

The origin of the modern Italian nephrology at the dawn of the 20th century

Le nostre storie: vite di nefrologi

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ABSTRACT

The author singled out the first decade of the 20th century as the time in which the renewal of academic medicine in post-unification Italy was concluded, while the changes that would be induced by the following war had not yet started. A bibliographic research relating to this period was undertaken with the aim of investigating the number and the quality of the studies on kidneys published by Italian scientists. A total of 176 publications of Italian scientists dealing with kidney diseases or physiology was retrieved, 10.8% of which was published on foreign journals. The analysis of the topics treated shows that they were up to date and comparable with the contemporary studies across Europe. Moreover, the issues raised remained of interest throughout the following decades up to our day. Top Italian researchers were fairly cited, especially if they published on international journals. While at the time the state of other organs was mainly assessed by examining physical signs and symptoms, kidney studies required laboratory facilities. This limitation meant that kidney scholars usually belonged to well established medical faculties. From these schools, a few figures stood out among the others for the importance of their studies, both physiological and clinical in nature. The same figures also gave birth to the major Italian schools of internal medicine from which, half a century later, originated the Italian Society of Nephrology. The findings of this research support the conclusion that the basis of modern nephrology can be traced back to that decade.

KEYWORDS: nephrology, history, Italy, clinical schools.

Introduction

Nephrology is the branch of medical science that deals with healthy and diseased kidneys. This term was apparently coined only recently, in 1945, by the British doctor Arnold Osman (1894-1972). The Italian Society of Nephrology was the first among other national associations to use this denomination. It was founded in 1957, later than other Italian specialties scientific societies [1]. In the few years since its formal foundation, Italian nephrology has become well known and its members have attained top world positions. In spite of its success, it is not clear when and how the seeds of this science in its present form were planted in Italy.

The turn of the 20th century was a crucial time for Italian medicine, for both historical and political reasons. At that time, the renewal of medical faculties that had begun at the end of the 19th century was mostly completed. When national unification was achieved, Italy had a legacy of several medical faculties originating from the different pre-unity states. Unfortunately, these schools were not uniform in territorial distribution, human resources and facilities. The efforts of the policy makers of the new state were aimed at making universities more homogenous throughout the country and at overcoming the “cultural crisis” of medical studies, denounced by many scholars [2].

German medical schools were chosen as teaching and research models. Major steps in this direction were the introduction of physiology chairs in all medical faculties and the introduction of apprenticeships in Germany for scholars and young researchers that would learn new teaching and research methods to be applied back in Italy [3,4]. The giants of German medicine of the time were the main source of inspiration. The Leipzig school of Carl Ludwig (1816-1895) had brought forward great innovations in physiology, especially in the field of graphical recording. The description of the mechanism of glomerular filtration was one of his main contributions to kidney studies [5]. Top Italian physiologists of the second half of the 19th century, Luigi Luciani (1840-1919), Angelo Mosso (1846-1910) and their disciples studied with Ludwig and, once back to Italy, applied the methods and the research interests of their master in their labs. Renal physiology was one important example: “scientific medicine”, i.e. medical lab research based on natural sciences methodology, was brought forward in antithesis to the traditional clinical method, based only on reasoning at the patient’s bed.

This renewal process took nearly 30 years to complete but eventually yielded its fruits in terms of research quality and international reputation. The 1906 Nobel prize awarded to Camillo Golgi (1843-1926) and the description of the sphygmomanometer by Scipione Riva-Rocci (1863-1937) are good examples of this revival of Italian medicine [6]. Therefore, we can identify the first decade of the 20th century as the time in which the foundations of *modern* Italian medicine were laid, after the post-unification renewal of academia and before the beginning of WWI, which changed all plans and prevalent interests for at least a decade. We know very little about kidney studies at the time. Since the analysis of scientific production is a sound method to assess the level of knowledge in a specific sector, we have looked at the studies on kidneys published by Italian researchers over that period. The aim of the investigation was to ascertain how widespread the interest in kidney studies was, who were the researchers, and where they worked. Finally, we assessed the quality of these papers within the larger European setting.

Material and Methods

The bibliographic research was performed on the Index-Catalogue of the Library of the Surgeon-General's Office (United States Army), followed by a cross-reference research. Keywords used were kidney, kidney disease, nephritis, uremia, albuminuria, and hypertension. The years considered were 1898 to 1910.

Results

We have retrieved 176 papers dealing with the subjects listed above; 19 (10.8%) were published on German journals. Articles are distributed among 62 medical journals, 9 of which were German. Among the publications retrieved, 9 are monographs (2 in German), and 3 are chapters in internal medicine treatises. The topics are shown in Table I. The most addressed subjects in the field of experimental and physiological research are urinary and plasmatic osmolality, urinary excretion of organic and inorganic solutes and the mechanism of glomerular filtration. These, especially when published on German journals, are the longest articles with an average number of pages higher than 30.

Subject	number	%
Nephritis	46	26.1
Physiological & experimental	41*	23.2
Uremia	16	9.0
Laboratory	16	9.0
Histopathology	15	8.5
Nitrogen metabolism	8	4.5
Albuminuria	5	2.8
Hypertension	3	1.7
Cystic disease	3	1.7
Diabetes	1	0.6
Unclassifiable	22	12.5
Total	176	100
*12 published on German journals		

Table I: Subjects treated in Italian papers about kidney (1898-1910)

The proceedings of the Italian Society of Internal Medicine, founded in 1887, produced 11 papers on kidney diseases. The authors are distributed among 14 centers (see Table II). We have found that 13 research papers were produced by surgeons (7.4%). The topics of these papers are experimental kidney ischemia, hematuria, cystic kidney disease and renal function tests.

We have also checked how well-staffed were the different medical faculties at the time, to try and understand how well-endowed they were. The centers with the highest number of chairs were Naples (33), Turin (22), Genoa (19), Florence and Pavia (17). The number of chairs at each faculty and the number of papers published are significantly correlated. The schools with more papers are also distinguished by the presence of internationally renowned institutes of physiology. The authors with the highest number of publications are Giulio Ascoli (1870-1916) with 12 papers, Filippo Bottazzi (1867-1941) with 12, Pietro Grocco (1856-1916) with 7 and Gino Galeotti (1867-1921). Galeotti, a famous pathologist, was the Italian scientist most cited abroad at the time [7].

City	% of Papers	Academic
Naples	23	yes
Florence	14	yes
Genoa	11.2	yes
Rome	11.2	yes
Pavia	8.1	yes
Turin	7.9	yes
Milan	7.3	no
Pisa	5.7	yes
Padua	4.1	yes
Perugia	1.7	yes
Siena	1.7	yes
Ferrara	1.7	yes
Venice	1.2	no
Parma	1.2	yes

Table II: Distribution of papers among Italian centers

Uremia was mainly studied by Ascoli, Carlo Forlanini (1847-1918) and his disciples Riva-Rocci, Ferdinando Micheli (1872-1937) and Angelo Ceconi (1865-1937) [8,9,10,11,12]. The relationship between kidney and hypertension was investigated by Forlanini, Riva-Rocci, Luigi Zoja (1866-1959) and Raffaello Silvestrini (1868-1959) [13,14,15,16]. Notable articles on nephritis and albuminuria were published by Ascoli and Zoja [17]. At that time, the leading figure in kidney pathology was Achille Monti (1863-1937) who wrote textbooks and presented papers at international conferences [18]. Likewise, the studies on experimental renal ischemia by Guido Ferrarini (1879-1953), a surgeon in Pisa, still have great value from a technical standpoint [19].

Laboratory investigations represent a fair share of the analyzed publications. They are authored by clinicians like Grocco and Micheli, or by surgeons like Roberto Alessandri (1867-1948) from the surgical Roman school [20,21,22,23]. Physiological studies have Galeotti and Bottazzi from Naples as leading authors [24,25,26] (see Fig. 1). Papers on cystic disease were published only by Alberto Michelangelo Luzzatto (1874-1924) from Ferrara [27]. Hematuria was studied by Davide Giordano (1864-1954), an eminent surgeon in Venice renowned abroad for the eponymous clinical sign [28]. Cesare Frugoni (1881-1978) studied the relationships between kidneys and neuro-vegetative nervous system [29,30]. Monographs or chapters on kidney diseases were written by Umberto Gabbi (1860-1933) and Silvestrini [31,32,33].

Notwithstanding the lack of a proper citation database for the observed period, we have looked at the citations of these Italian studies on foreign journals and textbooks. The more quoted papers are those published in foreign journals. Most of them deal with experimental or physiological research. Articles in Italian journals are usually cited in Italian papers, but there are a few exceptions. For instance, the work of Luzzatto on kidney cystic disease, although written in Italian, is also cited in high rated American research journals [34]. The same goes for the studies on uremia by Forlanini and Riva-Rocci. Their work ascribing the cause of uremic symptoms to “vascular spasms” and hypertension has been cited in the international literature up to the early thirties of 20th century [35]. The 1903 monograph by Guido Ascoli on uremia was also quoted extensively, although it roused much controversy [11,35].

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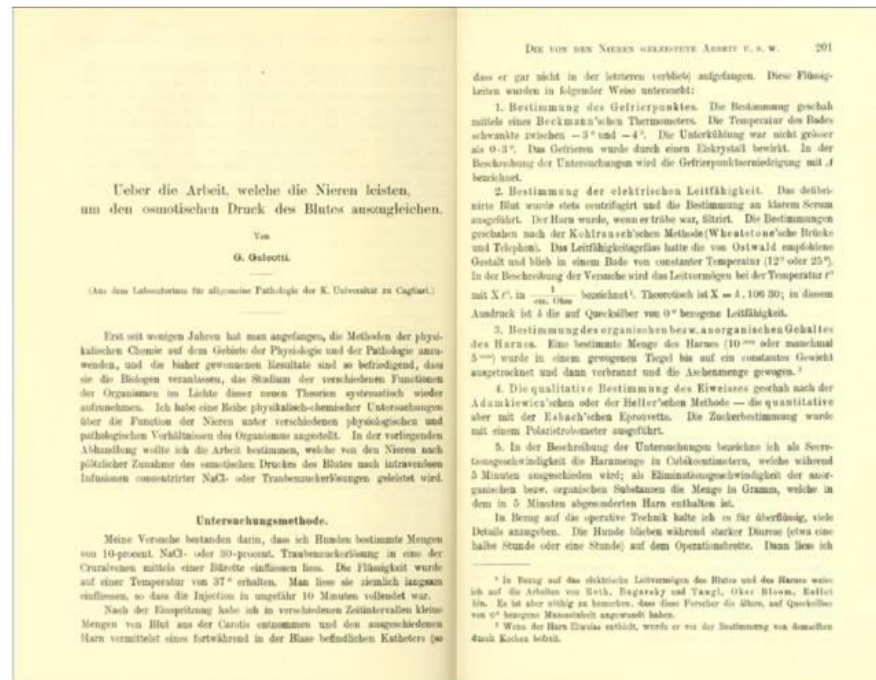


Figure 1: Title page of Galeotti's paper on the role of kidney on the regulation of plasma osmolarity published in 1902 (Ref n.25).

Discussion

The analysis of kidney studies published at the turn of the 20th century gives us an insight into medicine and medical research in Italy at the time and increases our knowledge of how *modern* Italian nephrology developed.

The number of Italian medical journals included in the present study is 53. This is a disproportionate number if compared to the number potential readers, which can be estimated by looking at the number of academics. At the time, there were only 267 chairs distributed among the 17 Italian medical faculties. In addition to the limited diffusion of the results, the dispersion of papers across many journals lead to an inadequate selection process for publication. Potential foreign readers were therefore hampered by the language and by the excessive number of journals and some important scientific results published in Italy were completely neglected. Conversely, Italian scholars who published on European journals received widespread notoriety. Bottazzi, also a Nobel candidate, and Galeotti are good examples.

To evaluate whether Italian kidney studies were up to date, we must look at the cultural context of the time. We have enough elements to suggest that Italian scholar were well informed about European research studies: a good piece of evidence is provided by a clinical journal "Il Policlinico", from Rome, that presented in every issue a selection of articles from major medical journals in Germany, France and England. Also, Italian scientists in the field of physiology had continuous and

direct relationship with European colleagues, with whom they would often work together.

To assess the quality of Italian nephrological research we must make a short technical digression. At the time, the most advanced exploration of kidney function was the analysis of plasma and urinary osmolality. This was made possible by the recent discovery of cryoscopy. The research by Bottazzi, Galeotti and by the followers of their Naples school in this field were certainly relevant and well-known to European scientists. Bottazzi, for example, was invited by the famous British physiologist Michael Foster (1836-1907) to give a lecture at Cambridge University. Galeotti became a world-leading scholar on the treatment of infectious diseases and was invited to give lectures as far as India and China. The same goes for other Italian physiologists working in Rome, Turin, Pavia and Florence who had all developed their research skills thanks to the physiology chairs established in the previous years and offered to leading foreign figures [36].

As far as clinical kidney studies are concerned, we must remember that the diagnostic process is based almost completely on laboratory procedures. At the time, this contrasted sharply with the diagnostics of diseases in other organs. In fact, x-rays and electrocardiography were not introduced in the medical practice until the early 20th century and heart and lungs were investigated exclusively through physical examination. Instead, urine analysis and the recently introduced measurements of blood urea and blood pressure were already the pillars of kidney disease diagnosis [33,37]. In the second half of the 19th century in Italy most clinical institutes did not have any laboratory instruments. This changed thanks to the champions of the new clinical methods based on biochemical-physiological know-how, Alberto Riva (1844-1916) and Grocco who both started their academic career as professors of clinical medicine at the university of Perugia before moving to more prestigious chairs throughout Italy [38]. From the records of the University we have learned that Riva got the chair in 1878 and set up the first clinical lab. When Grocco took over in 1884 the laboratory was enriched with new, modern equipment [39]. This modernization was opposed by many, as shown by the label of “chemical clinicians” that was ironically given to these physicians [40]. Nonetheless, at the end of the century, the renewal of the greatest Italian medical faculties was completed although it was restricted to major, properly equipped, universities. This is also confirmed by the results of our analysis: most of the relevant research papers were produced in Turin, Pavia, Florence, Naples and Rome, that also hosted renowned institutes of physiology. Moreover, knowledge of chemistry, physics and other sciences was needed to approach kidney studies. These necessary qualifications operated a positive selection among clinicians, as confirmed by the fame attained by these key figures and by their schools in the following years.

On the whole, the analysis of the publications at the dawn of the 20th century shows the great interest of Italian clinicians and researchers towards kidney studies. Their work was relevant and, when it managed to get the attention of European colleagues, was highly esteemed. Unfortunately, the diffusion abroad was restricted by the dispersion of papers among too many Italian periodicals and by the small number of studies published on international journals.

On the other hand, the work produced during this decade generated long-term effects that will be appreciated only after many years, after WWII interrupted kidney studies for quite a while, bringing forward more pressing needs. But the seeds were already sown: the cultural legacy of these scholars goes beyond the specific scientific achievements of the decade and actually represent a quantum leap from the previous century. Most of the clinicians who published studies on kidneys during the period considered here later became leaders of medical schools that influenced Italian medicine, and especially nephrology, throughout the 20th century. A few examples deserve to be mentioned. From the school of Grocco emerged Frugoni followed by Flaviano Magrassi (1908-1974) and his disciples Carmelo Giordano (1930-1916), founder of Naples

nephrological school, and Guido Melli (1900-1985), founder of Milan Nephrology specialty school. Micheli and Angelo Ceconi (1865-1937) funded Turin nephrological school, that was carried on by Pio Bastai (1888-1975), the founder of the first journal about kidney studies in the world, “Minerva Nefrologica”, in 1954 [40]. In Turin, the baton was later passed on to Pietro Sisto (1880-1964), whose followers Alberto Amerio (1918-2006) and Antonio Vercellone (1923-2000) became top figures of modern nephrology [41,42]. Umberto Gabbi (1860-1933), renowned for its studies on uremia in Parma, had Domenico Campanacci (1898-1986) as his disciple, who later became the founder of Bologna nephrological school [43]. We can clearly see the Ariadne’s thread that from that decade leads to modern nephrology. Surgeons also had an important role in this process: the surgical school of Alessandri in Rome, which had produced early research studies on kidneys, continued with Paride Stefanini (1904-1981) and his disciples, who in 1966 performed the first kidney transplant in Italy [44].

Conclusions

Our investigation shows that an important number of kidney studies were produced in Italy in the first decade of the 20th century thanks to key figures in the field of internal medicine. We suggest that the subsequent scientific progress in nephrology in Italy stemmed from the same selected group of clinicians that also gave birth to the greatest Italian schools of internal medicine [45]. The natural consequences were the full development of internal medicine on the one hand and the confirmation of the maturity of the specialty on the other, culminating with the foundation of the Italian Society of Nephrology.

REFERENCES

1. Fogazzi GB. 28 Aprile 1957: la fondazione della Società Italiana di Nefrologia. In Fogazzi GB, Schena FP. *Persone e fatti della Nefrologia Italiana (1957-2007)*. Wichtig Editore: 2007, p. 135.
2. Cazzaniga A. *La grande crisi della medicina italiana nel primo ottocento*. Milano, Hoepli: 1951.
3. Dröscher A. «Fallaci sistemi forestieri». I docenti italiani di fronte alla riforma della medicina, 1860-1870. In Ferraresi A, Signori E. (a cura di). *Le Università e l'Unità d'Italia (1848-1870)*. Bologna, CISU: 2012, p. 217.
4. Dröscher A. *Le facoltà medico-chirurgiche italiane: 1860-1915*. Bologna, Clueb: 2002, p. 213.
5. Ludwig C. *De viribus physicis secretionem urinae adjuvantibus*. Marburg, Elwert: 1842.
6. Riva-Rocci S. Un nuovo sfigmomanometro. *Gazzetta Medica di Torino* 1896; 50:1001-07.
7. La diffusione della ricerca biomedica italiana in Germania. In *Genetica, embriologia e ambiente: l'evoluzione in gestazione. Un progetto di ricerca: un Convegno di studi. «Il Veltro. Rivista della Civiltà Italiana»* 2011; 55:35-54.
8. Ascoli G. *Vorlesungen über Urämie*. Jena, Fisher: 1903.
9. Forlanini C. Nota clinica sopra un caso di accesso uremico curato col salasso; contribuzione degli studi sulla patogenesi dell'uremia. *Ist Lomb Acc Sci Lett Rendiconti* 1901; 34:203-16. (Anche in *Gazz Med Torino* 1901; 52:141-61.)
10. Ascoli G, Figari F. Ueber Nephrolysine. *Berl Klin Wchnschr* 1902; 39:634-36.
11. Ceconi A, Micheli F. Intorno alla questione delle nefrolisine. *Milano, Morgagni* 1904; 46:209-31.
12. Ceconi A. Del significato del cloruro sodico nella patologia della nefrite e nella genesi dei fenomeni uremici. *Riv Crit Clin Med Firenze* 1906; 7:661-701.
13. Forlanini C. Contributo allo studio della patogenesi dell'ipertensione arteriosa. *Gazz Medica di Torino* 1899; 50:561-72.
14. Riva-Rocci S. Le sostanze ipertensive del secreto renale; contributo allo studio dell' uremia. *Gazz Med Torino* 1898; 49:361-81.
15. Zoja L. Sopra un caso di nefrite senza ipertensione e con arteriosclerosi. *Boll Soc Med Parma* 1909; 2:168-74.
16. Silvestrini R, Verità G. Nefrite e ipertensione. *Riv Crit Clin Med Firenze* 1901; 2:840-53.
17. Ascoli G, Bonfanti A. Weitere untersuchungen über alimentare albuminurie. *Munch Med Wochenschr* 1903; 41.
18. Monti A. Contribution a l'histologie pathologique du rein. *Compte Rendues Congr Internat Med* 1904; 14:205-25.
19. Ferrarini G. Sopra le lesioni prodotte nel rene dall'ischemia temporanea e la loro riparazione anatomica. *Milano, Morgagni* 1903; 45:593-626.
20. Grocco P. La creatinina in urine normali e patologiche. *Ann Chim Farm* 1886; 3:211-28.
21. Micheli F. Della ricerca degli aminoacidi nelle orine e in altri liquidi organici in alcune condizioni patologiche. *Arch Sci Med Torino* 1907; 53-79.
22. Alessandri R. Contributo alla chirurgia renale specialmente in rapporto al valore comparativo e complessivo dei vari metodi proposti per l'esame della funzione dei reni. *Arch Soc Ital Chir* 1908; 303-76. (Anche in *Folia Urol Lpz* 1908; 2:137-57).
23. Dominici L. Intorno ai metodi di diagnosi della funzionalità renale nelle nefropatie di competenza chirurgica. *Fol Urol Lpz* 1909; 3:17-92.
24. Bottazzi F, Enriquez P. Ueber die Bedingungen des osmotischen Gleichgewichtsmangels zwischen den organischen Flüssigkeiten und dem äusseren Medium bei den Wasserthieren. *Arch F Physiol Leipz* 1901; Suppl. Bd:109-70.
25. Galeotti G. Ueber die Arbeit, welche die Nieren leisten, um den osmotischen Druck des Blutes auszugleichen. *Arch F Physiol Leipz* 1902; 200-42.
26. Galeotti G. Sulla secrezione renale nelle nefriti sperimentali. *Clin Mod Pisa* 1901; 7:217-19.
27. Luzzatto AM. La degenerazione cistica dei reni. I suoi esponenti anatomico-patologici e le sue forme cliniche. Venezia, S. Marco: 1900.
28. Giordano D. Die Behandlung der renalen Hämaturie. *Klinisch-therapeutische Wochenschrift* 1909; 16:1157-62.
29. Frugoni C, Pea A. Intorno al centro e ai nervi secretori del rene. *Lo sperimentale* 1906; 60:136-51.
30. Frugoni C. Sur les rapports entre le pneumogastrique et la fonction rénale. *Archiv Ital Biol* 1908; XLIV(2):213-27.
31. Gabbi U. Sulla patogenesi dell'uremia ricerche sperimentali e cliniche. Milano, Vallardi: 1895.
32. Gabbi U. *Malattie dei reni*. In *Trattato completo di patologia e terapia medica speciale*, diretto da A. De Giovanni, IV. Milano: 1901, pp. 3-113
33. Silvestrini R, Marchetti G, Steffanelli P. *Manuale di analisi delle urine*. Milano, Vallardi: 1909.
34. Bunting CH. Congenital cystic kidney and liver with family tendency. *J Exp Med* 1906; 8:271-88.
35. Volhard F. Die doppelseitigen hämatogenen Nierenkrankungen (Bright'sche Krankheit). In Mohr L, Staehelin R. *Handbuch der Inneren Medizin*. 2nd ed, vol. 3. Berlin, Springer-Verlag: 1918; 1149.
36. Candeloro G. *Storia dell'Italia moderna*. Vol V. Milano, Feltrinelli: 1968, p.78.
37. Picard J. De la presence de l'urée dans le sang et de sa diffusion dans l'organisme a l'état physiologique et a l'état pathologique. Strasbourg, These: 1856.
38. Cosmacini G. *Medici nella storia d'Italia*. Bari, Laterza: 1996, p. 112.
39. Pitzurra M. *Lo Spedale Grande a Perugia*. Perugia, Benucci Ed.: 1996, p. 168.
40. Andreucci V. 50 anni di nefrologia: tra scienza e sviluppo organizzativo. *G Ital Nefrol* 2010; 27:409-16.

41. Fogazzi GB. I classici della nefrologia italiana "I fondamenti fisiopatologici per la nosografia e la classificazione delle malattie renali bilaterali" di Pio Bastai (1888-1975) e Massimo Crepet (1911-1994). *G Ital Nefrol* 2008; 25:574-80.
42. Losito A. Intervista al Professor Alberto Amerio uno dei primi Nefrologi Italiani. *G Ital Nefrol* 2008; 25:89-93.
43. Sasdelli M. Un ricordo di un grande medico e dell'arte medica che fu. *Il Cesalpino* 2011; 10(27):27-32.
44. Santoro E, Ragno L. Cento anni di chirurgia. Roma, Edizioni Scientifiche Romane: 2014.
45. Federspil G. Le scuole cliniche italiane. Padova, Padova University Press: 2011.