INTERVIEW WITH DECOCK

(Decock): I think there is a lot that could be done and fairly with substantial scientific backup about the spread of the epidemic once it had been recognized which I think has never really been very well described.

You mention the example of China, the spread in Asia for example, nobody has really done a very good analysis I think of exactly what has happened there.

To some extent Africa throughout the 1980s, but to go back farther and start digging about where could it have come from and what did happen before we first recognized it in the United States is I think difficult because there is just so little information and it is not only difficult, as you well know, sensitive, it shouldn't be sensitive, but it is.

This should be kept between the two us. Back in 1983 I had just arrived in the United States and you know I had been interested in AIDS hadn't come across it very much but I had read about it while I was still working in Kenya when I first read about your work and so men in the United States for me who was interested in tropical medicine and working in East Africa where there is a lot of chaos it obviously peaks my interest. I left Kenya in 1982 and went back to London and wrote up my thesis and ended up working in an infectious disease unit for awhile and AIDS was beginning to be

talked about in London as well. Then I came to the United States in 1983 to work in Los Angeles where of course AIDS was heavily talked about. I was working on the liver unit at USC with a major interest in hepatitis which was my interest at that time, barely in the middle of it and started thinking and talking to people and I thought with my interest this doesn't make any sense, and eventually wrote an article which was published in the British Medical Journal. I wrote it in 1983 and it took a long time to get published because it got lost in the mail. It was accepted in 1983 before the virus was recognized and it was entitled something like AIDS, an old disease from Africa and I just wrote it for interest sake and I didn't know if it would get any attention or not. It got a huge amount of attention. Looking back now 1 or 2 years later it was kind of naive in certain things it said. It was at that time a reasonable attempt to put together different observations. Some of them were blatantly wrong.

(Gottlieb): But were there some African observations at that point.

(Decock): As a review of the literature, yeah. There were early African cases if you were to troll through the literature that just doesn't make sense there these people in Central African Republic and what link do they have to New York City. Anyway that article actually attracted and criticism from some parts which I thought was very unfair because it was not fingerpointing, it was purely a

speculative article saying how do you explain this phenomena, in view of the scientific literature.

(Gottlieb): Who protested?

(Decock): Most people actually were positive saying actually you pointed out, I got letters saying this is in insightful. Others would say, some Africans got upset. Somebody wrote a book about AIDS and racism or something which actually was a terrible book (an African married to a Brit).

(Gottlieb): How long had you been in Kenya and what did you go there to do.

(Decock): 1979-1982. I did all my medical treatment in England although my nationality is Belgian - the old Belgian/American. I went for two reasons, one was I was interested in infectious diseases and tropical medicine and had always said I would work in a developing country and secondly it counted as my Belgian military service. I was teaching internal medicine at the University of Nairobi.

(Gottlieb): There was a man I met recently who was a professor at the University of Washington in Seattle, older man who was in Nairobi at that time I think, maybe earlier. He may have left by then. But in retrospect from your years in Nairobi did you see

anything resembling AIDS.

(Decock): I remember seeing one patient who, no not really. You occasionally saw people who were extremely wasted and you would scratch your head and say what on earth is this. There were limited possibilities of investigating and you would end up saying it is either tuberculosis or disseminated living or something like that. As you know the pathology, a lot of autopsies were done, in fact a good friend of mine, whose name you probably know from the literature, Sebastian Lucas, he was working at the same time doing a lot of autopsies. He will say that the pathology of AIDS like the pathology of tuberculosis associated with AIDS is quite different from non-HIV TB. I didn't really see anything.

(Gottlieb): When did the first African cases turn up and who turned them up. Did they turn up in Africa or did they turn up elsewhere in Europe.

(Decock): If you go through the literature the first descriptions are clearly in Europe. As early as 1980-1982. There are then some other articles to try and look back. There are some important ones and I have them. There is one in the Scandinavian jungle of infectious diseases, there is one that documents 10 cases or so that go back before 1981 and as far as the 1960s, maybe one from 1950s. They are of disseminated chaos and multiple infections and so on.

(Gottlieb): Do you think there has been subsequent documentation by labs. Do you think they are reliable.

(Decock): When you read them you think gosh this is pretty plausible. For example white people who lived in Africa and died in Europe.

(Gottlieb): Like the Danish surgeon, the woman.

(Decock): You are talking about 1976.

(Gottlieb): Where was that published do you recall? And there was a Norwegian family as well.

(Decock): In abstract form, I have it. I think it was an abstract of a conference. I have a file of this sort of stuff and I make up a reading list for a course I teach at the London School.

(Gottlieb): Briefly, what has been the course of your career since. What did you focus on?

(Decock): I trained in internal medicine and was interested in infectious diseases and the problems of developing countries so I specialized in medicine and eventually went to Kenya with a diploma in tropical medicine in England and then to Kenya and did some sort of clinical research and then came back to London to write that

thesis at the School of Tropical Medicine. I wanted to do some further post-graduate work and thought of coming to the states. My sister lives in La Jolla. I was interested in ID but also in liver disease and eventually decided to go into fellowship in hepatology at USC. Al Redeker was really the man I worked with closest, because I had a major in hepatitis and we got interested in Delta hepatitis, but besides I did a fellowship, stayed on the faculty for a year and wanted to do some more research and was with CDC with the intention of actually doing hepatitis and just happened that there wasn't a slot I was advised at EIS and by the time I was leaving Los Angeles I was actually more interested in AIDS. Left L.A. 1986. Went to CDC, ended up working, actually wanting to do international AIDS work and really that is what I did from the beginning and worked with Joe McCormic. Worked in that branch and then I did some work in Zaire. We got funny in that retrospective study of up in northern Zaire, that ten year of testing the serum from 1976 and going back to that area. It was kind of a crazy thing to go and do, it was a shot in the dark and was a risky undertaking. The story was that in 1976 there had been this epidemic of _____ fever with a subsequent international investigation and studies were done and the serum came back to different institutes including CDC from serologic studies in the villages, so those were pulled out of the freezers in 1985, tested for HIV, there were 5 positive out of 659 specimens. My predecessor had gone back to that area to try to find out what happened to those five positive people and I went

back to do a serologic survey in the villages. It ended up being a useful study but it was a bit of an expedition. It is described in the New England Journal paper that he found two, three had died and two were still alive. I wrote it but I was the second author. The first author was Venzela and published in the New England Journal in 1987 or 1988.

(Gottlieb): Were there any isolates recovered.

(Decock): There was an isolate pulled out and that is published in JID, in one of the original 1976 serum. Published in 1987 - JID.

(Gottlieb): Are those sera still around or not. Do you need an isolate to trace his lineage. Who has these?

(Decock): You should be able to do it on the DNA. You would have to speak to Joe, Charles Schable.

(Gottlieb): One of the things that interests me is what still might be out there that could be restudied with newer technology and do you thinks that there are serum banks somewhere that have never been studied.

(Decock): I think they are weak. I think a lot of them have already been pillaged already for antibody testing.

(Gottlieb): You don't think that there are any treasure troves of serum that nobody has thought of or a source of tissue that nobody has thought of. What about liver biopsies in Nairobi. Do they keep slides of liver biopsies for the last certain number of years.

(Decock): That is actually quite a good idea. Histology material. Yuganda would have histology material. In 1986 I started working for CDC as an EIS officer, really doing mostly AIDS and some yellow fever as well. Yellow fever exists in Africa and Nigeria. I got interested in the subject of HIV 2 and it was clear that there was something going on in West Africa and there was total confusion about epidemiologically about one virus, two virus, so we got interested in West Africa and made contacts and argued very strongly at CDC for establishing a second AIDS research project in West Africa which I did for five years in West Africa (Ivory Coast). That project is continuing just as well because Conchasa collapsed and that is the main project in Africa. There was a major political disturbances and all the foreigners were evacuated. The person you should try to talk about the Conchasa research projects is Robbin Ryder at Yale, Bill Hayward in Geneva and Chris Brown, Skip Francis from Hopkins and John Mann was the first director. I am still involved with it and on leave of absence from CDC, I haven't exactly resigned but I am full time in London and we will see where I am going to go. I am writing up stuff that we finished.

(Gottlieb): Backtracking a little, we talked about hospital reservoirs and serum banks, I assume your interest in hepatitis is less.

(Decock): If you want to talk to people about serum banks the Belgians, the Institute of Tropical Medicine in Antwerp certainly had some. The people in Luvane had some and have published abstracts, nothing else. There is an abstract of serum having been tested from the mid-1970s of pregnant women in Conchesa. I think the earliest positive we have goes back to 1959, which is the sailor in England. The earliest apparent African specimen is supposed to 1959 as well.

(Gottlieb): Namius who just left me a message apparently had a serum that was positive in Essex's lab and that was published because its gone I think. What about the earliest HIV 2 in man. Have there been restrospectives of that.

(Decock): There is a paper from the letter in _____ in Japanese and again the earliest was in 1959 and 1960 which was from the Ivory Coast and Nigeria. If you want to talk about HIV 2 you need to talk to the Portuguese. They are not very organized. I think everything that can be squeezed out of there has been done. The sensitivity about them is that it was clear that the biggest, I think we could have learned a lot from looking at the old Portuguese soldiers and that was never quite kosher. There clearly

was some cases of HIV 2 disease in people going back quite a long time, probably to the 60s. That is seen as a disgrace rather than as a disease. They never tested the soldiers in an organized way. The intriguing thing about HIV 2 is outside of West Africa where else do you find it in Africa, only in these two other colonies and the explanation that people say is that they shipped troops, not only Portuguese troops but also indigenist troops because they figured they couldn't make local soldiers that they recruited, they couldn't make them fight the local people, but if they shipped them somewhere else they did mind fighting.

(Gottlieb): Why were the Japanese the first to detect a positive serum.

(Decock): Because they had access to a serum bank but I don't know which serum bank it was.

(Gottlieb): As an aside Gallow would always talk about Portuguese navigators sailing into ports in terms of HTLV 1 being a vector.

(Decock): The funniest thing is and I didn't mention it but it just struck me, in India, India is chaotic where you don't understand the first thing about descriptive epidemiology of HIV in India but all we can say is that HIV 2 is present probably from some German publications, but it is present in Bombay. The only other place it has been shown is Ghoa. Ghoa used to be a

Portuguese colony.

(Gottlieb): Do you know anything about the case in St. Louis.

(Decock): It as published in JAMA and that's all. They tested the serum from him and showed he was infected but can't remember how. But even in the United States it is conceivable there must cases we don't know about here and there. The virus presumably came into the country in multiple.

(Gottlieb): What is your thought as to how the virus got into the U.S. Randy Schultz in his book I think blames it all on the steward and he talks about in his first chapter of his book, it talks about the tall ships coming into New York harbor for the bicentennial in 1976 and says that epidemiologist speculated about with retrospect how that might have been the time of entry of HIV. Did you ever hear conversations like that.

(Decock): I thought that was one the weakest parts of the whole book. I thought that book was an achievement but there was some pretty major flaws in it. Clearly there must have been major amplifying events like that, certain individuals like that steward. CDC published this huge cluster at the very beginning. He was at the center of this cluster. You should talk to the people who did those investigations. He tells a good story, Darrow describes how he went around Los Angeles asking the cases have you have sex with

anybody who really stood out. He apparently went to somewhere on the West Side of L.A. and said to somebody, have you had sex with anybody in the last few months who really made an impression on you, somebody who sticks in your memory. The guy said yes I talked to this man who I had sex with who was extremely good looking and had bright blue eyes and spoke with an accent. He drove across town and went to Orange County and asked some other guy who was sick the same question and got the same answer. He said he practically fell off his chair. Those must have been exciting days, people who were involved with all that stuff, discoveries coming thick and fast.

(Gottlieb): I actually heard that CDC has Dugas' isolate. I want to talk to you about animals. Do you think that HIV 2 based o the information you have and HIV 1 entered human populations roughly the same time.

(Decock): I think HIV 2 probably got in earlier. These Portuguese cases. In Guinea Besow there was pretty good evidence that some people getting sick in the 60s and 70s from HIV 2 in Guinea Besow. It is in some of the early articles about HIV 2.

(Gottlieb): Why did HIV 2 cross species.

(Decock): It is hypothetical, plausible but not prevalent. I think because of practices exposing humans to monkeys. What

changed was human interchange. There is tantalizing hints about two interesting observations that need further explanation. One is the MRC group working in the Gambia are also doing work in Guinea Besow and they say that they are doing work in some villages in rural Guinea Besow. They say that they are seeing differential rates of mortality in older and younger people. There is HIV 2 in older people and it doesn't have a striking mortality effect where it does in younger people suggesting that there are different strains circulating. That is purely hypothetical. Older people to get exposed to monkeys in cooking and hunting. The second thing there was a Danish woman, who is a young woman who has been doing a lot of research on HIV 2 in Besow with Peter ___ who is anthropologist and she had started looking at human behavior in relation to monkeys and at some conference had a poster up with a risk factor and an odds ratio of cooking monkeys and stuff and again it was weak. She is in Denmark. I don't know how they prepare monkey meat. It is not done in all countries. It is considered good meat and no particular ritual with it. I have seen markets selling monkey meat.

(Gottlieb): Someone told me that it may be hypocricable that women who butcher monkeys or carve them up or slaughter them have a higher prevalence of antibody than others.

(Decock): I follow that literature and I have just reviewed it and I don't think that was published.

(Gottlieb): Do you think that HIV 2 crossed into humans several times or do you think there was one premortal event.

(Decock): I think HIV 2 crossing into humans is the most plausible explanation for this whole business. I think it is very difficult to prove things. I can't believe it went the other way. I tend to think epidemiologically more than from a basic science standpoint and I have major trouble with all of this molecular epidemiology, including Beatrice's work in that is extremely good and sophisticated but people are drawing hugh conclusions from observations you can count on one hand. If I went to India and said I found three cases of penicillin producing niceria gonorrhea and drew conclusions about PPNG and in India people would say your crazy. I think Beatrice's work is very good indeed and what she says is very plausible. The observations are limited.

(Gottlieb): You referred a few minutes ago that changing social patterns that changed things. Can you elaborate on that. What changed in West Africa in the last 50 years.

(Decock): To be more specific about it, you need to talk to some historians. But if you look at the late 20th Century and the developing world and compare that with 50 years ago, it is completely different, the huge expansion of cities, the huge mobility of populations, population displacement, international travel, these are social phenomena that influence the spread of

disease. Needles are important here and there. I think it is outstanding in rigid societies like China you have injecting drug use emerging as major vector of HIV. That is just a little piece of the puzzle. It is just the hugh amount of population mixing and movement. We see it, look at an extreme example in sort of natural experiment. The epidemics that we have just seen in Central Africa and the refugee camps, you had epidemics of cholera and possibly other things but certainly those huge epidemics. What's different. We know those organisms exist in that environment. It is the movement of people. Civil strife is a major example. The trouble is it is unmeasured most of the time, the effects it has. Look in West Africa. A country that has had very low prevalence of HIV was Liberia. With the civil war in Liberia have flooded across the border. They are integrated into the villages, they are the same ethnic group. What effect is that going to have on Liberia's program. It has to have an effect. You have the same in Malowi and Mozambique. Mozambique refugees in Malowi. Malowi is a very high prevalence, Mozambique is a very low one. These refugees are now going home. If there was one sort of conclusion from that kind of maverick New England journal paper from the Yambuku investigation we pointed out over this 10 year period the prevalence of HIV infection in rural Zaire hadn't changed. It was 0.8% and it really hadn't changed. The virus was there in 1976 and 1986. Some of the freezer specimens that I talked about that Nuvane might have they have done a survey on some hepatitis serum they stashed away. It is the old explanations of epidemiology,

host, agent, environment.

(Gottlieb): What about HIV 1 for a moment in terms of its origin. It seems closest to Chimp.

(Decock): Presumably these things cannot be a coincidence. The facts these viruses are so similar. If you look at where did HIV occur first in Africa rather than going back to saying what do we think it came from, where were the first cases from, they seem to be clustered around Central Africa. HIV seems to have been in Zaire at least as long as anywhere else. There is a bit of bias because the cases that have been recognized in Europe were going to Europe for medical treatment so that automatically they went to selective countries you know so if you detect a case in Belgium it is highly likely that that person will be from Zaire because a Nigerian would go to France not Belgium. Nevertheless there were many of those early cases who were Zairians. It is interesting that since the very beginning the prevalence of HIV in Kinchasa has stayed stable. It was never below about 6% from the very earliest work that was done and it hasn't escalated. That is not typical of an early epidemic. Usually in Bejam we watched it going up, it is now stabilizing a bit though. That makes me think that in Kampala we have seen it go up. The first observation of AIDS in Yuganda seem to have been around 1982. If you read that description of slim disease in 1985 showing an association with HTLV 3 antibodies they say in that paper that the villagers in the Rakai have started

seeing it around 1981 or 1982.

(Gottlieb): In terms of the range of Chimpanzee for a moment and I don't think people believe that that is truly the missing link there is there any overlap of the range of Chimpanzees with Central Africa and Zaire. Do you think there is a missing animal link in HIV 1. All the primate haven't been surveyed in the different types of monkeys and could there be another type of monkey that harbors a virus that is closer to human HIV 1 than this Chimpanzee virus.

(Decock): I really don't know. Animal epidemiology isn't very good. If it is deemed internationally important to figure this out, yes. Monkeys again, their sensitive because many of them are endangered.

(Gottlieb): Do you think it is internationally important to talk about stuff like this. Do you think this is just an intellectual game, a detective game, where did this come from that people are curious about or do you think there is any value beyond that or do you think it is a damaging thing to do.

(Decock): I don't think it should be damaging as long as it doesn't detract from other questions. Is it important? I can see it is scientifically important from the pure point of science of understanding philogenetics, I can see it is important. Does that

practical implications, are we more likely to get a vaccine or are we more likely to get fundamental understanding of HIV virology for therapeutics, no I don't think so. I think we have enough to be getting on with HIVE 1 and HIV 2.

(Gottlieb): Do you think there are other viral diseases out there that we might want to know about sooner, that we should be conducting surveillance or knowing about agents that we don't know about now.

(Decock): Yeah, I am a fairly strong supporter of this whole concept of emerging infections and what we should be doing about them. Inevitably there will be new agents coming out of obscure places.

(Gottlieb): Did you read that new Hot Zone book. He talks about the western shore of Lake Victoria, the Island of Plagues, the village of the western shore of Lake Victoria that is wiped out by AIDS. He tries to pinpoint the location of the AIDS epidemic.

(Decock): No data. He talked to me. Somebody has written a book, Laurie Garrett. Have you read hers. She is a pretty smart person.

End of Interview.

INTERVIEW WITH MYRA MCCLURE

February 2, 1995 - 9:30 - Washington, D.C.

(Gottlieb): Can you tell me a little bit about the major thrust of your work and how long you have been working on animal viruses.

(Response): I will tell you the bit that will relevant to you and that is many years ago we had a nature paper published way back in 1988 and that was looking at how you could take _____ lymphocytes from primates. Monitored the CD4 molecule that was on these cells to compare them to the _____ to the CD4 in humans and then also to take HIV 1 and HIV 2 and seeing whether or not you could infect those cells with the human virus. We have a table showing that some of the epitorps on the human CD4 were highly conserved to many of the primate species and indeed there was sort of evolutionary correlation that the closer the primate was to man the more of these epitorps were conserved on his CD4 molecule. As you might expect therefore these cells were more readily infectable with HIV 1 and HIV 2. All this is not directly relevant to you but in order to do that study we have to collect sells from a whole range of primate, old world, new world, and all the rest of that and as a result of that we were effectively testing animals as well because they said to us we can't give you blood samples from animals to do a research project but if you would be good enough to screen our animals for retrovile infection then we will allow you to do it. So we got into the screening thing which we do. We

doing graphics for nothing as a favor but has been terribly useful from both our points of view because we now have an enormous bank of serum cells from primates all over the world. We have isolated a whole lot of new viruses. Not all of them wild caught, because London Zoo for example breeds their animals. So we have been looking to see the range of infection in these captive animals and we have done a little bit of sequencing with some of the viruses that we have isolated so that is why I have become involved with monkey species.

(Gottlieb): Have you isolated any new viruses?

(Response): We isolated a brand new serotype of foamy viruses from the Orangutan that have never been no in that sort of higher primate. It has just been published in November of last year. We didn't actually isolate but we characterized another new virus from a gorilla. I have a net B type retrovirus. I have a new STLV 1 we were just talking about in there from a family of Mandarins. (Captive) So we don't really know whether, although I do have for some serum from wild mandarins so I can see whether or not, you know.

(Gottlieb): Is there a real worry that there is going to be a major difference between what you see in captive animals and wild animals.

(Response): I don't there is a real worry. I think people don't want to make the same mistakes that made before. For example the SIV, the sooty mangabey virus that you find. The sooty mangabey probably infected the macaque because you don't find macaques in the wild with SIV so it is an infection that they've got presumably for a sooty mangabey. That happened in American primate centers. Well everybody housed them together in those days because nobody knew anything about the potential of viral infection and people are always short of space and animal handlers, so they put the little monkeys all together.

(Gottlieb): How different is SIV macaque from mangabey and HIV 2 is very close.

(Response): Very close. There is divergence. The table that I will send you will give you a breakdown of how close each gene is, what the overall homology is between the three of them and it is very clear from these figures that the sooty mangabey in fact is the forerunner of HIV 2 as well.

(Gottlieb): How many monkey species are there.

(Response): Maybe 100. If you can't get there is a book called Napier and Napier and it is the Bible when it comes to primates. Why I hesitate is the macaques is one species of monkey but there are 13 subspecies in that family alone. If you just take the main

families I would guess about less than 100 but if you take all the subspecies as well then you have a lot.

(Gottlieb): What percentage of major families have been screened in work like your own.

(Response): A minority.

(Gottlieb): DO you think that there is more outreach to these communities.

(Response): Certainly, but the problem is (a) who is going pay for it and (b) how do you get the samples back quickly. It is alright to see it himself, I manage to get them back from Cameroon, Central Africa and all over the place. Serum sample is fine so you can screen the animals serologically and they actually tag them and we know which animal is which. But how to isolate a virus from that animal, I can't get fresh blood back to Britain in a hurry so that is a real problem. I have to do this out of another research fund because nobody will pay for this. Nobody supports this. I do it on the back of my other grants. I just use money for these, like a hobby and I am hoping that as I am beginning to publish papers o this stuff, I mean these are two good papers that nobody has paid for. I may go back to them and say I have this enormous resource here. Don't you think it is worthwhile looking at the origin of these viruses by sequencing them all, but they will say no because

if it is not causing a disease in man we don't want to pay for it.

(Gottlieb): The kind of work you are doing in terms of culture work is different from molecular work than you started doing, so do you have to gear up and get a whole viral culture lab.

(Response): No we do the two hand in hand and because you can do a lot with molecular biology, I mean you can choose your primate, screen to see if the virus is there, do a bit of sequencing, but really if you want to characterize the virus you have to get it growing. We like to isolate the virus, have it in our hands and actually see an EM of it.

(Gottlieb): So the techniques that you use for isolating the virus, are they very similar to the techniques used to isolate HIV.

(Response): Absolutely the same. Co-culture. The cells we use for co-sulture are human cells or primate cells. There are a lot of these as well. You know the apes is quite easy, they will adapt well to human cells. The new world monkeys that are a bit more difficult, a bit trickier, so I sometimes use macaques.

(Gottlieb): Has anyone done a serosurveys or any kind of surveys of humans who have been monkey handlers.

(Response): I have in a tiny little way because Britain does

everything in a quite small way, partly because we don't have a lot of monkey handlers and partly because they didn't want me to do a big study. They didn't agree to allow me to test. They being the handlers, the vets, the association of zoo workers. They didn't want to know. But the CDC have run or running up the minute exactly that study and if you talk to Harold Jaffee or Tom Folks then they found quite a high, in relative terms, 1% or 2% who are actually infected with, or sero-positive. Please check with them. Folds is the one who suggested to me that we should try and amalgamate the English study with theirs but I couldn't.

(Gottlieb): What is monkey B.

(Response): Herpes B. It is a fascinating virus because if a human gets herpes B it just kills them and they get really ill and they die, but the monkey just has cold sores and it is just exactly the opposite Herpes simplex, we just get cold sores but it kills the monkey.

(Gottlieb): It is a typical zoonosis where it is more aggressive. This guy with capacy carcoma stuff that they are finding a new Gallow Herpes in the capacy carcoma tissue and they are saying that so far it looks like the homologies are with Herpes virus simeri. That is what Flekenstein works on. That is a peculiar connection if it is one at all.

(Response): I'm sorry I missed that guy's talk yesterday because I got so involved in the sequencing thing. What I don't understand about that is KS really only affects men. Why would a Herpes virus affect men and women equally. Why would it only affect men. I don't understand that. It is not like a Herpes virus to be hormonal dependent.

(Gottlieb): A number of books have been written recently, did you talk to Laurie Garrett. Did the woman who wrote the book "The Monkey Wars" ever talk to you? She is a reporter in one of the Sacramento Newspapers. I found the book slightly outrageous. One of the lessons of the book, her agenda, is that we are far too cavalier about some of things we have done with monkeys in the past.

(Response): That is the real lesson that we have learned from it. This is why people in zoos and whatnot are actually interested. Partly because they want to protect their personnel, partly because they don't want to make the same mistakes they have made in the past like spreading a virus among primate. Partly because they want to know what the origin of the human viruses are so they cannot make the same mistakes if that is possible.

(Gottlieb): Is there evidence that this sort of thing has happened in zoos. In monkey colonies in research they bunched them together, there is no reason why you wouldn't expect it to happen

zoos but has it ever been documented to happen.

(Response): Nobody has looked. I don't know what the zoos are like in this country but you know at the minute the London Zoo is struggling for survival. It was only public demand that kept it open. They simply don't have the resources to look. That is why they have helped me. They have these enormous banks of serum. Every time a monkey dies or has a postmortem they keep serum sample, tissue sample and all of the rest of it. In terms of the foamy viruses I have been able to go back and tell them for example that this new Orangutan virus that I have, all their other Orangutans they have ever had in that zoo from the 50s have been infected with this virus so the question is where did it come from, did they get it from another monkey. They couldn't have gotten it from a human because the sequence data we have so far would suggest that it is not close to humans so they couldn't have gotten it from humans.

(Gottlieb): What about Orangutan in the wild?

(Response): Don't know, haven't been able to get any samples from them. Just as you were speaking I suddenly realized I had an address of a guy in Los Angeles.

(Gottlieb): The guy in Los Angeles, and it is controversial, says that he finds a foamy virus in people with chronic fatigue

syndrome.

(Response): That is not the guy I was thinking about. There is a guy in Los Angeles that has some connection with Orangutan colonies in Indonesia and I have been told to get in touch with him to get some wild serum from him. This Orangutan was interesting suddenly to us. I mean they isolated this virus years ago and we have put it aside, I mean who is interested in the foamy virus from an Orangutan that is causing no disease. But the funny thing was that when I got that blood sample and looked at the PBL there were huge syncytia in the PBL which you never usually see in the primary culture. It was so dramatic that I phoned up the zoo and said to them, what is wrong with this monkey. They said nothing he just came in to have his toe nails cut, he is perfectly healthy. Then two years later they phoned me up and said look we have to put this animal down because quite suddenly in the space of a week he developed an acute disease where he lost his balance and he was bumping into things, he couldn't climb, he had muscle wastage, all the rest of it, do you want tissue? So we went down and got all the bits and pieces. The reason we were interested in that was the man who cloned and sequenced the human foamy virus had taken the genal from the human foamy virus, put it in transgenic mice and within weeks the transgenic mice became ataxic, had muscle weakness, blindness, falling over, exactly the same disease. When we looked histologically, that base of pathology got the same guy to do it, it was exactly the same. In the brain and the cerebral

cortex, the optical canal, in fact the brain man that I took it to said was this animal blind because there was infiltration. I got the sample from him when he came in way back to the zoo in 1978-1980 and he had the same type of neutralizing antibody then as he had before he died. So we tried to publish this but Ron Dirozi rightly said that this is only one animal and science turned it down on the basis that it was only one animal, that I should give two or three incidence of this. We published it in J. Barrow without the pathology. We argued about it that this was relevant but we were trying to make it out that the association was busy and he said no.

(Gottlieb): Have you found any viruses associated with any human disease at this time?

(Response): They have suggestions that they have been associated with thyroiditis. Recently there has been a lot of crude publications suggesting that they have been associated with Motoneuron disease, but I think they are about to retract it.

(Gottlieb): Going back to your original work on the CD4 homologies, I assume you have somewhere sort of a family tree of the CD4s in your nature. I think I saw it at the time but I would like to see and in terms of HIV 1 and 2 and the species that have been associated with that so far, Chimpanzee.

(Response): Chimpanzee is an interesting one. I don't quite understand why so few Chimpanzee has been infected with this SIV CP Zed. that is another thing that Larry Arthur in New York, and ourselves and countless other people who, well we haven't used Chimpanzees but he has over a long period above Gallow, I mean the first thing they do is to check that these Chimpanzee aren't harboring their own HIV virus before they start to infect them experimentally and they never ever came across positive. I just don't understand it. The story that I heard years ago just before this paper was published about SIV CP Zed was that the animal had an infant animal and they both had been taken in watch the equivalent of the MRC and that these Chimps had been brought up by an elderly couple who treated them like children. Now that is a bizarre situation. Whether they were positive we don't know what they did with them, we don't know how close their contact was. I suppose it is a possibility that the infection went the other way, but you want to talk to someone like Beatrice who understands more about the sequencing and whether that is likely. What probably makes it unlikely is that there is one gene BPU in SIV CP Zed which is quite different, quite diverse from HIV 1 and that would tend to suggest that it is a real isolate because it is not that close.

(Gottlieb): Were the parent and the infant both infected?

(Response): Yes they were both infected. I think that there has since been another isolate by the people in Amsterdam or Belgium.

I can give you that reference as well. There were sikhs monkeys showing that there was huge variation within the species on their SIV and might be actually closing off if they sequence enough of them that it might be the forerunner of HIV 1. It has published already. Very nice people.

(Gottlieb): Do you have any particular insight into how or thoughts as to how these crossovers occurred. Do you think that there is the cut hunter or the cut butcher.

(Response): I don't think it is difficult really. I mean I haven't been to Africa but anyone I have spoken to who has been in Africa, for example the last time Robbin Weiss was there he said you only have to go into the bush to realize how easy it must have been for the transmission to have occurred from monkey to human. They live with their monkey. They are running around tripping over African monkeys for example where they were all the time. They eat monkey meat. They get scratched by their pet monkey. There are fertility rituals involved, all sorts of things where they use monkey blood, spleens, genitals, all sorts of things and they live a sort of rough life there to where they are bound to have cuts and abrasions.

(Gottlieb): Presumably the CD4 molecule evolution is not new, in other words the homologies have existed and the monkeys have existed and the humans have existed there for hundreds if not

thousands of years, do you think that from what you heard these are recent events, these crossovers or remote events?

(Response); I don't know, I listened to Beatrice the other day saying that these have always been there, but I remember that Roy Anderson wrote a very nice article, editorial in Nature a couple of years ago and he had worked out on the basis of sequence variation that this virus could only have been a minimum of 40 years and a maximum of 200 year old. Whether his opinion has now changed on the basis of more sequencing being available I don't know. I'm not sufficient of a molecular biologist to know.

(Gottlieb): There are some cases, you look back, it looks like HIV 2 might have been causing disease before HIV 1, but it doesn't look like it was causing disease much before the 60s.

(Response): I think that is right. The earliest HIV 1 sample we have is something around 60s, the Manchester sailor that apparently died from some unknown cause.

(Gottlieb): Then Namius in Atlanta published that the had a 1959 serum from the bank, but it is gone.

(Response): It wouldn't surprise me in the least if they came across some fossilized tissue that had HIV there, 400 years ago. What has made the difference to this infection is the way it is

being transmitted, I mean the group that it got into, their lifestyle, the fact that people travelled all the time, the behavioral changes have taken place, all this is the difference. Otherwise we may never have known anything about these infections.

(Gottlieb): Beatrice said the other day that there has been at least two crossovers of HIV 2 that at least two independent primate to human transmissions have occurred. I meant to ask her about that, where she is coming from on that one? (No) Have you ever worked personally with monkeys (No) or do you bleed them.

(Response): I go and see them, I like to see the monkeys that I have tested. In fact I took my two cousin's little girl to the zoo and at the top of their voices they shouted to me, have you bled this one as well?

(Gottlieb): I got wrapped up in some animal work at Stanford and I remember I worked with monkeys only briefly, I remember we really had no idea, no one ever told us about monkey B, no one ever told us, you have to be real careful around these guys. I remember walking through an animal room with my mentor and this monkey reached out and grabbed my mentor, they have very big teeth.

(Response): We screen all the wild monkeys that come into Britain, they are screened by the public health laboratory for things like Herpes B and whatnot and I really don't like handling the serum

even from a wild monkeys unless I know they have been screened.

(Gottlieb): What do they come in for these days and what do they do with them?

(Response): We have this big vaccine program so they are being used for SIV vaccine studies. We have a big vaccine program in Britain. It is the Medical Research Counsel that is running this. All our vaccine studies have been done with SIV and done by the MRC and they have been using, do you remember they have repeated the American experiments where everyone got tentatively excited with this fixed whole virus and they got protection and then it was the British crown who did it three years later, but when they did the control using uninfected cells that were fixed they also got protection on the animals. One wanders how come all these famous American scientists manage to do an experiment without the control. Nobody knows why they got the protection. There was no neutralizing antibody but it must be some molecule on the hostile surface that is just cross-protective, I don't know.

(Gottlieb): Just to quickly ask you about the more celebrated cases. The Manchester sailor, have you ever gone back and looked at the raw data yourself?\

(Response): I have never seen the raw data and have never been able to get access to the samples, but oddly enough I was

interviewed by a journalist who was writing a book as you are doing and he was acting as sort of middle man, but I don't know what happened to the book or journal. He has already written a book on slim disease. He was going to write a book a couple of years ago on the origins of HIV. I haven't heard of him for a long time now but I could probably dig out who he was. I guess he wasn't very successful.

(Gottlieb): Then there are a couple of other celebrated cases. Allegedly a case in St. Louis in 1969. As far as you know that is a real case? Apparently there is some doubt about that.

(Response): All I have seen is a rather bizarre correspondence where somebody sent me, because he believed this boy had been immunized with a polio virus that had been passaged through SIV AGM infected cells and they were asking me the question did I think that this is how this guy got HIV, but the epidemiology didn't hold up. For one thing SIV AGM doesn't grow all that well in human T cells and in any case they didn't use lymphocytes, they used African monkey kidney cells and there is no CD4 on those so the virus couldn't get in. It could have been contaminated with lymphocytes.

(Gottlieb): Has anyone ever gone back to look at those cultures and see if there was any lymphocytes and stuff.

(Response): You might want to go and talk to people at the Wistar. I don't think they would talk to anybody.

(Gottlieb:) Apparently there is a little girl in Chicago who has HIV and there is absolutely no epidemiologic association that can be found and her parents are suing the manufacturer of the polio vaccine based on this theory.

(Response): I don't think they have a leg to stand on, (a) the epidemiology of where the vaccine trials were going on doesn't correlate with the epidemiology of infection. Secondly the AGM virus is so distant from HIV 1 unless it is a particularly strange isolate. There is no rationale for thinking this.

(Gottlieb): Why do you think there is so much sensitivity in Africa about the origins? If anybody rationally looks at this you look at Kinshasa for HIV 1 and you know it just comes out and hits you in the face that this is where this all sprung up, why are they so uptight about it.

(Response): I don't know why they are so uptight about it, I mean I suppose it comes back to the white man/black man, you are accusing us of being the source of the epidemic. Nobody worried when they called the Asian flu for example that killed half of Europe. That wasn't racist. I suppose it is a slur on their lifestyle, their behavior, their morals, their hygiene, but nobody

should take that attitude. It is much more likely to be the sort of government class that are becoming infected or infecting prostitutes than the peasants.

(Gottlieb): For example what happened in Haiti with tourism, when the Haitians were singled out.

(Response): One of the first isolates came from Haiti. Bob Gallows. I think we have gone beyond that now and nobody is so worried about where it came from in a sense as to you better do something about it in Africa.

(Gottlieb): Do you think there is value in trying to think about where it came from?

(Response): I think there is value from the point of view of learning lessons from it and I think there is value in the sense that people want this sort of information. No matter where you go you are setting on a bus and people ask you what you do, if you mention AIDS, the first thing they want to know is where did this come from. Maybe its based on fear, but that is really what they want to know. I usually just say I don't know, nobody knows.

End of Interview.