

HISTORY OF ONCOLOGY

The great surgeon Eugène Doyen (1859-1916) and his disputable treatments of cancer

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Summary

We present the case of Eugène Doyen, famous Professor of surgery and gifted practitioner, distinguished by his surgical techniques and inventions but hardly criticized for violating the medical morals by his experiments on cancer

grafts and the development of an anticancer serum as noisy as ineffective.

Key words: anticancer serum, cancer grafts, Eugène Doyen, surgeon

Who was Eugène Doyen?

Son of Octave Doyen, Professor of surgery and mayor of Reims, Eugène Doyen (Photo 1) begins his medical studies with his father, then he pursues them in Paris. Internal in 1881 at the Tenon hospital, Paris, he leaves to study surgery in Germany (Heidelberg and Wurzburg) and in Vienna. In 1885 he supports his thesis on the epidemic cholera. Chief of anatomical works in Reims (Photo 2), Professor of clinical surgery, he is president of honor of the International Congress of Gynecology of Moscow in 1887. He settles in Paris, where he establishes a private clinic and a laboratory: the famous Doyen Institute. Intelligent, competent, active, daring, he is a surgeon of world reputation (Photo 3); he improves the hysterolaparotomy, thyroidectomy, nephrectomy, invents instruments (Photo 4) and uses cinematographic filming (Photo 5). He purchases a wine house of champagne (Photo 6) and becomes rich. Member of the Freemasonry, man of the world, he participated in duels and became a champion sportsman. He was also involved in the trial of Mme Caillaux, who had murdered Gaston Calmette, manager of *Le Figaro*. His accomplishments, his audacities, his vanity made him look suspect in the official medical milieu.

Doyen died in 1917 at the age of 57, when completing the plan for a “trench canon” from which wonders were expected.



Photo 1. Portrait of Professor Doyen.



Photo 2. Caricature of Doyen as a skinner.

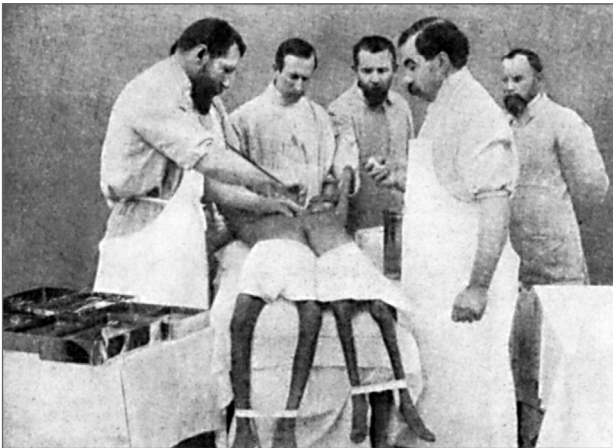


Photo 3. Doyen operating on the Siamese twins.

The cancer grafts affair of Reims

In June 25, 1891, a short paragraph published in *Le Temps* [1] was informing the public about an amazing communication for which Professor André-Victor Cornil (1837-1908) was going to give a lecture to the Academy of Medicine. A foreign surgeon, who wished to keep his anonymity, had confided to him, the previ-

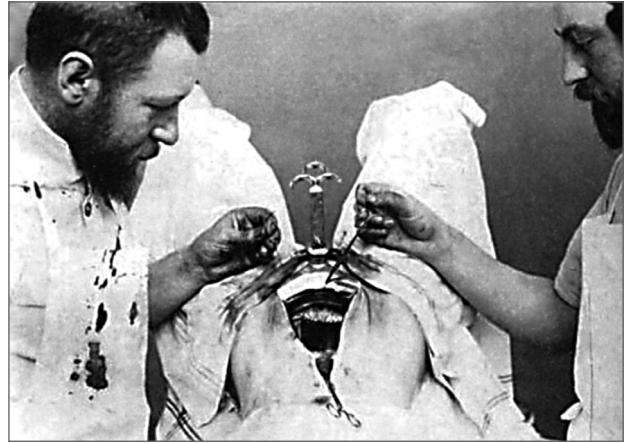


Photo 4. Doyen's dilator.

ous year, the result of two clinical observations of great scientific importance. As for their assumption, it was about reprehensible activities but by their conclusions, the proof of the infectious and contagious nature of cancer was finally demonstrated.

During the ablation of a breast tumor of two women, the surgeon had grafted to the other breast a small fragment of cancer tissue taken from the diseased part. The operation, which came off successfully in both cases, gave birth to a new malignant tumor and created the necessity for a second surgical intervention to one of the patients. The revelation provoked a general protestation from the Academy of Medicine and the press unanimously denounced this form of human vivisection. Very luckily, this was happening overseas. Being pressed by questions, Professor Cornil made it look like the audacious surgeon was American and, in order to reassure the tormented souls, the manager of Public Assistance made clear that such action was impossible to occur in French hospitals. To the Municipal Assembly of Paris, a member went up to the point to proclaim in a solemn way: "Nobody has to believe that in the hospitals anyone is surrendered to experiences *in anima vili*". [2]. The good people's rest did not last but for a little while. On the 1st of July, *La Cocarde* [3] in fact announced that the heretic surgeon was French and that the sacrilege had been committed in Reims. To sharpen the monstrosity the journal of Boulangists stated that these actions happened during the patients' chloroform sleep and without the last ones being aware of it. In the first case, the patient had to suffer the ablation of the other breast unduly contaminated. In the second case, the patient was left to her poor fate.

The case of the cancer grafts of Reims had just begun and, along with this one, the tormented career of a young Professor of Surgery in his thirties, Eugène

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Photo 5. Publicity of an operation by Doyen.



Photo 6. Caricature of Doyen advertising his champagne.

Doyen. Since July the 2nd, almost all of the surgeons of Reims presented in the *L'Indépendant rémois* [4] a communiqué made as protestation: "The undersigned surgeons of Reims, moved by the recent accusations expressed by a part of the press, assure that none of

them, in any time period, has effected any dangerous graft and they disavow any responsibility for offences charged". Only one surgeon had stayed in the shadow: Professor Eugène Doyen. It is precisely about Doyen that *L'Éclair de l'Est* was writing about the following days without naming him. In the interview that this doctor gave to a journalist of the *Temps* [5], at that time unknown to the public, he answered to the accusation with a little chagrin: "I know well to what they refer to", he said, "but what I can affirm, is that the denunciation, if there is denunciation, emanates from one of my colleagues. They envy me a lot here and they try to harm me in every way and by all means". At that point, the case had attained such an extent that the judiciary authority was led up to open an inquiry, but, due to lack of proof, Professor Eugène Doyen could not be inquired. The leakages went on. On the 26th of July, *Le Gaulois* [6] published the revelations of an eye witness of the event. This one had taken place at the *Hotel-Dieu* of Reims, in the service of Professor Arthur Decès (1831-1900), and in the presence of 8 of his students. Informed about the affair, Decès would exclaim: "Ah! As for me, I wash my hands off it". Two days later, 5 witnesses declared to the press a release certifying the exactitude of the acts reproached to Professor Doyen and Professor Decès. Facing the obvious, Doyen confirmed, in a letter addressed to *L'Indépendant rémois*, that he had never grafted the cancer. But, working in the wake of the great Louis Pasteur (1822-1895) he admitted having "just vaccinated" against cancer. "I have practiced", he was saying, "on a diseased woman having her 8th cancer recurrence, and who would wish at any cost to be saved from the suffering of a new operation, the attempt for vaccination for which I was scientifically authorized

by my previous works on animals. A fragment of tumor that had been subjected to a preliminary preparation destined to diminish its malignant potential had been introduced under the skin. This intent had been renewed by two other resurgences under the analogue conditions and for the same therapeutic purpose" [7].

Under this beautiful illumination, the Public Prosecutor's Office of Reims did not find "in the incriminated operations any culpable and worthy to chase action". But the investigation of the administrative committee of the hospices of Reims had to establish that the grafted fragments of cancer "had not suffered before any of the usual manipulations able to decrease the virulence". So the case was brought to the Tribunal of the Deputies' Chamber and, on information of the Marne Prefecture, the Minister for Home Affairs invited Eugène Doyen to put an end to such experimentations. Eighteen years later, Doyen dared to write about that: "The extraordinary campaign that had been undertaken against me in 1891, dealing with the instigation of some ignorant and jealous doctors, put an end to these researches. My first experiences are, however, interesting to recount, considering their date, since it is by the same procedure that Paul Ehrlich, almost 20 years ago, demonstrated the possibility to vaccinate a mouse inserting under this animal's skin a fragment of tumor of low virulence". [8]. In the absence of really scientific consequences, the daring experimenter had to settle immediately the legal consequences.

Les Morticoles, the novel of Léon Daudet (1867-1942), a virulent satyric of medical morals, denounced, since 1894, the dealings of Doyen through the conduct of the sinister doctor Bradilin. It is under the applause of his amphitheatre that this savant demonstrated the contagiousness of cancer inoculated with success on the young Lirot, boy of the poor neighborhoods: "Observe the axilla sirs, the ganglions are removed, The cancer follows its uninterrupted and fatal way, and I hope that in 2 sessions I will bring you liver and a spleen filled with cancer cells". The overdramatic Doyen, mocking, adds: "Sirs, I am surprised, like you all, by an ineffable attack that has to be put I am afraid on the account of jealousy... I think as most of you that the rights of science predominate over these of the individual, and I did what, in sum, was no more than to follow such illustrious examples" [9].

Doyen only had detractors among the people of letters. He also found admirers among the dramatists. In 1899, François de Curel (1854-1928) deployed successfully the fiendish "fastes" of medicine by representing *La Nouvelle Idole* on the stage of Antoine Theater. In this play Doyen incarnated doctor Donnat in the role of priest-doctor, excellent figuration of positivism at

the end of the century. Doctor Albert Donnat has a fanatic soul. A doctor, to his eyes, is a priest whose rights extend up to the sacrifice of human life for the good of the humanity. Seduced by this ideal, he "inoculates" the cancer to one of his patients, without her being aware of it. She is Antoinette Melat, a young and poor religious woman infected by tuberculosis. After a short stay in a nunnery in the countryside, she is cured thanks to this therapy. But Donnat notices with terror that the cancer is demonstrating exponential growth, without leaving to the unfortunate woman but a 6-month period of life. Thus, science is not infallible in every case. His idol betrayed him and turned him into a killer. The public opinion, the newspapers, justice and the jealous doctors get upset. Hurt in her consciousness, Donnat's wife, judges, accuses, despises him and cheats on him with her psychologist. Incapable to defend himself, Donnat thinks about suicide. But the intense need to serve humanity makes him resist against despair. What if he dies, so be it! But his death should be beneficial for the society. Thinking of himself as "a beast" for his murderous actions, he inoculates the cancer to himself and observes the inexorable and terrifying progress under the eyes of the finally calmed wife and those of the young Antoinette Melat converted her also to the ideal of the savant. As a proof of supreme love, Louise agrees in her turn to be submitted to cancer inoculation just before the curtain falls upon this general immolation [10].

Despite the literary weaknesses, this play, inspired by the Doyen's adventure, keeps an eloquent significance. Placing the cancer in the heart of an ethical and philosophical reflection, these two meet the ancient idol (religion) and the new one (science), putting on stage a nun of lower social class who finds her social justification in the sacrifice of her life, and, at the other edge of the hierarchy, a doctor who has, in the name of science, a right of life or death upon his patients, bending in a premonitory way over the cancer, badly inexorable that takes the place of curable tuberculosis, François de Curel went beyond his initial purpose. In the watermark of *La Nouvelle Idole* one could read the pretensions of a tumultuous positivism that was still expecting the time when the doctors would be awarded the right to dispose, in the name of science, of subjects in coma for experimental purposes. Even though the activities of Doyen were dedicated to tortures, *La Nouvelle Idole* was warmly received by the press, the public and the doctors that enjoyed celebrating "the elevation of thought and the greatness of the soul of this principal hero of the play" [11]. Yet, two critiques had been expressed with no sign of sentimentalism towards François de Curel. In the magazine *La Revue des Deux Mondes*, René Doumic can not hide the sense of anxiety and horror

that is inspired by this troubled fascination exerted by cancer: “For better compromising a side that, by itself was quite perilous, the writer chose the most disparaging kind of disease that he could find. From one point of the play to the other, he keeps our attention fixed, and in a manner of speaking, he makes our eyes wandering over a hideous malady, adding in this way to our moral anxiety a kind of physical torture” [12]. The second critique comes from a surgeon. Detail piquant, this surgeon is no other but Doyen himself. In the introduction of his medical ethics treatise “*Le malade et le médecin*” (1906), the writer of inoculations of Reims bears a severe criticism upon his proper theatrical transfiguration: “Inoculating the cancer”, he writes, “would be an aberration that would not excuse the love for science. This personage that has provoked at the Antoine Theater the admiration of so many persons that pass as intellectuals is simply an ignorant or a criminal, if not both” [13].

The same year when *La Nouvelle Idole* attracted the whole Paris at the Antoine Theater, the satanic medicine of cancer was blowing down new preys thanks to the progress of the gynecological surgery. This time, an excessive space was delivered to his appetite. With the exaggeration of removing the uterus and ovaries one of the most strange, the most discouraging and the most anxiety-generating myths of the *Belle Époque* was being epitomized: the myth of the doctors castrators.

The micrococcus neoformans or “the microbe of Doyen”

The personality of Doyen, that had already been illustrated in the affair of cancer grafts of Reims and

that was going to experience a new fame thanks to the greatest fraud of the century dealing with the cancer cure, is worth mentioning [14]. Professor of Surgery at Reims, he was known for his mastery in surgery that allowed him to perform the most complicated operations with such speed that the risks of a postoperative shock would be reduced to the minimum. Besides, it seems that he was one of the pioneers of vascular surgery. The first in France, he achieved, in 1910, to inoculate to a person a venous segment removed from a sheep [15].

With an adaptation capability and acute sense of publicity he also put, since 1898, the brand new cinematographic technique to the service of his surgical virtuosity by engraving on films of 5 minute-duration part of the procedures of his operations (Photo 7). Projected to the Faculties, to the surgery congresses and in commercial rooms, these documents made a world tour [16].

Doyen was after all an excellent surgeon. He notably introduced a surgical clamp allowing the surgeon to apply a pressure from 2000 to 3000 kg, reducing to the least the risks of blood loss [17].

At about the end of 19th century, he was a man fulfilled by success. Known to the whole world, notorious to the great press, Doctor of Laws of the University of Edinburgh, he was also the rich director of the Surgery Clinic of the Piccini street in Paris, and the founder director of the Journal *Revue Critique de Médecine et de Chirurgie*. But in France, it was difficult for him to be recognized by his colleagues. In many undertakings, he aspired without success the election to the Surgical Society. Not without good reasons, he was attributing this failure to jealousy. It also has to be said that an inauspicious reputation was stuck to his skin since the cancer grafts affair of Reims [18].



Photo 7. Caricature of Doyen filming an operation.

In 1887 and 1889, Scheuerling and Rappin discover, each one of them, intracellular micro-organisms which resemble *bacilli* or *cocci*. They cultivate them and demonstrate their action in the genesis of malignant neoplasms. At about the same period, Professor Charles Richet (1850-1935) isolates the *micrococcus pyosepticus*. But in this domain, it is the fabulous *micrococcus neoformans* of Doyen that draws the attention of the greater public, with thousands of scientists reserving an indifferent reception.

Doyen seemed to have big intuitions in terms of infectious pathology since he updated the bactericidal properties of some moulds. But because of the fact that he was capable both for the best and for the worst, he gave in terms of oncology the image of absolute cacophony, albeit he persisted all his life in considering himself as the Pasteur of cancer [19].

It was in 1900 that he managed, after many trials and errors, to obtain, from the peptonized broth of the breast of a cow seeded with some fragments of cancerous tumors, a pure culture of cancerous microbes that appear in the form of spherical mobile bodies. Such is the pathogenic agent of cancer that he names it with the pompous name of *micrococcus neoformans*.

The way since then is made by the illustrious predecessors, as Doyen says himself in his autobiography: "The still recent discoveries of Pasteur and his pupils on the vaccination against cholera of chickens, against the bacillus anthracis infection and the swine erysipelas, then against the plague, and the amazing results obtained by Robert Koch from the injection to tubercle bacillus of toxins of pathogenic bacillus showed me a first way: increase the virulence of cultures of the cancer microbe, study the toxicity of these cultures and search whether the action of the toxins and cultures themselves, after heating, could strangle the evolution of cancer" [20].

It was on a series of manipulations that had always been kept secret by the savant that the anticancer vaccine, finally developed, was ready for experimentation on humans. Precisely, the chance comes up in January 1901. The story of this grand premiere is touching. It reminds of the vaccination of Joseph Meister by Pasteur. We listen to Doyen saying:

"I have delineated the toxicity of the cultures on animals. Since I have known which doses could be injected without inconvenience, I waited for the occasion to experiment on humans. I had already prepared enough big quantities of *micrococcus neoformans* and I knew that their activity increased intensely by aging, when in 1901 I was called to examine, with doctor Tapret, a 37-year-old man who, in 6 months, had many recurrences of testicular cancer. The tumor overrun the line of groin and had the volume of a head. The opera-

tion, being the only chance for health, which I assented to undertake after the patient's demand, was as complete as possible. After 3 weeks, I had to remove near to the scar a recurrence that had the size of an egg. I proposed to the patient to give him subcutaneous injections in order to try to obstruct the re-proliferation of the tumor. He accepted eagerly. This patient received around 25 injections from my first vaccine, which was a blend of toxins and of a small quantity of -killed by the heat- microbes. He is actually, after 8 years, in perfect health".

The serum, collected from horses, treated by means of at least 20 weekly injections of *micrococcus neoformans*, was tested on humans 3 years later with the same success.

In 1903, Doyen announced officially to the Congress of Infectious Pathology held in Berlin that the anticancer vaccine and serum are finalized.

Proclaimed as the greatest bacteriologist of the world, he became a popular man ever since. He was in all the Congresses, all the Academies, and his discovery was making sensation to the big press. In November 1904, one could read in the *Le Journal*: "The biggest secret dealing with the laboratory experiences by which Professor Mechnikov and his assistants are indulged in the cancerous cultures deriving from the clinic of Doctor Doyen... Yes, we have reasons to believe that the *micrococcus neoformans* was found, at the Pasteur Institute, in doctor's Doyen cultures".

At about the same period, *L'Écho de Paris* was precisising: "No doubt that his microbe exists and his serum produces favorable modifications in the tumors".

As a matter of fact, the medical world was divided. If Ilya Mechnikov (1845-1916), Albert Calmette (1863-1933) and Emile Roux (1853-1933) seemed to have given for a moment to Doyen the security of the Pasteur Institute, many savants denounce the deception. Looking closely, the discovery was for a long time a figure of panacea, and, as months were passing, the healing percentages for which they had given credits to him started to melt like snow under the sun [21].

There is worse. Not only the authorities of Brompton Cancer Hospital of London, to whom Doyen had sent some of his ampoules, did not notice any change of the condition of the patients under examination, but also they perceived with astonishment that the famous *micrococcus* was nothing more than a crude saprophyte which is a common host of every individual, whether this individual is diseased or healthy [22].

This disappointing reality did not prevent the imaginative *micrococcus* which, referral to the *bacillus of Koch*, had become the *microbe of Doyen*, from reaching the hill tops of glory. Medical theses were making mentions to him up to Colombia and Professor Paul

Poirier (1853-1907) found himself being blasted by his students for having dared to doubt this sacred reality.

Meanwhile, in September 1904 it became known that the billionaire George Crocker, magnate of the Californian press, had summoned Doyen before the court for deception and fraudulent manoeuvre, moral violence, neglect of the patient and violation of the law of 1895 about therapeutic serums. During the process, that had to be conducted on January 1907, staggering revelations were going to throw blur light upon the personality of the new Pasteur.

The Doyen-Crocker trial

George Crocker, whose wife had incurable breast cancer operated many times, had been in contact with Doyen on 27 of April 1904. The practitioner, who met the couple in his Clinic of the Piccini street, seemed to be formal in relation with the efficacy of his therapy with anticancer serum, and despite the fact that he refused to speak in details because of respect to the professional secret, he insisted on beginning the treatment immediately. There was no question of honorarium. For him, he was saying, that was nothing but a “detail” which he did not use to attend to personally [23].

The treatment began on the 29th of April. Doyen, who did not use to attend personally to his patients, sent his assistant, Doctor Sée, to be on the bedside of Mme Crocker, at the hotel Vendôme, where the injections of horse serum treated with *micrococcus* were made. After every injection, a raise of fever shook the poor woman [24].

On the 11th of May, the temperature had reached 39° C. It was on that day when George Crocker received from Grenouillet, the mandatory of Doyen, a letter in which he was making clear that “all the necessary cares for the condition of Mme Crocker are included in the honorarium of 100000 francs”.

Thunderstruck, the billionaire sank deeper in a silence all the more as the health condition of his wife would not cease worsening all along the injections and by such processes he began to see the fraud. Indeed, it is difficult not to think that such an enormous sum for some injections of saprophyte seems really excessive, even for a billionaire. Grenouillet, who feared a fatal end, repeated eagerly his entreaties but without success.

When informed about the incident, Doyen picked up the phone and threatened Crocker that he would cease the treatment if the 100000 francs were not been deposited on time. It was at that moment that Mme Crocker foiled that viewpoint about creating to her husband the guilt which, in case of a fatal end, would torment him for

having put an end to this last expectation. The argument has convinced Crocker to pay the above sum.

In vain! On the 19th of May, Dr Sée relinquished gave up about making an injection that the patient could not support. On the 22nd of May the last injection was administered. On the 27th, Crocker decided to put an end to a treatment that was producing extra sufferance to his wife. Informed about this decision, Doyen acquiesced. The suspension of the injections of micrococcus led the patient to a transient improvement. At about the beginning of June, the couple Crocker shipped to the United States where Mme Crocker died on the 27th of July.

In front of the 1st Chamber of the Civil Court of Seine, chairman Chenu conjured the violence, the blackmail towards human beings stimulated by anxiety and asked for the return of the sum of 100 000 francs that the billionaire had promised to donate to the Pasteur Institute.

After having stigmatized the jealous persons set on against him, Doyen, via his lawyer Maitre Desjardin, settled for to notice that nothing was able to prove his bad faith and that was the price of such honorariums that he could be allowed to save the miserable from death. But, commanded to present his miracles to the witness box, he entrenched once more behind the professional secret.

With some exceptions, the medical body, yet in such solidarity towards the issues of honorariums, disclaimed the pretensions of Doyen. Since such demands were accepted for the domain of surgery, the simple administration of a serum with uncertain properties could justify them but still less than the serum of Pasteur, Roux or Yersin, whose efficiency was well known, had never made a penny fall into the purse of their inventor.

The 1st Chamber accorded his sentence on the 2nd of March 1907. Recognizing that “he is allowed to find exaggerating the sum of one hundred thousand francs asked as a honorarium”, this one confirmed the validity of “a treaty that had been made by a common agreement” between Doyen and Crocker, dismissed the last one and ordered him to pay the legal costs [25].

Doyen’s power of deception was such that his theories were kept, mainly overseas, by some scarce partisans until 1914. In 1907, a great Professor, the Argentine Sobre-Casas, wrote anew on this subject: “In France, and especially in Paris, the discovery of Doyen is empathetically combated by the surgeons in general that are dedicated to the study of cancer. But it is out of the question that the considerable effort and the intelligence that Doyen has deserves better than this. His discovery is indisputably of high scientific nature that has to be studied with calm and method and out of every prejudice”.

It was subsequent that the press would bring out the news, with or without his consent, spreading it all

over the world giving false hopes to thousands of desperate patients.

In Greece the Journals *Medical Progress* and *Medical Monitor* dedicated a few pages to the case Doyen-Crocker.

The use of Doyen anticancer serum in Greece

Among the proponents of the Doyen's anticancer therapy was also the famous Greek Professor of Surgery Nikolaos Alivizatos (1876-1945). He studied in Montpellier and Bordeaux and attended the famous French scientist's Clinic, his experimental researches and the application of his anticancer treatment [27]. When he returned to Greece he founded the Polyclinic of Athens in 1903 and later, in 1918, he was elected Professor of Surgery at the University. In 1927 he was elected rector of the University of Athens and was being elected repeatedly as Member of Parliament.

He taught the Doyen method to his colleagues at the Polyclinic through a series of lectures. He asked for and was sent to him by Doyen the serum which he administered to a small number of patients of the Polyclinic. In 1906, at the Pan-Hellenic Medical Congress he presented with enthusiasm the favorable results that he observed in the clinical picture of 3 cancer patients after the administration of the serum [28]. During the discussion following this communication, the famous surgeon of the Greek Hospital of Smyrni, Apostolos Psaltov (1862-1923) [29], noted that the medical community has already rejected the curative value of the said serum and that the clinical improvement that he observed was due to the impeccable surgical operations that he performed and not to the serum. At the same Congress Professor of Histology and Pathology Nikolaos Pezopoulos (1859-1911) [30] retorted with theoretical arguments the value of the anticancer serum during his introductory speech at the start of the Congress.

For the cure of cancer by the Doyen serum, the opinion and conclusions of the committee of eminent French doctors consisted of Paul Berger (1845-1908), Edouard Kirmisson (1848-1927), Charles Monod (1841-1921), Charles Nélaton and Pierre Delbet (1861-1957), among others, were: "It seems that Mr. Doyen is a victim of illusions that so often induce the inventors to confuse their expectations with reality" [31].

When, at the beginning of the 20th century, Doyen and Alivizatos administered the anticancer serum, they were thinking that they were using a medicine that would probably be proved saving in the fight against cancer. If time did not do justice to them and their ex-

pectations proved to be vain, they are neither responsible nor accountable to the History of Medicine.

Conclusions

Even though the French scientific discoveries have often served the prestige of France overseas, it is difficult to say that for the *micrococcus*. The case Doyen-Crocker reflects also the origin of a real movement of Francophobia in the transatlantic press.

According to Bainbridge, Doyen's vaccine had still partisans in 1914. As far as it concerns George Crocker, he found an object good for relief by consecrating a part of his fortune to the fight against cancer in the mark of the foundation carrying his name.

The Doyen case showed once more the need for keeping cancer and cancer patients away from charlatans.

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