

GIANTS IN NEPHROLOGY

Gabriel Richet: the Man and the Scientist



Raymond Ardaillou¹, Pierre Ronco²

(1) Académie nationale de médecine, Paris, France

(2) Service de néphrologie, Hôpital Tenon, Paris, France

Address correspondence to: Raymond Ardaillou; Académie nationale de médecine, 16 rue Bonaparte, 75006 Paris; Cell:331 42345782 e-mail: raymond.ardaillou@academie-medecine.fr

Abstract

Gabriel Richet who died in Paris in October 2014 was the fourth of a brilliant dynasty of professors of medicine including a Nobel prize, his grandfather, Charles Richet. He behaved courageously during the Second World War and participated in the Campaign of France in 1940 and in the combats in the Vosges Mountains in 1945. His family participated in the resistance during the German occupation of France and three of his parents including his father, one of his brothers and one of his cousins were deported in Germany. At the end of the war, he was with Jean Hamburger the founder of French nephrology at Necker Hospital in Paris. He realized the first hemodialyses in France and was involved in the first allogenic transplantation that was not immediately rejected. From 1961 to 1985, he was the head of a school of

nephrology at Tenon Hospital and attracted in his department many young collaborators and scientists. He was the first to describe the role of specialized cells of the collecting duct in the control of acid base equilibrium. He was the subject of a national and international recognition. Founding member of the International Society of Nephrology in 1960, he was elected his President from 1981-1984. His fame could be measured by the number of fellows and visiting faculties from countries all over the world. When he retired in 1985, he left an important legacy involving several departments of nephrology directed by his ancient collaborators. After his retirement, he was an active member of the French Academy of Medicine and devoted much of his time to the history of medicine and, particularly, of nephrology. The main qualities of the man were his constant research of new ideas, his eagerness to work and his open mind to understand others.

Introduction

Gabriel Richet died on October 10th 2014. He was ninety-seven years old. His career is intimately linked with the birth of nephrology and its early development. He is considered as a giant in this discipline.

A brilliant dynasty

Born in 1916 during the First World War, Gabriel Richet represents the fourth generation of an illustrious series of medical doctors, all of them professors at the Faculty of medicine in Paris. His great-grandfather, Alfred Richet, surgeon, took care of the wounded soldiers in 1871 during the siege of Paris by the Prussian army. His grandfather, Charles Richet, was awarded the Nobel Prize in 1913 for the discovery of anaphylaxis. His father, Charles Richet junior, was a specialist in human nutrition and took care, at his return in 1945, of the internees in the concentration camps. On the maternal side, his mother, Marthe Trélat, was one of the first women who became residents in the hospitals of Paris. She was the great-granddaughter of Ulysse Trélat, minister during the Second republic. The aim of Gabriel Richet was to add his first name to those of his ancestors, in which he succeeded beyond all hopes.

A courageous man during the Second World War and also later

Gabriel Richet was 23 years at the outbreak of the Second World War. He had just become resident in the hospitals of Paris when he was enlisted in the

French army and took part to the military campaign in France. He was decorated with the War Cross. After a short captivity in Germany, he was released, came back to Paris and started his activity of resident. All of his family members participated in the struggle against the German occupants. Three of them were deported to concentration camps, his father to Buchenwald, one of his brothers, Olivier, also to Buchenwald, then to Dora and finally to Bergen Belsen, and his cousin, Jacqueline Richet-Souchère to Ravensbrück. At their return, they published a book on their captivity entitled “*Les trois bagnes*” (The three convict prisons). His mother, Marthe, was jailed at Fresnes, close to Paris. Soon after the liberation of Paris, Gabriel Richet enrolled in the army under the high command of General de Lattre de Tassigny. In the beginning of 1945, fights continued in the South of Alsace where Gabriel Richet served as a doctor in the French commandos. He was wounded in Durrenentzen, a village close to Colmar, received three military citations and was decorated with the award of “*Chevalier de la Légion d'Honneur*” by General de Gaulle in Karlsruhe in April 1945. After 45 days in a military hospital, he returned to the commandos up to the end of the war and was demobilized in summer 1945. He was attached to Alsace and until his old age he regularly attended the meetings of the veterans of the commandos in Durrenentzen.

The cofounder of nephrology at Necker Hospital

Demobilized from the army, Gabriel Richet joined the department of medicine directed by Louis Pasteur

Vallery Radot, a grandson of Louis Pasteur, where he met Jean Hamburger (Figure 1). He was immediately attracted by his personality because at that time, Jean Hamburger was persuaded that the period of a purely clinical medicine was ended and that it was essential to understand the mechanisms of the diseases with new methods based on laboratory and histological investigations such as those in progress in United States. He followed Jean Hamburger in Necker Hospital to establish with him the first French department of nephrology (Figure 2). He worked together with Jean Hamburger during ten years and both are considered to belong to the post-war rebuilders of the French academic medicine. Gabriel Richet after having spent three months in Boston in the department of nephrology directed by John Merrill introduced the treatment of acute renal failure with the artificial kidney and he could with this new method considerably improve the prognosis of this disease associated mainly at this time with post abortum sepsis and crush syndrome. Research studies were carried out and many discoveries were realized, for example the presence of a transient decrease in the number of bone marrow erythroblasts in acute renal failure leading to the hypothesis of a renal hormone controlling red cell production [1]. He also demonstrated that most patients with advanced renal failure died from serious electrolyte changes including hyperkalemia, acidosis and hyponatremia rather than retention of waste products such as urea [2]. Hyponatremia was shown as a consequence of the retention of endogenous water due to lipid oxidation [3]. Introducing the percutaneous kidney biopsy pioneered by Claus Brun in Denmark, Jean Hamburger, Renée Habib and Gabriel Richet contributed to the routine histological diagnosis of glomerular diseases. Together with Paul Michielsen, they performed the first studies of renal histology using electron microscopy. In 1952, Gabriel Richet was involved in the first allogenic renal transplantation from a mother to her son who had lost his unique kidney after a traumatism [4]. The patient was irradiated before the graft in order to attenuate the immunological reject. The kidney graft was not immediately rejected as observed before but, in contrast, kidney function persisted about three weeks opening up exciting new therapeutic perspectives in living related transplantation. In 1955, together with Jean Hamburger and Jean Crosnier, he developed the concept of renal intensive care aimed at correcting disorders of the major fluid electrolyte, acid base and other metabolic functions, thereby markedly improving the prognosis of acute renal failure [5]. The concept was rapidly applied to other medical disciplines leading to the creation of the first departments of intensive care. All these advances were permitted by major technical progresses including rapid determination of plasma concentrations of sodium and potassium with flame photometers, plasma protein separation with electrophoresis, pH meters and new performant optical photometers.

The head of the Tenon school of nephrology

In 1961, Gabriel Richet became head of a department of medicine at Tenon Hospital that he transformed into a department of nephrology over the four following years (Figure 3). To fulfill this objective, he recruited assistants who initially were Claude Amiel, Liliane Morel-Maroger, a brilliant pathologist, and Raymond Ardaillou. He succeeded in obtaining the construction of a new building by the “Assistance Publique-Hôpitaux de Paris” and the University with an intensive care unit, a hemodialysis unit and research laboratories. He could thus develop his team with new members including Jean-Paul Fillastre, Françoise Mignon, Jean-Daniel Sraer, Alain Meyrier, Pierre Verroust, Eric Rondeau and Pierre Ronco (Figure 4). A second wing was built some years later by the “Institut National de la santé et de la recherche médicale (INSERM)” with only research laboratories and Gabriel Richet was appointed as head of an INSERM research unit. Gabriel Richet spent 24 years at Tenon Hospital. It is not possible to describe all the discoveries obtained during this period. Gabriel Richet had his own research program. One of his essential contributions was to demonstrate with



Figure 1.
The staff of the department of medicine at Broussais Hospital (1947). Louis Pasteur Vallery Radot, head of the department, sits in the middle of the second rank. Gabriel Richet is the seventh on his right and is easily recognized by his cigarette.



Figure 2.
The staff of the department of nephrology at Necker hospital (1955). Gabriel Richet is the second on the left of Jean Hamburger.

Jacqueline Hagège and Manfred Gabe that intercalated cells of the rat collecting duct, also known as dark cells, secreted bicarbonate during metabolic alkalosis and respiratory acidosis and were morphologically different from other cells that secreted H⁺ ions as shown by scanning and transmission electron microscopy. Therefore, he described for the first time the role of specialized cells of the collecting duct in the control of the acid base equilibrium and distinguished the A and B types of intercalated cells showing that they were different functional forms of the same kind of cells [6]. He also studied with monoclonal antibodies made in the laboratory Tamm Horsfall protein in plasma and urine of patients with renal diseases [7]. He participated in many clinical studies with his collaborators. Thereby, his goal to create in Tenon hospital a department of national and international excellence for renal diseases was largely reached. Moreover, he succeeded in stimulating research in other disciplines and the hospital which was at his arrival an establishment uniquely devoted to clinical activities became a center of investigations and research. He frequently proposed to his collaborators unsolved questions as new topics of research. Like in the parable of the sower, many grains of wheat died, but some of them sprang up and allowed new discoveries to be done. In fact, he let a great freedom to his associates in the choice of their own research project, followed the progress of their research with much interest and was very happy when they reached international recognition.

An international and national recognition

Gabriel Richet is one of the early giants of French and international nephrology. He was a founding member of the international Society of Nephrology (ISN). Among his many roles in the leadership of ISN, he was co-General Secretary of the ISN's first Congress in Geneva and Evian in 1960 chaired by Jean Hamburger, and ISN President from 1981-84. He received many awards including *Honoris Causa* Degrees; among those awards, the most prestigious probably was the Jean Hamburger Prize of the ISN in 1993. His fame could be measured by the large number of fellows and visiting faculties from coun-

tries all over the world, who trained or did research in this multilingual and multicultural Tenon community, a virtual nephrological tower of Babel. Gabriel Richet provided a unique atmosphere of intellectual curiosity and creativity by providing support and guidance to each of them, while at the same time leaving the freedom to all to develop their own projects. Thanks to his generosity and his warm personality all who worked with him would consider him as a "father" figure, a position that he accepted and filled with a lot of humor and joviality. Thus doctors from around the globe will remember him with warmest personal feelings, and each could contribute an anecdote testifying to his humanity, tolerance and personal support. It is not possible to cite all of them, but only those with whom permanent links were established such as Detlef Schlondorff, Morris Schambelan and Gary Striker (USA), Stanislas Czekalski, and Hanna Debiec (Poland), Emilio Podjarny (Israel), Kiyoshi Kurokawa (Japan), Diego Lopez Novalez (Spain), Vicky Cattell (UK), Judith Withworth (Australia), Václav Stefanovic and Miloš Budislavjević (Yugoslavia), Lise Giroux (Canada), Pierre Cosyns (Belgium), Hedi BenMaiz (Tunisia), Tullio Bertani (Italy). Gabriel Richet was particularly attached to the relations with China. His department welcomed many students including Nan Chen who is now head of the department of nephrology at Rui Jin Hospital in Shanghai and John Cijiang He who is professor of nephrology at the Mount Sinai Hospital (New York). Gabriel Richet was appointed Grand Officer of the French Legion of Honour by the French government in 2012 (Figure 5).

The legacy

When Gabriel Richet retired in 1985, he left as a legacy, two departments of nephrology, one for the patients with chronic renal failure and those treated with hemodialysis, the other for transplanted patients and patients with acute renal failure, a department of clinical investigation in ambulatory patients and a research unit depending of INSERM. All of them were directed by his former collaborators.

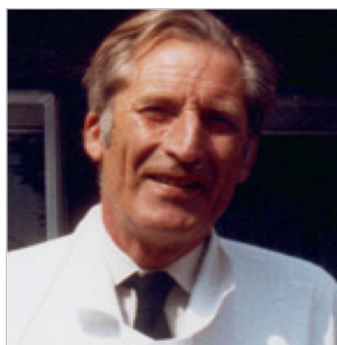


Figure 3.
Gabriel Richet head of the department of nephrology at Tenon hospital (1961-1985).



Figure 4.
The staff of the department of nephrology at Tenon hospital (1964). Gabriel Richet sits in the middle of the first rank between Raymond Ardaillou on the left and Claude Amiel on the right.

Moreover, several others became heads of departments of nephrology in different cities of France including Rouen, Limoges and Evry. He started annual meetings where they all met for discussing difficult patient records including the histological data.

The retired nephrologist and historian of medicine

After his retirement on September 1st 1985, Gabriel Richet was an active member of the National academy of medicine. He was interested by improving the conditions and methods of teaching in the medical faculties and cosigned several reports on this question for the government. He also devoted much of his time in historical studies, mainly on the history of nephrology and on the work of his grandfather Charles Richet. He published articles on the discovery of anaphylaxis [8], the report written by Georges Cuvier on the situation of public health in France at the time of the 1st Empire [9], the nephrolithiasis at the turn of the 18th and 19th centuries [10], the work of Pierre Rayer who was a precursor in the studies of renal diseases [11] and Bona-

parte's expedition in Egypt [12]. A particular mention has to be done on his studies with Italian colleagues interested in the history of medicine. Together with Carmela Bisaccia and Natale G de Santo, he studied the renal stones of Montaigne [13], the medicine in the "*Encyclopédie of Diderot et d'Alembert*" [14], the build-up of clinical science [15], Desault and the birth of nephrology [16], the contributions of Bertin [17] and Ferrein [18] to renal histology. This enumeration shows that Gabriel Richet continued to work many years after his retirement. He also received at home his ancient collaborators and discussed with them the results of their recent studies.

The man

What was the real personality of Charles Richet? He describes himself in his last lecture at Tenon Hospital in October 1985 as a distressed intellectual ("*un angoissé intellectuel*") who from the beginning of his medical career refused to be satisfied with a purely descriptive medicine, but was distressed by the thirst for knowledge, which directly accounts for two others of his qualities: his eagerness to work and his open mind to understand others. When he recruited a future resident, the two qualities to which he was the most sensitive were imagination and the taste for working. He searched in the others his own characteristics. Like Alceste, the main character in the "*Misanthrope*" by Molière, Gabriel Richet could have said "*Je veux que l'on soit homme, et qu'en toute rencontre, le fond de notre coeur dans nos discours se montre*" which could be translated into "I want to see a man in any one of us, and at every encounter, words show the depth of our heart". Gabriel Richet was essentially a generous man who showed a real interest for the life of his pupils and assistants. He was proud of their successes and sad of their failures. He will remain for the medical community an example of cleverness, humanism and nobility of character.



Figure 5.
Gabriel Richet speaking when he was appointed Grand Officer of the French Legion of Honour.

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