

A Note from History: The First Histopathologists

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Although compound microscopes had been available since the 17th century, skepticism about the value of microscopic examinations prevented their use in medicine. However, in the late 18th century, optically corrected lenses and microscope objectives began to be manufactured. These technological advances signaled a new era in microscopy, histology, and histopathology.

Marie Francois Xavier Bichat (1771-1802) (Fig. 1) was born in the year that Morgagni (1682-1771) died [1]. Bichat studied medicine in Lyon and Paris. After graduation, he became an army surgeon and during the French Revolution he was a physician on the staff of the Hotel Dieu, the preeminent hospital in Paris. He used his military connections to obtain permission to dissect and experiment upon the fresh bodies of those who were guillotined. His experiments led him to conclude, for example, that cardiac excitation by electricity occurs only when the heart is stimulated by direct contact, an observation that is not too far from present day shocking the heart [2].

Although Bichat devoted relatively limited time to microscopy, he identified more than 20 different types of tissues. In his first "Traité" and his "Anatomie générale" [3,4], Bichat concluded that the various tissues in different organs are the building blocks of life and that their alterations in diseases are manifested by structural changes. He recognized that diseases are the result of characteristic and



Fig. 1. Marie Francois Xavier Bichat (1771-1802)

identifiable microscopic changes in specific tissues, rather than simply the result of gross alterations of the organs. By these insights, Bichat transformed the old doctrine of organ pathology into the new doctrine of tissue pathology.

Bichat discovered that the parenchyma of an organ is a combination of different tissues and he perceived that understanding the tissue changes in disease might lead to a cure. He challenged doctors

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to think about diseased tissues instead of diseased organs. He wrote in his “Anatomie générale” that “You may take notes for twenty years from morning to night at the bedside of the sick, and all will be a confusion of symptoms, ... but start cutting bodies open and the confusion will soon disappear.” He concluded “What is [clinical] observation worth, if we are ignorant of the [pathologic] cause of the disease?”

In his second “Traité” [5], Bichat introduced the terms “organs of animal life” (ie, external organs such as voluntary muscle and sense organs) and “organs of vegetative life” (ie, internal organs such as lungs, heart, and liver). He drew a time honored conclusion that we live internally almost double the time that we exist externally.

Bichat became a lecturer in medicine at the age of 26, and he completed four substantial texts of pathology within the next five years, before his untimely death at the age of 31. Bichat’s principal legacy was introducing the notion, 20 years before the word “histology” was coined, that diseases occur as the result of pathologic changes in tissues.

Gabriel Andral (1797-1876) of Paris (Fig. 2) was only 4 years old when Bichat died, but he showed himself at an early age to be a worthy exponent of Bichat’s tissue doctrine. Even before he completed his medical education, Andral published several papers and notes on his clinical observations with pathological correlations. For example, he observed that influenza, a disease of unknown cause, came and went as an epidemic and that death from influenza was attributable to bronchitis and pneumonia.

In 1828, the year before the publication of his 2-volume “Précis d’Anatomie Pathologique” [6], Andral was appointed Professor of Hygiene in Paris. From 1839 until 1866, he was Chair of Pathology and Therapeutics of the Faculté de Médecine in Paris.

Andral had an analytical mind. He collected scattered facts and by adding them to the results of his own observations he was able to construct a new system of pathological anatomy – tissue pathology. The first volume of his book [6], devoted to general pathology, was divided into 5 sections covering



Fig. 2. Gabriel Andral (1797-1876)

matters such as circulatory lesions, ulcerations, ossifications, and secretions. The second volume was devoted to special pathology and covered the tissue changes in diseases of the alimentary tract, lungs, heart, lymphatics, blood vessels, lymphatic ganglia (nodes), liver, spleen, breast, gonads, and blood. Andral’s book was a great success; it established his international reputation as an anatomic pathologist. The two volumes were translated into English and printed in the United States [7] within a couple of years after their original publication in France.

Midway in his career as a pathologist, Andral focused his attention on microscopic alterations of the blood. In 1843 he published another highly successful book, the first concise treaty on pathological hematology, “Essai d’Hématologie Pathologique” [8]. In this book, readers can find a number of first-described entities. He referred to pus in the blood as an increased number of globules (white blood cells), indicating leukocytosis. He

described anemia as a diminution of the globular elements (red blood cells) of the blood, noting that anemia can vary from mild to severe depletion of these elements.

Another of Andral's innovations was measuring the proportions of constituents of the blood, such as fibrin, globules, solids, and water, in health and diseases. He introduced the recording of body temperature and its variations in diseases and noted that high fever was associated with rapid heartbeat and an excess of globules (cells) in the blood. His examination of blood from patients and from the deceased led him to conclude that there are primary blood diseases [8]. By investigations of blood and detailed case studies with laboratory findings, Andral created a new field in medicine – hematology.

In conclusion, Professors Bichat and Andral performed studies of tissue pathology that are of fundamental importance. Their scholarly contributions to understanding the alterations of tissues in pathological conditions forged links between the organ pathology of Morgagni and the cellular pathology of those who were to follow.

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