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Classics in Oncology

Peyton Rous (1879-1970)

Introduction

The viral etiology of cancer was first suggested by Amedee Borrel in 1903 and actually demonstrated by Ellerman and Bang in 1908 when they achieved cell-free transmission of avian leukosis. At that time, avian leukosis was not considered a neoplastic disease and it was not until Peyton Rous's famous experiment in 1911 that a definite link between tumors and viruses was established.

In 1909, a local poultry breeder brought a Plymouth Rock hen with a large tumor on its breast to Rous's laboratory in the Rockefeller Institute. When Rous excised the tumor and examined it microscopically, he found all the characteristics of a spindle cell sarcoma. He then made a "soup" of the tumor and injected it into the original hen. New tumors formed, invaded the surrounding tissue and killed the hen in several weeks. In his first report (1910) Rous was mainly concerned with transplantation and propagation of the tumor he called "Chicken Tumor I" and which he described as the first solid avian neoplasm to be transmitted within the same species. He also mentioned, almost in passing and without much enthusiasm, projected attempts to transmit the tumor using cell-free filtrates.

In the following reprinted paper, Rous reports the virtually unexpected results of these experiments—the tumor, a true neoplasm, was successfully induced in live hens by means of a cell-free filtrate and the tumor behaved in the new hosts very much as it had in the original hen.

Nowhere in this report, nor in any of his subsequent reports during the next twenty years, did Rous use the word "virus." Even after an electron microscope photographed the Rous Sarcoma Virus, he continued to call it a "tumor agent." Nevertheless the implications were clear, the properties of the filterable "agent" corresponded very closely to those of a filterable virus. But in 1911 every scientist knew that Virchow's doctrine of cancer causation from within the cell, not without, was fundamental and that Rous was at best mistaken—the tumor was not a tumor, or Rous's technique was faulty and the filtrate did have cells in it—in any case, viruses could not cause cancer. As recently as 1958, at the Seventh International Cancer Congress, one investigator dismissed the Rous sarcoma virus as a "laboratory mutant . . . responsible for a variety of economically important diseases in chickens." Rous may well have been in the audience at the time; he was 79 and had gone to London for the Congress.

Peyton Rous had reached an important milestone in the history of cancer research, but he had made his discovery at a time when the scientific community was not yet ready to go beyond a too literal interpretation of Virchow's "Omnis cellula e cellula." He was working in America when research and important scientific ideas were still considered the province of Europe, and lastly he was using a very unfashionable laboratory animal—the chicken!

Soon afterwards, Rous, perhaps depressed by his colleagues' rejection, put aside cancer viruses and turned to other work.

Francis Peyton Rous was born in Baltimore on October 5, 1879. Even as a youngster his scientific observations brought him into conflict with the experts. He was interested in botany and submitted his own classification of ferns to a contest in Baltimore—the prize was a microscope. The project was certainly ambitious but ran counter to the established authorities of fern classification and he lost.

He received an M.D. from Johns Hopkins Medical School in 1905 and then trained in pathology with Aldred S. Warthin at the University of Michigan. In 1909, Rous accepted Abraham Flexner's invitation to join the Rockefeller Institute for Medical Research where he stayed and worked for the next sixty years.

After he shelved his tumor virus work, he developed a method for storing whole blood which made possible the blood bank. The use of hens' eggs as media for cultivating viruses and trypsin to isolate cells from tissue was first developed in his laboratory. Rous's studies of the liver and gallbladder led to delineation of the gallbladder's chief function, the concentration of bile.

In 1932 Richard Shope's discovery of a causative virus in rabbit fibromas gave support to Rous's earlier work and invited a return to cancer research, which occupied him for the remainder of his life.

Dr. Rous received honorary degrees from at least twelve universities, including Cambridge where he spent one of his happiest years. Indifference to the possible viral etiology of cancer began to dissipate and he received

numerous awards including the Distinguished Service Award of the American Cancer Society and the National Medal of Science. He served as Editor of the *Journal of Experimental Medicine* for fifty years and was an articulate and inspiring writer and speaker.

In 1966, over half a century after his first report on "Chicken Tumor I" Peyton Rous was awarded the Nobel Prize in Medicine. He was in the midst of an attack of femoral thrombosis and was advised not to make the trip to Sweden, but he had been nominated for the prize more than 20 times and had waited 55 years for recognition of his early work. At the age of 87, he went to Stockholm to receive his award in person.

Dr. Rous died in New York City on February 16, 1970.—*Editor.*