

Peyton Rous

PEYTON ROUS



A NOTABLE
CAREER IN
FINDING OUT
PEYTON ROUS

1879-1970

The Rockefeller University Press

NEW YORK • 1971

Frontispiece *In his laboratory 1958*

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LIBRARY OF CONGRESS CATALOGUE CARD NUMBER 77-160731

STANDARD BOOK NUMBER 87470-016-7

PRINTED IN THE UNITED STATES OF AMERICA

introduction

ON MAY 19, 1970, relatives, associates, and friends gathered in Caspary Auditorium for a simple memorial tribute to a great scientist and an inspiring human being whose death three months before had ended one of the most distinguished careers in the history of medical research. Peyton Rous spent more than 60 years of that uniquely productive career at The Rockefeller Institute for Medical Research, founded only eight years before he joined its staff in 1909. Dr. Maclyn McCarty, who planned the memorial to a beloved friend and colleague, has noted that as a result of this remarkable record of sustained service — undiminished even during 25 years of "retirement" — Dr. Rous's absence will continue to be felt in many ways in the coming years.

On the pages which follow are the texts of reminiscences voiced on a May afternoon by four men who were fortunate enough to know Dr. Rous not only in the laboratory but also in many of those other worlds through which he moved with such enthusiasm and joy, observing and discovering. Warm and distinctively personal though they are, the four tributes are remarkably consistent. Certain words and phrases recur again and again. From myriad facts, events, and occasions, they reflect a single unblurred image of a whole man — Peyton Rous, scientist and humanist.

Frederick Seitz, *President, The Rockefeller University*

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a view from the center of a world

P EYTON ROUS's activity as a naturalist came early to the public notice. A frog he had brought with him on a boyhood visit to the Chelsea Hotel jumped out the window and down the blouse of a chambermaid sweeping the courtyard below. This result was reported by the headwaiter at lunchtime as he returned the creature to its young master.

Rous really wanted to be a botanist or a writer and, indeed, had already been both in his early teens. But circumstances dictated that he take training in medicine and then in pathology. Finally, quite against the advice of his own teachers, he accepted Simon Flexner's challenge and took up cancer research.

From this distance it is easy to discern who the great experimenters were whom he joined. Rous came to equal these giants and breasted all of them in their own particular pursuits. Some he simply surpassed in the unraveling of a special aspect of the cancer problem. At least one he proved absolutely wrong. And in doing that, with his exquisitely straightforward observations on a chicken tumor transmissible by a cell-free agent, he founded a school of cancer research all his own.

How is it to found a school? Not all gaiety.

Intellectual support for what had been called "the virus hypothesis of cancer" was at its lowest ebb when elegant, experimental proof of it issued from Rous's laboratory. But tumor after tumor, in the broadest sense of that noun, had had infectious causes ascribed by the heroes of nineteenth-century bacteriology. And since the cancers — or true tumors, as they were called — were different, it began to be taken for granted that the difference must

lie in their causelessness or spontaneity. The destructive corollary of this — that if you had found its cause you hadn't a tumor — doomed Rous's discovery to many years in limbo. A half century later the Seventh International Congress Against Cancer could still hear, and hear with equanimity, that the Rous sarcoma was a laboratory artifact which had misled cancer researchers for fifty years.

That was in 1958. But already things were changing. And at the present time more than half the published work on cancer causation stems, and stems not at all remotely, from Rous's 1910 discovery.

Fortunately, throughout this long, dark period of acknowledgment deferred, Rous received wholehearted Rockefeller support. I say fortunately not for Rous, but for all humanity. For during that time of acclaim withheld he gave us a whole series of epochal discoveries. From them derive blood banking, tissue-culture harvesting, and our most modern understanding of several physiological and oncological linchpins.

When at last the well-earned awards materialized, it was felt that he was worthy of each on any one of several counts — and that he might have had the Nobel Prize for literature as well.

What manner of man could be so many things to all mankind?

My late chief had inexhaustible energy. It was I, fifty years his junior, who showed the more fatigue at the end of our days together. He had enormous power of concentration — or was persistent to a fault — depending on one's view of the occasion. He had maintained, despite his high literacy and profound scholarship, the curiosity and power to observe with which most of us pay while

A VIEW FROM THE CENTER OF A WORLD is by James S. Henderson, Professor of Pathology in the University of Manitoba Faculty of Medicine. From 1957 to 1970 he was on the faculty of The Rockefeller University and a close associate of Dr. Rous.

still children as the price for learning. He was educated to a fine pitch, yet had lost none of that infinite resonance which let him see things anew. This made him a delightful companion.

His laboratory was a playroom: his assistants, neighbor children, asked to play for awhile. But, in the games we played with animals and tumors and cells and viruses and chemicals, no fantasy was allowed. The prize in the game had to be a hard fact, although the facts, without the context of the carefully garnered experimental evidence, would have seemed fantastic enough. Some of them sufficed to rock the world of biological science — nay, to change its very axis. Rous's work did much to shift that axis from Europe so that it came to pass right through the Rockefeller campus. The view from his lab in Theobald Smith Hall has been a view from the center of a world.

With dramatic irony, the panorama which was his backdrop there had changed of late. When I first joined him I could look up from our bench to the phallic grandeur of the Empire State Building and to the chaste harmoniousness of Rockefeller Center. Now these are screened by buildings close around and for the most part mean and sterile — built, it would appear, to the end of income for today and no thought of inspiration for tomorrow.

His lab is strangely quiet now and my thoughts as I look out on this alone are that it is well that Rous and our older colleagues built so carefully here, tending so conscientiously the architecture and literature and scholarship inseparable from their science. For the tide that threatens everywhere to reduce great callings to sordid careers has already run strong and might, had it been otherwise, have engulfed all.

But there will remain joy from experimentation — and from the memory of Rous's enthusiasm for observing phenomena. How he enjoyed his visits to Israel, where he was thrilled by the violent clash of the new against the old. How he reveled in the bright light

of Stockholm, where, on feeling a recurrent thrombosis, he dosed himself with anticoagulant so as not to spoil the fun for anyone. How he delighted in his breakfasts at the British Embassy, where he contributed to one of those deep friendships which transcend national and generational boundaries.

He was at home all over the world, whether in Nature's solitary company or at the center of the most urbane group. He extracted the most possible from the city jungle and from the forest primeval.

Perhaps it was in that forest that Rous received his greatest challenge. In the hemlock woods near his Connecticut home there lived a hermit who, more surly than wise, said to Rous on their first encounter: "From the city, ain't ya? Ye'll starve up here." But the pessimistic prophet was confounded. Many years later — after Houston, Philadelphia, London, Washington, Frankfurt, and Stockholm had made their obeisance — the Medical Society of Connecticut took the plunge and elected Rous an honorary member. He was particularly proud of this, for it showed he had earned that which is dearest of all — honor at home.

He will be remembered there and here and everywhere as long as biologists have scholarly concourse.

his sparkling versatility

IT HAS been said that "a prophet is not without honor but in his own country, and among his own kin, and in his own house," but surely that quotation from the gospel does not apply to Peyton Rous. He has been held in the highest esteem by all of us, his scientific kin, and in his own scientific house, The Rockefeller University, as well as in his own home, and by his friends throughout his country and the world. Deservedly so.

With the passing of Peyton Rous, I feel that we have experienced a sort of *Götterdämmerung*, the passing of one more of the old giants — that small group of able men who came early to The Rockefeller Institute for Medical Research and who, by their efforts, carved out the mold and form which that Institute was to assume for the next fifty years. It was largely through their efforts that the infant institution flourished so successfully that not only did the founders increase their interest in it and aid to it; but many other donors throughout this land endowed and supplied other institutions to further the great adventure of medical research for the good of mankind. Indeed, lacking only a few years, Rous's presence at Rockefeller occupied almost the entire span of its existence.

To be sure, great and able men have come since and are with us now and will continue to do fine work, but today medical research has become such an accepted part of university life that the glamor and most of the excitement has gone. However, the early establishment of the value of medical research to a somewhat ignorant and hostile public was one of the great feats accomplished by those early workers.

Peyton Rous's famous, first demonstration of a viral cause of certain fowl tumors has changed the whole pattern of cancer research through a slowly growing awareness of its significance, but the fact stands out that this work, which was largely responsible for his Nobel Prize, was done about sixty years before the award was made. This proves once again that "The March of Science" is not as swift as we are led to believe, if an investigator is so far in advance of his fellows that even carefully executed and beautifully documented work is not appreciated until more than half a century later.

Now the Rous sarcoma is known to almost every high school boy interested in science. It is being used in scores of laboratories all over the world.

It is not necessary for me to try to tell you who knew him what manner of man he was: the dynamic, brilliant, eager, broadly informed person; the man who was loaded with honors and bore them lightly; who walked, when more than ninety, with a firm step and at a fast pace and filled his days with active and excellent work.

Instead, I want to recall here his sparkling versatility — which some who knew him but slightly may not appreciate — because it led him to several careers. The first, already mentioned, covered the period of his work on the chicken tumors before World War I. The next involved him in a host of experiments too varied to list, such as the protection of bacteria by phagocytic cells, and the separation by trypsin of living cells in tissue culture — a technique that he used to advantage later.

Then there was another most important work. As it became

HIS SPARKLING VERSATILITY is by Phillip D. McMaster, pathologist and microbiologist, who has been associated with The Rockefeller University since 1919 when he became a Fellow and an assistant to Dr. Rous. He is now Professor Emeritus.

clear that this country would become involved in World War I, Rous, with his associates Joseph Turner and Oswald Robertson, began a search for fluid substitutes for blood that might be given to the wounded. But none of the substitutes tried satisfied them unless red blood corpuscles themselves were present. At once, therefore, he and Turner sought ways and means to preserve red blood cells outside of the body for emergency infusion into the wounded. We must realize that this idea seemed fanciful and visionary to many at that time, when transfusions were made only directly from man to man by a surgical procedure too difficult to attempt at the front. Transfusions were not commonplace, as now, aided by a wealth of anticoagulants. Through well-conceived experiments, Rous and Turner succeeded in preserving corpuscles for three or four weeks, whereupon Robertson joined the U.S. Army Medical Corps and had himself transferred to the British Expeditionary Force. Behind the lines in Belgium and France, in a makeshift refrigeration unit made of packing cases, he preserved red blood corpuscles by the Rous and Turner method. Many lives were saved thereby, for this was the first blood bank the world had ever seen, and it was effective.

Even as late as World War II, during the London blitz and in our landings on the South Pacific islands — so far ahead of their time were these experts, Rous and Turner — blood was often preserved by essentially the same methods, although between the two wars many attempts had been made by others, especially by the Russians, to improve upon the technique.

By now, thousands of lives have been saved, and Dr. George Corner, in his *History of The Rockefeller Institute*, cites the work as one of the two greatest contributions made by this institution to clinical medicine, yet it came from the nonclinical laboratory of Rous and Turner.

There followed work with the National Research Council in

Washington during the war, and afterwards return to experimental pathology and excursions into physiology and even immunology.

I first knew him after World War I, when he was interested in liver disorders, bile formation, and even in gall stones — subjects far, far removed from cancer research. To follow these interests he had to become an expert experimental surgeon — another evidence of his versatility.

I was struck by his scholarship, by his apparently complete mastery of everything written about cancer research, and of the lore of physiology and of pathology, as well. How could one man accumulate such a fund of knowledge? It seemed to come about by a coupling of his keen mind and exceptional ability to a tireless effort directed to the highest principles of perfection. This combination yielded an uncanny judgment about what work to undertake and what not to attempt, and it gave him a surefootedness on the steep ascent to success. Even with these advantages, he devoted every minute of the laboratory day to the work at hand with an almost fierce intensity.

I can see him now — arriving in the morning, stepping from the elevator, and calling to his secretary as he passed her room on the way to the laboratory, commencing dictation to her even while hanging up his hat and coat. When the secretary left, the door closed and remained so for hours while he wrote. Absolutely no one dared to interrupt this retreat. When experiments were under way his most outstanding characteristic was a capacity to become totally engrossed in the problem and techniques at hand. He was a true perfectionist, testing meticulously every possibility for failure, with a strong feeling that something might slip up either in the planning or in the execution of an experiment.

In the laboratory he never fraternized with his associates; there simply was no time for it. Even at the lunch hour he seldom joined them, believing it was better for them to mingle with the others on



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the staff to broaden their viewpoints. On the principal that "the poor you have always with you," the leisurely human contacts were put off; they could be indulged in at any time. But unfortunately we were all too busy, and the time seldom came. When it did, it simply revealed again how many sides there were to this man's nature!

I recall him in the early nineteen-twenties at his summer place on Long Island, where we waded up to our shoulders in the waters of Peconic Bay, feeling about with our feet on the soft bottom for scallops. On feeling something promising, we would duck and try to seize our prey. Again, there were hours of fishing in the quiet waters of the bay. Such moments were a revelation to me. The living dynamo I knew at the laboratory was relaxed and thoroughly carefree.

Thoroughly, indeed! The use of that word brings me to still another aspect of his versatility. He despised that word and, as an editor, deleted it from most papers that came upon his desk. We are all aware, of course, that he was as well known for the excellence of his writing as for his experimental work. He was a master of the English language. If genius is the infinite capacity for taking pains, in writing, as in his experimental work, he was doubly a genius. Each of his papers was written over and over and over again and then refined further.

Often, when he was writing in seclusion, he could be heard reading his sentences aloud for balance and cadence, just as did Daniel Webster, another master of the English language, when preparing his great speeches a century earlier.

Besides exhibiting this capacity for meticulous writing, Peyton Rous spent an unbelievable amount of time in editorial work, into which he entered with equal zeal. For years and years he carried practically the whole burden of the editing of *The Journal of Experimental Medicine*. Under his expert leadership it became the

Atlantic Monthly of medical journals, and this was a Herculean task, considering how badly most medical researchers wrote and, unfortunately, still do. He was almost alone in his continuing battle with authors, often as not typical prima donnas, who presented slovenly written manuscripts. I know whereof I speak, because, even in my room across the hall from his, I could not help overhearing heated arguments between the editor and the would-be authors who — when told that they must rewrite their papers for the fourth or fifth time — came to feel that the editor habitually regarded a clean, uncorrected page of manuscript as an abomination to be assailed and mastered simply because, like Mount Everest, it was there.

Although giving so much of his time to editing, he was also most generous when it came to publication. Frequently papers from his laboratory carried the name of some unknown youngster in the department as the leading, major author. Peyton Rous's own name was either at the end of the list or, as often as not, absent altogether, when, as a matter of fact, he himself had either written the whole paper or rewritten the greater part of it. Further, he labored on such papers with just as much care as if they were all his own.

As we gather here in this modern auditorium on this beautiful campus, I return to my original theme. It is because of men like Peyton Rous and a few other luminaries that the small Rockefeller Institute became worthy to grow larger and then greater, until we now see the University as she stands today.

But let me prophesy: the day is coming, and indeed may not be far off, when all this magnificence will seem small in comparison with the value to mankind the world over of the first proof of a viral cause of tumors. This will stand as a sort of Rosetta Stone leading to the interpretation of these dread diseases, and future generations will have to thank Peyton Rous.

stay as close to nature as you can

FROM the flood of memories that crowd in upon me, I shall here refer only to a few that seem to me to characterize Dr. Rous as man wedded to life and to science. They are memories that I cherish.

Physician he was in the noblest sense of that term — a liberally educated physician having wide knowledge and deep understanding of his profession and manifest compassion for the ill (as also for the downtrodden). In addition, he was a soundly trained general pathologist and a superb experimental pathologist. As experimenter he was whole-souled, pursuing his curiosity avidly and responsibly throughout a long life, with an eagle eye out for the new and a sharp sense of the significant.

That he was a medical scientist, and the things he achieved as such, are widely known. But for the here and now, I shall recount other and more personal recollections, which have to do mainly with the *how* of some of the things he did, maybe here and there a glimpse of reasons *why*.

Most vividly my recollections remind me that Dr. Rous was a *naturalist*. By that I mean one who scrutinizes, reflects upon, and speaks or writes about phenomena of nature, however created. Indeed, while still a boy he became a professional naturalist. Years ago he told me with pride that the first money he had ever earned was made in this way; Mrs. Rous now reminds me that this initial endeavor consisted in his writing for a Baltimore newspaper a series of essays entitled "Flower of the Month" — this when he was about 20 years old. See pages 28 and 29, included here through the kindness of Mrs. Rous and the permission of the *Baltimore Sun*.

When I first came to The Rockefeller Institute for Medical Re-

search in 1934, Dr. Rous had recently become interested in the neoplastic attributes of certain cutaneous papillomas that occurred naturally in western cottontail rabbits and were caused by a virus that had been discovered by his friend Richard Shope; he wrote feelingly of this interest and of Dick Shope in his Nobel Prize Lecture "The Challenge to Man of the Neoplastic Cell."¹ During the ensuing several years, Dr. Rous and his successive associates — Joseph Beard, William Friedewald, and I — spent countless hours studying the natural growths (and the cancers that sometimes originate in them) in cottontail rabbits that had been trapped in Kansas by Earl Johnson, another friend of Dick Shope's. We spent further hours planning and executing experiments to disclose more about the doings of the Shope virus. Rous and Beard first found that the papillomas caused by it are true tumors. Then, after Beard had devised an easy way of producing discrete papillomas with the virus, we produced and studied them extensively in tame domestic rabbits, in western cottontail and jack rabbits, in swamp hares from east Texas, and in snowshoe hares from Maine.

However the growths had come to be, and in whatever species, Dr. Rous always examined them one by one, himself. His ways of doing so interested me enormously. First he would look closely at the growth with his naked eye. Then he would palpate it, ascertaining the fleshiness of its margins and its penetration of, and attachment to, underlying structures. Often he would draw freehand sketches of the tumors, with many erasures and penciled labels. Often, too, he would call Mrs. Stebbins, his secretary, into the laboratory; then, while John Pomerico, his well-trained senior technician — much respected and leaned upon by everyone in the

¹ *Cancer Res.*, 1967. 27: 1919-1924.

STAY AS CLOSE TO NATURE AS YOU CAN is by John G. Kidd, Professor of Pathology in Cornell University Medical College. In the 1930's he was first an assistant, then an associate in Dr. Rous's laboratory at Rockefeller.

lab — held the rabbit before him, Dr. Rous would dictate elaborate, precise, vivid descriptions of its growths. These descriptions, everyone knew, were to be typed promptly on heavy five-by-eight-inch cards, corrected in his own hand, and kept readily available in the middle right-hand drawer of his desk. Finally he would call upon the knowledge stored in his capacious mind and upon his wide-ranging imagination, as he summarized his observations and interpreted them.

Watching and listening to him, you perceived at once that the tumor was an evolving biological entity, a part of nature now gone wrong, and you were led to wonder how it had come to be what it was, and to speculate on what the future might hold for it and its host. Good fortune it was for all of us that the Shope virus gave rise to growths situated on the skin — at hand, inviting scrutiny, their characters open to those inclined to sense and able to discern.

So striking to him were the visual (and intellectual) impressions gained from his gross examination of a tumor that he frequently deemed gross photographs imperative. When these were to be made, the rabbit's fur had first to be shaved or clipped from about the growths so that they were as conspicuous as the jewels in Tiffany's window. Then Dr. Rous, John Pomerico, rabbit in cage on small laboratory truck, and Dr. Rous's associate (possibly emulating Dr. Flexner, he usually limited himself to but one at a time) would make their way en masse to the Illustration Department, which was situated on another floor in an adjacent building. There, with everybody focusing on its growth, the rabbit submitted more or less graciously to the professional ministrations of Mr. Schmidt or Mr. Haulenbeek, the Institute's professional photographers. Occasionally Dr. Rous found it necessary, in order to conserve his time, to delegate to his associate the task of posing the growth for photography, but he always managed to scrutinize the developed, wet negatives before the rabbit was brought back to the laboratory.

Whenever it seemed to him that the precise character of the growth had not been captured, retakes were made on the spot.

Biopsies were often taken, too. Precise surgical and anesthetic techniques were employed, Dr. Rous being master of them all. He habitually used a jeweller's monocular magnifying lens in selecting those portions of the biopsied tissue to be prepared for microscopic examination or used in transplantation studies. After Miss Delano, his Boston-trained histology technician, had stained her beautifully flat and unusually thin microtome sections with methylene blue and eosin, then embedded them in choice Canada balsam, and mounted them on slides under spotless cover glasses, Dr. Rous spent long hours studying the slides with his student-grade binocular microscope, the pertinent experimental records spread out before him on his laboratory bench. Again he frequently called upon Mr. Schmidt or Mr. Haulenbeek for assistance in the preparation of photomicrographs, seeing to it that the image displayed in the prints duplicated precisely the one seen under the microscope.

He next spent days, weeks, and months going over the laboratory records — correlating the experimental procedures and the recorded observations in minute detail, "squeezing dry" the findings of each experiment, comparing those of like sort and looking closely for contrasting findings. He then reexamined the observations and inferences that he had made and compared them with findings already hewn out and reported upon by other workers with other materials. He knew firsthand the treasure trove that is the scientific literature of cancer, notably the precise observations and reflections of that army of well-trained German pathologists of the last half of the nineteenth century who had explored cell by cell the innumerable growths of diverse kinds that occur naturally and in great profusion in man and animals. (How he managed to wade through all that difficult German and keep the findings sorted out were secrets I never fathomed.) Finally, everything was to be

written up for publication in *The Journal of Experimental Medicine*, but that is another story.

A personal recollection from long ago reveals how strongly Dr. Rous believed the experimental pathologist should remain close to nature. During my first year with him, I made an observation about the "spontaneous" regression of virus-induced rabbit papillomas, which led to an inference that ran rather counter to one he cherished. Realizing that he would accept factual observations, I produced in several experiments varying numbers of discrete papillomas with three different strains of Shope's virus. (The purchase of the more than six dozen domestic rabbits required for these experiments, and the charges for their maintenance during several months, strained Dr. Rous's laboratory budget severely that year, but that, too, is another story.)

I then carefully followed the course taken by each papilloma in each rabbit. In one of my experiments, for example, 30 rabbits had a total of 920 of the induced tumors, which had to be observed at intervals of two to seven days during about eight weeks' time. In order to record the enlargement (and occasional disappearance) of the numerous papillomas — the large number was necessary if the results were to be meaningful — I procured some sheets of rigid transparent plastic, each about as big as a rabbit's flank (again making rather free use of Dr. Rous's laboratory budget, this time with assistance from Tony Campo, the Institute's Purchasing Agent). By placing a sheet of the plastic against the flank of the firmly held rabbit I could quickly outline with a sharpened glass-marking pencil all the tumors the rabbit possessed.

The chartings, transferred to a number of sheets of white bond paper measuring about three by four feet, constituted a graphic record of the course of events, tumor by tumor and rabbit by rabbit. After we had spread the chartings over every laboratory bench and much of the floor of his large laboratory and had looked to-

gether at all the happenings, Dr. Rous readily accepted the new inference, as I had surmised he would do.

But when it came time to present the findings before an audience of scientists and to write them up for publication, my graphic chartings seemed to me boringly voluminous. Hence I decided to present the findings mathematically. I constructed a simple straight-line graph of which I was rather proud; it reflected accurately the relationships exhibited by the chartings and had the merit of being concise. I imagined that it would have pleased Pythagoras and that it would please almost any editor because it would save him precious pages. (Dr. Rous had long edited what we youngsters referred to as *THE* journal, hence was acutely aware of page costs.)

But my graph didn't please Dr. Rous. Gently he pointed out to me that, in biological work of the sort I had been doing, a fellow needs to describe exactly what he did, and to show exactly what he had seen; then the inferences would follow naturally. Whatever you say or record should be as close as possible to the natural phenomenon. Don't let mechanical or electronic gadgets, or anything else, get in between you and whatever it is you're studying; and when you report your findings stay as close to nature as you can.

While becoming a professional naturalist at an early age, Dr. Rous simultaneously became a professional writer, as I have said. My memories of him as writer are also vivid.

He approached writing with a zest that was remarkable in a zestful man. When he had a job of writing to do you could set your watch by the time of his daily arrival in the laboratory: it was 10 A.M. Proceeding immediately to his desk, he would sit there, pointedly undisturbed, writing steadily, until about 1:25 P.M. If a crucial decision about a particular point concerning the afternoon's scheduled experiment had to be made by him, you could interrupt him for a couple of minutes during the morning. But nothing dis-

cursive, nothing that could be put off until the afternoon, would he talk about.

One morning I needed to talk with Dr. Rous about the afternoon's work and was waiting in his laboratory when he arrived. After he had greeted me in the courtly manner that was natural for him, he noticed that my attention was fixed on his desk. Experimental records lay in a thick pile all over it, randomly distributed and admixed with numerous sheets of lined yellow paper, each covered with his fine handwriting, the margins filled with countless alterations. We both knew that somewhere in the jumble lay hidden his old black fountain pen, now laboratory patched with ink-stained surgical adhesive tape, but having a fine point of the sort he liked and a barrel congenial with his fingers. After a moment, Dr. Rous smiled and said: "Rearranging my desk each morning helps me collect my thoughts."

The afternoon's experiment took precedence over everything else. This usually required all hands until about 6:30 P.M., sometimes an hour or two later. When it was finished, Dr. Rous walked briskly home, leaving his writing to be tackled joyfully again the following morning. However, I imagine Mrs. Rous might like me to say at this point in the interest of accuracy that all too often he arrived home in the evening carrying a briefcase full of scientific papers, with which, soon after dinner, he would retire to the library, not to be seen again during the evening.

During his lifetime, as everyone knows, Dr. Rous published scores of detailed scientific reports on a number of diverse themes. Without exception, these were written in exquisite English. But like most scientific reports of our times they were essentially ritualistic narrations, tending strictly to the business of "telling it like it was." The *it* was important and so were the papers. The latter were distinguished by his uniquely rich and brisk style and, even more, by

FLOWERS OF APRIL

When harsh March weather is past and gone and April's sunny showers give glad promise of another summer, every plant that grows makes ready its apparel of the coming season. And what a vast stir there is, to be sure! Every seed that has been waiting impatiently since autumn, every shrub that should in virtue of its age take spring philosophically—only it doesn't—all of these commence to swell and bud and put forth their leaves. Positively, from the rapidity with which some of these wood denizens make their appearance in new splendor, it would seem as though there were a premium put on haste, as if there were an eclat to be gotten from an "early spring opening" in the vegetable world, just as among milliners. On one day you have bleak, bare winter earth and on the next—presto!—a thousand flow-ers are dancing confidently in the weak sunlight.

It would be hard to tell which is the earliest species to blossom forth. So many different kinds are there, and so much depends on advantage in position—on the protection afforded by a hillside, on the warmth from a nearby spring—that there is no accurate order of succession. But among the first come the skunk cabbage. One of our earliest signs of spring is the queer, irregularly blotched flower of this plant. It exactly resembles a miniature monk-cowl peering from the surface of the earth in the moist woodland where it grows. The bright green leaves, whose shape and odor give the plant its name, appear a few days later sprouting up around the flower.

A far more beautiful, and pleasant acquaintance is the blood-root. Its white blossoms, with king-gold center, are known to all who have sought to pluck them only to find that the petals shatter with the slightest ill-usage, and that the juice of the stem stains the hands a bright orange. Nature can give no stronger indications that this subject of hers is to be admired in its native haunts and left undisturbed. But there grow others not so tender. The quaint, fuzzy little liver-wort is scattered all through the woodland, and at this season of the year the light blue or cream-colored or even plucky flowers and trilobed leathery leaves of the plant are dear to every rambler. Or perchance the find may be a colony of the rue-anemone—most delicate adventurer of the new year. Every wind that blows sets the pink-tinted blossoms quivering on their fragile stalks as if in dread of a frosty death.

Indeed, a frosty death is an only too common occurrence. Truly, the good die young. No one ever saw a frozen skunk-cabbage—such louts thrive, lusty and malodorous—but who has not gone into the wintry woods, his mind set on arbutus, and parted the dead leaves only to find the flowers underneath, that should have been starlike, waxy and fragrant, brown and withered? The spice-bush also, which perfumes the thickets with its yellow blossoming twigs, is another frequent sufferer—and the dog-tooth violet. Oh, I could name only too many overconfident species that pay bitterly for their rashness!

FLOWERS OF MAY

We city people, with our narrow, urban view of nature in general, come to look on April as most joyous with the fragrance and splendor of spring. But we are much mistaken, for April is merely the month of transition. It is true that our sidewalk trees come into foliage then, but that is due to the warmth from the numerous furnaces that have not yet given over their winter activity and to the protection afforded by the houses round about; and if one goes into the country he will find the forest still in cold, gray severity, save for the reddening of some maple or the timid green of a budding willow. So if the rambler but time his visits aright he may have the pleasure of two separate vernal seasons—the more artificial, when the horse-chestnut, elms and lindens on our streets put forth their leaves; and the later, natural development in the wild-wood, when every oak twig is tipped with new foliage and the withered, brown leaf-skeletons that have rustled on the beech since fall give place to a translucent greenery. This latter rustic quickening ordinarily takes place during the last few days of April, so that by the first of next month there is overhead a canopy of leaves, light emerald and stirring with every chance breeze that idles through the boughs. And beneath a wild luxuriance of herbage spring up plants of all sorts, the good and the noxious, the brilliant and the insignificant, flourishing alike side by side.

The flowers that bloom now seem to me vastly superior to those of April, in that they possess a much greater elegance and delicacy. Anyone may note this difference for himself if he but compare the perfections of a blood-root blossom and a violet; the one is handsome, but the other has a far more graceful and well-bred prettiness. The earlier blossoms are impressionistic; they are, as it were, sketched in by Nature in the scant intervals between snow and sleet; and they bear all the crudeness of their hasty origin. But the flowers that come later have had longer to mature; more trouble has been bestowed on them; and they show a correspondingly greater grace and finish. This distinction becomes all the more evident as the year passes by, for each blossom seems more highly wrought, more cultured, more lavishly decorated than its predecessor, till finally the golden-rod and purple aster of the fall seem almost overornamented in elaboration of design, richness of coloring and general splendor.

... The dogwood, though it presents no such treasure, is yet full as dear to the wood-lover. Nothing can be more artistic than its branches spread with creamy blossoms. Science whispers that the large petals that compose the square-patterned blossoms are not true petals, but merely changed leaves around a minute inflorescence at the center—but, fiddlesticks! Let's turn a deaf ear to our informer if she try to shatter our prettiest beliefs. A dogwood blossom will remain a blossom for all that can be said to the contrary.

Excerpts from columns written by Peyton Rous for the Baltimore Sun during 1900. They were signed either "F. Peyton" or "Frank Peyton."

FLOWERS OF JULY

Naturally, in the strife for existence all sorts of wiles are resorted to. Some species come into blossom early in spring, when there is little competition because of the risk from snow and frost; others are particularly adapted for a life on rocks or in sandy ground, while yet others flower all summer long, thus making the chances better for an abundance of seedlings next year. These last are usually weeds, for the original inhabitants bloom in regular cycle. Thoreau once said that were he to wake up some fine morning in the woods near Concord he could tell the date to within three days by his knowledge of the flower almanac. Had he been placed in one of our modern, weedy fields he would have found it difficult to determine the time to within two weeks.

At the tip of every stem of the St. John's wort is a host of gay stars, orange-yellow, with many stamens radiating from the center of each. Not so shy of blooming as the primrose, the plant yet holds more aloof than does the butter-and-eggs, whose stalks, crowded with quaint flowers, are seen nearly everywhere in waste places. These dragon-faced flowers are one of the delights of childhood. By gently pressing at the sides they may be made to open their lips and yawn terrifically in true monster fashion.

Look at their color—literally that of butter and eggs. Few would wear the combination, think you? Yet here it is very charming. Nature has a certain subtle and ethereal quality to her hues. She can choose almost any shades and blend them in a mixture that is somehow never incongruous, though frequently in dye-stuffs it would be hideous. The difference is that these are live colors, just as the green of water is alive and the blue of skies, whereas all manufactured hues are dead. Such are the mere corporeal bodies of colors and lack the soul that natural tints possess. It is as impossible to create a real color as it is to make flesh and blood.

Of the sun-dew no doubt exists that it kills insects, though not for mere destruction, as it has been shown to draw nourishment from them. Darwin has based a whole book—"Insectivorous Plants"—on experiments performed with an English representative of the sun-dew genus. You may find our species growing at the edge of any botanically well-regulated pond. They love sunlight and damp sphagnum moss, where a sufficiency of moisture is always present. The small, white flowers that are uncured on a fragile stalk early in July are entirely harmless; the leaves do the insect-trapping. Each of them is thickly beset with red bristles, tipped with a minute glistening drop of viscid liquid; hence the title sun-dew. When an unwary gnat alights he finds himself caught on one bristle, and, what is worse, all the others near by bend over by some devilish ingenuity and add their drop to the one in which he is struggling. So he succumbs, and after death is assimilated in some manner. How? Ah, well! That is what Darwin wrote his book about and is hardly to be explained in a sentence. The two kinds that we have around Baltimore are both very small—a good specimen will be hardly more than a couple of inches across—and they are usually found together. Their leaves are respectively round and shaped like the blade of a paddle.

FLOWERS OF AUGUST

The flowers of August, in their beaming supremacy of color and form, always put me in mind of a florid middle age; they seem so entirely fitted for the adornment of a buxom dame or a portly gentleman. The cloistered petal maidens of the spring woods have a sweet character of youth and innocence; the brilliant June laurel carries itself with the stalwart grace of a strong prime; our autumnal everlastings have a quiet gray that seems akin to the silver of an old man's hair, and the witchhazel's beauty is like the faded glimmer of his smile. Just so the goldenrod resembles nothing so much as a stout, jovial merchant of 50 years; and the wild sunflower has quite the appearance of his good wife, bustling, somewhat ponderous, yet quick and kindly withal. Of course, all August's subjects do not partake of this nature. As there are people who never grow old with the years, so there are flowers, which, dwelling with these dignified neighbors and of exactly the same age, yet keep a child-like simplicity.

The cardinal flower illustrates this point to perfection. Once see it standing in molten dignity beside some sluggish water course and you will always recall its scarlet as the most magnificent you have known. The shape of this individual blossom is peculiar to the genus, and they are arranged in a certain order to make a stately appearance; but the color will best identify the new plant, and, when you chance on its radiance for the first time, the conviction will be absolute that this is the cardinal flower.

Two or three other members of the family are common, but they are blue; only one escapes insignificance—the great lobelia. Were it not for his scarlet eminence this promising species might cause quite a stir in the world. As happens, however, its stalks, crowded with bloom, gain admiring notice only when the cardinal does not grow nearby. Among the Rarer kinds the Indian tobacco of straggling habit and diminutive inflorescence is noted more for the harm it accomplishes than for aught else. Gray refers to it as "poisonous and a noted quack medicine."

With almost as evil a reputation is the blue weed, or viper's bugloss, an emigrant from Europe. Indeed though, the blue weed's only crime is in looking somewhat wicked and bristly and in preferring fields for its residence—which is certainly accounted very wicked, according to the vegetable code of morality. If these trifling details be overlooked the plant is really very interesting for the curious combination of the red on its stamens with the prevailing purplish-blue of the flowers.

But of all August's flowers the oenothera or meadow beauty is dearest. The Maltese cross of her petals has such a sweet simplicity; and just enough of purple tinge is mingled with her pink to suggest passion joined to an infinite purity. Standing serene and lovely in her meadow home, she reminds one of a delicate woodland lyric. But our good earth is a famous poet anyway. He will take the most commonplace materials and mold them to beauty. Stones are his prose, but animals and plants possess the living principle which marks a genuine inspiration.

the depth, range, and quality of the work being reported. His scientific papers were invariably dignified and more or less formal. They were a trifle full for some people's taste; yet always his thought and prose marched briskly forward, seeming sometimes about to break into a spirited gallop. Nothing more will be said here of these reports except to list a few of those published from 1910 to 1962, primarily in *The Journal of Experimental Medicine*, having to do with cancer. The titles themselves are revealing: "An experimental comparison of transplanted tumor and transplanted normal tissue capable of growth"²; "A sarcoma of the fowl transmissible by an agent separable from the tumor cells"³; "A virus-induced mammalian growth with the characters of a tumor — the Shope rabbit papilloma"⁴; "The progression to carcinoma of virus-induced rabbit papillomas (Shope)"⁵; "The carcinogenic effect of a virus upon tarred skin"⁶; "Conditional neoplasms and subthreshold neoplastic states. A study of the tar tumors of rabbits"⁷; "Experiments on the cause of the rabbit carcinomas derived from virus-induced papillomas. II. Loss by the Vx2 carcinoma of the power to immunize hosts against papilloma virus."⁸

His scientific lectures and reviews were different; here he joyously brought life to the literature of science. For example, his Harvey Lecture entitled "The Virus Tumors and the Tumor Problem" begins: "Not long ago in the dark ages of medicine, one could think nearly anything about disease because one knew almost nothing." And ends: "The tumor problem has withstood the most corrosive reasoning. Yet since what one thinks determines what one

² *J. Exp. Med.*, 1910. 12:346-366.

³ *J. Exp. Med.*, 1911. 13:397-411.

⁴ *J. Exp. Med.*, 1934. 60:701-766.

⁵ *J. Exp. Med.*, 1935. 62:523-548.

⁶ *Science (Washington)*, 1936. 83:468-469. See also *J. Exp. Med.*, 1940. 71:787-812.

⁷ *J. Exp. Med.*, 1941. 73:365-390.

⁸ *J. Exp. Med.*, 1952. 96:159-174.

does in cancer research, as in all else, it is well to think something. And it may prove worthwhile to think that one or more tumors of unknown cause are due to viruses.”⁹

When Dr. Rous was 85, he wrote a hard-nosed scientific review entitled “Viruses and tumor causation: An appraisal of present knowledge.”¹⁰ It is certainly one of the most cogent dissertations extant on the theme. Carrying a serious scientific message, the paper hewed strictly to the line. Yet his ways with words would out; in the second paragraph, as sanction for his categorization of certain tumor-causing viruses as “do-all” viruses (meaning thereby viruses having the capacity to “do-all” etiologically — i.e., to exist in nature and to produce real neoplasms in living organisms under natural conditions), he cites the *Greater Oxford English Dictionary* and *Pepy’s Diary* (1701) as references. A sampling will illustrate further his thought and style: “Neoplasms seldom if ever arise spontaneously; nearly all are occupational diseases of the body, acquired while running the gauntlet of life. . . . No one can tell what experiment may next reveal as concerns tumor causation. As William Blake once wrote: ‘To the man of imagination, Nature is imagination itself.’ ”

In response to a letter of congratulation about this paper, Dr. Rous wrote to me in September, 1965: “Perhaps you will be interested to know how the paper came to be. Begun as a ‘must,’ to deal with the tumultuous virus facts, it soon took on the size of a constructive effort and held me in its grip throughout a whole year, nearly all my time going to it. Now at last I’m free again. Whoopee!”

In the convocation address given at the Medical School of the University of Michigan in 1938, Dr. Rous spoke on a theme close to his heart, “Nature and the Doctor”¹¹:

⁹ *Amer. J. Cancer*, 1936. 27:233–274. (Reprinted by permission of the Harvey Society.)

¹⁰ *Nature (London)*, 1965. 207:457–463.

¹¹ *Science (Washington)*, 1938. 88:483–489.

Every good doctor is a naturalist, and there is none more whole-souled or with a larger task. . . . [He] has always deemed himself eager to listen to Nature and to carry out her commands. Her name has been as often on his lips as that of Liberty on those of the social philosophers. Always he has spoken of aiding her, of not offending her, of letting her take her course (as if she would not take it anyhow by hook or crook) and time and again he has invoked the *vis medicatrix naturae*, conceding that Nature is the best physician, an admission not the less wise because the fact has so often been glaringly evident.

In a seldom-read little book entitled *The Modern Dance of Death*¹² — written while he was on a sabbatical as Fellow of Trinity Hall, Cambridge — Dr. Rous displays a truly phenomenal knowledge and understanding of man, of the nature of his diseases and his adaptations to them (essentially the same today as long ago), and of the attainments and potentialities of modern medical science (including morbid anatomy, clinical medicine, and experimental physiology):

In the time of Thomas Linacre, man had a passion — strange it now seems to us — for pictures in which they danced with Death. Rather was it Death that danced

When one takes up the important diseases which cut man off before age is upon him, grouping together those which . . . are extraneous, a significant fact emerges, namely that in direct proportion as a malady is understood does it come to appear avoidable or if not avoidable remediable.

Was argument for basic medical research ever more compelling?

In a labor of love, "Pathology and the Glare of the Future,"¹³ Dr. Rous dealt with the discipline for which his friend Aldred Scott

¹² 1929. Cambridge University Press, London.

¹³ *Contributions to Medical Science*, dedicated to Aldred Scott Warthin, 1927. George Wahr, Ann Arbor, Michigan, pp. 19–22. (Privately printed.)

Warthin had trained him — with its place in the hierarchies of science, and with the kind of training experimental pathologists of the future should experience:

Time was, and not long ago, when the pathologist knew himself to be the child of fortune. Cells were then novel things. To look at them, stained red or blue or brown, arranged in ordered intricacies fraught with meaning, was almost enough. But the pathologist had far more. His task it was to recognize the vagaries in form brought about by disease. These too proved orderly in their strange fashion, like writings in unknown tongues upon the morphologic background. . . . Everything that the pathologist saw had scientific worth. . . .

The role of the pathologist [implies] a special attitude of mind and a distinctive training. At present the attitude of mind is more evident than the training. In it, indeed, lies the pathologist's one immediate advantage. He has only to consult the physiologist upon some question involving morbid activities to learn what crude misconceptions there can be — when indeed he finds any conceptions at all — upon the problems which seem to him so importunate. The pathologist can comprehend the gist of the physiologist's endeavors, but the latter . . . neither understands nor cares what the pathologist seeks after. The two differ as markedly as the two worlds of health and disease which they study. The strength . . . of the pathologist lies in his acquaintance with the immense gamut of morbid disturbances and his curiosity about them. Out of his strength something worthwhile should come. . . .

It may be some considerable while before the need for adequately trained pathologists is conceded. But perhaps the conquest of the immediately accessible amongst morbid causes and effects will force a recognition of it. The front line monsters of disease have been hewn down rapidly in the last fifty years. Already one can perceive signs that many of the others lie hid . . . in regions to which only those equipped with a fundamental science and with a first-hand knowledge of morbid processes — this the hilt to the sword — can pierce unerringly.

Dr. Rous's writings about some of his contemporaries who were also physicians and pathologists are at once perceptive and revealing.

For example in "An inquiry into certain aspects of Eugene L. Opie"¹⁴:

In the long run the experimental pathologist expresses himself as surely as the artist. He does it despite the cryptic, the surprising and the negative results of his labors, the demands of his fellows that he stick to the truth when telling of these, and the ritualistic character of modern scientific reporting. A single early paper may tell little of a man, being so often the product of chance and the prepared mind of some older associate, but as years pass his researches delineate him. . . .

Steadily and unavoidably Opie became a humanitarian, in a telling sense of the word. . . . Reading [his] papers, going along with him from year to year by this means, one sees venturesome thought and imagination, directness, simplicity, and a devotedness, which are the man himself. . . .

Everyone who deals with the phenomena of pathology soon comes to know that nature often speaks her secrets with a still, small voice out of a dense thicket of happenings. He who would hear and comprehend can have no pride of intellect, no fixed preconceptions; he can only listen intently and ask himself what he may have heard. This has been Opie's way in science — and in life.

And in "Karl Landsteiner, 1868–1943"¹⁵:

Few men who work at the problems of human disease come to the mental stature of which they are capable. So much there is to see and to do by the way, such opportunity to gain large practical ends by small mental means, so much pulling and hauling by the lay public and such wide applause for second-, third-, and fourth-rate achievement, if only it be of use, that to fall away from the line of the intellect is all too easy. A few men there are, though, who cleave to it through thick and thin. Karl Landsteiner was one of these.

When I first came to know Dr. Rous he was 56 years old and his hair was mostly gray, tinged with fading auburn. He was warm, fun-loving, and spirited — nowhere more than in his home, surrounded by his devoted and lively family, or in your home on family and

¹⁴ *Arch. Pathol.*, 1942. 34:1–6.

¹⁵ *Obituary Notices of Fellows of the Royal Society*, 1947. 5:295–324.

other social occasions. But he didn't suffer fools gladly. For he had long since become what the young of today might call an "action person," and, again possibly from observing Dr. Flexner, had learnt the usefulness to himself of reticence and dispatch vis-à-vis the point at hand. He set for himself high standards of performance in the laboratory and expected the same of others; sloppy laboratory work he simply would not have, nor doctrinaire assertions or asseverations. He spoke out forthrightly about anything and everything, so that you were seldom in doubt about what he thought. Somewhere though he had learnt that infinite patience is required from those who deal with the inexperienced, as also gentleness and (often) accommodations.

Dr. Frank Sladen, who had known Dr. Rous when they were young men at Hopkins, once told me that Dr. Rous was redheaded (Dr. Sladen had red hair himself), the implication in context being that Dr. Rous was spirited and more or less ready to engage in controversy over scientific matters that were close to his heart. For whatever reason, when confronted late in life with the assertion that cancers are caused by somatic mutations, Dr. Rous rose trenchantly to controversy, without explanation or hesitation. The assertion ran counter to something that as pathologist he knew. From countless microscopic observations of cancers in man and animals, made by innumerable pathologists during more than a century, and from several decades of experimentation with laboratory-made chemicals that bring on cancers, Dr. Rous and other pathologists (notably Leslie Foulds) had found out that cancers generally don't arise full blown and in a flash. By contrast they often originate in a series of step-like processes during long periods of time, by means of which they go from a variety of non-neoplastic states to the neoplastic, from benign neoplasia to malignant, then to successively more anaplastic states (from bad to worse, in Dr. Rous's phrase), *always in a single direction*. During his cogitations about somatic

mutation, Dr. Rous marshaled numerous facts for and against the idea that the process might be responsible for the generality of cancers. He wrote down the arguments pro and con, evaluated them, and submitted the gist of his thoughts for publication in a paper having the title "Surmise and fact on the nature of cancer;"¹⁶ then he went about his business.

On semiformal scientific occasions, when he knew he was amongst friends, Dr. Rous delighted in letting himself go. Invited to address a group of virologists in 1956, he began: "Have you ever tried putting up a title like a target and shooting at it in the hope of [gaining] new and amusing thoughts? Take, for instance, 'The Influence of Sugar on Love.' This theme if taken seriously would really be a matter for a committee, and the committee could work on it for a very long time. I will shoot at a title today. It is 'The Viruses and Us': not what we do with the viruses but what they have done to ourselves."¹⁷

Long after attaining emeritus status, Dr. Rous wrote three creative and witty essays, which surely are related more to vibrant life than to lifeless science.

In "The Disagreement Amongst Doctors,"¹⁸ which he read before an audience of physicians in a city some distance from his home, Dr. Rous deftly uncovered an abiding shortcoming of his profession — reliance upon rationalized "systems" instead of soundly acquired knowledge in treating diseases. In the past, this shortcoming was manifest in many practitioners, not a few of them eminent — Benjamin Rush for example; it often gave rise to strong disagreements. Dr. Rous recognized that the disagreements will doubtless continue until we learn everything there is to know about all of man's diseases

¹⁶ *Nature (London)*, 1959. 183:1357-1361.

¹⁷ *Perspectives in Virology* (Morris Pollard, editor). 1956. Harper and Row, New York, pp. 305-308.

¹⁸ *On Cancer and Hormones: Essays in Experimental Biology*, 1962. The University of Chicago Press, pp. 49-56.

(factitious systems will then, of course, have no place in the sun). But Dr. Rous wished everyone to know meanwhile that good often comes from such disagreements — the displacement of dogma by fact.

In "Henry James and the Mouse,"¹⁹ Dr. Rous tells us, in slightly less than two printed pages, much about The Rockefeller Institute of yore; about Henry James and his nephew "Harry," who had become the Institute's first Business Manager; about social customs in 1911 ("conduct was conduct with no intrusive hormonal mitigations"); about cancer research; and about himself. In response to a question from Henry James, he tells also about a devoted mother-mouse who, having dutifully raised two experimental foster-broods in rapid succession, killed her third such brood overnight at just the time when, "judging from how [the young mice looked] — bright-eyed and joyously frisking about in their world of wooden walls and shavings — [life obviously seemed to them] utterly good." Dr. Rous explains the mother-mouse's behavior: "It was an act of self-preservation; the urge to live had overcome maternal feeling. . . ."

The third of these delightful essays bears the title "The Lamentable Decline in Self-Satisfaction."²⁰ It was read before a group of his friends in New York, mostly nonscientists. Here Dr. Rous abundantly documents his assertion that "To be self-satisfied in the world of today is possible [only] to certain gifted personalities. . . . This is lamentable since self-satisfaction is an economical [and harmless] way of pursuing happiness and catching up with it." The good doctor then prescribes: "Man needs to recover somehow a measure of self-satisfaction. This he must have if he is to put forth his finest efforts; he must think better of himself and of his capacities if he is to attempt transcending deeds. . . . At the very first chance we should turn

¹⁹ *Perspectives in Biology and Medicine*, Vol. 7, No. 4, 1964. The University of Chicago Press, pp. 433-434.

²⁰ *Perspectives in Virology and Medicine*, Vol. 9, No. 4, 1966. The University of Chicago Press, pp. 439-449.

our gaze from what we unhappily are and must remain, to what we have done or fashioned that is good. . . . Instinctively as part of our will to live [we often long to say cheerfully]: *To Hell with it!* . . . But our greater need is to warm ourselves at the fire of our own being and [to] hear our secret clock tell us softly, over and over, 'All's well, well done!' 'All's well, well done!' "

In 1946, with the deepest of feelings, Dr. Rous wrote three characterizations of Dr. Flexner, who had opened wide for him as a young man the doors to discovery, and had thereafter remained his friend: — of Simon Flexner forged by his times and by superb family influences into practical man and pathologist; who, as imaginative, far-seeing, and self-sacrificing Director of The Rockefeller Institute for Medical Research during its lengthy formative period, made strong and enduring personal associations having great value for medicine;²¹ — of Dr. Flexner as spokesman and pioneer for medical discovery in America;²² — and of Dr. Flexner in perspective as man, pathologist, renowned medical scientist, and medical statesman.²³ Needless to say, these writings, as also his biographical sketches of Opie and Landsteiner, disclose much about Dr. Rous.

He wrote with deep feeling too about this University, which he loved. His humanism shines through in his "Hail to the greatly fortunate,"²⁴ in which he refers to the devotion and enduring loyalty which the University inspires in those who are privileged to work in it, and to ". . . the introduction into our working lives of music, poetry, and philosophy, superb architecture, assembly rooms adorned with modern art, all existing amidst exquisite gardens . . .

²¹ *Simon Flexner, 1863-1946*. 1946. Memorial Meeting. The Rockefeller Institute for Medical Research, pp. 13-21.

²² Simon Flexner and medical discovery. 1948. *Science (Washington)*. 107:611-613.

²³ Simon Flexner, 1863-1946. 1946. *Obituary Notices of Fellows of The Royal Society*. 6:409-445.

²⁴ *The Rockefeller University Review*, 1967. 5:16-19.

[this boding] well for the future since the word *scientia* in its original use included all knowledge.²⁵ Humanism will have its way in the end. For are we not of man- and woman-kind?"

In sum, Peyton Rous found much in life that seemed to him worth striving for — family, friends, fun, humanism, health, work; nature, medicine, science, discovery, intellectuality. Not least of these good things was the noble institution that enabled him to do with all his might the things he did, head high and free; his escutcheon might well have shared its motto, "Pro Bono Humani Generis."

²⁵ The deeper meanings and relationships of science, as touched upon here by Dr. Rous, have long been of interest to reflective humanists — see for example numerous writings of Thomas Jefferson; Brailsford Robertson's telling sentence ("Science is the first and greatest of the humanities," *The Spirit of Research*, Adelaide, 1926); and Michael Woodruff's eloquent statement in a recent issue of *The Lancet* (Jan. 24, 1970, p. 186).

his business was finding out

AN INCREDIBLE cascade of notable discoveries flowed for 60 years from the laboratory of Peyton Rous at The Rockefeller Institute for Medical Research (now The Rockefeller University). This astonishing productivity was forged at the laboratory bench by his head and heart and hand. He was a complex man, endowed with a felicitous facet of great simplicity that enabled him to communicate with Nature. Dr. Rous had an unusual singleness of purpose; nothing could deflect him from his goal. He was highly creative and his concepts were crystal clear. In the history of science, Dr. Rous will stand in the front rank with the greatest biologists of the ages. With Bernard and Pasteur he founded the vast and important field of experimental medicine. The French savants contributed to the new discipline, respectively, physiology and chemistry; Dr. Rous added pathology to these. He was a genius and a genial one.

During the six decades from 1910 to 1970, the Institute was the heart of a Periclean creation built by the talented faculty brought together by Simon Flexner. It was the first house established expressly for the work of a scientific elite in America. The creative ferment was stormy. Early among the cohorts were Oswald Avery, Karl Landsteiner, Max Bergmann, James Murphy, P. A. Levene. Dr. Rous was in the center of the intellectual maelstrom that the young investigators were establishing. He loved the Institute, for it was a good place for gifted experimentalists to work and reflect. His contributions to it and to science were fabulous. Unto him much had been given and of him much was required and nobody was disappointed — he returned an overabundance of value. He set standards of excellence in life and in work, and he did both supremely well.

Doubtless, because of Dr. Rous and his confrères, Family Rockefeller derived satisfaction concerning the worthwhileness of their medical project at the Institute.

Dr. Rous found out much which was at variance with all previous experience. He disdained to call his work discovery, because this sounded puffed up; his business was "finding out."

The pearls of Dr. Rous were always big and lustrous:

The first agent to cause cancer;

A virus (Rous sarcoma, RSV) that evoked solid tumors of animals, thereby creating the vast field of the cancer viruses;

The first blood bank (with J. W. Turner and O. H. Robertson);

Rous-McMaster biliary fistula, which determined the function of the gall bladder in digestion;

Isolation and characterization of reticulo-endothelial cells;

Outlying acidosis;¹

Factors that urge on malignancy of animal cells.

In Dr. Rous's laboratory, J. G. Kidd, one of the disciples, found that normal guinea pig plasma can cure a malignant tumor of mouse.

Many more wonderful things did he come upon.

Peyton Rous lived in a small world of his own, comprising his family, a few choice friends, a small band of students. His unquenchably happy interest in every aspect of living made him a vital person. The Rous circle was surrounded by a wall which was impenetrable but necessary. Isolation was painful to him, for he was fundamentally gregarious and had a great zest for life and people, but he knew

¹ Outlying acidosis is a term introduced by Dr. Rous for localized acidosis in tissues, independent of the pH of the blood. Rous, P., and D. R. Drury, 1925. *J. Amer. Med. Ass.*, 85:33-35.

HIS BUSINESS WAS FINDING OUT is by Charles Huggins, William B. Ogden Distinguished Service Professor of the University of Chicago. He shared the Nobel Prize in Physiology and Medicine with Dr. Rous in 1966.

that a cloister is prerequisite for high creativity. Admission to the inner circle was attained by aspirants to the badge of excellence. The Rous Virtue rubbed off on the fortunate ones and there resulted an adornment of character. A junior and well-loved member of the Arbeitskreis puts it: "We had a good time."

Peyton Rous possessed the wonderful mystique needed for continuing discoveries. He was born with this rare and awesome talent and he cultivated it assiduously lifelong. Fortunately, he made a great discovery while young; RSV was found out in 1910 when he was 31.

Peyton Rous regarded himself as a naturalist. He was an autodidact because creativity can be demonstrated but not taught. He was a perennial child of Nature. He grew flowers and learned much about them. He loved his cottage in the country with his garden and a softly flowing river, the wildlife, and the drowsy hum of insects on a hot summer day.

Peyton Rous was a master of the graceful and difficult art of belles-lettres, which is fast becoming forgotten. It's a delight to re-read his numerous offhand letters, received and treasured during three decades. They are wonderful — but there is nothing surprising about that, since Dr. Rous was a perfectionist. Let us feast on excerpts from some of the gems — part letter, part song.

You ask how people have behaved when they made a great discovery. I'll make a try. Isn't it wholly a matter of temperament? Archimedes, running down the street shouting, "Eureka," after he'd discovered how to measure specific gravity; and Ronald Ross writing a poem that's still quotable on the magnitude of his find, the malaria parasite. I can't recall whether Pasteur ever gave any sign of elation. Perhaps he was too intent, an earnest man. (1965)

All goes well here in Cornwall Township except that its greenery is becoming sere as a result of hellishly persistent drought. (1965)

You speak of A. as ensnared. My guess is he's on his way, perhaps only half aware, to becoming a university president or other big shot in

122 EAST EIGHTY-SECOND STREET

N.Y., N.Y. 10028

Feb. 7, 1965

Dear Charlie,

How incidents do alter cases! Last week an engraving of Benjamin Franklin fell from my wall and its frame was broken at a corner. When mending it I found a memo. at the back telling that we'd found it in France at Mayenne in 1926. He was 72 when the engraving was made, and at his best. He looked out reprovingly upon me, so here I am writing you. He'd never have put it off!

There's been a large reason ^{not} why I've been trying for weeks to bring order into the tumultuous facts about the tumor viruses, with the aim of a comprehending paper. What a task! It wedges me in the middle of the night and I think of little else. Actually it's an exciting adventure in discovery by thought.

Almost as exciting as to read what "humanus" has just done. (Please send me reprints of all your recent papers but some slip by.)

Yours and Margaret

Rayton Howe

"an engraving of Benjamin Franklin fell from my wall"



Duplessis Pinel Paris 1778.

Tiré du Cabinet de M. Le Roy de Chaulmont &c.

Chouillet d'après.

"He looked out reprovingly upon me"

administration. When a doer in science is no longer eager to do it again, he has had his scientific climacteric, with the padded red leather chair not far in the offing. But he'll make a good president for he's warmly human as well as shrewd.

B. of the thunderous brow is like Lucifer to me — fallen and fated to fall again in his relations to men, yet with the grandeur that cannot be marred of the true discoverer. Come this way soon. (1952)

And here's a quotation in exchange for yours, though it will have no pertinence to you now; it's from Samuel Johnson to Boswell: "If a man does not make new acquaintance as he advances though life he will find himself alone. A man, Sir, should keep his friendships in constant repair." This wasn't shrewdness on Johnson's part. It came natural to him. (1962)

Yesterday, hearing that Dick was indeed back in his lab, I went in at once to see him. Yes, there he was syringe in hand injecting a mouse held by his secretary, Ginger Rogers, while his black technician stood by. On withdrawing the needle he waved the syringe at me joyfully while Ginger Rogers picked up another mouse. He was in a state of exhilarated happiness. Almost as happy, I went away. (1965)

This comes to you from a delicious little town, bright with flowers at their spring best, on the northern side of the Thousand Islands. I'm here for a reason that may seem to you whimsical. After the meeting in Toronto that ended Saturday I couldn't bear to fly back to New York and then fly again next Saturday to St. Lawrence University on the other side of the River where I'm booked for their commencement. What a chance to jump over the fence and be completely out for a week. So with Marion's high approval I've done it, wandering along and finding in Gananoque a first-rate hotel with a still better cook and as yet no summer visitors. I stroll and admire tulips two feet high, poised like long-necked pretty girls, and watch what happens on the River and read novels and get amusement from thinking, or more truly from the thoughts that come of themselves. It's a dreamy life without any dreams other than itself. I'm like a bee asleep in a corolla. . . . Too long a letter, that bee seems to have waked up. (1962)

We came to know Sterling Childs quite well for he had us as house

guests several times. He delighted in all the small happenings of outdoor life with never a word on cancer and the Fund. He was in act unassuming and kind. (1962)

How incidents do alter cases! Last week an engraving of Benjamin Franklin fell from my wall and its frame was broken at a corner. When mending it I found a memo at the back telling that we'd found it in France at Mayenne in 1926. He was 72 when the engraving was made, and at his best. He looked out reprovingly upon me, so here I am writing you. He'd never have put it off. There's been a large reason why not. I've been trying for weeks to bring order into the tumultuous facts about the tumor viruses with the aim of a comprehending paper. It nudges me in the middle of the night and I think of little else. Actually it's an exciting adventure in discovery by thought. Almost as exciting as to read what X has just done. (1965)

New virus deeds incessantly reported keep me as watchful as a shooter standing at a butt in England while beaters are making the pheasants fly over. There's an urgency to my task which is exhilarating. (1965)

Ever since the London Congress I've been getting together a blast entitled "Surmise and Fact on the Nature of Cancer." Needless to say it deals with the somatic mutation hypothesis; viruses are mentioned only when they corrode this. It's taken a lot of delving, and even more thought, but the hardest part was to write it in such a way as to undeceive without enraging. N.B. I'll not mind a bit if some people get enraged. (1959)

But the present strange attitude of scientists with regard to the viruses (enthusiasm \rightleftharpoons denunciation) makes it worth the try. (1959)

Marion was eighteen and I thirty-five when we became engaged and, shortly after, we spent a weekend with Sinclair Lewis and Gracie, his first wife. "Red" was then doing advertising for a publishing house, and still in his rawboned youth. He was outspoken in telling us that our marriage could not last, so great was the difference in our age. It will have lasted half a century next June. (1964)

More than 50 years ago Marion Eckford deKay and I were married. She was the daughter of a scholarly commentator on the arts. We

brought to each other different likings that have delightfully widened the enjoyment of our lives together. (1965)

Here I must stop. Not even the first page of my stated lecture has been written. Grindstone! Here is my nose. (1966)

A thousand Swedish medical students held a formal dinner in Stockholm in honor of Dr. Rous. The evening was punctuated with many drinking songs. Through a mist of tears one remembers Peyton (age 87) very late in the evening standing on his chair with glass in hand singing *skoal* with the young students.

Peyton Rous died of cancer on 16 February, 1970, after a brief illness.

This is

OCCASIONAL PAPER SIXTEEN

of which fifteen hundred copies

have been set in Garamond type and printed by

The Rockefeller University Press

in April 1971 for the family and friends of

PEYTON ROUS

