F-V RASPAIL, THE MOST REVOLUTIONARY OF ALL MICROSCOPISTS

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OVERVIEW

The aim of this article is to present to modern-day microscopists an overview of the work of **François-Vincent Raspail** (1794-1878)*, a man universally recognized as the Father of Histochemistry. It is not our intent to present a biography of Raspail here; several biographies of him have already been published. That his immensely varied work covered fields as diverse as agriculture, geology, meteorology, and medicine, is well recognized. We will here review his microscopic work, giving a limited biographic background to help to put his life and work in perspective. Finally, we will notice how Raspail's pioneering work has developed into the modern histochemistry, a branch of science that is revolutionizing biomedical research.

*** Masthead: An ink portrait of Raspail from the Petit Larousse Illustré, Nouveau Dictionnaire Encyclopédique of 1918 (library of LCT).**

Figure 1. Raspail with his microscope in the background. This circa 1825 portrait projects the combative personality of the sitter.

Raspail's microscope.

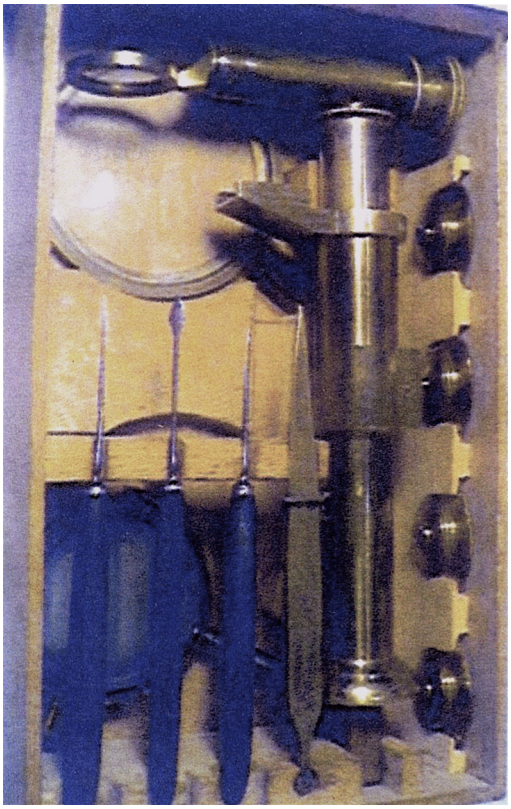
Raspail designed a type of simple microscope (figure 1) which was manufactured by the Parisian microscope maker Louis Joseph Deleuil (1795-1862), (figures 2a and 2b). The design represents an improvement over what it was (wrongly) known as the "Ellis Aquatic Microscope." We cannot resist going into an aside here. As Brian Ford notes in his History of the Simple Microscope (Ford, 1985):

Students of microscopical history know aquatic microscopes by a fuller title - "the Ellis Aquatic Microscope". As you might by now expect, the instrument was not invented by John Ellis at all."

Actually, that type of microscope was invented by Abraham Tremblay before 1744 (Recoules, 1991a) to assist him in his memorable studies on the biology of the Hydra (Lenhoff & Lenhoff, 1986). What Raspail did was to add a precisely controlled advance movement to the lens by means of a helical screw (see figures 1 and 2a). As we said, Tremblay used his instrument for the study of the Hydra, and Henry Baker used one similar for the discovery of the amoeba. Naturally, all those observations were made in small pools of water, hence the name of Aquatic Microscope. Others, as Raspail, were studying fragments of vegetal tissues mounted in at most, a few drops of a liquid medium, therefore the name of Botanical Microscope. Recoules pointedly observes that the major difference among the two microscopes was who was using it (Recoules, 1991b). In fairness, there was a minute difference; the Botanical has a flat glass for stage, the Aquatic a watch glass - "*vive la difference*!"

Figure 2a below left, shows a Raspail microscope. Notice the side knob controlling focus and the knob located at the proximal end of the horizontal arm. The latter was Raspail's contribution to the design.

Figures 2b to the right, shows the contents of the base that doubles as carrying case. The disassembled microscope, dissecting needles, a lancet, and four objective, plus the mirror, are conveniently stored into it.



Raspail creates Histochemistry.

Since 1814 it was known that iodine reacts with materials rich in "fecule" (starch) producing a violet coloration - now called the starch iodine reaction. In 1825 Raspail applied the method to microscopic samples (Bracegirdle, 1968a; Simone Raspail in Weiner, 1968a), in particular to the study of embryos in the seeds of grasses. The method worked beautifully, histochemistry was born. The idea had the simplicity of genius. The test was quickly adopted by microscopists in Europe and America and is still in use today. Raspail soon developed three additional reactions for the histological detection of sugars, proteins and oils (Raspail, 1828).

Previously, he had described the use of freezing mixtures to harden the tissues for sectioning (Raspail, 1825), a technique used in histochemistry and surgical pathology to this day. While Raspail is remembered for his histochemical work, the fact that in a 1825 paper he introduced the freezing method was forgotten until given generous recognition by Bracegirdle (Bracegirdle, 1968b).

Raspail the Public Health practitioner.

Unfortunately, Raspail did not persevere in his microscopic work. He felt he could be more effective in helping humanity by providing medical advice and by creating new medicines. This he did. Raspail started offering medical services to anybody, and particularly to the poor. His claim was that he had invented a "New System of Medicine," whatever that was. He had found a medication suitable for almost every ailment, camphor. Camphor is a strongly aromatic compound obtained from the Asian camphor laurel. He dispensed it in alcoholic solution, in powder form, even in cigarettes. His success with the public was remarkable; the sales of his medications, books and pamphlets brisk. All along his theories and practice were ridiculed by the medical establishment. Today, in spite of its long lasting popularity, the therapeutic use of camphor is discouraged by the Federal Drug and Food Administration of the USA on the basis that safe and effective alternatives are available. But there was a more serious problem; Raspail had no license to practice medicine, not even formal education in it. His only academic experience was as a student at Paris School of Science. How long he attended it is not known, but he did not graduate (Simone Raspail in Weiner, 1968b). Finally, in 1846 he was brought to trial for practicing medicine without a license. It was and still is a very serious offense, however his scientific knowledge and good humanitarian intentions were recognized by the court, and even by the prosecutor. Apparently political considerations influenced the outcome; the government did not want to make a martyr out of "the doctor of the poor"; at least not at that precise moment. He was fined fifteen franks and allowed to return to his illegal practice where his contributions to urology at least, were original and significant and are remembered to the present (Androutsos, 2006).

Raspail the revolutionary.

Practicing medicine without a license was not the only activity that took Raspail away from his pioneering microscopic research. Nor was it his actuation as editor in 1834 and again in 1848 of the anti - governmental periodicals, the "Reformer" and the "Ami du Peuple." He was active in party politics, trying to change the status quo by non-violent or even violent means. He was wounded in street fighting during the 1830 revolution. The wound was minor, but his revolutionary activity cost him twenty seven months in jail. As we will see later, it was not going to be his last revolution and neither his last stay in jail.

Raspail the Presidential candidate.

Surprising as it may be, the revolutionary/microscopist Raspail did run as a candidate for the Presidency of the French Republic. That was in 1848. He was the candidate for the extreme left. His opponents were not kind to him, or to each other (hardly a surprise to us watchers of a major 21st century presidential campaign). Here is a sample.

Voulez-vous du micmac?
Choisissez Cavignac.

Voulez-vous d'la canaill'?
Choisissez M'sieur Raspail.

Voulez-vous un coquin?
Choisissez Ledru-Rollin.

Mais voulez vous du bon?
Choisissez Napoleon.

A. Maurois (1948)

Would you like nonsense?
Choose Cavignac.

Would you like the trash?
Choose Mr. Raspail.

Would you like an arrogant?
Choose Ledru-Rollin.

But would you like a good man?
Choose Napoleon [the 3rd].

(Loose translation, MdC 2007)

Nobody will think that the anonymous "poem" represents the best of 19th century French poetry, but it didn't hurt Napoleon's chances. Six candidates run; here are the results for the four already mentioned:

Louis Napoleon:	5,434,226
General L-E Cavignac:	1,448,107
A-A Ledru-Rollin:	370,119
F-V Raspail:	36,900

Figure 3. Louis Napoleon (1808-1873), as Napoleon III Emperor of France (1852-1871).

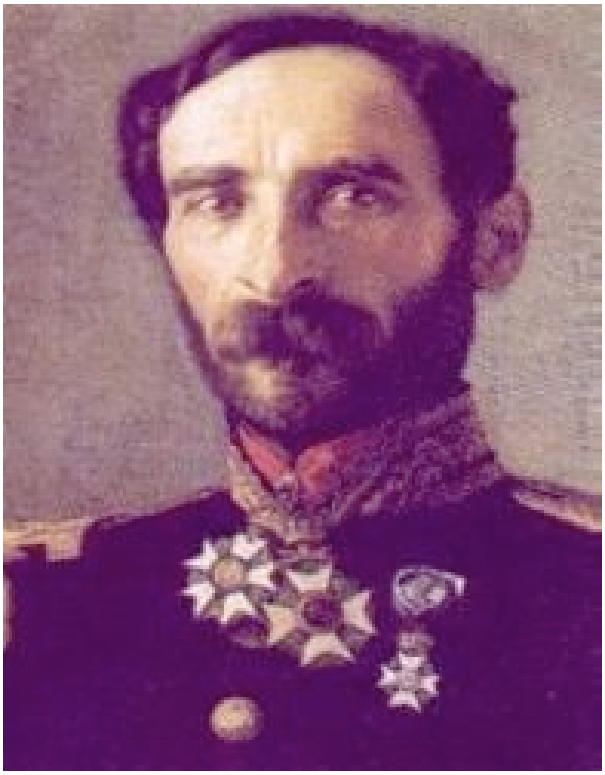


Figure 4. General Louis-Eugène Cavignac (1802-1857), a law-and-order man who used an iron hand to put down the 1848 Parisian uprising. His political appeal, although far greater than Raspail's was not match for that of Louis Napoleon.

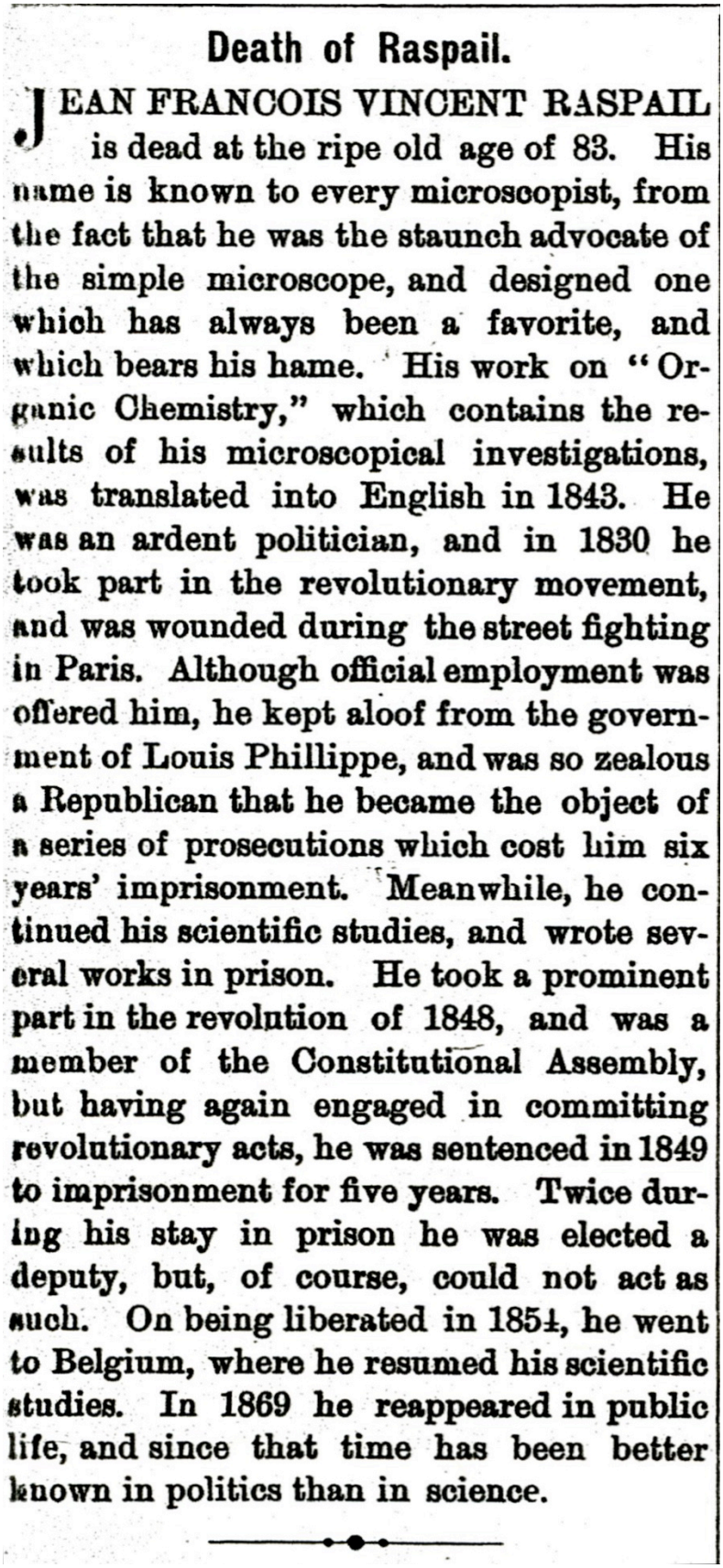
It is a melancholy observation that if at the end Napoleon's III government brought disaster to France, Raspail's extremism might have fared no better; of course he had no chance.

The revolutionary in jail again.

The election results were humiliating; Raspail obtained less than a tenth of the votes obtained by the third-place candidate, the more moderate leftist Alexandre - August Ledru - Rollin (1807-1874). It should be noted that Raspail was running his campaign from a jail cell. As we saw before, his previous incarceration had been for twenty seven months for his 1830 participation in the revolution against King Louis Philippe. This time it was even more serious; he had been sentenced to six years in prison for his active participation in the revolutionary movement of 1848. When Raspail's wife died, Napoleon III commuted his sentence to exile. Still he spent a combined eight and a half years in jail and nine years in exile.

Raspail goes to Congress; triumph after tragedy.

Back in France, the 1869 election for Legislators sent Raspail to the National Assembly, as a deputy for the city of Lyons. He remained in the Legislature for years, always idealistic, but generally ineffective. There was still a one year home imprisonment, this time for publishing a Farmer's Almanac with opinions too strong for the government liking. Finally, his age made of Raspail the Senior Deputy of the French Legislature. As such he received honors from the military guard. Raspail commented: "This is the first time soldiers with bayonets salute me rather than taking me to prison." The old revolutionary had not lost his bitter sense of humor.



Death of Raspail.

JEAN FRANCOIS VINCENT RASPAIL is dead at the ripe old age of 83. His name is known to every microscopist, from the fact that he was the staunch advocate of the simple microscope, and designed one which has always been a favorite, and which bears his hame. His work on "Organic Chemistry," which contains the results of his microscopical investigations, was translated into English in 1843. He was an ardent politician, and in 1830 he took part in the revolutionary movement, and was wounded during the street fighting in Paris. Although official employment was offered him, he kept aloof from the government of Louis Phillippe, and was so zealous a Republican that he became the object of a series of prosecutions which cost him six years' imprisonment. Meanwhile, he continued his scientific studies, and wrote several works in prison. He took a prominent part in the revolution of 1848, and was a member of the Constitutional Assembly, but having again engaged in committing revolutionary acts, he was sentenced in 1849 to imprisonment for five years. Twice during his stay in prison he was elected a deputy, but, of course, could not act as such. On being liberated in 1854, he went to Belgium, where he resumed his scientific studies. In 1869 he reappeared in public life, and since that time has been better known in politics than in science.

Figure 5, left. Raspail's obituary published in the January 1878 issue of The American Journal of Microscopy and Popular Science (Anonymous, 1878).

Posterity.

Raspail died the 7th of January of 1878. What Lord Stanley of Alderley wrote of Hilaire Belloc (Stanley of Alderly, 1928) could have been written for Raspail,

"[He] was prejudiced, but there were few who knew him who did not love his prejudices, who did not love to hear him fight for them, and who did not honor him for the sincerity and passion with which he held to them."

So it was with Raspail's friends, but not with his enemies, and of those he had too many.

"You amount to very little if your death is not desired by many."

This overly pessimistic maxim by the venerated neurohistologist Ramón y Cajal (1920/1959) does, unfortunately, apply here.

In death as in life Raspail received both due recognition and disapproving silence, or worst. A few examples will illustrate the point.

For all of his advocacy of the use of the simple microscope, Raspail is never mentioned in Ford's History of the Simple Microscope (Ford, 1985).

Professor L. Lison wrote a book of histochemistry in French (Lison, 1960) that was the most comprehensive treatise on the subject published to that time. The eight hundred and forty-two pages of text contain a single reference to Raspail. That reference is not to Raspail's fundamental work on the histochemistry of sugars, lipids, or proteins, but to his developing of a technique for micro-incineration; a technique that was becoming obsolete by the time Lison's two-volume work was published.

Neglect went further in the work of Professor M. Langeron. In none of the four editions of his widely acclaimed manual of microscopy and micro-techniques, published from 1916 to 1949 a single reference to Raspail is to be found. Mentioning the fact that in its fourth edition the book covers 1430 pages (Langeron, 1949) gives a measure of the extent of the oeuvre and of the extent of the neglect. The Paris Medical Faculty had not forgiven Raspail even seventy years after his death.

It is comforting, however to see that even in his lifetime his fame had cross the Atlantic (Anonymous, 1878). Credit to his work was given once and again by Professor Lucien Cayeux who begun his 1914 course at the Collège de France by saying he was honored to proclaim Raspail the founder of "micro-chemistry." Similar accolades were given outside France by researchers in Europe, and the USA by authorities in the field such as Chamot and Mason (1938) and Pearse (1968). The longest boulevard in Paris is named after Raspail. Several biographies of Raspail have been written, including a very comprehensive one (Weiner, 1968) and to this day France honors his name as a scientist as as an advocate of those down and out in society.

Quo vadis histochemistry?

Raspail's legacy, whether acknowledged or not, rests on the prodigious developments in the branch of science that he created: histochemistry. His path-finding research was followed by that of others that enlarged and refined the original techniques. Differential methods were developed for the identification of various sugars, proteins, and lipids. Techniques were developed for the precise identification of RNA and DNA, even before the role of these nucleic acids were fully understood. The activity of enzymes was demonstrated at intracellular level. All this and more had been achieved by 1960, the year Lison published his extensive compendium. Ten years later another golden era started for histochemistry, an era that continues to this day. Developments included the wide-spread use or radio-isotopes and of auto-radiography. Ploem's brilliant invention of a practical system for epifluorescence microscopy (reviewed in Ploem and Tanke, 1987) were some of the advances that heralded the new era. Then came the introduction of highly specific fluorescent markers used in conjunction with confocal microscopes which are backed up by impressive computer power. These have brought histochemistry to a realm never dreamed off: real-time observations at the molecular level within the living cell. Technology that will allow tracking the motion of a single molecule within a living cell is been developed

(Clemson University, 2007). We have to mention also the incredibly sophisticated technique of in-situ hybridization that permits, for example, to detect in a tissue section even one copy of the HIV genome lodged inside an innocent-looking cell. This world of wonder rests on the foundations laid by François - Vincent Raspail. At the end, he was a far more successful revolutionary with the microscope than with the rifle.

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