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Reminiscences: My Forty-Year Romance with Malaria

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REMINISCENCES:

MY FORTY-YEAR ROMANCE WITH MALARIA

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Prologue

Looking back some 55 years since beginning my graduate studies, I have come to appreciate my good fortune: (1) to have inaugurated and carried out, over a period of some 35 years, a three-pronged research program (birds, simians, and man) against the world's most important infectious disease—malaria—and during two-thirds of that time, carrying worrisome administrative responsibilities; (2) to have participated in national and international efforts towards alleviation and control of that disease; (3) to have had a remarkable group of professional and subprofessional people who shared all kinds of problems; (4) to have received full support of my scientific efforts from the Directors of the National Institutes of Health, and last, but not least; (5) to have a wife who accepted my sometimes extended peregrinations, here and abroad, necessitated by my commitment to the problem of malaria. A reporter might ask, "How did a native Nebraskan, brought up with winter's snow and hot dry summers choose a tropical disease career?"

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After receiving the B.A. degree from the Grand Island Baptist College, an M.A. from the University of Nebraska, and a teaching interlude, I contacted Dr. E. R. Becker of Iowa State University about studying with him for the Ph.D. He invited me to visit him and during our conversation he asked me if I had a problem in mind or if he should select one. I wanted to work on blood protozoa and suggested studying the relapse phenomenon in *Haemoproteus columbae,* sometimes referred to as pigeon malaria. He approved the problem, and I won the degree.

Armed with this new parchment, I learned of an opening in the biology department at Nebraska Wesleyan University. After a conference with Dr. Claude Shirk, chairman of the department, I was offered the position and went there as an associate professor. My teaching duties were less than arduous; research was encouraged. In that atmosphere I expected to continue for an extended period. However, the depression which struck the midwest in 1932 soon saw the university in financial straits augmented by the failure of the Peters Trust Company in Omaha, where most of the university's endowment funds were on deposit. Our salaries were reduced by one half and for a period of five months we received no money.

Luckily, a position opened at the Peru State Teachers College for which I applied and was hired. The college was established to train teachers for the Nebraska schools—hardly an atmosphere for a research-minded associate professor of biology. As it turned out, there were compensations.

My studies involving *H. columbae* had whetted my interest in true malaria. At that time there was a broad interest in avian malarias but in-depth studies were limited to infections in the canary, which carried only a small amount of blood. This could be overcome with a malaria in a larger bird. Peru was located in a major flyway, and non-migratory birds were all about. One of them might be carrying a true malaria that would grow well in a larger bird attuned to laboratory conditions—a chicken or the common pigeon. I decided to study the bird parasites of that bird population with one object only: to find that parasite!

During the next four years I described and named some 15 new species of protozoan blood parasites, but the prize was missing—no true malaria. Owls, crows, magpies, and other

birds, carrying protozoan blood parasites, were kept caged in the laboratory and, as a sideline, so to speak, their infections were treated using the then available antimalarial drugs. These initial studies in chemotherapy were reported in several short papers, but I attached no particular significance to them. As it turned out, those preliminary studies pointed the way for my subsequent career.

Among the male members of the Peru faculty I was an oddity. I didn't play golf, I didn't hunt, and I didn't follow the fate of the athletic teams. All I did was teach, roam the woods, and work in the laboratory. According to my lights, the elusive malaria parasite would not be found on the golf course.

Mourning doves nested on the campus and each summer no malaria parasites were found in their blood. In 1937, however, a nestling was found with a true malaria. It was identified as *Plasmodium relictum.* With that "find" the paramount question was: would it grow in the chicken, other doves, or in the pigeon? Before those questions could be answered, the same species was found in a young pigeon taken from a nest under the wheel-house of the college observatory. Were they the same parasite? They were, as determined by cross infection experiments. In the pigeon the parasite produced a fulminating infection, even death. I had found the long-sought malaria parasite!

I reported finding this "new" parasite at the fall meeting of the American Society of Parasitologists, was congratulated on my good fortune, and had numerous requests to share the parasite with other investigators. I was not anxious to do so until I had time to study it myself. This reluctance was understood by other investigators.

In early 1938, I received a letter from Dr. L. L. Williams, in charge of malaria research for the U.S. Public Health Service, asking me if I would share my new parasite for extended studies by the Public Health Service. It took me less than five seconds to make up my mind about that. In my reply, I told Dr. Williams that I had spent almost five years in search of that parasite and if the Public Health Service wanted it they could have it but they would have to take me too. If the ploy worked I would be in full-time research.

After a series of negotiations and an interview in Washington, D.C., I was offered an appointment to the research staff of the Williams Malaria Research Laboratory located at the South Carolina State Hospital in Columbia. The malaria-infected pigeons and the Coatney family, which now included our four-year-old daughter, moved to Columbia.

When I reported for work there I met Dr. Martin Young who, I learned later, had called Dr. Williams's attention to the new pigeon malaria. Martin was engaged in studies dealing with the biology and mosquito transmission of human malarias, especially vivax and malariae, used by the medical staff for treating central nervous system syphilis (lues nervosa). My pigeon malaria studies moved ahead, but I lost no time in joining Martin in cooperative studies dealing with the human malarias.

Early in 1938 the Surgeon General of the Public Health Service (PHS) saw that war was imminent. If it came, American soldiers would have to fight in highly malarious areas of the world, and quinine was the only drug then available for its treatment. In order to try and improve that situation, he initiated a program at the National Institutes of Health (NIH), under the direction of Dr. Lyndon Small, for the synthesis of potential antimalarial compounds. These new compounds would have to be tested initially against malarias in lower animals. That part of the program called for someone with drug-testing experience. A survey of the PHS personnel found only one person with such experience—myself. As a result, I was transferred to the NIH to set up such a program. That move brought the family, which now included our two-year-old son, into the Washington, D.C., area which was our home for the next 25 years.

The Department of Agriculture, for obvious reasons, had barred the importation of *Plasmodium gallinaceum,* a malaria parasite of chickens, but now, with war on the horizon, they relented. As a consequence, I chose to use day-old chicks and the gallinaceum parasite in evaluating new potential drugs. The chemists had several compounds ready for testing, but my procedure for their evaluation failed to satisfy a certain medical officer, who had control of the program. I am sure he was qualified as a physician but, in my opinion, he was not a qualified experimental scientist. I refused to modify the program and notified the director that I was ready to go back to South Carolina. The impasse was settled by my being given sole responsibility for the testing program.

Under an increased staff, a goodly number of compounds were tested, none of which showed promise, until we tested NIH 204, a phenanthrene amino alcohol. It was vastly superior to quinine against *P. gallinaceum* in the chicks, but would it work in man? The answer might be found at the St. Elizabeth's Hospital in Washington, D.C. The physicians there used vivax malaria in treating luetics. When their patient had experienced the required treatment, the disease was terminated with quinine. Why not test the effectiveness of our new drugs, like NIH 204, in terminating those infections? If the trial drug reduced or terminated the infection, we would have a lead, or a new drug, for further tests. I could see no difficulty in PHS physicians working with physicians at St. Elizabeth's Hospital. The problem was that my staff did not include a physician. Where was I to get one with a flair for research to evaluate NIH 204 or other test drugs? I appealed to Dr. Henry Sebrell,

my institute chief, for help. A few days later he told me about a young M.D. who wanted to join the PHS but was then working for a master's degree in bacteriology at Johns Hopkins University. I went over his *Curriculum Vitae* and immediately asked that he be assigned to me at the NIH. Dr. Clark Cooper joined my staff on 13 December 1941, six days after Pearl Harbor. We worked as a team for the next eight years.

Arrangements were made quickly with the St. Elizabeth's staff, and Cooper took over the testing of NIH 204. It proved to be an excellent drug, but certain side effects prevented its general use. He then tested a whole series of compounds of similar structure, but each of them exhibited the same limitations. It was obvious that we would have to move in a different chemical direction.

A National Malaria Program had been organized by the Committee on Medical Research under the Office of Scientific Research and Development and its activities, on a nationwide basis, had progressed to where test compounds were coming to us from other laboratories. The testing of those compounds, as well as our own, soon exhausted the supply of available mental hospital patients. With that avenue cut off, another source of human test subjects had to be found.

Cooper and I were discussing this sorry state of affairs in my office one afternoon when we were joined by Dr. David Ruhe who had recently joined our staff. Dave listened to the discussion for a time and then said, "Chief, have you ever thought of using prisoner volunteers?" I was struck by the idea and decided to investigate the possibility at once.

The PHS supplies physicians for the Federal Prison Service and Dr. Marion King was the Medical Director. My course of action was—go to your friends first. I went to see Dr. King the very next morning and explained the situation to him. There was a war on and a pressing need for new and better drugs for the treatment of malaria. Could it be arranged so that potentially effective drugs could be tested in prisoner volunteers? Dr. King knew and approved of our work but made it clear that using malaria for treating lues in mental patients was an acceptable practice; employing prison volunteers for testing new drugs was quite another matter. I fully appreciated his position. He was being asked to approve a program contrary to accepted medical practice. After a time he agreed to endorse the program but made it clear that final approval rested with the director, James V. Bennett. Fortunately, the director's daughter was one of my technicians, and I hoped that might contribute to a favorable decision. When we saw Mr. Bennet I laid the problem before him stressing the fact that after Pearl Harbor the Japanese had cut off our quinine supply, our stockpile was low, and the United States needed effective new drugs for the treatment of malaria. He listened carefully and after some time he turned to Dr. King and said, "Marion, what do you think of the idea?" His reply was that "If Dr. Coatney is to be in charge, I'm for it." Mr. Bennett then wanted to consider the best place for the project. I suggested the prison in Atlanta, Georgia, because it was close to Milledgeville, Georgia, and to Columbia, South Carolina, where Drs. Geoffrey Jeffery and Martin Young of the PHS could easily supply infected mosquitoes for the project. Also, Atlanta was easy for me to get to from Washington, and the prison population should supply ample volunteers. Mr. Bennett was quick to point out that Atlanta was hardly a minimum security prison. He finally agreed that Atlanta was the best place under the circumstances and to make our work easier he called Mr. Sanford, the warden at Atlanta Prison, and told him that he had approved a project which Dr. King and I would present to him in a day or two.

Dr. King and I went to Atlanta and found Mr. Sanford far from pleased with the proposed drug-testing project. He had a contract for making mattresses for the army and mail bags for the post office which yielded Prison Industries about $2 million per year. In his light, he had reason to see us gone. I pointed out to the warden that there was a war on and that $2 million was a mere pittance in terms of the war effort and the crying need for better antimalarial drugs. He finally agreed and invited me to return in a few days to present the project to the inmate population. When I next visited Atlanta, I took Dr. Ruhe with me. The warden brought the men together in the Great Hall of the prison with its catwalk near the ceiling and guards with rifles. It goes without saying that I was not exactly calm and collected under those conditions. The warden gave a short talk and then turned the meeting over to me. I explained the need for new antimalarial drugs for the armed forces and the need for volunteers in assessing the effectiveness of the new drugs.

I made it doubly clear that participants would have to be of military age; in excellent physical condition; be willing to accept infection with malaria, either by mosquito bite or by blood in inoculation; and to accept medication and routine tests as required. Each volunteer would have to agree to stay with the project for a period of six months. At the end of that period he would receive an honorarium of $50 (later raised to $250) and six months would be taken off his sentence. In addition, he would receive an attractive certificate signed by the Surgeon General of the PHS and other dignitaries certifying as to his participation in a research study with broad significance to mankind. I was careful to point out that many of them would be sick and some so sick that they would wish they had never heard of us and the drug-testing program. I went on to say that there was little likelihood of a fatal outcome and that our physicians would take care of all their medical problems.

With that coverage of the program, I invited those who

might like to take part in the program to meet me at the foot of the steps. I stepped down onto the floor and the men came forward like a wave. One fellow said to me, "Doc, did you say that all our medical problems would be handled by your doctors?" I replied that that was exactly what I had said and the man on his left, Dr. Ruhe, would do exactly that. The questioner turned to those behind him and said, "Boys, let's go." They were with us! I am proud to say that was the only time we asked for volunteers. Over the years the project spoke for itself in enlisting more than one thousand volunteers from that institution.

With the support of the warden and the inmates, the way was cleared for remodeling the hospital to accommodate us and for enlisting a complete staff. It was not until St. Patrick's Day 1944 that the first 15 volunteers were infected with vivax malaria following the bites of infected mosquitoes. It was my privilege to take part in applying infected mosquitoes on that historic occasion. I say "historic" because not only was this the only country in the world where prisoner participation in such a study was permitted, encouraged, and sanctioned by law, but what makes it stand out even more is that it was only the second time in the history of the United States that prisoner volunteers took part in solving an important medical problem.

Let us turn back for a moment to the first of these volunteer studies. Alex St. Martin was shot in the left breast and stomach in 1823. Dr. William Beaumont, serving in the Michigan Territory, dressed the wound which, due to adhesions, failed to heal properly, allowing access to the stomach. Alex was unable to work and became Beaumont's body servant. With Alex's permission, Dr. Beaumont began the earliest extended studies of the physiology of digestion in 1825. The idea of participation in medical problems then lay fallow until 1915, a span of 90 years, when Dr. Joseph Goldberger, a PHS medical officer working in Mississippi, employed 11 prisoner volunteers in solving the cause of pellagra, at that time the scourge of the south. The volunteers who participated in that important study were promptly released from prison, but their contribution was forgotten. The governor was berated by the public and the Mississippi medical profession for allowing their participation. Goldberger went on to receive many honors, but his landmark was pellagra. Again, the idea of prisoner volunteer participation in solving a medical problem lay fallow, this time for 29 years, to be broken on 17 March 1944 as mentioned earlier.

We have not forgotten the outstanding results, to be delineated later, of the volunteer studies begun in 1944, but we seem to have forgotten that it was prisoner volunteers who made the results possible. At this writing, prisoners in the United States are not permitted to participate in studies aimed at solving medical problems, suits in our courts to the contrary notwithstanding. But now back to the main theme.

The effectiveness of test compounds was measured in terms of their quinine equivalent against St. Elizabeth's vivax malaria. As a consequence our initial work included intensive studies of the biology of the parasite and the effectiveness of quinine against it. With that basic information, evaluation of several groups of drugs, including a series of 4-aminoquinolines, got underway. Among that assemblage was SN-7618, now known as chloroquine, which proved to be an outstanding drug. It gave complete suppression of the disease, when taken once weekly, and was highly effective as a therapeutic agent. Unfortunately, it did not cure the underlying tissue infection. Chloroquine rapidly became the drug of choice the world over and still holds that position at this writing.

By 1946, we had exhausted the supply of suitable patients at the Atlanta prison which made it necessary to move the project to the Federal Correctional Institution in Seagoville, Texas. At that facility studies were carried on to determine the effectiveness of pamaquine, isopentaquine, chlorguanide, and several antibiotics.

In view of the favorable activity of chlorguanide, it seemed essential that we undertake assessment of chloloroquine and chlorguanide in the field. To implement that activity, a field unit from the Seagoville staff was set up in Guatemala in early 1948. This study was made possible through a cooperative arrangement with that government, the PHS, and the Pan American Sanitary Bureau. All went well until the unsettled conditions in that country made it necessary to terminate the work. However, the results demonstrated clearly that each of the drugs reduced the incidence of malaria significantly; the greatest reduction occurred in areas under chloroquine suppression.

In 1949, those in "high places" decided that with the war over and an excellent drug in hand, malaria was of minor importance. As a consequence, it was suggested that I might turn my energies to a more important problem—the common cold. I was not interested in the common cold and said so, knowing full well that as a commissioned officer I could be ordered to study it—I wasn't.

The Seagoville installation was closed, and I decided to take a vacation. I had not had one since the war started except for six weeks in the hospital nursing a bleeding ulcer in 1946, if one can call that a vacation. We bought a new car, and the Coatney family took off for the West Coast on a two-month trip, hopefully without a telephone. All went well until while in Yellowstone Park, waiting for Old Faithful to erupt, the car radio was turned on and I learned that President Truman had sent troops into South Korea.

It was plain that our vacation was about over because I could see that Commander Coatney would soon be back in

prisoner volunteer malaria studies again. The life pattern of Korean vivax malaria was well known to me, which made it obvious that many surgical cases flown to Walter Reed Hospital in Washington, D.C., would experience attacks of malaria about Christmas time. While those patients were in Korea they were on weekly doses of chloroquine, but when taken out of the area the drug would be withdrawn allowing the disease to express itself. What was needed was a curative drug. We had quit too soon!

There had been a few trials of primaquine, a new 8-aminoquinoline, by Dr. Alf Alving at the Statesville prison in Illinois which showed it to be four times as active and one-fourth as toxic as pamaquine. There would have to be a more exhaustive evaluation of that drug before it could be recommended to the armed services. In other words, the Atlanta operation would have to be reactivated, which involved hospital space, a source of infected mosquitoes, and a new staff. I could handle all but one part of that setup, namely finding a capable physician with a research bent and willing to work behind bars. It would be unfair to ask Dr. Cooper to come back for he was then Chief of Medicine at the U.S. Public Health Hospital in San Francisco. However, in desperation I called him, mentioning that we were again at war and that I needed him. He came and stayed five months until Dr. Al Myatt was ready to take over. The primaquine studies in our volunteers showed that when employed at a dosage of 15 mg daily for 10 to 15 days, a regimen recommended by Dr. Leon Schmidt, it cured vivax infections. This was important information but, in the absence of extensive toxicological data, it was deemed necessary to study the tolerability of the drug in soldiers rotated home from Korea.

That study was carried out in 1951 involving a thousand army personnel at Fort Benning, Georgia, and at Fort Knox, Kentucky, under my supervision and Dr. Alving, respectively. Those tests demonstrated the overall safety of administering a single 15-mg dose of primaquine daily for 14 days to military personnel on full duty. Following that demonstration an order was issued stating that all soldiers returning from Korea by ship would be given 15 mg of primaquine daily for 14 days. That was done beginning in December 1951. The navy, on the other hand, had a shipload of marines ready to return to the States. The order said "soldiers" and these were marines, so on that basis they were not given primaquine. That decision was unfortunate in one respect and extremely fortunate in another.

We had estimated that the malaria seed-rate in all returnees from Korea would be about 20%. Among the returned soldiers, about 280,000, the relapse rate following primaquine treatment was close to nil. However, in the marines, most of whom went to Camp LeJuen, more than 19% came down with malaria. The navy was embarrassed, but we were elated because the navy had unwittingly performed the crucial experiment to prove that primaquine would cure infections of vivax malaria.

We next turned our attention to a new type of antimalarial drug, produced by the Wellcome Laboratories in New York, known as pyrimethamine. Therapeutic studies in lower animals and the prisoner volunteers showed that it had the highest activity against blood forms of the parasite of any known antimalarial. One of the technicians in our NIH testing laboratory told me, with a twinkle in her eyes, that she was afraid to open a bottle of the drug in the laboratory for fear it would cure every infection in the room. However, resistance to pyrimethamine developed quickly against the blood infection in avian, simian, and human malaria; more disturbing was the fact that the resistance factor was transmitted unchanged through the mosquito. Subsequent studies showed deleterious changes in the bone marrow and kidneys of man. It was an excellent drug whose disadvantages outweighed its usefulness.

As a consultant to the Parke Davis Company, I made frequent trips to their home plant and always made it a point to needle the chemists about their failure in developing a highly effective injectable drug that would give protection over an extended period. They seemed to shrug off that suggestion, but in the end they developed an effective drug known as Camolar. A single injection gave protection against a sporozoite-induced malaria in volunteers for upwards of one year. Such results were unheard of in the management of malarial infections. On the basis of such extraordinary results, it was decided to test the drug in the field. At the invitation of the Government of Pakistan, Dr. Peter Contacos and I went there only to meet up with the problem of resistance to chlorguanide, the parent form of the drug. That coupled with the disadvantage of distress at the site of injection caused us to terminate the trials. Another case where many are called but few are chosen.

I know at some time during this essay, time should be given for a more complete account of the volunteers and their contribution to the biology of the human malarias, to the search for new antimalarial drugs, and to their attitude toward participation. I shall do so now.

Those men considered themselves the elite of the prison population and, in a sense, they were. They had been selected first by the custodial staff and selected again by our medical staff. As volunteers they were exempt from many of the prison rules. All their illnesses, except surgery, were handled by the project physicians, and they had the only wide-screen color TV in the prison. To project their elitest view they designed their own patch with an embroidered MP (malaria project) in bright yellow on a blue denim background, which they sewed on their left sleeve above the elbow.

On our side, we instituted a series of strict routine procedures necessary for the scientific accuracy of the study and for 24-hour overall control of the project. The staff received relatively few complaints concerning these procedures, because the volunteers understood the need for them. A few objected and considered withdrawing from the study, which they had every right to do, but in so doing they would have to give up their good time, their elitest status, and withstand the scorn, or worse, of their project-mates where the maxim was: we are all in this together. Among approximately one thousand men, fewer than a handful withdrew.

Administration of test drugs was decided by lot. This was fair and necessary because it prevented any semblance of favoritism by the staff. When a man drew a number, that was it. If a test drug was not effective, the volunteer would come down with the disease: high fever, etc. If effective, he would be protected. The same procedure was used when testing drugs for therapeutic effectiveness. The men saw this as "the luck of the draw." Once while interviewing a volunteer I asked him why he wanted to join the project. He replied, "I have a brother in the army and this is the only way I can fight." We took him.

One day Dr. Cooper told me that "Jones" was having a tough time. I went to the ward to see him. He had just gone through a prolonged vomiting episode, and as I approached his bed he gave me a faint smile. I asked him how things were going. I will never forget his reply: "Doc, I wouldn't go through this again for a million dollars, but I'll go through with it this time if it kills me." I could only say, "Thank you. You're a real soldier."

On another occasion I was awarding certificates to those who had completed their six-month participation. As one man's name was called, he stepped forward a couple of steps and asked if he could say something. I agreed and he said, "Please send that certificate to my mother. I don't want to touch it. It's the only honest thing I have ever done." That mother got the certificate and a letter from me praising her son's participation.

I think I should include one more example for, to my mind, it gives the attitude of the volunteer as he saw it. The Parke Davis Company was considering setting up their own drug-testing facility in the Florida State Prison at Raiford. I was invited to go there as a consultant, and as I was walking along one of the hospital corridors an inmate, who was mopping the floor, looked up and said, "Hi, Doc. Are you going to set up a malaria project here? If you are, I want on it." My reply was, "Thanks we may need you." That man had been a volunteer in our Atlanta prison project, received his good time, and was then serving time in Florida. He was a walking advertisement for our volunteer program.

Up to 1960 I had worked mainly in two fields: (1) the blood parasites of birds, including malaria; and (2) the biology and chemotherapy of the human malarias. Then came a decided change. On 5 May I was sitting at my desk at the NIH when a call came through from Dr. Don Eyles, in charge of our Memphis laboratory, and I heard him say, "Bob, I have monkey malaria." I was incredulous. I told him not to take chloroquine until we were sure. He replied that he expected I would say that so he had taken the drug before he called. In other words, he was the one suffering the chills and fever—not I. Prior to taking the drug, he had drawn 20 cc of his own blood and injected a portion of it into an uninfected monkey. I asked him to send the remainder to the Atlanta prison for transfer to volunteers. That was done, and in a few days the recipient monkey and each of the volunteers came down with malaria. *Plasmodium cynomolgi* of monkeys would grow in man and produce disease. Malariologists, including myself, knew that monkeys harbored malaria infections, but erroneously we thought malaria in the monkey was for monkeys and malaria in man was for people. That tenet would have to be discarded. The greater question was: is monkey malaria a true zoonosis, an anthroponosis, or both?

At the time of the Eyles accidental infection by mosquito bite, three species of simian malaria were known from Malaya. The species responsible for his infection had been isolated from a monkey in northeastern Malaya. Under the circumstances it seemed worthwhile to go there to study the simian malarias. When I presented the opportunity to Eyles, he was enthusiastic and went there in August with a small staff. He had three main objectives: (1) to study malaria in the indigenous monkeys, (2) to determine their natural vectors, and (3) to investigate the possibility of the natural transmission of monkey malaria to man.

The productivity of the Eyles group was phenomenal. During less than four years they identified two dozen vectors of simian malaria and described five new species (one was named for me). When those are added to the three already known, Malaya is surely the birthplace of malaria and, I like to think, maybe the Biblical Garden of Eden. Dr. Eyles's untimely death cut short a brilliant career and eventually resulted in our closing the laboratory.

The simian malaria program at the Atlanta prison was in the charge of Dr. Peter Contacos, and as the Malayan and other species of simian malaria became available they were sent to him for possible transfer to prison volunteers. Contacos established five simian species in man and carefully described their parasitology and clinical manifestations in studies involving some 225 volunteers.

At this juncture I had spent some twenty years in charge of studies involving human and simian malarias, their biology,

and treatment. The human hosts for these studies were prison volunteers, as mentioned earlier, who willingly accepted the rigors of the disease and the uncertainty of the test drugs. Their antisocial conduct had landed these men behind bars, but they proved to have honor too. If they made a commitment, they kept it. I can certify that the PHS kept its commitment to them. I was privileged to work with these men longer than any staff member. It was an experience of a lifetime, and I cherish the opportunity.

Most of what I have dealt with here has had to do with the evaluation of new drugs in man and with the possible threat of simian malaria as a zoonosis, but I am not unmindful of the work carried on in our laboratories at the NIH, Columbia, South Carolina, and Memphis, Tennessee, in support of those studies: the initial testing of potentially effective drugs against blood- and sporozoite-induced *P. gallinaceum* infections in day-old chicks, a program that embraced more than 2,000 compounds; the intensive study of all aspects of *P. gallanaceum* infections in young chicks; Miss Helen Trembly's management of the insectary where countless thousands of mosquitoes were raised for transmission of malarias to the chicks and to humans; the basic studies on drug metabolism by Drs. Howard Bond and John Sherman; Dr. Joseph Greenberg's discovery of synergism in antimalarials; and Dr. Joe Held's technique for locating malarial exoerythrocytic bodies in the liver of infected monkeys. These highlights, plus others too numerous to mention, came about with me, in terms of the game of football, as coach and quarterback. However, let it not be forgotten that it was the members of a remarkable staff who carried the ball. My philosophy was, and is, that team research hinges on finding someone else to do what I want done because he wants to do it.

In 1960 I was named chief of the Laboratory of Parasite Chemotherapy and continued in that capacity until terminated by the law that states that commissioned officers of the PHS must retire at age 64. *Tempus vitam regit.* As a consequence, Captain Coatney became a civilian following his retirement on 31 May 1966.

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Epilogue

Prior to my retirement I had been invited to accept a position as Professor of Pharmacology at the Louisiana State University School of Medicine in New Orleans and had accepted. My teaching schedule allowed ample time for research, and upon inquiry I learned that several chimpanzees at the Delta Regional Primate Center, at nearby Covington, Louisiana, were available for studies involving malaria. The availability of these animals gave an opportunity to study *Plasmodium schwetzi,* an ape parasite, which had eluded us earlier. Through a series of fortunate circumstances two chimps were infected by the inoculation of infected blood and, in due time, through the cooperation of Dr. Contacos, then in charge of my old Atlanta project, prisoner volunteers were infected through the bites of infected mosquitoes. The malaria parasite which infected the volunteers was not like *P. schwetzi,* as expected, but like *P. ovale* which we knew quite well as a tertian malaria parasite of man. When the parasite was transferred back to an uninfected chimpanzee the resulting infection was *P. schwetzi* again. At that point I decided to let some other investigator unravel the *P. schwetzi–P. ovale* riddle. Those confusing results remind us that when we ask questions of nature the answer may be pleasant, shocking, or wrapped in an enigma.

After three enjoyable and scientifically profitable years in New Orleans, I decided to retire a second time. We moved to Atlanta, Georgia, a beautiful city with a mild climate, many old friends, and former colleagues.

During a luncheon with a group of former staff members, the question was raised about finishing the book on the primate malarias begun in 1966 and abandoned. Drs. William Collins, McWilson Warren, and Peter Contacos agreed to collaborate if I would assume overall responsibility. We all got to work and *The Primate Malarias* appeared in 1971. Our aim was to present a comprehensive treatment of all the primate malarias. If that aim was realized, and I think it was, it is an important addition to the literature of the primate malarias.

Now I am a true retiree—mowing the lawn, getting reacquainted with my malaria-related stamp collection, and enjoying an introduction to historical horology to the extent of collecting and writing about early American clocks. Retirement is wonderful if one can get used to it.