

## HISTORY OF ONCOLOGY

# Cancer's conceptions of Marie François Xavier Bichat (1771-1802), founder of histology

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*"On a total of fifty million bipeds, it was really difficult to find another mind thinking like Bichat"* (Schopenhauer, 1852).

*"Open up a few corpses: you will dissipate at once the darkness that observation alone could not dispel"* (Xavier Bichat, 1802).

*career. Although the training of Bichat was exclusively that of a surgeon, his scientific interests embraced all of medicine, especially descriptive anatomy, histology, pathological anatomy and histopathology. His important contribution was to point out that organs were not homogeneous structures but were composed of different tissues.*

### Summary

*The French doctor Bichat had a brief but outstanding*

**Key words:** anatomy, Bichat, histology, pathological anatomy

### Introduction

The discovery of the human body was made in a number of steps. The 16th century had identified the visible principal structures, visceral masses, organs, and part of their connexions. The following centuries perfected this knowledge by going further into the details, and the microscope, still ungainly, began to intrigue people.

The 19th century looks more discerning: Bichat identifies the categories of tissues making up the body architecture, and Rudolf Virchow (1821-1902) [1] discovers the cell, which he identifies as the fundamental unit of the entire human physiology and pathology. The next generations move from histology (study of tissues) to cytology (study of cells). Thus, bodies that are ever smaller attract man's attention.

Since the mid-20th century, a new step has been made towards infinite smallness. Doctors are now interested in molecular anatomy, each perturbation of which causes a disease.

### Bichat's life and carrier

Bichat (Photo 1) was born in November 11, 1771



**Photo 1.** Bichat's bust from terracotta by Joseph Chinard, Lyon's sculptor.

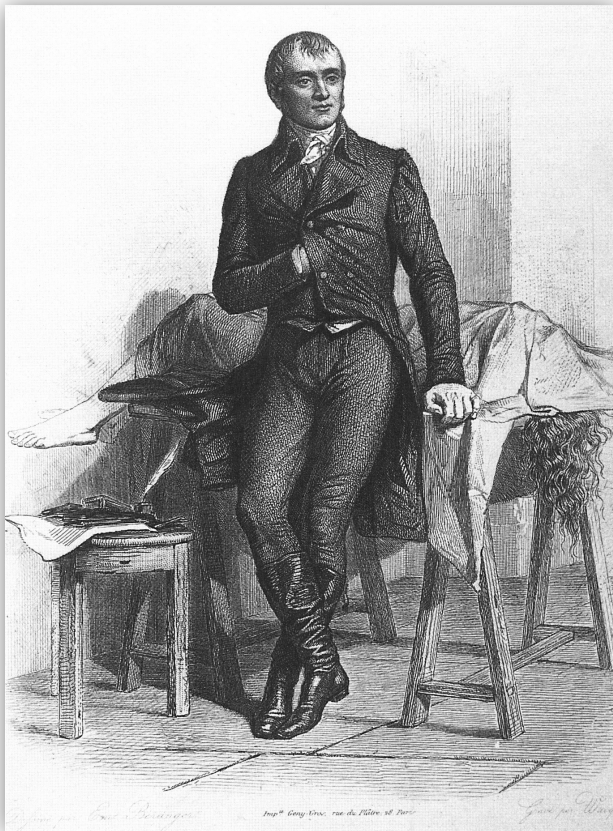
in Thoirette in the Jura of France, the son of a provincial surgeon. His initial surgical apprenticeship was taken in his native region. He then worked in Lyon for more than a year (1791-1792) with Marc-Antoine Petit (1762-1840) and Louis-Vincent Cartier (1768-1839), both students of Pierre Joseph Desault (1738-1795). The outbreak of the 1793 war between France and most of its surrounding neighbors, collectively known as the first Coalition, interrupted Bichat's education. He served in the French army, holding positions at several military hospitals, where he received much practical training.

Bichat journeyed to Paris in 1794, where he joined the crowd of students who were regularly following the practical instructions given by Desault. The latter, aided by recommendations from Petit and Cartier, was quick to perceive the young surgeon's potential. Desault was so measurably impressed by Bichat that he invited Bichat to live with him and take charge of his private surgical practice. Furthermore, Bichat acted as his corresponding secretary, answering for him all the requests for advice that came to him from every district

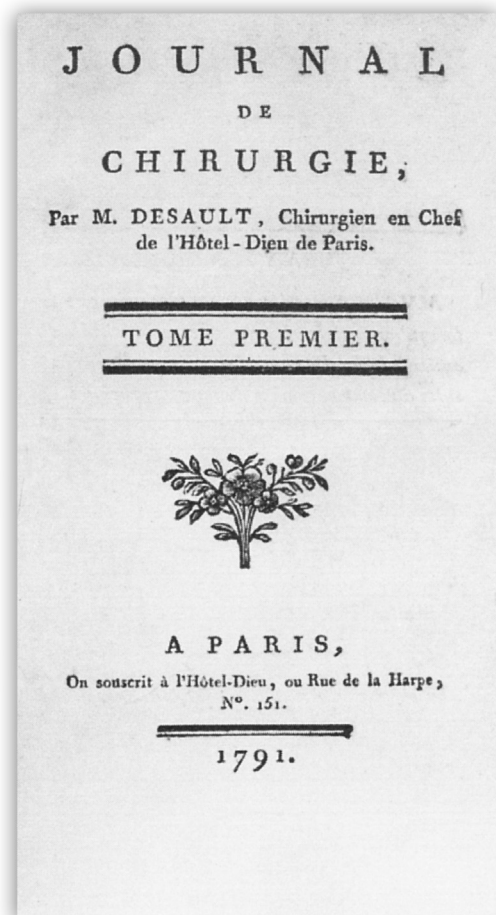
of France. Bichat also assisted Desault at all his operations (Photo 2) in private practice [2].

In 1795, during the last year of Desault's life, Bichat was also entrusted with the editorship of the *Journal de Chirurgie* (Photo 3), which had begun to languish because Desault lacked the time and desire to carry out the duty. Bichat, at 24 years of age, authored all three final volumes of the journal. After Desault's death Bichat's interests gradually shifted from surgery to internal medicine. In 1798, he published the works of his master Desault [3]. In 1799, he abandons surgery to dedicate himself to physiology. Although he gave up the practice of surgery, he remained convinced that the discipline illuminated general medical principles: "...devoted for some time to the study of medicine, then to hospital practice, I can no longer concern myself with surgery except insofar as it is an essential basis for all medical knowledge, an important means of analogy in a multitude of difficult cases, and a guide without which the physicians would often proceed haphazardly" [4].

In 1800, he is appointed as a doctor in the Hôtel



**Photo 2.** Bichat at the dissection table. Following the fashion of the time, Bichat affected the mannerisms of Napoleon in his hairstyle and in the placement of his right hand inside his coat.



**Photo 3.** Title page of his *Journal de Chirurgie*.

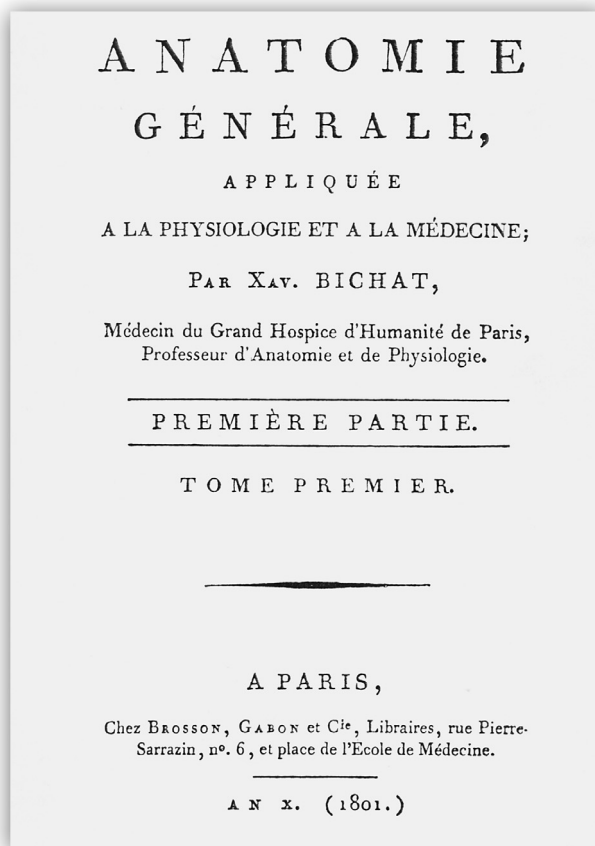
Dieu of Paris, where he will apply his anatomoclinical method with rigour. In the same year, he will publish his brilliant *Recherches physiologiques* in which he distinguishes between animal life and organic life, and gives his admirable scientific definition of life: "Life is the total sum of functions resisting death".

In 1801, he published his *Anatomie générale appliquée à la physiologie et à la médecine* (Photo 4) and started his monumental *Traité d'anatomie descriptive* that was to consist of 5 volumes, but, unfortunately, remained unfinished due to his premature death.

It's on the great stairway of the Hôtel Dieu, where he will be attacked by the disease for the first time; it was to take him away in only 14 days despite the treatment of Corvisart.

Bichat died prematurely in Paris on July 22, 1802 due either to galloping phthisis or tubercular meningitis. The latter cause is a plausible one. It is a strange but common fact that tuberculosis patients show hectic activity before the illness reaches a terminal stage, and Bichat would have been a shining example. He dissected six hundred bodies in a single winter. During his last three years, he produced three thick books including new ideas.

Bichat died at the age of thirty-two (Photo 5), at the age when scientific life is just about to start for the majority of men. He passed away while in all his glory and was laid to rest in triumph; he died without having



**Photo 4.** Title page of his treatise *Anatomie Générale* (1801).



**Photo 5.** Bichat dying, relieved by doctors Esparron and Roux.

the chance to finish his work, but also without having seen the construction of his doctrines collapse.

When Bichat expired, Jean Nicolas Corvisart (1855-1821) wrote to his master Napoleon: “Bichat has just died. Nobody ever did so much in such a short time.... but there is not even enough money in the house to pay for the funeral....” [5].

Bichat was buried in Père-Lachaise. His head was studied for the purposes of phrenology.

Bichat was dubbed as “the Napoleon of medicine”. Corvisart, in his funeral oration, spoke of him: “None accomplished so many things, so well in such a short time”.

### His works

Bichat’s *Recherches physiologiques sur la vie et la mort* (1800) [6], *Traité des membranes en général et des diverses membranes en particulier* (1800), four-volume *Anatomie générale appliquée à la physiologie et à la médecine* (1801) [7], and five-volume *Traité d’anatomie descriptive* (1801-1803) opened entirely new fields for anatomists, physiologists, and pathologists. He emphasized tissues as the units of which organs were composed, introduced the terms animal and vegetative system to descriptive anatomy, and is eponymically linked with many anatomical and descriptive terms.

In 1800, he publishes the *Traité des membranes* and the *Recherches physiologiques sur la vie et la mort*. The four volumes of his *Anatomie générale* were prepared, written and published in 1801. Without taking a break, he attacks pathological anatomy. So, what is left of the age-old construction of humours? Nothing. Over two millennia collapsed in a few months.

Bichat’s work as a pathologist was to be published in 1802, but his *Traité d’anatomie pathologique* was never printed. Bichat was about to complete the collection of data for it, when the disease exacted a fierce revenge upon an opponent, who had struck a major blow against it [8].

He came up with the idea for the *Traité d’anatomie descriptive*, of which he only published the first two volumes. The third one, almost complete, was compiled by his colleague, friend and cousin, Régis Buisson (1774-1805), who was also the author of the fourth volume, whereas he left the fifth one in the hands of Joseph Philibert Roux (1780-1854).

Bichat described the internal tunics of arteries, the fatty jugal point, the arachnoid membrane, the great cerebral fissure and the sacrospinous ligament.

The *Anatomie générale appliquée à la physiolo-*

*gie et à la médecine* (1801) is the most well-known work of Bichat [9].

### The foundation of histology

Long before Bichat, Aristotle had distinguished in the human body structure the organs or dissimilar parts, and the similar parts (fibres, membranes, flesh, bones, cartilages, nerve substances) or tissues. In practice, organs were considered to be indivisible individualities, up until Bichat who, although without using a microscope, identifies different sorts of membranes (to be called tissues) in the human body, each having its own structure, and, particularly, its own well-defined role in our system; therefore, he assigns an anatomo-functional role to them, and also argues for the necessity of physiological studies, thus opening the way. However, Bichat remains attached to the abstract theories of that century.

Bichat proved by dissociating different organs that these were made up by a number of elements found in many of them, which he called tissues. Just like chemistry has its simple bodies that give birth to complex bodies, anatomy has its simple tissues, the combinations of which form organs. There are 21 sorts of tissues, but only 6 of them form the fundamental canvas of all organs (cellular, arterial, venous, exhaling, absorbing, and nervous). Their study is the object of general anatomy. The techniques employed by that science are dissection, desiccation, combustion, maceration, putrefaction, ebullition, coction, and corrosion with acids and alkali. Bichat distrusted the microscope and didn’t use it. The microscopic study of the fine structure of tissues will be conducted a few years later, and it will be called histology. It is the notion of tissues that led Bichat to conceive a proper technique for intestinal suture. He demonstrated that it wasn’t necessary to face, among them, tissues of the same nature, and that it would be best to take advantage of the adherence properties of the peritoneum [10].

Virchow is dedicated to pathological histology. It is the cell that gives to a tissue its specificity; this is Virchow’s theory, extending the foundations laid by Bichat [11].

Bichat emphasized the tissues, rather than organs, in pathological theory: “We cannot, therefore, deny that a change in just one of an organ’s tissues is frequently enough to disturb the functions in all the others; yet likewise, it is in only one of them that the evil originates”.

His insistence that tissue was the prime element in the study of pathological anatomy facilitated the

transition from the Morgagni's theory of organs as principal components of the body to the doctrine of Virchow that the cell was the basic unit.

Pathological anatomy became more fully systematized with the publication in 1800 of the *Traité des Membranes* by Bichat, who focused particularly upon the histological changes produced by disease. As developed by Morgagni, pathological anatomy had dealt with organs [12]. Bichat changed the focus: "The more one will observe diseases and open cadavers", he declared, "the more one will be convinced of the necessity of considering local diseases not from the aspect of the complex organs but from that of the individual tissues". Bichat's *Traité des Membranes* heralded the pathological anatomy of the nineteenth century. This work in which he individualizes the notion of tissue in histology (term invented by him), led to him being dubbed as the father of histology.

### **His researches on physiology and pathological physiology**

As a physiologist, Bichat is known to us by his treatise *Recherches physiologiques sur la vie et la mort* (1800) and the *Discours sur l'étude de la physiologie*, published in 1811 by Arène in *Archives d'anthropologie criminelle* (N° 207). He had an enormous influence on his contemporaries. He made a clear distinction between animal life linked to the nervous cerebrospinal system, and organic life which depends on the sympathetic system [13].

The sympathetic system is considered to be an autonomous system of which each ganglion "constitutes a small brain", which is absolutely independent from spinal nervous centres.

According to him, passions appertain exclusively to organic life. Fear is related to the stomach, anger to liver, goodness to heart, joy to viscera etc. Bichat made the distinction between physical properties (elasticity and extensibility) and vital properties (sensitivity and contractibility) of tissues. The life of the organism is the total of partial organic and tissue lives that add up to it, following the necessary adjustments and combinations. It seemed to him that it was the result of a conflict between the individual's vital force and physico-chemical forces the predominance of which lead to death.

On an intubated and tracheotomised dog, Bichat demonstrated that, transversally in the organism, arterial blood acquires the characteristics of venous blood, and that in asphyxia, arterial blood becomes black. He insisted on the importance of three vital organs (heart,

lung, brain), the functional synergy, and resistance to oxygen deprivation of which he studied.

In 1800, Bichat repeated the experimentations already done on the introduction of air in the veins. He demonstrated that just a few air bubbles were enough to cause death. He also studied, on animals, the effects of blood transfusion. Bichat also conducted the first crossed circulation experiments with arterial anastomosis in such a way as to obtain an animal-donor and an animal-recipient.

Bichat's vital doctrine did not last for a long time, but it was the beginning of all research leading to today's developments.

Bichat intended to replace the first part of his treatise *Recherches sur la vie et sur la mort* with reflections on the alterations of functions in diseases. This pathological physiology would be completed with an experimental section. To this purpose, he studied galvanic action on the brain, nerves, heart, stomach, intestines, and muscles both on animals and decapitated bodies, 30-40 minutes after the torment. Bichat's principle was: "Life is the sum of the functions that resist death" [14].

Bichat, who had an enormous influence on the younger generation, had dreamt of a complete teaching of medicine, covering from anatomy to therapeutics. He used to say: "To dissect in anatomy, do experiments in physiology, attend patients and open corpses in medicine - there lies a triple path outside of which there can be no anatomist, physiologist, or doctor". He added: "We know that chemistry made Paracelsus; we know that physics makes mechanics; we have not forgotten how many physiologists wrote novels. And if we have a fair idea of what is called wisdom in medicine, we make the best out of other people's mistakes by always walking on the path of experimentation and observation". A thorough analysis shows that Bichat distinguished between two classes of phenomena Morgagni had mixed up: simultaneous manifestations of a disease, and those preceding death. According to Giovanni Battista Morgagni (1682-1771) [15], the location of a lesion is the last link in the chain of causality, whereas according to Bichat, this is the initial place from which the lesion originates. Therefore, he was among those who opened the way for anatomoclinical medicine [16].

### **His conceptions on cancer**

Doctors were still considering humours, while Bichat, since 1798, has studied tissues in terms of their form, structures, development, and functions. Thus

was born general anatomy. Then, by demonstrating that “all types of cadaveric lesions show identical characteristics in the organs of the same system”, he formulated the fundamental law of macroscopic pathological anatomy which establishes a link between tissue lesions and the disease.

With regard to oncology, Bichat proved that cancer is not the product of a hypothetical humour but a random tissue, the physiology of which follows the same rules as normal tissues. Therefore, it is not a singular condition affecting the whole animal economy, but a primitive and localised disease with a tendency to generalise. Meanwhile, the old division in open cancers and closed cancers was deprived of content since these concepts represent two different aspects of the same pathological tissue. Hence, it was appropriate to classify cancers, not with respect to their position, but with respect to their histological specificity. Thus, four types of cancer tumours arrested Bichat’s attention: tuber, scirrhus, encephaloid, and melanosis. These are the foundations of tissue theory (histology), which the young scholar was to bequeath to his successors as a spiritual testament.

Bichat divides random tissues or tumours into two large categories: those having their homologues in animal economy, which form homologous tumours (fibrous, cartilaginous, adipose products...), and those not having equivalents in normal tissues, which form heterologous tumours of cancerous nature; these are tuber, scirrhus, encephaloid and melanosis.

Tuber and scirrhus were well-known. That was not the case for melanosis, of which none had heard of until that day, nor for encephaloid, which described those soft tumours that seemed to be a little similar to the cerebral substance due to their structure. Bichat points out that such products have a life of their own from day one until their last day, and that, for example, scirrhus is not a benign tumour susceptible to degenerate into a malignant tumour, but a random product having its own tendency towards malignancy. The progress made was enormous. For the first time, cancers were the object of a coherent classification [17].

Since 1802, Bichat has imposed the anatomopathological method. In the age-old theory of alteration of humours, which had brought oncology to a standstill, he substitutes the notion of organic lesion, thus paving the way for tissue, and then, cellular theories of cancer. The second turning point, which occurs in the late century, is associated with the introduction of the first parasitic theories of cancer. Bichat’s fortune represents an exceptional phenomenon in medical history.

Overall, Bichat introduced the new concept of the role played by tissues in the onset and development

of diseases. His work was taken up by his students Guillaume Dupuytren (1777-1835), Gaspard Laurent Bayle (1774-1816), and Théophile René Laennec (1781-1826). Cancer was still one of the least known diseases. The concept of an infectious virus was at the heart of the experience, in 1771, of Bernard Peyrilhe (1735-1804), who had attempted to inoculate a human cancer into an animal. This was resumed by Jean Louis Alibert (1766-1837) and his assistants, who tried in 1808 to inoculate into themselves human cancers, without being successful. Dupuytren also failed in transplanting human cancer into animals [18].

In pathological anatomy, just like in normal anatomy, Bichat considered that tumours are made up of tissues. He insisted on the individuality and the unity of cancer, which is not the product of hypothetical humours, but a pathological tissue different than normal tissues. He also specified the structure of tumours in which he discerned the cancerous parenchyma of the supporting tissue or stroma. On the basis of that concept, Bichat denied the classical doctrine of degeneration and divided tumours into homologous and heterologous depending on whether they seemed like normal tissues or not. He contrasted hard cancer (scirrhus) and soft cancer (encephaloid or vegetating). These concepts were resumed by Jean Cruveilhier [19] (1791-1874) who added the notion of the pathognomonic cancerous sap (1827).

Bichat considers cancer to be a pathological tissue different than normal tissues, and insists on the unity of cancers. He also points out that sudden death is due to the interruption of perspiration and cerebral circulation and function, and that the brain cannot function without being supplied by blood [20].

## Discussion

Apart from surgery, to which Bichat had only paid a tribute of gratitude, he came up with the idea of restructuring the entire medical construction on a new basis, and, as if he had a premonition of his imminent death, he put himself to work with feverish passion. Two and a half years were enough for him to produce this tremendous work *Traité de l’anatomie*. Before him, anatomy had no pretensions beyond the description of organs and systems. He understood that beneath the exterior form, eminently mobile, texture was hiding, which is considerably less mobile, and very important in a different sense mostly from a pathological standpoint. None before Bichat had established any links between identical tissues disseminated in different organs, none had classified them, nor had anyone

studied them from all sides and with every known process; in short, general anatomy did not exist; he created it from nothing, and his work even feels like a hasty production. Beyond comparison in terms of its descriptive part with respect to anything having to do with physical studies, though incomplete with regard to inner structure, whereas the author's imagination often takes the place of observation. The details of the organism cannot be revealed to a naked eye, and Bichat despised the microscope. One sees whatever he wants, he used to say, when looking into the uncertainty. He was forgetting that it was through that uncertainty that the phenomena of circulation in the capillaries were made apparent, one hundred years earlier, to the amazed eyes of Marcello Malpighi (1628-1694), and that the microscope had given to Harvey's immortal discovery the last sanction it was missing; he was forgetting all that Anton van Leeuwenhoek (1632-1723) [21] had learnt more than a century ago; but this investigational method is slow when it comes to producing results, and Bichat did not have time to wait. One had to wait for a number of years to go by for microscopic observation to take the place it was worthy of in science.

Whatever it is, and despite its minor imperfections, his *Traité d'anatomie générale* was nothing less than an outstanding book with regard to the project, prodigious in terms of the abundance and novelty of the subject matters, the solidity of bases and the power of insights; he produced a revolution in science. The ingenious doctrine of vital properties was also favourably welcomed, and its mark is found in all the works of the generation that followed. It did not take long for Bichat's ideas to disseminate throughout Europe, where they were welcomed with enthusiasm.

The study of tissues in their normal state was to lead to that of their diseases; pathological anatomy was only one step away from general anatomy, but the one who took it wasn't Bichat: he had gathered all the elements of this work, he had already communicated them to his pupils during his courses in the winter of 1802, his *Traité d'anatomie pathologique* was to be published some time that year; death did not allow him to have the final word, but the impetus was given and motion was not going to stop. This youth greedy for progress, with a passion for work, which he had gathered around him when establishing the *Société médicale d'émulation*, decisively followed the way he had drawn, and created the *anatomopathological* school [22] that restructured science on new bases and operated in France as a movement similar to that produced by John Hunter (1728-1793) [23] in England twenty-five years earlier.

Concentrating medical education at the hospital reinforced the links growing ever since Andreas Vesalius (1514-1564) [24] between surgery and anatomy; and helped establish the anatomolocalist perspective on disease that became so prominent in the hospitals of post-Revolutionary Paris, stimulated further by Bichat's work on tissues. By Bichat's day, the radical reform of French medical education imposed in 1794 had led to surgery being taught alongside medicine to all students. The prominence of the hospital in the post-1789 medical system and the prestige of pathological anatomy elevated the status of French surgery.

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