigiani CA. Giuseppe Gradenigo. *Acta Otolaryngol* 1926;9:401-3.
 41. Umansky F, Elidan J, Valarezo A. Dorello's canal: A microanatomical study. *J Neurosurg* 1991;75:294-8.