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Simon-Emmanuel Duplay (1836-1924) and the conceptions on epithelial cancers in the 19th century

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Summary

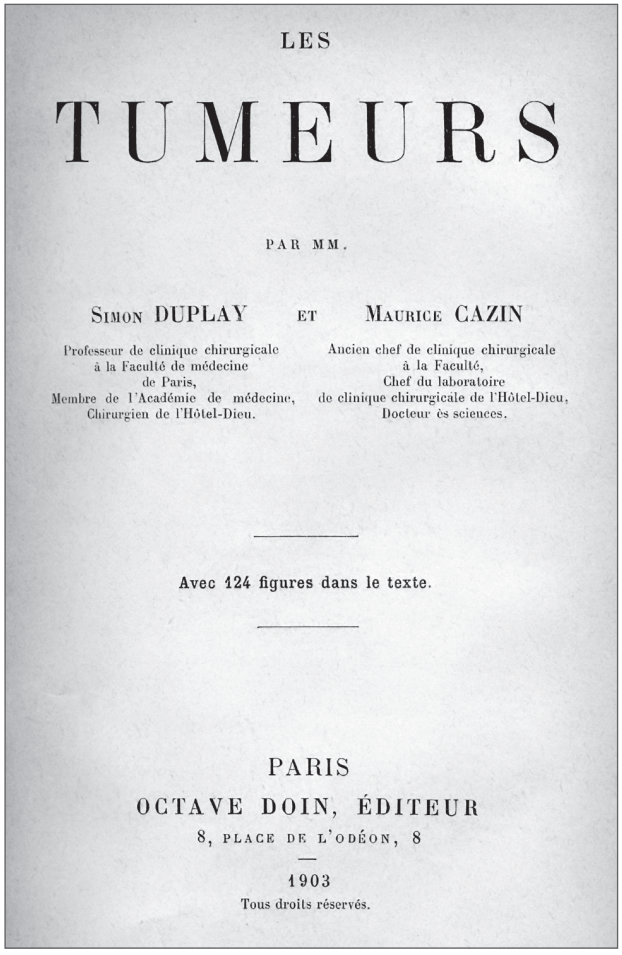
In this article we present the conceptions of the 19th century physicians for the epithelial cancers. The studies carried out by Professor Simon Emmanuel Duplay and his contemporaries on cancer in the mid-19th century are interesting and promoted cancer research in the clinical, epidemiological, therapeutical and experimental fields.

Key words: epithelial cancer, Simon Emmanuel Duplay, 19th century oncology

Introduction

At the end of the 19th century cancer was a major scientific problem. The incidents were increased dramatically and, even if it was a disease known from antiquity, it had never been studied methodically.

The French clinico-pathological School, by undertaking researches into cancer emphasized the need to go beyond anatomo-clinical attempts. Simon Emmanuel Duplay, an eminent professor of clinical surgery at Hôtel-Dieu, Paris, found an "Anti-cancer league" in 1892, with the help of several of his colleagues in the Faculty of Medicine like Paul Reclus (1847-1914) and Ellie Metchnikov (1845-1916) of the Pasteur Institute Laboratory [1]. The idea of that project was to combine all medical specialties capable of tackling any aspect of cancer as it was the only way to increase knowledge in this field. Furthermore, Duplay with his collaborator Maurice Cazin published in 1903 a book entitled *Les tumeurs* where they collected and commented the knowledge of their contemporaries over cancer (Figure 1).


LES

TUMEURS

PAR MM.

SIMON DUPLAY ET MAURICE CAZIN

Professeur de clinique chirurgicale à la Faculté de médecine de Paris, Membre de l'Académie de médecine, Chirurgien de l'Hôtel-Dieu.

Ancien chef de clinique chirurgicale à la Faculté, Chef du laboratoire de clinique chirurgicale de l'Hôtel-Dieu, Docteur ès sciences.

Avec 124 figures dans le texte.

PARIS

OCTAVE DOIN, ÉDITEUR

8, PLACE DE L'ODÉON, 8

1903

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Figure 1. Frontispiece of the book *Les Tumeurs.*

Simon - Emmanuel Duplay's life and carrier

Duplay (Figure 2) was born in Paris on September 10th, 1836. Coming from an illustrious family, his grandfather was Robespierre's personal secretary and his father Mathieu Simon Maurice Duplay (1805-1872)

Figure 2. Simon-Emmanuel Duplay (1836-1924).

an eminent doctor of the Parisian hospitals, Simon completed his studies in Paris Medical School and in 1872 he became in charge of the clinical surgery lessons in the Faculty of Medicine. In 1880 he was appointed professor of external pathology and in 1890 became professor of clinical surgery at Necker hospital and later at the prestigious Hôtel-Dieu. Member of the French Society of Surgery he became Academician in 1879 and in 1887 he was decorated with the medal of the Officer of the Legion of Honor. During his carrier he modified and improved the surgery of hypospadias (the so-called Duplay operation is a plastic procedure for the congenitally deformed penis), he described first the subacromial or subdeltoid bursitis named Duplay disease, he developed a method for the reduction of transversal fractures and he conducted researches on the treatment of cerebral trauma.

Besides his books on surgery, Duplay left an important scientific work on cancer. His essays entitled *The tumors, On contagion and inoculation of cancer, Report on cancer's etiology, The parasitic theory of cancer, Experimental researches on the transmission of cancer* promoted cancer research in the clinical, epidemiological and experimental fields.

Simon Duplay died on 16th January, 1924 in Paris [2].

Definition of tumors

The 19th century scientists believed that it was very difficult to formulate a definition for tumors satisfactory enough in all viewpoints so that would not give place to any criticism for ambiguity or misinterpretation. As Duplay and Cazin write: "Any abnormal mass developed in a part of the body can be so named, so we began by arranging in the group of tumors different diseases that could not find place in groups of well-defined affections, such as wounds, fractures, dislocations. Also the ancient medical authors placed in the group of tumors the cutaneous diseases, inflammations, edemas, erysipelas, hernias, syphilitic gums, tuberculomas" [3].

But as they mention, it is necessary to reserve the name "tumor" for conditions resulting from the overgrowth of the tissue and, according to the definition given by the French pathologists André-Victor Cornil (1837-1908) and his collaborator Louis-Antoine Ranvier (1835-1922), tumor is any mass constituted of a newly developed tissue (neoplasm), tending to persist or to increase [4]. Duplay and Cazin divided the tumors into benign and malignant and, regarding malignant tumors, they mentioned that their main characteristics are their non-precise limits, dissemination by way of the lymphatic system or blood, invasion of the proximal or distant internal organs, tendency to recur even after complete surgical excision and their rapid progress leading to death. They also classified malignant tumors into those developed by connective tissue cells named sarcomas, by endothelial cells - endotheliomas, by ganglionic tissue - lymphadenomas, by epithelial cells - epitheliomas, and by various cells named mixed tumors [5]. In particular, under the name "epithelial cancer" they included all malignant tumors of epithelial origin. The term "epithelioma" seems to have been introduced by the leading Danish histologist Adolphe Hannover (1814-1849) in 1843, in order to indicate the malignant tumors of epithelial origin developed in the skin or the mucous membranes [6]. But a certain number of the 19th century pathologists refused to adopt the definition proposed by Hannover and distinguished the malignant tumors of epithelial origin under the names of carcinomas or epithelial cancers.

Causes and epidemiological data on epithelial cancer

For the 19th century physicians heredity was considered as exercising an indisputable influence on the development of neoplasms and more particularly on epithelial cancers. It was a common observation the

predisposition for malignancy in some consecutive generations, the cancerous heredity [7].

Duplay mentioned that nutrition was considered to have an influence on the development of cancer, either by creating a predisposition or by being a vehicle to the cancerous agent. According to the observations of physiologist Peter-Ludwig Panum (1820-1885), among the inhabitants in Faroe Islands and in Iceland, where the consumed food was exclusively of animal origin, cancer was unknown. On the other hand, André-Claude Duchaussoy (1755-1820) indicated cases of cancer in a sect of vegetarian Swiss, concluding that neoplasms were more frequent in people with a vegetable-based diet. Roger Williams observed that death from cancer was more frequent among the low economical classes, like workmen, but the incidence was higher among the rich "easy life, rich diet", and for Williams this was the cause of cancer; he mentioned that mortality from cancer was doubled in England because of the increased meat consumption [8].

Among the local causes believed by Duplay and Cazin as being able to play a predisposing or determining role in the development of epithelial cancers, inflammation is noted in a large number of observations. For breast cancer, Sprenger indicated in 30 of 100 studied cases the existence of a previous mastitis. Also, all the classical medical authors of that period insisted on the predisposing influence of chronic gastritis for cancer of the stomach, of trachelitis/endometritis for uterine cancer and of cutaneous ulcer for skin epitheliomas.

Another cause implicated in many cancer cases was the use of tobacco. According to Tillmann, of 77 cases of cancer of the lip, 4 developed in women, among whom 3 were heavy smokers. In another statistics, in 245 cases of cancer of the tongue, 230 were noticed in men and 15 in women; all of them were smokers.

For others, alcohol seemed to increase the incidence of cancer of the esophagus, as well as lithiasis for the gallbladder cancer.

Duplay and Cazin insisted a lot on the influence of leukoplakia in the development of oral epithelial cancer. They were certain that epitheliomas of the oral mucous membrane succeeded frequently leukoplakia (leukoplasia, leukokeratosis), especially in the tongue, lip or the internal surface of the cheek [9].

Surgeon Edmond Monod (1843-1921) reported cases of vulvo-vaginal leukoplakia (kraurosis) having undergone an epitheliomatous malformation and urologist Adrian-Joseph Hallé (1859-1927) observed a similar cancerous tendency of leukoplastic lesions developed on the mucous membrane of the bladder and ureters. According to dermatologist Henri-Camille Leloir (1804-1897), the epitheliomas can originate not only at the leukoplastic plaque itself, but also in its circumference or at the edges of the mucous membrane [10].

In his researches professor Jean-Baptiste Bousquet (1792-1872) noticed the leukoplastic epitheliomatous evolution at the level of the plaque. In one of his preparations he comments on the voluminous bud of squamous-lobular epithelium with epidermic globes developed over the leukoplastic surface, invading the muscular layer, the fascicule of which was transversely split (Figure 3). As Leloir demonstrated, the epitheliomatous transformation occurs especially in the dekeratinized parts and not in the places where the hyperkeratinization is considerable, and Cazin concluded that the cancerous degeneration is considered to be the ultimate stage of leukoplakia and it is almost always fatal [11].

From the epidemiological viewpoint, it seemed that in the mid-19th century the number of cancer patients was increased gradually in most of the countries. In the same period the eminent French physician Etienne Lancereaux (1839-1910), based in epidemiological studies, declared that cancer is more frequent in Europe and Asia than in Africa, and that it was common to the white populations of America. Researches supplied by Roger Williams, Evans and Nasmyth, demonstrated that the frequency of cancer increased in considerable proportions in England and Scotland. In 1840 in England, cancer was causing 1 death in 5,646 inhabitants or 177 deaths in 1 million of inhabitants. In 1894 it killed over 1,403 patients (713 per million inhabitants). In 1895 the victims of cancer in England were 4-fold higher than 50 years ago. According to Joseph Bryant, in USA cancer mortality in 1850 was 9 in 100,000 people; it became 11.7 in 1860, 16 in 1870, 26 in 1880 and 33.5 in 1890; the increased rates included cancers from all parts of the body, but mainly those of the digestive

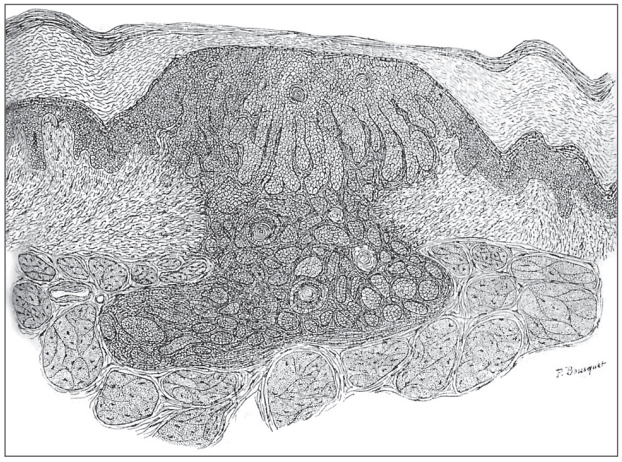

Figure 3. Squamous-lobular epithelium of the tongue developed in a pre-existing leukoplakia (a Dr. Bousquet preparation in Hôtel-Dieu Laboratory).

tract and the author adds: "the patients were more than 45 years old" [3].

Epithelial cancers' symptoms

Duplay and Cazin insisted that an epithelial cancer begins in an insidious way because of the characteristic absence of pain. Pain as a symptom could appear later either because of secondary infections following ulceration, or when the nerves are invaded or compressed by the tumor or enlarged lymph nodes. Patients with cancer of the skin or of the mucous membranes observe first a hard projecting mass like a kernel. For epithelial cancers developing in the internal organs, the beginning escapes completely and the lesion can give symptoms only after a long period of time, either when the tumor acquires a considerable size and becomes clinically palpable or creates complications like bleeding and ulceration.

By palpating an epithelial carcinoma, Duplay and Cazin emphasized the irregularity of its shape, its hard consistency and the abnormal vascularisation resulting from the dilatation of the venous networks. They considered one of the most important signs of epithelial cancers: the premature invasion of the lymphatic system, provoking hard and painless adenopathies.

Ulceration with its hemorrhagic and infectious complications establishes the terminal phase common to all epithelial cancers. Ulceration can also occur in the internal cavities and on the surface of teguments and will provoke bleeding of the affected organ such as hematemesis, melena, metrorrhagia or hematuria. Also an epithelioma of the scalp can penetrate the vault of the skull, a breast cancer will penetrate into the pleural cavity, an epithelial neoplasia arising from the uterus will communicate either with the bladder or the rectum.

Finally the two authors declare that the evolution of epithelial cancers is invasive and rapid, and prognosis is variable and depends on their location, shape and the patient's age [3].

Treatment

The revolution achieved in surgery since the introduction of the antiseptic method by Joseph Lister (1827-1912) simplified the excision of tumors. The unique treatment of epithelial cancers in the 19th century consisted in their complete surgical removal. The recommendation was the excision of the malignant tumor without delay as soon as the physicians have noticed its presence and recognized its nature. This absolute rule had however certain number of exceptions which we shall indicate.

First of all they used to abstain from any operating procedure in patients having an epithelial cancer concomitant with a serious systemic disease, as for example advanced-stage tuberculosis. Diabetes, albuminuria and haemophilia were also considered as contraindications even for the mildest operations.

It was also not allowed to operate when there were signs of cancer generalization, especially in the internal organs or in regions more or less away from the primary location of the tumor (liver, lung, spine). This rule did not include, however, the case in which the proximal lymph nodes were invaded by neoplasia; in that case they used to remove the totality of the lymph nodes at the same time with the tumor [3].

Another concern for surgery was the nature of the neoplasm and the knowledge of its usual evolution. So in certain forms of cancer with extremely fast evolution, named as *acute cancers*, the operation was considered rather harmful than useful, as recurrence and disease dissemination following surgical excision seemed to be accelerated. In this category Duplay and Cazin placed breast cancer, testicular cancer, ocular cancer and melanoma. For those neoplasms they used to treat only the symptoms and complications, such as severe pain, bleeding and septic infection. Finally we have to mention certain palliative operations that they were believed to prolong the patient's life, like in cases where the tumor was creating severe functional problems such as compression and blockage of the respiratory, digestive and urinary tract. In these conditions the surgeon was practising an incomplete tumor excision in order to restore the permeability of the affected organs [3].

Concerning the non-surgical treatment methods proposed for epithelial cancers we will quote some of them that the 19th century scientists regarded as palliative and in some cases even curative.

Numerous medical authors in that period reported cases of epithelial tumors that had been cured or modified in a very considerable way following an accidental erysipelas infection. After the discovery of the pathogenic agent of erysipelas, streptococcus, German bacteriologists Frederic Fehleisen (1854-1924) and Albert Neisser (1855-1916) inoculated cultures of this germ to cancer patients. They noticed some improvement, especially in cases of sarcoma, but the results did not seem satisfactory as the majority of the patients died from sepsis as a consequence of the inoculation [9].

Emmerich and Scholl tried to treat malignant tumors with sterilized serum coming from sheep, submitted previously in injections with streptococcus. The results published by these authors were seriously

discussed and the efficiency of this method was not confirmed. It is also interesting to mention a whole trial series of anticancer serotherapy, started in 1895 by Charles Richet (1850-1935) and Jules Héricourt, who immunized dogs, donkeys and horses with a human sarcoma and then transferred the serum to patients with advanced cancer. The idea was to raise an antiserum for treating the patients but this method failed too [12].

Treatment with quinine was a consequence of the coccidian theory of cancer. Knowing its efficiency against malaria's *plasmodium*, scientists had experimented with this drug in the treatment of malignant tumors in cases where they believed they recognized the existence of sporozoaires and especially since they considered that cancer was relatively rare in malaria-treated patients. Mathieu Jaboulay (1861-1913), professor of surgery at Lyon Medical School, tried the salts of quinine in the treatment of cancer by administering them orally, subcutaneously or intramuscularly and he noticed that pain was less, the foul-smelling exudates disappeared, the bleeding tendency diminished, the cancerous tissues cleaned, the swelling of the lymph nodes decreased and the general status of the patient improved. Jaboulay considered that this treatment must start at the first stages of cancer and continue for a long time in order to have some benefits and avoid relapses, and advised the administration of quinine pre and postoperatively.

The administration of *phytolacca decandra* was also popular as it was believed to exert an elective action on epitheliomas due to the potassium hydroxide and the oxalic acid that the plant contained.

French surgeon Louis Guinard (1864-1939) recommended the usage of calcium carbide with good results in inoperable forms of epitheliomas of the uterus and ulcerated carcinomas of the breast as it stops bleeding, dries up exudates, and relieves pain.

Finally, we have to mention the method of the German surgeon Albert von Mosetig-Moorhof (1835-1907) based on methylene blue administration either by interstitial injections or by embedding plasters. The purpose of this method was to destroy the cancer cells by provoking chemical necrosis of their nuclei. Dominique Domec (1846-1885), professor of clinical surgery and anatomy at Lille Medical School suggested for the treatment of cutaneous epitheliomas first the cauterization by galvanocautery, then the application of chromic acid in the ulcerated surface and finally the methylene blue powder with satisfactory results in the majority of the described cases [13].

Conclusion

The conception the scientists of the 19th century had on epithelial cancers is quite interesting, comparable with our current knowledge on oncology.

The studies held by the French Medical School and especially by Simon Emmanuel Duplay and Maurice Cazin inaugurated the modern period of oncology.

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