The First and Next 25 Years of AIDS Science and Medicine: The First 25 Years: Advances in Science and Medicine
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BOB MEYERS: For those of you who haven't joined us before, we are an independent, non-profit organization. We have two missions: The programs for journalists and awards for accomplishment. We are indeed honored this morning to be at the American Public Health Association. I want to tell you in a moment a bit more about our program, but first I want to introduce our host, the president of the American Public Health Association, Dr. Georges Benjamin.

GEORGES BENJAMIN, M.D., FACP: Well good morning. I am Georges Benjamin. I am the executive director of the American Public Health Association. APHA is the oldest and most versed association of public health practitioners in the world and Bob; I really want to thank the National Press Foundation for being here. We were absolutely ecstatic that we would get a chance to host you in our home. You know, the HIV/AIDS pandemic has taught us a lot about the importance of medical research. It has taught us a lot about our capacity to solve very complex problems to improve human health, but obviously we all know that we need to do more. We need to do more faster. We need to do more creatively, and we have incredible scientists in this country, and we applaud their efforts on this terrible, terrible epidemic. As our nation today debates a potential new pandemic of avian influenza, I just want to encourage us also to not forget to continue to

redouble our efforts on the one that we have in hand. This has been a very fascinating, troubling in some ways, 25 years, and hopefully we don't want to go another 25 years before we have the cure, but again we have done just wonderful work. I think all of us have lived through this terrible epidemic and it's important as we think forward on how we can improve the health of Americans that we pay some attention to the lessons that we have learned on the past and the lessons that we can not have to go through in the future. Again, I want to welcome you all, and just tell you to have a really wonderful conference. Bob, I will turn it back to you.

BOB MEYERS: Thank you Dr. Benjamin. Our foundation has done programs for the last 10 or 15 years on HIV/AIDS. Actually, at some of our public health programs Dr. Benjamin has been a speaker. In addition to individual programs, both in Washington and around the country, we have for the past four years collaborated with the International AIDS Conference on training programs for journalists who receive their fellowships and we did it in 2002 in Barcelona, in 2004 in Bangkok, and we will do it again this summer, August, in Toronto. We started out with 30 journalists. They provided fellowships, too. We now have 90 who will be coming in, half of them from China. So, this kind of program becomes very important for both our learning experience to help other

journalists. In this morning's program, we are going to start with one of the most significant figures in AIDS research, Dr. Anthony Fauci, who has been head of the National Institute of Allergy and Infectious Diseases for 22 years I believe, and it is significant that as we look at the anniversary publication of the first MMWR article on HIV/AIDS, recognize that Dr. Fauci's leadership basically parallels the epidemic, so it is an extraordinary honor for us to have him as a speaker. He will make a presentation, then we will have Q&A and then we will move to our first panel. As all national press foundations are, this one is on the record of course, so Dr. Fauci, thank you so much for joining us.

DR. ANTHONY FAUCI, M.D.: Thank you very much, Bob. I appreciate your kind introduction. Georges, thank you for hosting this for us. As you can see from this first slide, I am going to talk about the first 25 years of HIV/AIDS medicine and science. I have a half hour to do that and I am going to entertain questions after that so just time constraints alone will only allow me to just point out to you some salient points, events, and trends over the last 25 years to actually be a food for thought and discussion.

This is actually the first in what I think is going to be a series of similar talks on the different venues that I will be giving over the next several months. I think the

next one will be probably in Toronto when we go to the Internation AIDS Meeting and some thereafter, to talk about the various perspectives of the first 25 years of HIV/AIDS, so I am going to go through this with you historically and point out what I believe are some of the important issues that have arisen, so let's see.

This is the MMWR that Bob referred to. For me, it has a very special meaning. As you can see, the date is June 5, 1981, so we are a few weeks from 25 years, and I can remember, I didn't know it at the time and I will just give a little personal note here, I was sitting in my office at the National Institute of Health Clinical Center and had been for the previous 8 or 10 years that involved in studying the host immune response, its suppression, and its tendency to be infected when you have immune suppression, so I was fundamentally an infectious disease person and an immunologist at the same time so I was one of those overtrained, doubly trained people and I remember sitting in my office picking up the MMWR and hearing about and reading about these five gay men from Los Angeles who presented with Pneumocystis pneumonia, not really having any idea what was going on. Everything that was going through everyone's head, is this a toxic drug that they have been exposed to, is this some kind of mutated form of CMV? I felt a bit uncomfortable about it but really didn't take more note of it than just

putting it on the side of my desk, but things really started to happen exactly one month later, on the 4th of July, when several more patients from New York and California with not only Pneumocystis but Kaposi's sarcoma and over the ensuing months, I made a decision which now retrospectively certainly was the right decision, but a lot of people were looking at me like there was something wrong with me at the time. I decided that starting with that fall, I was just going to change the entire direction of my research which had been going on for 10 years and study this very unusual disease which was called GRID at the time, for gay related immune deficiency, so I converted my laboratory into an AIDS lab, and as I mentioned many of my mentors and senior figures told me that I was making a career destroying choice because I was studying this very unusual disease that was very restricted to an unusual population.

Now obviously as events turned out, it became clear over the ensuing months and this is a *Washington Post* article by Christine Russell who had been following HIV closely at the time about the gradual but nonetheless frightening spread of this mysterious lethal disease in the United States, so now we fast forward 25 years and we see that what was somewhat skeptical among people about whether this was going to be anything but an epidemiologically restricted disease has exploded historically into one of the most devastating

pandemics in the history of civilization. The numbers you are very well familiar with, 40 million people living with HIV, 5 million new infections just last year, and 3 million deaths, which means that HIV/AIDS has now transcended malaria and tuberculosis as the leading cause of microbial death in the world. Remember malaria and TB were the two big killers before then, and just a couple of years ago HIV/AIDS has superseded them.

Now I am going to show you historically, I am going to be going back and forth. I am going to try to keep this in a historically orderly way, but you have to go back and forth to look at what happened with the research budget when I first began being responsible in 1984 as you can see that the amount of resources were not very good, but remember at the time, there was a lot of skepticism on whether this was anything that was going to be a major event or a major public health catastrophe, but what has happened thankfully over the years is that the resources for HIV/AIDS have dramatically increased such that HIV/AIDS research now occupies 12-percent of the entire NIH budget of 28 billion dollars, so it is about 11-percent now because of the flattening of the budget, but it has gone from a miniscule amount to between 10 and 12-percent of the NIH budget.

Now the advances, and I often talk about the AIDS model of what it means when you can make investment, not only

resource and capital investments but infrastructure and intellectual capital, getting people to work on it, the number of advances in AIDS research from 1981 over the 25 years to 2006 are listed here and I am going to go over some salient components of each of these. It is noteworthy that if you look at the number of papers that have been published and that are listed in PubMed for HIV/AIDS, it is extraordinary. Almost 200,000 HIV related papers, so can you imagine if you are in the AIDS field and you are trying to keep up with the literature, what that means? If you really read anything more than the abstract, you are probably going to spend about 15 hours a day trying to keep up with the literature. It has really almost gotten out of hand. It's the reason why we have so many meetings and conferences to try and get people to stay up on it.

Here are some of the important landmarks. If you talk about what is the most, and I get asked this all the time now with the 25 year anniversary, what are the most important scientific advances? I think you have to say that the actual discovery of the etiologic agent first and it's sort of interesting, you know of the controversy they've gone on, this is a series of papers that had been published in *Science* in 1983 and importantly, several of them were from the Gallo group from Max Essex, which danced around a bit that this was a retrovirus, not quite sure what is the

relationship to HTLV1 was. François Baraceluce [misspelled?] from Luke Metenier's [misspelled?] lab isolated what was looking like a retrovirus and published an electron micrograph of it in *Science* in that issue, and this is actually the first electron micrograph of what turned out to be HIV/AIDS. What in fact they did not do in that paper was make the direct connection between this virus and the causation of the syndrome that they were looking at for a variety of reasons, of not being able to grow the virus or do any serological epidemiological proof. It wasn't until the following year in a series of papers in *Science* in which Bob Gallo and his colleagues actually made the direct connection by not only isolating the virus but by getting a serological test where you can match the people who are infected with the people that you got the virus for and that is the reason why you refer to them as the codiscoverers. It was really isolation and identification and then proof of causality.

Now, what happened in the next few years was really a marvel of scientific advances. The next most important thing that happened was the immediate transference of this knowledge to the developing of a rapid sensitive and specific blood test for HIV, the now famous ELISA test, which is confirmed by a western blot, and the reason why this discovery the following year in March of '85, one year after the *Science* papers from Gallo and then Montonier

[misspelled?] is that it was able to protect the blood supply first completely in the developed world and then gradually in the developing world, diagnosis could be made early which has important relevance a couple of years down the pipe when therapy became available because we don’t only treat people now on the basis of their being deathly ill the way it was early on and then also they do epidemiological and natural history studies to be able to say that x-percent of people in this particular region are infected with HIV. Obviously you would never be able to do that if you didn’t have a sensitive and specific test.

Another important point that is more of a scientific issue than it is an issue that the general public would really appreciate is the extraordinary advance and amount of knowledge that was gotten into the molecular virology and epidemiology of HIV. This is probably the most intensively studied virus of any of the viruses that we have been studying for the last many decades. First, the identification of it as a retrovirus, a bit different from previously described retroviruses such as HTLV1, 2, as well as some of the animal retroviruses, like murine, leucemia virus, and equine leucemia virus. The virus was very rapidly cloned, sequenced, and its genes were delineated, and this is a map, I know you can’t read what the functions are and it is not meant for you to read except to say to remind me to tell

you that there are three structural genes and six regulatory genes and even today we are learning more and more about how the functions of these regulatory genes contribute to the pathogenesis of HIV. We also learned a few years down the pipe, so I am going to have to fast forward a bit here, that when you looked at the molecular epidemiology of the virus in humans and its evolution over a few decades, compared to a virus isolated from a chimpanzee, it is now quite clear that somewhere several decades ago, in Central and Southern Africa just beneath the equator, likely in the area of Cameroon and Zeae, now the democratic republic of the congo, that this virus jumped from the chimpanzee to human and only because of a variety and a constellation of socioeconomic events of moving of populations did it actually take hold and explode into a much more of a human to human virus as opposed to an animal to human virus, as it adapted itself to the human species. In its molecular adaptation, we now know that there are different clades or subgroups, all HIV-1 but a little bit different when you look at the molecular make-up. No real major difference in its pathogenesis but for example, we have a predominance of the B-clade in North and South America whereas in Africa there is a predominance of the C-clade and to a lesser extent the A-clade. It is a curiosity of the molecular evolution of the virus. It does not have a lot of relevance when you talk in terms of pathogenesis. Speaking

of pathogenesis, I could probably spend the entire half hour talking to you about pathogenesis. I would like to because that is what I do with my own lab work, but it is something that I just want to point out some salient features to you. [Silence] I think I'm going to do that.

Okay I think we got it. This is a slide that I made several years ago and updated. What it tells you. It is sort of interesting, it was kind of historically important for me to point out to you, the first few patients that I admitted to the clinical center in the summer of 1981 when I decided I was going to convert my efforts to studying this interesting new disease, patients came in with a high viral load, which I had no idea what that viral load was because we couldn't measure viral load because we didn't know what virus it was, and very low CD4 counts. It was only until a few years later that we realized that this was not a two-month or a one-year disease, but a disease which had a mean time from infection to the actual manifestations of serious symptoms of about 10 years. That is a lag that is of important relevance when you think in timing of treating people. We learned a lot, and this is where I came in because I was doing immunology and infectious diseases that there was a very interesting effect on CD4 positive T-cells by a number of mechanisms ranging from an increase in turnover and aberrant activation to direct killing to innocent bystander apoptosis

in a variety of other mechanisms. Still today, very interesting papers are coming out about pathogenesis. We also learned early on, like virtually every other virus, there is a human cell receptor which the virus has co-opted to allow it to affect human cells. In this case, it is the CD4 molecule, which is an important immunological molecule in antigen recognition and cell triggering. So the virus did what any virus does when it wants to get into a human cell. We also learned soon thereafter that there was a co-receptor that was discovered by Ed Berger and then subsequently others indicating that the virus not only needs the CD4 molecule, it also needs a molecule like CCR5 or CXER4 in order to bind and fuse. That is important because we now have therapies that are directed about that, and we also learned the very sophisticated elegant way the virus first binds to the CD4 molecules, undergoes a conformational change, allows it to bind to CCR5, and then the membrane fuses with the cell and that is how you get infected, showing us once again that viruses evolutionarily are geniuses when it comes to how they can infect the human species.

My own lab has been studying for many years the fact that despite the fact that you can control this virus with therapy, that there is a latent reservoir of HIV which has essentially made eradication of HIV impossible, leading to the understanding that the virus has the ability to insert

itself into the genome of a cell and even if you block the replication of virus, not a single individual on record has been able to clear the virus completely. Just think about that. Sixty million plus infected, not one documented case of complete irradiation either with drugs or naturally with the immune system. So, everybody that any competent scientist has looked at who is HIV infected, no matter how well they are doing, you can isolate the virus for them. That bodes very poorly for “a cure for HIV,” even though our control of the virus by treatment, which I will get into in a moment, is actually doing very well. This is the proof positive of what I just said. Rick Davy in my own lab had been looking at patients who have been on therapy for three years with no detectible viral load. We empirically interrupted therapy in all 18 patients, in every single one of them, despite having undetectable virus for three years. In every one the virus bounced back to the level where it was before; again, some sobering news for the issue of trying to irradiate.

So let’s go forward now to the treatment of an HIV infected individual. We have learned a lot about how to treat opportunistic diseases including those listed on this slide which are actually the direct killers of patients as opposed to the HIV virus itself. It has been historically very interesting. Maybe of you will remember in 1987 the

original paper that showed the efficacy of the first drug, AZT, and to refresh your memory it was given to people who had advanced disease. Why? Because the only way you can identify somebody with HIV is when they had advanced disease. They were given a placebo or AZT and this was the data that led to the approval of AZT as the first drug; 19 deaths in the placebo group and one death in the AZT group. That was the good news. The bad news that we suspected but weren't sure of was how long the AZT effect would last before resistance would develop, and it wasn't very long. It was measured in months. In fact, if you look at 1987 with AZT monotherapy, this is weeks and this is viral load. We had a modest decrease in viral load which, after a few weeks, about a year, went right back up to the baseline because of development of resistance. Things got better with two drug therapy, it lasted a little longer. Remember AZT and DDI or AZT and DDC? But things really started to happen when three drug combination, particularly with the protease inhibitors came in, in 1996, in which the viral load in patients who had never received therapy before was able to stay below detectable level for a considerable period of time. Now, fast forward, 2006, we have multiple targets, not only the reverse transcriptase inhibitors and the protease inhibitors, but we have licensed drugs that are used for fusion and entry inhibitor and a very promising drug for integrase inhibitor.

This is very important to keep the pipeline of drugs going, even though we had been very successful. We need better drugs, easy to use, and importantly we need drugs that will substitute for others when resistance emerges. An interesting fact that I often speak about, these are the FDA approved drugs for HIV. We always say when you put resources in you get results, so there is hardly a scientific problem that you can't solve if you concentrate on solving it. It is of note that we have more antivirals that are approved by the FDA for HIV/AIDS than the sum total of all of the antivirals for all of the other viral diseases combined. Now that is very, very interesting, and I think that really tells us that if we wanted to really target a number of other viruses, we could probably have a lot more effective antivirals against other viruses. The results have been striking. These are the number of newly diagnosed cases. These are number of deaths, and this all happened in the mid-90's with the availability of antivirals. The green circles that increase which are persons living with AIDS in the United States is only because as less people die and we have a constant number of 40,000 being infected each year, then obviously do the math, the number of people living with HIV are going to increase.

Now when you talk about treatment, when you talk about the history of AIDS, you cannot mention the role of

HIV/AIDS activism in the science of HIV, and it was really founded on the community, in this case very heavily weighted towards a very well informed activist gay community demanding a say in the availability of drugs and how trials were conducted. It started off as a confrontational relationship. This is a picture of now my very close friend Larry Kramer who we have some very experiencing experiences with over 25 years, particularly when he wrote that article in the *San Francisco Examiner*, a full page magazine section which said in an open letter to Dr. Anthony Fauci, “an incompetent idiot.” [Laughter] I will never forget that. Go back, and you will see that was in the 80’s, but we have become actually very, very close and warm friends since then and he has been very helpful in getting the activist scientific community together. This was a sign when octant was storming the NIH and this is right in front of our building when they were coming. They actually were directing it. It was a frustration that they were directing at the wrong people. They wanted drugs approved more quickly, but the NIH doesn’t approve drugs that should have been up the Rockville Pike a little bit. [Laughter] But nonetheless it was important because I asked them into my office and was able to sit down and finally find out what it was that they really wanted to do, and they made some very good points. I think that was the birth of the very good relationship. Now if you fast

forward 15 years, this is exactly what went on at the Derby meeting in South Africa in 2000 where the South Africans were actually, it was eerie to see, because I was at both of those demonstrations, to see the South Africans asking the same question, why can't we have access to treatment the way the AIDS activists in the United States are saying we want access to unproved drugs, the South Africans were saying we want access to all of the approved drugs which they weren't getting. So that really led to the ground swell of movement which led to things like the President's Emergency Plan for AIDS Relief, which is aimed at preventing 7 million infections and treating 2 million HIV infected individuals and caring for 10 million. I don't have time, but I could tell you the story of how this came about. It actually came about when President Bush sent me and Secretary Thompson at the time to Africa to see if it would be feasible to do a program to get drugs for Africa. We reported back that it was and in a wonderful way, I think many people did not expect he actually launched this very ambitious program which has turned out to be very successful. Now we have the President's program, the Global Fund as well as individual bilateral agreements. The impact has a long way to go, but we have seen something that no one would have imagined. We now have over a million people who are on antivirals from low and middle income countries. When this started a few years

ago, it was like 10,000 people outside of the developed world who were receiving antivirals. We still have a large percentage more that need to be covered, but it is a very important step in the right direction. This is one of those slides of individuals who we saw prior to therapy and then a year later on therapy with his son. It's very, very interesting how the miscalculation on the part of so many people that you can't deliver drugs on a daily basis in a developing nation setting, and the people who did the low-tech public health issues proved everybody wrong, because Paul Farmer did it in Haiti, and a lot of people are now doing it in Subsahara Africa, so this idea is if you have millions of people that need drug who don't have a good health care system, you could never get any drugs to them. That is completely incorrect, and a real misperception.

Finally, I want to close on the issue of prevention. In order to fight AIDS, you got to have both treatment and prevention. These are a large number of approaches to prevention. I am going to highlight three of them because of lack of time. The first is education and behavioral modification. Now I am going to tell you a story maybe some of you don't know because it is something between the surgeon general and I but this is a picture of C. Everett Coop when he was surgeon general. He is a very close friend of mine. In fact, I actually was his private physician which we didn't

want to make public because since I was an AIDS doc, people would think he had HIV, but he didn't. He was just a guy that was under a lot of stress who is doing very well right now. He is 90 years old and we are going to celebrate his birthday in a month or so. But Dr. Coop, who was the surgeon general at the time, was asked, believe it or not, by President Reagan to go out and put some information out on HIV and he did a bit more than they expected. He actually came out with the surgeon general's report that many of you may realize which was a no nonsense discussion of what HIV was and how to prevent it, and we had a very interesting mixed reaction in this country. The people who were extremely conservative were actually horrified by the use of the word sex and condom and things like that, and this is actually a cartoon from that time. "If anything comes in the mail from the surgeon general, don't open it." [Laughter]

It's interesting because they told him to do the surgeon general's report but they didn't give him any money to put it out, so he and I worked out something where I transferred some funds from my institute to him and he was able to actually put out the surgeon's report with NIAID money, an interesting, pretty well kept secret. Not that it's news, but it's just interesting.

The other one is interruption of transmission from mother to child. A very interesting story, one of the big

successes was the protocol 076 in which AZT was given to mothers during pregnancy, delivery, and to the baby. The results were striking, with the number of HIV cases at birth rapidly going down to essentially being a handful in the developed world of the United States, but the situation globally is abysmal with 700,000 children infected in 2005, which led to the Novaripine study which was a single dose to the mother and a single dose to the baby which has now dramatically decreased the transmission of HIV from mother to child in a way that really was unprecedented in the developing world. The other is topical microbicides, I'm sure you are going to hear a lot more about that from Zeda [misspelled?] so I am not going to spend much time on it, but it is really a necessary prevention technology for a variety of reasons, not the least important of which is that women have really no means to protect themselves if their partners do not wish to use a male condom or allow the female condoms to be used, and there are certain situations very clearly where abstinence and being faithful are not likely to protect people, particularly married women or those who are sexually abused, so this is another important area; and finally, the area of vaccine, vaccination which has been one of the most important stumbling blocks in our prevention mechanisms because it is still a scientific issue. HIV is different. The natural immune response is inadequate, unlike other

viruses in which 90-percent plus of people can clear the virus. If you look at even the important killers like small pox and polio, HIV hides from the immune system. It destroys and targets the immune system, and it mutates rapidly. There is a lot of effort going on now in trying to develop an HIV vaccine. It is fundamentally not a logistic problem. It is a scientific challenge, and that is the reason why we are now rethinking and looking at ways in which you can present the antigen to the body in a manner that is even better than natural infection, with regard to recognition by the host, and we could spend probably a whole day talking about that, but it just remains the lesson and the bottom line message to you is that it is still an important scientific challenge, and finally what about the way forward in the 21st century? It's very clear that we have had many successes with HIV/AIDS, fundamentally emanating from the basic and clinical research, but it is very clear now that to confront AIDS in the 21st century, you have to have a combination of prevention, treatment, and care. Any one of these alone is not going to be the solution, particularly when you have a situation where you have a global pandemic involved in the developing world in which resources are not nearly at the level as they are here. So, I will stop here and I would be happy to answer any questions. Thank you.

BOB MEYERS: If you have questions, please come to the microphone. [Inaudible]

MALE SPEAKER: Thanks. Tony, could you talk a little bit about how all of this money that has been put into HIV has had an impact upon other aspects of infectious disease in terms of both basic science and treatment?

DR. ANTHONY FAUCI, M.D.: Yeah it's been extraordinary. First of all, particularly at the level of basic science and even at some applied science, I can give you a couple of examples. The ability to dissect out the immune system with one of the most tragic experiments of nature, you know when we first started studying the naturally occurring congenital immune deficiency, the father of immunodeficiency was a fellow named Robert Good back in the 60's and the 70's and he referred to them as experiments of nature. This is a very catastrophic experiment of nature where you interrupt or destroy specifically certain aspects of the immune system and by doing that, studying how the immune system is regulated has given us insight into any of a number of diseases, cancer, rheumatic diseases, allergic diseases, that is number one. Number two, the whole issue of the viral biology, how viruses work, how they evolve, the ability to rapidly sequence and annotate the genes of viruses, we have done that before but it has been raised to almost an industrial level where you can do it rapidly. The

sequences that we can do now are in a matter of a day or so as opposed to months, so viral biology is another, and the other is the entire arena of targeted and screening of antiviral drugs, which has had a lot of spin-offs. In fact, some of the drugs that were developed for HIV are drugs that are being used for other infections like hepatitis. If you look at drugs like tenofovir and drugs like that, Denavir, all of those now are spinning over to other diseases, so we could go on and on but a large number of basic science advances that easily able to be extrapolated to other diseases.

FEMALE SPEAKER: Could you talk a little bit about how AIDS jumped from chimpanzees to humans and what that means for the prospect of an influenza pandemic? And do you think the pandemic is coming and would care to say, would you care to give a time line? [Laughter]

DR. ANTHONY FAUCI, M.D.: Sure. Thirteen days and four hours. [Laughter] Let's start with HIV first. Seventy-percent at least of all of the emerging new infections, if you trace them, SARS, pandemic flu, HIV/AIDS, Nipa virus, Hantavirus, 70-percent of them are zoonotic, namely they are fundamentally an animal virus that has jumped species. When animal viruses jump species, more often than not it's a modified dead end. In other words, they don't adapt themselves molecularly enough. They can jump from a

species to a human, but they don’t allow themselves by a variety of circumstances to efficiently adapt themselves to human where they can spread from human to human. Sometimes, however, that happens. That was the case with HIV/AIDS. It is very likely, given the history of butchering chimpanzees in Central Africa as a very important source of nutrition and food, that there were these infected chimpanzees and over decades and decades, they were getting butchered. Someone cut their hand, got infected, infected their wife or sexual partner, and it was a dead end, because at the time there wasn’t a lot of sexual co-mingling. Then what happened likely in the ‘50s and the ‘60s and the early ‘70s was that these jumping of species from chimp to human occurred, at the same time where there was profound socioeconomic perturbations in Southern Africa and Subsahara Africa, with the end of colonization, the breaking up of the family unit, people living in the rural areas, working in the city, the truck routes, commercial sex work, all of that exploded in Subsahara Africa, which allowed what might have been a form frust of an infection turn out to be an explosive infection, and it happens to be transmitted sexually, which is a universal physiological phenomenon, and you’ve got all the right components of a perfect storm and that is exactly what happened.

With regard to influenza, influenza II, at least pandemic flu is a zoonotic, because I'm sure most of you know because we've been talking about flu a lot, that flu is fundamentally an infection of water fowl. It has over a long period of time evolutionarily been able to jump and adapt itself to humans, so right now we have human influenzas which are fundamentally H1:3 and N1:2, so you have H3-N2, H1-N1, H2-N2, there are 16 H's and nine N's, and many of those are fundamentally animal viruses. The way H5-N1 is fundamentally a bird virus, which infects water fowl, but has adapted itself to be extremely lethal and transmissible among domesticated chickens. In its evolution and high exposure to humans, it has adapted itself in a very inefficient way to go from chicken to human, 205 cases, 113 deaths. That is very inefficient when you have tens of millions of chicken and hundreds of thousands if not millions of people exposed to those chickens. The question is will the virus molecularly adapt itself to be able to efficiently go from human to human? No one can answer that question, but you can say, and this is important and I say this so many times and I hope people get it right, that there is the preparing for the worst-case scenario and the question mark likelihood of a worst-case scenario. The government, the state, the local, all of the people who need to prepare must prepare for the worst-case scenario, the things that you read about now, the

upcoming TV shows that they are going to show, the worst-case scenario. The worst-case scenario means the 2006 version of the 1918 pandemic, which was the worst public health catastrophe we probably ever experienced. What is the likelihood of that happening? We don't know but it is a very complex array of molecular and virological genetic events that is going to allow this virus, if it ever does, to go efficiently from human to human, so even though you can theoretically say we are a mutation away from a pandemic, in reality it is much more complicated than a mutation away, so I can't say there is no chance, because there is a chance, nor can I say that there is a very good chance because given the complexity of the situation, you really can't say but in preparedness, you have to prepare for the worst case scenario but I wouldn't want the American people to go to bed at night and wake up thinking that they are one mutation away from catastrophe, because it is unlikely that is the case. As public health officials, should we be cavalier and say well then why prepare for it? No, you have to prepare for the worst case scenario. The problem is communicating that message to the public of how do you tell the public you are preparing for the worst case scenario but don't worry about the worst case scenario? It is a tough message, but that really is what the message is. I don't think people should be waking up in the morning worrying that the sky is going to

fall but public health officials, myself, the secretary Julie Gerbany [misspelled?], we should be worried about it, not the American people, because that is what we do. We worry, right? [Laughter]

FEMALE SPEAKER: Dr. Fauci, you were good enough to highlight the efficacy of prevention of mother to child transmission and then you also indicated the number of new infections among children today, almost 700,000 a year, the life cycle in adults of the disease, as you pointed out, obviously is often 10 years before we really see the complications of the disease, and yet in the developing world we are seeing as many as 50-percent of those children that are born infected die before they are two years old, I wonder if you could speak to the scientific needs around the research for children, be it with continued research and treatment and particularly for vaccines for children?

DR. ANTHONY FAUCI, M.D.: That is a very good point. Well, first of all let's just take treatment. The developing immune system of a child is much more sensitive to the ravaging effects of HIV. If you treat a child appropriately early enough, their cost will be as favorable as if you treat an adult early and appropriate, so it isn't as if even with treatment there is this big dichotomy between the effect of drugs on children vs. the effect of drugs on adults, so that 50-percent two year catastrophic projection that you are

talking about is a reflection of not getting drugs to the children, most of whom are in the developing world, so that I the answer to that.

Vaccine, when you talk about vaccines it's very tough to talk about vaccines for children because a child is either infected or they are not, and I don't think you would want to vaccinate anybody unless they were in a risk category, so I don't see HIV vaccine being the next measles, mumps, rubella, and haemophilus influenza B, you will be vaccinating people who are in the high risk category which, if a child does not get infected from a parent, either perinatally or through breast feeding, that child is not at risk until they become sexually active and if they do become sexually active, under what circumstances do they become sexually active?

MALE SPEAKER: Dr. Fauci, one of the items you have on the approach to HIV prevention that unfortunately you didn't touch on because of time constraints is treatment, prevention, and drug alcohol abuse. My question is how do you think or when would science influence policy not only in the U.S. but worldwide to allow a greater, more extensive use of harm reduction systems to prevent further spread?

DR. ANTHONY FAUCI, M.D.: It's a tough call. I don't know. We know what the data shows. We know that when you treat drug abuse that you stop, if you treat injection drug use by methadone, you have less injection drug use. When you

have less injection drug use, you have less transmission of HIV. We also know scientifically that when you exchange needles for clean needles that in fact you have less infection with HIV and you don't promote injection drug use. We knew that. We knew that for a long period of time but we haven't had a change in policy. I might point out to you that the lack of a change of policy transcends all administrations, so when we presented the data to the Clinton administration that this would work and they did not allow the use of federal money for needle exchange, so you can't say if this administration versus that administration, it seems to be sort of across the board in the United States.

MALE SPEAKER: If I would ask one more question, please, what role, going from science to basically outreach, what role do you think that the community groups, largely non-profits, have in research?

DR. ANTHONY FAUCI, M.D.: In research? Well it depends on what the research is. There is all kind of research. Preventive research, getting the message into the community, their role is huge. It's probably more important than the tertiary medical center people. If you have somebody at the community level who goes in to downtown Washington in the inner city or Newark or New York City or the Bronx, you certainly want to have community people doing

that. You don't want somebody dressed in a suit who looks like a fed.

FEMALE SPEAKER: Do you think industry has adequately incentivized to pursue HIV therapeutics?

DR. ANTHONY FAUCI, M.D.: Overwhelmingly so, because there is a lot of money in it, and I don't mean that in a facetious way. There are some, and I have met a few, extremely altruistic pharmaceutical companies, even when they want to be altruistic sometimes their board of directors and board of trustees do not allow them because there is a bottom line to it, but unfortunately we have a terrible epidemic with HIV. Fortunately that the development of drugs is a very huge profit for many of them, so I don't think we have a problem with incentivising companies to get involved in developing new drugs. We have a little bit more of a problem incentivising than to get involved in vaccine research, because vaccine is perceived by many of them that if it comes it will be an entitlement that the need for it will be so great that it will essentially be given away. We are having the same problem with pharmaceutical companies when you're dealing with the issue of making vaccines for things that are not yet a threat, biodefense countermeasures as well as influenza, which is the reason why a lot of the president's program for the 7.1 billion dollars that he asked for, of which there is 3.8 being spent this year, is going to partner

with industry to help them convert to a much more consistent reproducible way of making vaccine through cell culture versus egg based, so we have to help incentivize industry when the product is not perceived by them as a blockbuster drug whereas with HIV there is plenty of opportunity for a blockbuster drug.

MALE SPEAKER: Dr. Fauci, given the particular biological nature of this virus, do you think HIV will ever be able to be cleared by any kind of treatment that medical science can devise?

DR. ANTHONY FAUCI, M.D.: I can't say no, I don't believe that, because that would be counter to the efforts that we are putting in to try and solve that extraordinarily important problem, but it is going to be really tough. If you look at the way HIV acts, how it integrates itself into the genome of a cell, and you have patients like I've been following for eight or nine years who have had a level of virus in their blood below detectible levels for eight plus years, and then when I look for the virus, it's still there, I'd have to say that you never say never, and you never say always in biology, but if in fact we do, it is going to be very tough to do, so I am not totally optimistic that we are going to be able to truly eradicate virus from huge numbers of infected people. We may do it rarely in an individual at

first, but I don’t see this happening as a routine phenomenon.

FEMALE SPEAKER: Dr. Fauci, can you tell us a little bit about how big a problem adherence to therapy is for patients infected with HIV and what might be done to improve it?

DR. ANTHONY FAUCI, M.D.: Yeah. Adherence is probably not as much of a problem as people think it is, but it is a problem, and it was more of a problem when it was logistically more difficult for people to take therapy. The era of 35 pills with the maximum three to four drug, we had to take five or six per day every four hours or what have you, then it became very, very difficult. As we have gotten better and better at making the drugs user-friendly like one or two pills once or twice a day, adherence has remarkably changed. There will always be in human nature people who are recalcitrant to adherence. There may be some groups that because of what other things they are going through, make it more difficult for them to adhere, but in general it is not really today in ‘06 as big a problem as it was in 1997, 1998.

FEMALE SPEAKER: Doctor, I would just like to ask about in terms of developing countries like Southeast Asian countries, how much more catch up will they have to do in terms of treatment and prevention, and the role of developed countries in helping them out?

DR. ANTHONY FAUCI, M.D.: Southeast Asian countries, it's sort of very interesting because it really varies widely from country to country, Thailand is a very good example of a success story, Cambodia less so, Indonesia less so. It really relates much more to the leadership of the nations involved than it does to outside countries helping them. Now that we have very inexpensive drugs of generic type or others, the excuse that the drugs are too expensive is still relevant but not prohibitive. The assumption that you don't have the infrastructure to deliver the drugs, I think is based on a lot of misperceptions and Africa and Haiti has proven that to be incorrect. So, when you are talking about delivery of drugs, it is mostly political will. We have seen extreme dichotomies in Southern Africa of countries in which the political will is there and something happens or the political will is not there and you are still dealing with a high percentage of people who are infected and very little movement towards getting them treated, so I would say that the developed world always has a role in helping out the developing world but when you are talking about the question you asked to me, it's more the leadership of the individual country.

FEMALE SPEAKER: [Inaudible] political will in China?

DR. ANTHONY FAUCI, M.D.: Boy that's a big question. The political will of what? There are a lot of things going

on in China, and China unfortunately, and I won't get into trouble with this because I have said it before [laughs], and not gotten in trouble. [Laughter] China is a very, I'm telling people who know more about China than I do, is a very complex country and there has been a history of tardiness in realization of a problem or admitting a problem, and it goes back from the tainted blood supply in China that took so long to get recognized as a real issue in the spread of HIV infection. That was really a shame. You could go to pandemic influenza with H5-N1 where there goes from no chickens infected to a lot of chickens infected. No human cases to several human cases, so although it looks like, as we get further and further towards better openness economically and otherwise, that the situation is improving, but China has always been a bit of a problem in getting the straight talk out at the time you need it. It would have been so important early on to have had proper recognition of the tainting of the blood supply in China several years ago. It would have made a huge difference.

MALE SPEAKER: This has been great. Thank you very much. [Applause]

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[1] kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.