Dr. William Collins Interview

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Dr. William Collins Interview

This is Leo Slater. Today is January 11th, 2005. I'm interviewing Dr. William E. Collins at CDC in Chamblee, Georgia. This is part of my Stetten Fellowship on history of malaria research at NIAID. I just want to confirm to you Dr. Collins that we are taping our conversation today.

WC: Yes.

LS: Very good. I thought we could start with the earliest days, start with your family background, your early education. You grew up in Lansing, Michigan is that correct?

WC: Yes. I was born there in 1929. And I grew up and went to high school there. My parents both emigrated from Canada. My father was an artist, a performing artist so to speak: He sang and he was an actor. But in the Depression you worked in a factory. Nobody made any money, so he worked in a factory whenever he could get a job and he sang at funerals, he sang at weddings, he acted in local theaters and that sort of thing. My mother worked as a clerk in a garment factory. They had no money, absolutely none. My father had first come to the United States in 1926. They got married in 1928 and came to the United States. They both immigrated legally.

They became citizens, I think, in 1935. In 1939, my father was in New York studying at some theater group and in September 1939 he was called back to a war plant and my mother was in Michigan working. He never went back to the theater because all during the war he was doing factory work. He was not a big man. He was a small man so he was a supervisor rather than a machine operator. By the end of the war, he had been hurt in a factory. He was totally disabled. In 1947, I started college, but he never worked after that. My mother continued to work as a clerk in a factory. He lived quite a while but he had a disability pension and that sort of thing. My mother continued to work.

LS: Do you have brothers and sisters?

WC: No, I am a single child.

LS: Were you one of these kids who was very interested in insects from an early age?

WC: By the time I was 10 or 11 years old I was studying insects. That was my passion, collecting insects of all various sorts. What I wanted to do was collect insects. Back then it wasn't frowned upon for people to run around with a butterfly net or collect insects. Now it would be frowned upon. People don't do that sort of thing as a kid anymore.

LS: Tell me about college.

WC: I went to the local college, Michigan State in East Lansing in 1947. Now it's a university. I worked in an insurance company all through college as a clerk: I essentially worked my way through school but Michigan State was only $47 a quarter. It was dirt cheap if you were living at home. I graduated with a Bachelor of Science degree in 1951.

LS: What did you major in?

WC: Entomology and then a Masters degree in entomology the following year. Then I moved on to Rutgers in New Jersey with a fellowship. In New Brunswick, too, you could live in a boarding house, eat at a local greasy spoon, and get by there.

LS: How did you choose Rutgers as the place to do your PhD?

WC: It was a swap. The professor at Michigan State owed a graduated student to Rutgers because he had recently hired a staff member from Rutgers. You know, it's one of these: they trade off graduate students. He had hired someone, so I had no choice. I had never been out of the state of Michigan. I'd been to Ontario and Toledo, Ohio: that's the farthest I'd ever been from Michigan. To go all the way to New Jersey was to go to a foreign country, and it was quite a jolt to go to New Jersey: Boy, that was a foreign country as far as I was concerned. I met some real foreigners when I went to New Jersey.

LS: Who was your professor at Rutgers?

WC: Bailey B. Pepper was head of the department, but I worked for Phil [Philip] Granett who developed 6-12 insect repellent as his thesis project. I was into mosquitoes right away. Bailey B. Pepper was the one that I really liked. Because of the draft board pushing me, I finished a Ph.D. in two years, again in entomology, minor in plant pathology, and thought I could escape by going to work for industry. That lasted three months. I would have thought I would have rather have gone to work for a university or something like that, maybe teaching. In fact, I applied at several universities, but Diamond Alkali Chemical Co. offered me a job right out of college, and I thought, "Well, this is a good opportunity to work for Diamond Alkali as a technical advisor," and technical development was what it was: insecticide development. I had an opportunity to work with a very interesting man, Dr. [Leonard] Gordon Utter. We went to various places looking at field stations and that sort of thing. Diamond was kind of interesting: During the three months there I learned an awful lot, but it didn't last long. The draft board found me and dragged me off into the army, but fortunately because of the IBM machines working very diligently, they pulled my card out so that I was sent to the biological warfare laboratories at Fort Detrick, Maryland. When I went into the army Bailey Pepper, from Rutgers, called a friend who was at Fort Detrick and told him to try and find me and get me into Detrick. Fort Detrick turned out to be almost a post doctoral program, where I was allowed to do research on biological warfare for the U.S. army for the next two years. Once you got in the army, you made such big money you know, $77 a month. Once I got married I got $150 a month; hey, big money then.

After regular basic training, I didn't go as an officer that's for sure, I went as a private and when I got to Fort Detrick it was very interesting. It was one of those situations where every enlisted man had either a master 's degree or a Ph.D., so my barracks had 23 people and 41 college degrees. Each barracks was basically the same. It was essentially a graduate or postgraduate program and we all went to research labs each morning.

LS: You stayed on there even after your obligation to the army had been fulfilled?

WC: Well, I met my wife there. My wife was a microbiologist and we got married and it sounded like a good opportunity to stay on another year and get some money. It was good, but it was secret. For someone who wanted to do research being secret was not good: You knew your career was eventually going to go down the tube if you didn't publish and you never could publish there. Nevertheless, it was a beautiful environment. It was biomedical research -- animals, viruses, entomology and that sort of thing were involved. It really was a lot of fun, at least from the research standpoint, and it moved me away from agricultural research totally into biomedical research, pathogens. There were excellent facilities, supplies, everything else, but you knew it wasn't going anywhere.

LS: As an entomologist, then, you were previously very focused to agriculture and not medical zoology? How did that fit in at Fort Detrick?

WC: I had classical entomological training: Ninety-six semester hours of entomology as an undergraduate and graduate. I knew insects front and back so when you start working on mosquitoes when you're in research, that's great. Some people don't like mosquitoes, but I've always liked mosquitoes. So that was what I did at Fort Detrick. Let's just say I worked on mosquitoes.

LS: And after Fort Detrick?

WC: I contacted people back at Rutgers: did they have a job for me? Instantly, they had a job. When I went back to Rutgers, I went back into plant work. I was an extension entomologist and did whatever they wanted me to do. We dealt with everything from cockroaches to plant pests, gardening pests, etc.: That was the job of an extension entomologist -- to serve the public. I worked mostly with garden pests, household pests and so on. Extension entomology was a federal job, so that continued my federal employment.

LS: That was New Brunswick?

WC: New Brunswick, New Jersey, yes. It was part of the U.S. Department of Agriculture support to the university. It lasted a little over a year, and then I had this strange phone call, an absolutely strange phone call out of the blue. It happened because a job opened up at Merck. They had an opening and the department chairman at Rutgers said, "Would you be interested in going to work for Merck?" I really was not interested in going to work for Merck, but I said, "Well I'll go talk to them." In the process they sent out a telegram to one of the people [Robert Ingram] I had worked with at Fort Detrick who now was working for the Public Health Service. All of a sudden a man who I had never heard of, Dr. Martin Young of the Public Health Service, called me on the telephone and said, "Would you like to come work for the Public Health Service in Columbia, South Carolina?" It was an NIH lab. I didn't know the NIH had a lab in South

Carolina, but he said NIH and it always intrigued me: "Gee, could I go work for NIH?" That sounded pretty good to me. I said, "I might. Yeah." Well my wife was not too fond of New Brunswick, New Jersey. She said, "Look into it," and Martin Young said, "You know, if you want the job you probably could have it," on the recommendation of the man I had worked with at Fort Detrick. So we took the job sight unseen. I'd never been to South Carolina but he said, "It's NIH." And so we moved to South Carolina.

LS: Young had found you without you being in the loop?

WC: I'd never applied for the job, but Young took it on the recommendation of Robert Ingram who was working in the field station in Memphis, again an NIH field lab in Memphis.

LS: So you first worked for NIH at the Columbia field station in 1959. Did you work on things besides malaria there?

WC: I basically went there to work on viruses. When we arrived Martin Young said that the thought was that this lab was on its last legs so to speak: Malaria was on its way out. Geoffrey Jeffery was working on intestinal parasites at the time also trying to develop other things to do in the laboratory because malaria they knew was going to take a back seat. They had been told to stop training malariologists, that malaria was basically on the ropes but that there were other things to do. But they had an insectary there and they were trying to find out what the *Anopheles* mosquitoes would do with viruses. I had a lot of experience with viruses having worked at Fort Detrick. I knew a lot about mosquitoes and they wanted me to work on it. Everyone had been trying to find something else to do with these mosquitoes. They also wanted me to work on the insect tissue culture which I didn't have much experience with but I was going to give it a try. Insect cell culture was relatively new to me and relatively new to everyone at the time. We started collecting caterpillars, catalpa caterpillars. There's a plant in South Carolina from which everyone collects these catalpa caterpillars for fishing. We would collect catalpa caterpillars and try and culture the ovaries off them and see if we could raise viruses on the ovaries. It wasn't very successful. I tried. Other people were successful. I wasn't, but that soon took a back seat to the malaria work. It was fun for a while, but malaria never took a backseat to anybody – it's holding its own. I think I arrived there in April, but within a matter of several months Martin Young got in a supply of blood from Texas and it went into a patient and it turned out to be chloroquine resistant *falciparum* malaria. He couldn't believe it. No one in the laboratory could believe it. The patient didn't respond to chloroquine. That Saturday morning everyone was sweating blood because the patient was not responding and the word went out in the lab: We've got chloroquine resistant *falciparum* and we're back in business. All of a sudden it didn't matter whether I was going to work on viruses or not. We were back into malaria and I became deeply involved then in the mosquito work.

LS: Can you tell me more about day-to-day work and facilities at the South Carolina State mental hospital?

WC: With the South Carolina State Hospital, we were located in the basement of the Caucasian, or the main, hospital. It was an old, old hospital. What happened is that each morning Jimmy Skinner would drive out to the African American hospital out in the country. It was a fair trip out there,

and he would make the blood films on the patients out at that hospital. Most of the patients were out there and then there were a few patients in the main hospital where we were. The hospitals were basically the same as far as age. The main hospital was located in downtown Columbia. There was a part of the hospital was used for research on intestinal parasites. There were a lot of intestinal parasite studies going on at the time so that you were doing a lot of drug studies on intestinal parasites and the malaria was just part of it. Then also we'd do some virus work in there and the insectary was relatively small, although we had three or four different species of mosquitoes that we were raising there. It was a pretty good facility. Martin Young had his office down on one end. It was fairly regimented. At 10 o'clock you all met for a break and Martin would tell us the news of the day, so to speak, and they'd discuss what patients were going on. Then Martin would, once a week, have a meeting with the senior staff. Martin was the chief, no question about it, Martin was the chief. And you had Geoffrey Jeffery was the assistant chief, so to speak.

LS: You have mentioned Memphis already. We are talking about Columbia. Can you tell me a little something about how the field stations, the NIH field stations, were organized?

WC: As far as I understand the field station in Memphis was working on monkey malarias. The one in Columbia was working on the human malarias in the mental patients.

LS: All this was run from Washington, D.C., by G. Robert Coatney?

WC: Oh yes. Now Coatney had started his work in Columbia, then when World War II came along he moved up to Washington. Earlier, Dr. Coatney had worked in Nebraska and he had isolated a pigeon malaria and during the Depression NIH wanted the pigeon malaria. Coatney said, "You can have the pigeon malaria but you've got to hire me," because he wanted a job so desperately he said, "Give me a job and I'll bring you my pigeon malaria." So he was assigned to work in Columbia, but he was a real go-getter, a really dynamic individual. When he got to Bethesda during World War II, he was a dynamic worker and he headed the operation out of Bethesda. Martin Young did the operation in Columbia and the lab in Memphis was run by Don Eyles. Don Eyles was a tremendous biologist, a botanist as well as a parasitologist. He really was outstanding.

LS: Do you remember if Coatney would come down? I mean how did he run these stations from D.C.?

WC: On the phone and with periodic trips. He very seldom came down. He ran the prison project more than he ran the lab in Columbia.

LS: What was your relationship with the Atlanta Federal Penitentiary project when you moved to Atlanta in 1963?

WC: In 1963 we moved over because basically they had a cut back in personnel and they had to close the field labs. There was a drastic cutback in personnel so they closed the field labs in Memphis and in Columbia and they moved us here to Atlanta so that they could support the prison project.

LS: How was Columbia wound down? Was it just ended and people moved ?

WC: Yes. It was cut off. Martin Young moved to NIH and then Geoffrey Jeffery did a year at Yale, and I was the last person to close the Columbia lab. I swept the floor: I got rid of the desks, finished it all off, closed the door, locked it and moved over here to Atlanta.

LS: And the records?

WC: The records ended up in my attic and now they're in the lab here. They were never destroyed.

LS: You had mentioned to me before that sometimes Coatney would run into problems getting resources or getting things done and he had a special relationship with James Shannon. Can you tell me a little about Dr. Coatney's management style?

WC: My understanding is that Bob, who was a very dynamic individual, would not take no for an answer. My understanding is that he would fight for his personnel. He would fight for his beliefs to the point that if someone above him said no, he would keep on going higher and higher until he finally got what he wanted. And he was able to fight. He was a small man, something like a bantam rooster, and he would fight and fight until he got done what he thought needed to be done for both his personnel and for his beliefs. He was extremely successful. He was a very good friend of mine in his older years. He died here in Atlanta. He retired here to Atlanta and he lived to be a very old man, but he sometimes ruffled a lot of feathers, but I liked him a great deal. His wife will be 101 years old in February and his widow and my wife continue to talk to each other on the phone about once a month. She's retired up in Connecticut in a nursing home.

LS: Was he hands-on scientifically?

WC: In his younger years, yes, he was, but when he was a chief he acted as a chief. By gosh he demanded things and if you crossed him he would put on his uniform and those four stripes carried a lot of weight with the junior officers.

LS: In the late 1940s or early 1950s, he still had a big avian malaria project running up in the D.C. area. Was there some kind of give and take with the kinds of research he was doing there on drugs and the kind of work you did? Either in Columbia or here with the prison project as far as drug development was concerned.

WC: The drug projects that were done here in Chamblee were all in the primates and at the prisons were all in humans. There was a quantum leap between what was screened in programs like that and the avian studies. By the time you get to the human studies, or into the primates, it's totally different. By the time a drug gets to that level, it's gone through an awful lot of steps, that's something you should know. We thoroughly believed by the time we got to the primate work that we had got to a point that human studies no longer needed to be done. We could do everything in primates. We could do all the drug work in primates we no longer needed to do any studies in humans.

LS: What kind of models were you using at that point?

WC: By the early 1970s, we had gone even beyond the rhesus monkeys and into the New World monkeys. We had *falciparum* and *vivax* going into the New World monkeys and we had chloroquine resistant strains of human malaria growing in our New World monkeys. We could test drugs. At the present time we test vaccines in them, so that we had replaced any human studies. Because of the criticism by international organizations of doing any human studies, we had replaced these with monkeys. Of course, now you have PETA and these organizations saying you shouldn't use monkeys. We replaced humans with monkeys but there comes a point where computers cannot do it. Computers cannot mimic immune responses. This was really the great accomplishment of Coatney: to push ahead and strongly support using monkeys to replace humans. He also strongly supported the studies in the Far East Research Project out in Malaysia. He thought that -- by knowing more about the relationships of monkey malarias to humans and more about what parasites were mimicking human malarias -- we could find the models that could be used for drug testing. So Coatney supported Don Eyles and McWilson Warren out there in South East Asia -- looking to see if humans were being infected with monkey malarias and for monkey malarias that might infect humans. Coatney really pushed forward the frontiers of replacing humans as models for testing drugs and vaccines. He really pushed it hard and a lot of that work continues to this day.

LS: Was there any industry involvement or industry interest in any of this?

WC: Coatney worked a lot with industry. He needed the relationships with industry to get the drugs that were developed, both the U.S. and the German industries after the war. I know one of the things that he wrote about the development of chloroquine was that an American company actually knew about chloroquine but wouldn't tell the Americans about it until almost two years after the Americans developed chloroquine. Then it was made known that they knew about its properties for years, but because of confidentiality agreements between the German companies they wouldn't let it be known. They had delayed the development of the drug, which was unfortunate, but it eventually was brought out that chloroquine was such a marvelous drug.[1] All the new drugs that are being developed nowadays to replace chloroquine don't last nearly as long as chloroquine lasted. Chloroquine has lasted decades where the new drugs are lucky to last, five years, eight years, and then they begin to fail. His, and other people's, development of drugs during World War II and shortly thereafter was remarkable.

LS: Can you say anything more about the prison work?

WC: Dr. Coatney really pushed hard to convince people that these people at the prison really wanted to volunteer, that they wanted to participate in the effort. There were a number of mental hospitals involved. At the time malaria was a treatment for neurosyphilis. Without penicillin it was a treatment. Later malaria therapy became a shadowy area because as penicillin became widely used there was no need for malaria to be used. Then it became borderline ethical to use malaria for the treatment. If you don't use malaria for the treatment of neurosyphilis then you should probably not use malaria and therefore you shouldn't use drugs then to treat these patients after you give them malaria. That left a void. How are you going to test new drugs?

[1] Coatney, G. Robert, "Pitfalls in a Discovery: The Chronicle of Chloroquine," *American Journal of Tropical Medicine and Hygiene*, 12, 1963, 121-128.

Now this may be a backward way of thinking about how you're going to develop new drugs, but he thought then, well, we probably need volunteers. The volunteers in his mind were the prisoners. This borders on ethics, a great deal in ethics, but a lot of the prisoners wanted to volunteer, particularly during wartime. Therefore, he was able, in 1944, to convince the Bureau of Prisons that these people would actually want to volunteer and they did. Therefore, the Bureau of Prisons asked these people if they would volunteer and an agreement was made for them to volunteer. It was set up at the U.S. federal penitentiary here in Atlanta for them volunteer and a number of them –- actually hundreds of them volunteered to take malaria. He was very proud of them and he put it to the prisoners, and the prison system put it forward to the prisoners that it was their contribution to the war effort, and they continued that through the Korean War and so on. It actually lasted until the early 1970s. There was a great deal of criticism that the prisoners could not volunteer. That a prisoner could not or would not volunteer, but there are many indications that they did volunteer. We had public health officers spend a great deal of time trying to talk them out of volunteering, so to speak, and explain to them "you don't have to volunteer, you can stop it anytime you want," and yet they did not. These prisoners actually volunteered. We used mosquito bites rather than blood passage and they were strictly monitored, as the Public Health Service officers and medical officers were there all the time. The federal penitentiary here in Atlanta was a totally controlled environment. Here in Chamblee, which is only about 10 or 15 miles away from the prison, we had insectaries in which we could infect mosquitoes. We generally took mosquitoes down there to infect them and then brought them back here to hold them. The mosquitoes were not held at the prison. The prison would monitor the daily blood films down there or bring them back here for us to monitor. It went on, I would say, from about 1944 to about 1972.

LS: I want to move back to the neurosyphilitics in the hospital environment. You could inoculate when you wanted to and follow the disease course throughout -- that is latency, recurrence, etc. -- in a controlled environment. Can you say a little bit about the use and the value of that research including the ethical issues you just raised?

WC: The patients, of course, were in a hospital environment so that they were always under care and not allowed to go home. [The Nobel Prize was awarded for the treatment of neurosyphilis with malaria therapy.][2] It was a treatment that was not as effective as one might think. It resulted, if given fairly early in neurosyphilis, in about a third of the patients being benefited enough so that they could probably go home. In perhaps another third, it stopped progression so that if they were already damaged neurologically it didn't progress, but it didn't make them better. In another third of the patients, malaria therapy had no effect at all. That is not great therapy by good medical standards, but a third of the patients probably had a beneficial effect. A third of the patients is better than none, you might think, but the patients in whom you only arrested progression are still in the hospital. From the hospital management standpoint that's not good because they may live in that hospital then another 10 or 20 years. Neurosyphilis is a terminal disease, and untreated, the patients would eventually die. From the hospital's standpoint, they would rather they die, and that is a bad outcome from the patient's standpoint.

[2] Julius Wagner-Jauregg received the 1927 Nobel Prize in Physiology or Medicine for "his discovery of the therapeutic value of malaria inoculation in the treatment of dementia paralytica."

What happened with malaria is this. While malaria was given as a treatment it was an opportunity for the public health service -- for malariologists -- in these locations, to see what happened. We learned so much about malaria. We could have just given malaria and seen what happened to the syphilis, but to have expert malariologists stand by and see what happened to the malaria was a marvelous opportunity. Now it's, shall we say, a crass scientific thing to do, but we were getting the benefit from the malariologist standpoint, of seeing, for example, that the parasitemia goes up, but it comes down. "We're getting immunity here." We had to feed mosquitoes to transmit to the next patient. We learned so much. We found out that the mosquito infects more on every other day or that the mosquitoes infected more on the ascending phase then on the descending phase or that the mosquitoes are infected more when there are male gametocytes than female gametocytes. We learned all these little tiny pieces from looking at 10 or 20 patients. Soon patterns emerged that we could not or did not observe by going out in the field and looking at even 100 patients where we didn't have any idea when they got infected. We learned a lot out of these patients who were being treated for neurosyphilis and this was used by the great British scientist George MacDonald who worked out the mathematical models. He took these data and then developed models that now are the standards for determining what happens when people have malaria. And malaria was a hope. Syphilis is an awful disease. At the turn of the century it was estimated that 10 percent of the adult population would catch syphilis. It was a fatal disease. It was an awful thing. Sexually transmitted diseases are awful as we all know from AIDS right now. At that time syphilis was our sexually transmitted disease. It was awful. Though malaria was a hope, I am glad penicillin came along.

LS: In recent years you and Dr. Jeffery and others have published papers by essentially going back and mining the old clinical data from these neurosyphilis experiments. What gave you the idea to do that?

WC: When the development of vaccines came along, people were making -- I won't say wild statements -- but they were making some statements that didn't seem to ring a bell. Such as that people don't develop fevers until they get to a parasite count of 1,000, that sort of thing. And we'd say, "Oh no, you're wrong: People develop fever of 104 as soon as the parasites start to appear," and they'd say, "How do you know that?" So we'd go back to the data and get a few little tidbits. Jeffery and I would get a few numbers and someone said, "Can't you provide a few more numbers?" So we decided we'd provide a lot more numbers. We got a lot of numbers and put out a small separate, well actually it was big separate, piece for *The American Journal of Tropical Medicine Hygiene*.[3] Then the people in Europe said, "Can you provide us the raw numbers?" And they wanted it on a statistical database so that they could use it for *falciparum*, which we provided to them. Dr. L. Molineaux and a few others over there wanted to have it and we gave it to them. Then they said, "Can we make this available to the European community?" We said, "Of course." Then they asked, "Can you do it for *vivax*?" So we have started putting things together for the *vivax*. Someone later said, "Can you make a review *ovale* and how about *malariae*?" And so we continued to mine this thing.

[3] W. E. Collins and G. M. Jeffery, "A Retrospective Examination of Sporozoite- and Trophozoite-induced Infections with *Plasmodium falciparum*," *American Journal of Tropical Medicine Hygiene*, 61 (Supplement), 1999, 4-48.

It's not in a computer database. It's old records that date from the 1940s. It's not something you can plow, you know. They're handwritten records most of them, and I go through those records occasionally and someone will come back and say, "Do you have these data, such as how about hemoglobins?" "Oh there may be some hemoglobin data. I'll have to look." And you just go through these old yellowish daily records hunting. Often I find out that it's there. So it pays not throw anything away. We had thought that it would be valuable to keep these old records mainly because when the vaccines come along we want to predict what will happen. And the vaccines *will* come along. We want to know what to expect because people develop immunity, natural immunity, and every one of these patients that was infected developed immunity. Some of them were infected more than once during their treatment and they developed immunity. Now we think that anytime someone wants to ask a question from these data, we have an obligation to go back and look and see if we can find the answer. We go back and look. No one has offered us any money to go back and look. Jeffery is retired and our administration here at CDC questioned whether we should. So they called in a panel of ethicists. They went outside and they – our administration – called in a panel of, I think it was five, outside ethicists, fairly expensive to call. They were from various parts of the country and they sat here all day long: "Was it ethical to write up data from the 1940s and 1950s when these people had not gone through IRB?" Finally they concluded that it was a treatment at the time that was ethical and so now it was ethical to go back and write up data, write up information based on data from these treatments. As you'll notice in the prelude to the report they called in another ethicist from Canada who came to the conclusion it was ethical and then we were able to make the data available to the Europeans and everyone else.[4] Otherwise we wouldn't be able to publish on them. Now it is unethical to write on data from prisoner of war camps and that sort of thing from Germany. That's already been determined, but the ethicists in the panel that was called together by CDC came to the conclusion that it was ethical to write on these patient treatments based on the fact that it was an ethical treatment at the time they were given in the 1940s and 1950s.

LS: These were the records that you had in your attic for a while?

WC: When we cleaned out the records in South Carolina we had no place to put them here. Now we have a nice new building here in Chamblee, but when we first moved over here we were in a trailer. So they were sealed in boxes. I didn't know what to do with them because I had no space. After about 10 years, once we had space, they were moved here. They sat in file cabinets until, I would say, about 15 years ago. I had my beautiful 24 X 36 office. About two years ago, I was moved into this nice lab building but with the cubical office which I have now, but I have a storage room. In the storage room I have beautiful file cabinets. Now the records are in a beautiful file cabinet all in order, beautiful.

LS: And you have other records, in addition to those from Columbia?

WC: There was another field laboratory in Milledgeville, Georgia, with the mental hospital there. That operation ran for about 7 years. Those records were preserved and are in the file cabinets here. They are also in excellent condition.

[4] Charles Weijer, "Another Tuskegee?" *American Journal of Tropical Medicine Hygiene*, 61 (Supplement), 1999, 1-3.

LS: I just wanted to talk a little bit more about the details of this research. I was looking at some of the publications: I'm quoting from one but I think this sort of statement occurs in most of them. "Treatment with non-curative doses of anti-malarial drugs was often necessary to modify and control the early stages of the infection with *P. falciparum*, when needed parasitemia was also modified by the administration of bismuth thioglycolate." [5] What were you trying to tune with these sorts of non-curative interventions in the disease? How were trying to shape the disease course?

WC: I'm a PhD. I do not treat patients. The staff treated the patients. So the medical staff treated the patients and they would determine that the patient was having too much fever and needed the infection to be "cooled off." They would want the patient to be treated with something that would slow down the infection, but they didn't want the infection to be cured, because the object was to get more and more fever. Therefore, the patient was treated with either quinine or with bismuth thioglycolate. This was used in a large number of the patients to kill off part of the cycle, to get it 'into synch' so to speak. It was given in many of the patients in which you had double broods: It would kill off part of the brood and get the infection back in synch so that you had fever more or less every other day instead of every day. Or quinine would be given just to slow the infection down for a day or so and then get it back. The physician didn't want to cure the infection because then they would have to start over again and re-inoculate.

LS: Malaria here was a therapy and therefore it's the therapy that's being tuned with these interventions.

WC: And they wanted to keep the infection going but they wanted the patient to have a little, shall we say, mid-treatment rest.

LS: Do you want to say anything more about the changes in human experimentation and patient consent or IRBs?

WC: Fortunately, since I now work only with monkeys, I don't get involved with IRBs: We go through animal care and use committees for our monkey work. In the past, any IRB work and that sort of thing, whether with prisoners or mental patients, was handled by the medical staff or, I presume, through Coatney's office in Washington.

LS: Moving back to primate malaria you've mentioned Don Eyles, you've mentioned the work in Malaysia, can you tell me a little bit more about that?

WC: The great thing that happened with Eyles was he got malaria He got monkey malaria in the lab in Memphis and he called up Coatney. He said, "Hey guess what? I've got monkey malaria." And then they intentionally fed mosquitoes on people in the lab there. Now that wouldn't have surprised Don Eyles or his staff but they intentionally tried to infect themselves.

[5] W. E. Collins and G. M. Jeffery, "A retrospective examination of sporozoite- and trophozoite-induced infections with Plasmodium falciparum in patients previously infected with heterologous species of Plasmodium: effect on development of parasitologic and clinical immunity," *Am J Trop Med Hyg.*, 61(1 Suppl), 1999, 36-43, on p. 36.

LS: But the first one was an accident?

WC: Yes. The first one was accident and then they intentionally tried to infect technicians in the lab. They had no permission to do that. They just did it, but people do that on occasion. You know, they just want to see if it can be done. After that, it was all done in the prison project: They intentionally tried to infect prisoners at the federal penitentiary with monkey malaria. Even that went through IRBs in Washington. They were very successful. They did it repeatedly with several different species of monkey malaria. Now we did not intentionally try to infect any technicians in our lab here in Chamblee because the prisoners volunteers there were available to be infected with *Plasmodium knowlesi*, *cynomolgi*, *inui*, *schwetzi*, and *brasilianum*. These five species readily went into the prisoner volunteers which established that monkey malarias do go into humans. But is it a serious public health problem? No. But it is an interesting thing. Could it be a problem in parts of Borneo or something like that? Yes. Is it going to sweep worldwide? Heavens no. Could it confuse people in certain parts of the world such as Borneo? Yes. It's been reported out in Borneo recently and everyone got a little excited about it. It's a curiosity. It shows that monkey malarias can be models, really interesting models. There are so many things that we could do with monkey malarias. As we make vaccines, could we use these related parasites to test models? Could we use them as vaccines themselves? If they are related enough could we use them because they may create enough immunity, but maybe not disease? Look into it, you know.

LS: In 1971, you and Drs. Coatney, Peter G. Contacos and McWilson Warren published *The Primate Malarias*. Can you say a little bit about this project?

WC: In 1971, Coatney and Warren decided to write a color atlas on the species of monkey malaria. As they did the illustrations, they produced marvelous drawings. As they got into it they thought, "You know maybe we should start putting in the rest of the stuff, the biology of the parasites and so on." So they came down here to Chamblee and started talking to Pete Contacos and me about it and they said, "You know if we decide to expand this into a larger book instead of a color atlas, we could make this quite a book." Pete Contacos said, "You know that would take away about 25 publications that Bill has been writing?" And they said, "Bill could put together quite a bit on that" and I said, "Well, yeah, I could – we've got a lot of stuff we've been accumulating on it, but we haven't really got it all together and with the delay it would take us about six months to put together all the text on the mosquito work, but we probably could put it together." Coatney said, "Let's go for it." "And we require also Mac Warren to put together some biological stuff, a couple of chapters there." Instead of being just a color atlas, we decided that we would expand it and write it well. That made McWilson Warren a little bit mad: At the time Mac Warren was getting ready to take a job in El Salvador and this made a lot more work for him to do. Pete Contacos went along with it. We decided that we'd put aside what we were doing and work on the book. Well, Coatney got real ambitious. He decided he'd make a big book out of it and he came by every morning demanding some pages, some models. He got to be a real pest. He drove McWilson Warren up the wall. Warren got so upset at him he didn't want to speak to him and that made Coatney upset. And so Coatney said, "Okay you're no longer second author you're third author," which made Warren unhappy. I don't think they spoke to each other again after that. So instead of being Coatney, Warren, Collins and Contacos it became Coatney, Collins, Warren and Contacos and that pissed off Warren no end. I had

nothing to do with that. I said, "That's not right," but Coatney was adamant. In the end, I probably wrote sixty percent of the thing, but it had nothing to do with me. It was just that Coatney got mean and said, "Well Warren isn't getting his chapters in on time; he doesn't deserve it." So then Coatney got mad and went to the director of CDC and demanded Warren get his chapters in on time. Well, that didn't go very well with Warren either.

It really got to be awful: They wouldn't speak to each other. Warren eventually got his chapters in and they were good chapters, but they hated each other's guts. By the end of the thing they really hated each other's guts. When it got done, it was a really good book and then the printers asked – I don't know who the printers were – "You think anyone would want this book?" Coatney said, "I think some people would want it. Why don't you print off 1500 copies?" So they ran off 1500 copies. I said, "I'm going to give away a bunch of copies. I'll buy 50 copies." They sold out right away. I gave mine away. I gave the dishwasher, animal caretakers, and everyone a copy. Then people came to me and said, "I'll buy a copy off you, whatever you want, I'll buy a copy." You could now sell them for $50 a copy. I should have bought a 100. They were nice books. They sold for $7. I thought it was a good deal. It was a cheap book to give away.

LS: Did you do a second printing?

WC: No, it was the government printing office. You can occasionally see them on *eBay*. It's like Percy C. C. Garnham's book.[6]

LS: I have a couple of names that I'd like to ask you about. First is Dr. Sol McLendon.

WC: Sol McLendon was head of the State Park Hospital. In South Carolina, when we were working there, there were two hospitals, one for the Caucasians patients and one for the African American patients. They were totally different facilities, two different locations. Sol McLendon was in charge of the hospital that held the African American patients. He was a real nice man. Many of the patients treated were at the facility that had the African American patients. Because they were given *falciparum, y*ou had to manage them a little more carefully. Sol McLendon was a really good physician and he had a lot of experience with malaria.

LS: He's the one that the strain of *falciparum* is named for?

WC: The McLendon strain, yes, a very famous strain of *falciparum*, which is used a great deal.

LS: You maintained a variety of strains, such as the El Limon and McLendon stains of *falciparum* -- that's part of what your lab contributed to the project?

WC: Yes. We maintained strains of malaria either continuously in patients or we froze them. Geoffrey Jeffery developed the technique for maintaining the parasites in a frozen state.

LS: The other name was Jimmy Skinner.

[6] P. C. C. Garnham, *Malaria Parasites and Other Haemosporidia* (Blackwell Scientific Publications, Oxford; 1966).

WC: Jimmy C. Skinner, yes. Jimmy Skinner was the senior technician for years and years. In fact, I'm having dinner with him tonight. He and I published over 100 papers together. He worked with Martin Young for a number of years and then when we moved here – to CDC -- he and I worked together for years. Jimmy was an excellent microscopist before he retired. He really was a fine lab technician, senior technician. It was interesting: When Professor Garnham used to visit our laboratory, one of the first people that he wanted to see was Mr. Skinner. He really had a great admiration for Mr. Skinner and his work.

LS: You mentioned Martin Young. Can you tell me a little bit about him?

WC: When I first came to South Carolina I knew nothing about malaria. I mean I knew a lot about mosquitoes and some viruses. I came to a nest of malariologists when I came down there. I didn't really realize that I was coming to some of the foremost malariologists in the world when I came to South Carolina. In fact when I first talked to him on the phone I heard this voice saying, "This is Martin Young" – you know ending the voice in the high pitch; it really was kind of startling. But Martin Young really was a fine malariologist, one of the foremost malariologists in the middle part of the 20th century. I liked Martin Young a great deal and he was going to teach me -- and make me pay for my education in malaria. He would say, "I'll bet you the gametocyte count will be higher tomorrow; that'll cost you 10 cents." If you're going to bet with him, that is. Or "I'll bet it will be lower, that'll be another 10 cents." Almost always he got the dime because he knew what was going to happen. He had the experience. I really had a great admiration for Martin and Gedelle his lovely wife. Gedelle lives up in North Carolina now, I think.

LS: Let's move on to 1974 and the CDC?

WC: When the lab closed it was decided that, if the prison project closed, either I would go to Bethesda or I would go to work for CDC. Well, there was a job freeze. It was, "Uh oh, what do I do?" At that time almost all the people I had worked with were working for CDC, Peter Contacos who had been head of the lab here was now working for CDC. Geoffrey Jeffery was working for CDC. McWilson Warren was working for CDC. I was the only one left. So they went to CDC and said, "You don't have a malaria research lab. You have epidemiologists, you have a field lab in El Salvador, but you don't have a malaria research lab. Wouldn't you like to start a malaria research lab?" And so David J. Sencer said, "In the middle of a job freeze the director of CDC has some discretion, I can come up with five slots. I can come up with a slot for Bill Collins and for only four technicians. I can come up with a slot for Jimmy Skinner, Bill Collins and you can pick three other technicians." So I did.

LS: How big was the previous group?

WC: We had 11.

LS: Was that tough?

WC: Yeah. The others could retire. They were all eligible to retire or find another job somewhere. So I picked the other ones and we decided that, "Well, that'll be pretty good, what can I take?" Fortunately NIH, which moved a great deal of stuff up, said I could keep the monkey records, and I could keep three freezers full of sera and frozen parasites and some of the equipment, which they didn't want to move. Some of the stuff they moved, but most of the stuff wasn't worth moving, it was junky equipment. But I could keep the monkey records. And the three freezers full of parasites and sera got me going and Dr. Robert Kaiser who was head of the work here, the Bureau of Tropical Diseases, was able to buy me 20 New World monkeys and 20 rhesus monkeys to get me started. And we were off and running with my four technicians.

LS: Did the work that you were doing change much?

WC: Not at all. I was working with Geoffrey Jeffery and McWilson Warren. They were down in the field. They were in El Salvador.

LS: The names of the divisions within CDC that you have been associated with have changed from time to time: for example, the Bureau of Tropical Diseases, Vector Biology and Control Division, Host-Parasite Studies Branch became the Center for Infectious Diseases, Division of Parasitic Diseases, Malaria Branch in 1981. Do these sorts of organizational changes impact the work that you do?

WC: Well, funny as it may seem I haven't changed what I've done at all. I was for a short time a branch chief on vector borne diseases, but everyone realizes I'm not a branch chief. I don't function as a branch chief.

LS: That is an administrative post?

WC: I don't administer anything. I'm not an administrator. I'm a researcher and I'm a writer, more or less. I gather data and I put it together and I publish. I like to write about 8 or 10 manuscripts a year on the data we accumulate. We have a very small group and we always have had a very small group and we work on malaria in monkeys and mosquitoes and we test vaccines and we develop models. That's what we do. And I've had technicians who are extremely productive and extremely loyal and dedicated to the projects. Sometimes, someone says they don't understand how I have avoided being an administrator, but if you avoid being an administrator you can get something done. I'm in the Senior Biomedical Research Service which is a group that can do research without having to be in an administrative position. I don't have to attend administrative functions and that sort of thing.

LS: Right. You said that one of the things you do is develop models. Could say a little bit more about models and monkeys or models and vaccine development? What kinds of inputs go into that?

WC: I've been looking at developing a model for testing vaccines or drugs against *Plasmodium vivax*. *Plasmodium vivax* is still an important parasite of humans and we've put it into squirrel monkeys. Squirrel monkeys are fairly easy to handle. They're a small animal. They're fairly available and easy to work with, but there still are some problems with *vivax* and squirrel

monkeys. Getting transmission by the sporozoite stage requires a lot of sporozoites to get an infection. We sometimes don't get very high parasite counts, and, with infection by sporozoites, the prepatent periods aren't as short as we get in humans. But there is a parasite, a monkey parasite that grows much better in squirrel monkeys that is almost identical to *vivax*. In fact, many people think it is identical to *vivax*. It's a South American parasite called *Plasmodium simium*. We've worked with *simium* for many years and from a molecular standpoint some people think, and I might agree with them, that it is either a subspecies or a variant of *vivax*. Having worked with it for a number of years, I think that it is *vivax*, just a variant of *vivax*. And the more I work with it, the more I think it's a better model and we can actually test a *vivax* vaccine using *simium* instead of *vivax*. The prepatent periods are half that of *vivax*. It infects mosquitoes very well. So why not test *vivax* vaccines using *simium*? We could test anti-sporozoite vaccines. We could do liver stage vaccines with *simium* because we could get much better liver stages. We get higher parasite counts. We could test the effect of blood-stage vaccines much better with *simium*. It's a better model, but as our former branch chief Kent Campbell says, "Bill you're the only one that knows anything about *simium*." He says the reason people aren't using *simium* is they don't know anything about *simium*. Why don't you tell them?" Well, we haven't written it up yet, but if I had a good vaccine against *vivax* in my hands right now I'd like to test it against *simium*, or test in that model system. But everyone is so enamored with *falciparum* that they aren't developing *vivax* vaccines. Now there are some *vivax* vaccines probably out there, but no one puts any money for *vivax*. They always are looking out to say, "Hey let's make a new *falciparum* vaccine," because they want the Nobel Prize next week. God there's a lot of people sick with *vivax* and, I don't know, I just think that the second line is going to be *vivax*. We've got such an opportunity to do this work. I don't generally work at the front line. I'm always at the back edge of the knife, but *simium* is a marvelous model – it's just one of the models that we have available. There are other models, monkey models, that we have. There is another one, *fragile* another bizarre parasite, comes from Sri Lanka. There are some good indications that we can - again in squirrel monkeys - probably use *fragile* as a model to test *falciparum* vaccines. We can transmit it by sporozoite. We also can use *falciparum* as a model in monkeys to test *falciparum* sporozoite vaccines. We here have systems to test vaccines in monkeys, but we can't test all vaccines in monkeys: We don't have enough monkeys; we don't have enough personnel. But there are, let's say, ninety vaccines in the pipeline and there are only two or three facilities set-up to do testing in monkeys, therefore monkeys are not in the critical pathway. But we can provide some excellent studies that can contribute to the testing and development of these vaccines. I won't say that we are critical. But we can provide a lot of useful information and we have developed models and that sort of thing that will be very beneficial. We never have said we're critical, what we are is beneficial in the development of vaccines: If we can provide information that is useful, why ignore us? Some people say, "Hey I don't want to go to a monkey because if it doesn't work in a monkey then you won't go ahead in humans." Well that's not necessarily so, but if we can provide information that is useful and say, "Hey, it works in a monkey." It doesn't say it will work in a human and if it doesn't work in a monkey it doesn't say it won't work in a human. It just might provide useful information. Let's take a look and see.

LS: Earlier you commented that, when you started at NIH, malaria was viewed as finished as a research topic. Malaria eradication was in its heyday…

WC: That's because they thought chloroquine was it and DDT was it, and, you know, it was. Basically they had the tools and the world was totally prepared to get rid of malaria, but now we've got problems. We still have some marvelous drugs in the pipeline and available. There are still some great things out there. We have insecticide treated bednets. They are really marvelous tools. We have some great insecticides that are still useable, and we have some great drugs now. The artemisinin combinations are really great drugs. We still have a couple of million people dying each year but we have a lot more people at risk. To have a couple million people die but still the tremendous population at risk means that we've made progress. Yet we still have a couple of million people dying each year. NIH has this transmission blocking vaccine. I really like the transmission blocking vaccines. We have been fortunate to have an opportunity to work with some people at NIH on some of the testing for their transmission blocking vaccine and have been very impressed. I think some of the new vaccines coming along are extremely impressive. If you combine those with the bednets and some of the other drugs that are coming along, there's progress, a lot of progress. But there's still malaria out there, and I like working with malaria. I really like working with malaria. I had a lot of fun.

LS: It's interesting organism?

WC: Oh, it's a lot of fun. Everyday I work with five or six different species, every day in our monkeys, and we keep a colony here of about 325 monkeys all the time. We do vaccine trials, we do a lot of biological studies looking at different species and how they're behaving. It's what we do.

LS: How big is the group now?

WC: Our group is very small. There are two senior scientists, John Barnwell and myself and then we have about five senior technicians and about three junior technicians. That's it and we publish a lot.

LS: Is there anything I should have asked you about today that I didn't ask you about? Some people I that should have mentioned?

WC: Peter Contacos was a person that I worked with for a long time. He was my boss for 14 years. Peter Contacos ran our prison project for a long time. He was an M.D.-Ph.D.and really was a leader in the running the prison for Dr. Coatney. Dr. Coatney was the boss up in Washington, but for day-to-day prison operations and the operations here at the monkey malarias, Contacos did a marvelous job and then he retired. Why he retired I have no idea, but he retired with 20 years in the corps. This is what disappointed me a great deal about the Public Health Service. They force their people to retire, which is unfortunate. Now I worked 50 years in the government, but I'm a civilian. The corps officers are forced to retire after only 30 years or they give them an extension up to one, two, or three years if they ask for it, but for a scientist who is working on research that can be very young, and to force them to retire is, I think, just a waste. Now Geoffrey Jeffery and I continue to have a lunch every Thursday and he has been publishing continuously since the 1940s, 1950s, 1960s, 1970s, 1980s, and we've published again last year. He has not stopped publishing, but he worked 15 years as a civilian. After his stint as an officer, he left NIH and came to CDC and worked as a civilian, fortunately. Then, after he retired as a

civilian which meant he had over 40 years of service, he and I continue to publish together. Not gainfully employed, he publishes as a retired public health officer with me. So he has continued to be extremely productive. But a lot of the public health officers have no gainful employment; they've been lost -- fine malariologists. Peter Contacos was one of those. He was a great public health officer, an M.D-Ph.D., and we've lost his contributions to the public health service. It's just unfortunate. Another one is Dr. William (Bill) Chin who worked at the prison project for a number of years. Then he left and went to USAID in the Far East for a while, but he was lost to research. He did a lot of work in the malaria field and then retired and was lost. I think it's unfortunate that the public health service has lost people who could have stayed on for a number of years doing very fine research. It's unfortunate because if you look at a lot of malariologists, some of them productive, particularly the British, for years and years. Garnham, for example, was productive into his 80's. Now I keep working after 50 years, maybe I'm not productive but I keep working because I've got nothing else to do. My wife, Janet, retired after over 40 years in the government She was a microbiologist and worked for the Veterans Administration. She says, "Don't quit working," because she's bored out of her gourd so to speak walking the dog every morning. So I keep working. We have a lot of interesting things going on here – we have a parasite which has yet to be described. We've had it for about 10 or 15 years and we don't know what it is. It is a parasite that we got out of a mandrill out of Gabon. We know it's different. It's a really bizarre parasite and we've had it in a whole bunch of monkeys. We have no idea what it is.

LS: But you're able to propagate it?

WC: Oh yeah we can grow it in culture. We've had it in rhesus monkeys, in New World monkeys, it's a bizarre primate parasite. We can't grow it in any of the mosquitoes we have, but it's a weird parasite and we think it's a new species. We're not quite sure. We haven't described it as a new species because there is a parasite that's been described from Africa and one that we're not quite sure about -- that this might be. But the one from Africa hasn't been described well enough for us to be sure that this isn't it, but it's different than anything we have here. So we've been playing with it for a number of years. Had it in a lot of monkeys. We have various manuscripts that we've been working on for two or three years so we just keep going along, various vaccine trials that we've finished up, you know a year ago or two years ago we haven't written up yet, so it gives us something to do. We have ten different species of mosquitoes that we grow in our insectary. We just have a lot to do. I like to come to work. I come to work at 7 o'clock every morning, go home at 5 and have fun. Hey, what more can you do?

LS: You're doing it.

WC: I have one senior technician and I have two in the insectary, and that's it.

LS: This is a nice facility.

WC: It's a very nice lab. It's very comfortable now. The government pays well. This is much bigger than I need. JoAnn Sullivan and I have this lab. Of course, we'll move out of here in 2009 to the new building, the monster building they're building at Clifton Road. The insectary will be

underground and the animal facilities and the labs -- it's going to be bigger than all the Chamblee campus put together in one high-rise building.

LS: All of your animals and mosquitoes are in this building someplace?

WC: No, we have an animal building. We have an insectary building.

LS: So logistically, that'll be easier for you?

WC: Yes, the giant building they are building at Clifton Road will handle it all.

LS: Thank you.

End of transcript