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Jan Sapp's interview with Joshua Lederberg

July 26, 1995 / *Re:* [Ciba Conference on Man^m and His Future]...

L: ..that was my first venture into social commentary, at least published social commentary. And I talked about eugenical issues, what molecular genetics would do for us. I was in a little bit of a debate there with H.J. Muller and with Huxley who were the positive eugenicists, and I was saying it's hard to quarrel with that but why use such a clumsy method and with such uncertain political and social overtones. If there's a problem, the technology fifty years downstream will be so far superior; but what you're proposing that we can deal with it more effectively and let's use the time and the interval and try to decide what it is we really want to do. And that's when I introduced the term euphenics as the counter program to eugenics, at least for the...

S: Why? Because it's at the phenotypic level...

L: Yeah; and a footnote yeah, that's medicine, education.

S: Exactly. It's all the social factors. So this is '62.

L: Yeah.

S: What does Nigel Calder have to do with this?

L: He was the editor of The New Scientist. Yes, I actually did publish a rather hysterical short one-page version of it in The New Scientist - Crisis in Human Evolution, namely. The kind of stuff Sinsheimer was touting very strongly a few years later on. But I was saying, "Look, there's an issue; let's think about it" and a lot of other people said "Oh, how awful. Let's shoot it down". I just wanted to look at it.

At any rate, I bumped into him a couple of times. I think this is the COSPAR, the Committee on Space Research - the international conglomeration of scientific activity of a lot of the non-governmental and governmental efforts in international cooperation in space. They had a symposium in Nice; I gave a paper about the

biologist's interests in space exploration - worrying about quarantine on the one hand which is another cosmic environmental issue; and on the other the positive programs of the cosmos determinants of biology that are around all the time.

[I coined the term exobiology around this time]. And I think I was sitting next to him on a flight either to or from Nice that he approached me and said, "Would you be interested in writing a column [weekly or monthly or whatever] for The New Scientist on social impact of science". I said, "That's an interesting proposition" and I mulled it over for a while. And ... this is a rule of life I'll pass on to you: whenever you're faced with an opportunity, never just grab it; if you find you're interested in it then say, "Look, what do you really want to do with it" rather than what's presented to you. So I followed that heuristic and said, "Look, if I'm going to do that sort of thing, I want to put it some place where it'll have a broader impact than in The New Scientist". And I asked around some friends in the newspaper publishing industry. I would have been very happy if the New York Times had agreed to it, but as it turned out, the Washington Post is the one that was receptive. I guess it was David Hamburg who introduced me to the publisher.

S: And where were you institutionally based when you were doing that?

L: Stanford. I hadn't been there very long, but I got there in 1959.

S: So what's the deal with Washington Post - weekly?

L: They agreed on a weekly column. It's dated - as you can tell by the title - it's called "Science and Man". Didn't have much fuss about that ("sexist") distinctions in those days. And so it went. Howard Simon was my protector there. He was the science editor for the Post, and I needed one because his publisher was constantly badgering him - "Nobody can understand what this guy is saying. What are we publishing it for?" - etc. etc. And he would sometimes protect me from mutilation of my text. He was quite keen on it. The fact is it had a pretty good play, and my target audience were congressional staffs if I were to try to identify what kind of person was I trying to get to.

S: Congressional staffs?

L: Yeah. These are the people who actually read the technical stuff that might have policy implications and pass it on to their bosses.

S: How common is it (this is what, '66?).

L: Yeah. Nobody else was doing it.

S: I was going to say... there wasn't a science reporter or science editorial column for ...

L: I did not know of any working scientists at that time who were making regular contributions of this kind.

S: And later on people such as Lewis Thomas whose book I read recently, *The Youngest Science*, talked about his contract with *The New England Journal of Medicine* and that's '72.

L: Yeah. No, it's the public press that I'm interested in. Morowitz must have been doing it; I don't know when Steve Gould started. But even to this day, there is no regular column of this kind.

S: So how long did it last?

L: About six years. It was quite a strain.

L: Well, '66 through '71. I didn't actually get started until '66. I'd forgotten. It was '64 or '65 when I talked to Nigel. And more and more I got into environmental questions and there was hardly any environmental reporting in those days. So issues... hazards from lead or whatever else just thinking environment and so on - weren't being very much talked about.

S: But this is a demanding thing to be writing. Once a week you're doing this plus you're at Stanford at...

L: Oh, yeah, running a department.

S: And were you also involved in any international affairs?

L: Not as much then as now. And in fact, this did come to some crisis because at one point for example I was asked to serve on the PSAC, on the President's Senate Advisory Committee, and I decided I couldn't do it, that while I was writing a column for public consumption that I really could not be the recipient to confidential information. I would be having to hold things back from a public that would be expecting the contrary.

S: But was this your entry into those kinds of relationships?

L: In some measure. Not totally, but. Yeah, my connections with government up to that time were NIH and NSF study sections which didn't involve broad policy considerations. I might have been once in a blue moon asked on some other commission or whatever, but it was not a regular commuter.

S: And can you measure how successful your series was?

L: It's very hard to say. I keep running into people who tell me that they used to read it and...

S: Actually, I have met lots of people.

L: But when I asked myself, I didn't know how to measure it.

S: Isn't that interesting?

L: But the kind of people we're talking about told me that yeah, they read it; they looked forward to it. I'd get a little bit of flack in the mail and so on.

S: I was going to ask you that. So did you get governmental feedback from these Congressmen that you were addressing?

L: From time to time. I'd get three or four letters a week of response which sounds like it's not very much but when I'd run into people..well, you know: how many people bother to write?

S: Okay. Now, there was something else you mentioned on email...

L: Let me make another point about that, though. This was also syndicated; it wasn't just the Washington Post. It appeared probably in a couple dozen newspapers all around the world. In fact, you may have seen it in The Age in Melbourne. I know it was there for a while. This is just an example.

S: And this raises another issue which is.. on the one hand we have a scientist going into, in effect, journalism reportage but basically bringing the public up to date with current events within the scientific community of things of interest to scientists.

L: And there were very few things I was a strong advocate of. It was mostly, again, "Let's take a look at this. There are some issues that deserve consideration. Life is more complicated than you think, that simple settled answers are likely to be overly simplistic". If I had any meta message, it would be in that

dimension.

S: But what's your other message at the level of writing? What does it say about journalists reporting about science. I mean, did you have a sort of chauvinist attitude of "Here's a scientist. I know what I'm talking about" as opposed to journalists screwing it up?

L: Well, yes. One reason I did this was that (I can't recall the specific incidents, but) I was very disappointed in the way the press ever dealt with anything I ever had to say. And I came to the conclusion if I'm going to be in the press, I want it to be in my own words. I understood their constraints; I had a lot of sympathy with what they had to do, especially when I could sort of do it one day a week and what they do is seven days a week. But I just felt there was a need for that alternative.

So there was some explication of current science, but it was focused on "What does this mean for humanity"; that's the headline rather than a policy dimension of these kinds of discussions.

S: What about your colleagues. Did they look askance at this? Did they say "Here's Lederberg going..."

L: A few did, yeah. Well, yeah.

S: Was it seen as political activity?

L: Yes. It was mixed. And even some of the same people said, "Gee, I'm really glad you're doing this for us" and at the same time said, "Gee, that's not really science, is it?" But I wasn't playing headlines the way that Carl Sagan does. I was not personalizing it in that sense.

S: It wasn't a huge money maker.

L: Oh God, no. No, it was nothing.

S: And so from the point of view of scientists, for you doing this...

L: I had mostly positive reinforcement: "I'm glad somebody's doing it, but it does mean dropping your science, doesn't it?" I said, "Well, I try to walk with two feet".

S: What does it do for breadth? Does it give you more breadth?

L: Let me explain why I stopped. I would read my columns and I

would get even more interested in the subjects that I raised, and I've got a foot of files for every topic that I brought up which might have taken ten columns over a period of a year or two to talk all around a given set of issues. But I would continue my self education and self criticism far beyond the time the thing as published. Well, that's not a journalist's approach; that's a scholar's approach. And I decided in the end that I was a scholar and not a journalist and I just couldn't keep doing that, that I really should go into more depth on the topics that I did want to study and be able to do a better job. So there was just the mental indigestion that was involved. It was close to six years' worth.

S: That's a long time.

L: There were about two hundred fifty columns.

S: Is that right?

L: Yeah.

S: And where are they now? Have you even pulled these out?

L: I've checked my own copies of them. I've had them all transcribed so they're ready for publication.

S: You've got them on CD ROM or something?

L: Not yet; they will be. I've just got them in computer files at this stage.

S: How did you get them into computer files?

L: I had my staff here transcribe them. If I had been more patient, I might have waited to get them scanned and done in that way. But don't kid yourself: by the time you've edited a text like that, you're not very far from the amount of effort required to just type it in in the first place. I think it was not an inappropriate choice. The columns could be scanned by a human interpreter about as efficiently that way as the formal scanning. When you get scientific material, there's an advantage to scanning it in, having the page images on tables and things of that sort.

S: Okay. So this takes you far off the bench, but from the point of view of a bacterial geneticist.

L: Very few of the...well, one in ten might literally have to do with genetics or microbiology. I didn't avoid that topic, but it was much broader. So nuclear policy, arms control.. got kind of excited about Vietnam and wanted to be some voice of temper and campus revolt and that sort of thing. So some of that crept in. But I'd get a little admonition now and then from Howard who said, "Look, we've got a lot of other people who think they know as much about that as you do".

S: Who's Howard?

L: Howard Simon, my editor. It was not a heavy hand, but a little reminder now and then. So he gave me some latitude. But I couldn't go week after week on things that didn't have an obvious centre of scientific and technical expertise. It was my credential for being the one to do it.

S: I know when you sent me the article on the Sea Level Canal, it was quite interesting what you said from the point of view of a geneticist interested in evolution. I'd be interested in first of all the taxonomy of the organisms in the Caribbean before the Pacific Ocean rushes in.

L: Well, there's an analogue to that with planetary quarantine.

S: I was about to say the exact same thing. It reminds me of your story about the moon, when you were worried about the moon being contaminated.

L: Mars is what I was worried about.

S: Excuse me; Mars, that's right.

L: I'd given up on the moon. If we're going to send astronauts to the moon, the moon's going to be contaminated.

S: Well, is the moon contaminated?

L: Undoubtedly stuff has been left there. I'm not sure how consequential it is; there's no atmosphere and it's probably heavily bombarded with radiation from space, so it's self sterilizing in very large measure. But if we were to find a spore on the moon, we'd have to seriously worry that it was not the result of terrestrial traffic.

S: Do you remember when Carson's book came out?

L: Rachel Carson? That was in the late '50s, so it was a little bit before I was responding to...

S: It came out in 62.

S: Did it have a big influence on you when it came out? It didn't go smack right between the eyes with respect to environmentalism?

L: Not to me, but I could see what was happening to the public more generally. It was certainly a major point of arousal. I thought it was greatly hyperbolic, and I thought the toxicity of DDT was greatly exaggerated and so on. The one thing that's come up that we didn't know then is what it does to egg shells and birds. I think that part is indisputable. But I think that's the only part of its ecological impact that's really reliably founded. So I tended to take a quietistic attitude about some of that stuff, but I felt against the vacuum that we'd had before, it was a matter of if the pendulum's gonna swing violently from one side to the other, let's find what some central point might be.

S: Okay. Can we jump now to emergent viruses for a minute?

L: Yeah.

S: I have two questions. I need to understand what happens in '88, what you people are doing in Washington, what the alarm is. And then I have another question which I'd like you to think about and undoubtedly you already have which is "Is there a new paradigm for understanding virus outbreaks that has emerged in the last ten years or less" which seems to be indicated in Morse's book, "Emerging Virus" and things of that nature. I keep seeing pictures of this stuff. There is an ecology of viruses as opposed to killing them.

L: Well, I can mostly give this in a personal perspective which is what you want. I had been exercised ever since I can remember about the hazards in biological weaponry and the subversion of microbiology as military agencies. I was quite well acquainted with the programs that had emerged since World War II. A lot of folks who had been at Fort Detrick during the war were at Wisconsin afterwards; there was no secret about any of that. I felt we had to defend ourselves, but I was appalled at the idea that these things would ever be used. At the time, I didn't think much about terrorists in the lower level activity but more as it's being incorporated into the arms race in the U.S. and the Soviet Union. That's sort of background Item 1. I didn't do much about it during the '50s up to the middle of the '60s.

And 2), I was very much impressed by the outbreaks of Marburg and Lassa fever in the middle '60s, and I wrote a couple of columns about it. I also remarked that this is nature's war and I also connected them with how much more terrible it would be if these kinds of agents were to be adopted as well as BW agents.. So I had a dual program - one at the political level, the arms control aspects of it - and the other is to worry about these emerging viruses. I didn't use that expression at that time. I think the paradigms are mostly rhetorical ones; I think the basic ideas go back a very long time.

In '67 and/or '69 (I forget which one of those it was) I brought this issue up again at a Nobel Foundation conference and didn't get very far with it.

S: What issue?

L: The hazards of emerging viruses. I talked in particular about influenza through recombination. We'd had two major antigenic shifts of flu, one in '57 because I remember that happened when I was in Melbourne -- the Asian flu -- and there was another one in the '60s. And I read up on it, had long known about the influenza epidemic in 1918 and what a devastating impact that had.

Oh, there were seminal books on this. I did medical school, had microbiology and so on, but Hans Zinsser wrote Rats, Lice and History and that's probably the guiding text on this issue. O'Neil wrote essentially the same book a little later on plagues in history -- not much that's different in there. The Zinsser book is really the paradigmatic _____.

S: So as far as the influenza epidemic of 1918, 1919 -- is that what you mean?

L: Well, about the role of plague as a historical phenomenon, that it had as much to do with shaping human destiny as wars had. Then as far as the ecology of microbes are concerned, the books by Dubos especially, Theobald Smith and Mac Burnet -- Mac wrote one on the natural history of Viral Disease I think it's called; it goes back quite a way. It's provided the main intellectual substance of thinking about it and the paradoxes of co-evolutionary adaptation of micropredators and their hosts. The short run is towards higher virulencies through transmissibility - those are pyrrhic victories; and the long run is co-adaptation closer to symbiosis.

Now, I am reminded also of the general background of my interest in symbiosis that you know all about, the 1952 paper and so forth. So that's even part of the background -- the ecological relationship -- which comes under the general heading of symbiosis study.

S: Agreed. But when I look at -- and you mentioned a moment ago -- that perhaps there is no new paradigm but there's a sketch for rhetorical purposes or polemical purposes - but what is that polemic? Is it a polemic that, "Oh, we've killed these damned things"? And our aim is to kill them. And, by the way, if we get reinfected or if there's an outbreak, this is because they're new viruses. And the new paradigm would say your object is not just to kill them, it's to learn how to live with them and the reason for that is that -- guess what -- they may not be new viruses at all and that this is not simply a matter of mutation but a matter of transmissibility; and maybe what we're doing is speeding up the rates of cycles of infestations or cycles of epidemics. Is that an accurate depiction of -- that's what I...

L: I'd have to put at somewhat greater length and more subtly than that. If we could only do it, our aim is to kill them; but they're hard to kill, and that's a huge biosphere out there. I'd calculate there are about a mole of potential pathogens! And those are very big numbers. So you better take that into account if you're going to talk about eradication as a paradigm. I've been skeptical about eradication, maybe overly so. It took me a long time to when I was....

S: Maybe overly so, did you say?

L: Yeah. In some particular context, I was something of a hold-out on Advisory Committee on Medical Research at WHO on declaration that smallpox had been eradicated. And it was okay to wait another year or two before claiming victory on that. It probably didn't do any harm, but turned out...

S: When was that?

L: '81

S: And what did it turn out? Was there eradication?

L: Yeah. It's never shown up again. Now, it still lives in the freezers in the laboratories, and there's a debate going on about destroying them. It may still live in the frozen Arctic

in the old cemeteries, and Sandakcheev is digging them up to see. And I think it's very important to find out whether that potentially exists. I'd rather have them dug up in very carefully-controlled conditions than have it happen inadvertently with unvaccinated personnel and so forth.

S: So eradication to you as a paradigm -- you're skeptical about it because of the impossibility of success and because of the large numbers of variations of these organisms. Is that...

L: I think there are so many ways in which there might still be lurking remnants and quite apart from the issue about reformation, *de novo* from its evolutionary progenitors that... There's a tacit assumption of special creation that public health people have about infectious agents. They really have not understood their continued evolutionary process. The ease with which they talk about the Great Plague of the 14th century being *Yersinia*. Okay, maybe it was. I wouldn't guarantee it. But they don't have another category to think of it. And if it is *pestis*, what's the identity, the strains and so on and so forth? But I've been working on microbial evolution all my life, so the idea of plasticity is one that I'm much more deeply imbued with.

S: And is it the plasticity of the viruses, for example, that makes them so difficult to eradicate.

L: Yeah. Well, the whole set of issues. We don't have good chemotherapy for them. They're easy to eradicate if they have unique hosts, and that's what makes smallpox almost a unique paradigm; there's no other known host for it nor another reservoir for it. Maybe the same will be true for polio. So far, that's worked in the western hemisphere. What we will do if we're smart is to replace virulent polio with Sabin polio and have that still circulate as an essentially innocuous attenuated virus that will get around a little bit so it isn't only the inoculated individual who gets the benefit of it.

S: Does it make sense to talk about -- as in other kinds of invasions, not the kind of invasions that Elton talked about in terms of the transmission of plants and animals by humans like the zebra mussel kind of stories but -- other kinds of, let's call it, naturally occurring outbreaks? Does it make sense to talk in terms of virus outbreaks in the sense of cycles, thousand-year periods of cycles; where are we in this wave? I mean, there's a way in which one speaks about....

L: I don't know why there would be a thousand year cycle. I could

imagine there being a fifty year cycle having to do with immunity and that certainly has happened with flu. So an outbreak leaves survivors with a very high degree of immunity. Until those have died out, you're not gonna have a fresh wave. But that's about the only basis for any cyclical behavior that I could visualize and that implies that there's some continued reservoir, either in an animal host per se or recreation through regeneration.

S: But if you talk about an ecology of viruses, how can you talk about for example -- and again, comparing it to other kinds of invasions where we may argue, "Well, we may not be causing these outbreaks but we may be increasing the frequency of recurrence of these outbreaks"...

L: Oh, human behavior has a lot to do with opportunities of viral spread. A lot of people want to pin down all the awful consequences of capitalism and so on. I say, "Yes, and there's one outstanding one and that is people travel a lot and to an unprecedented degree". And the statistics I throw out is that a million people a day fly across an international boundary. A million people a week travel between developing and advanced countries. That's a new fact in human existence. I don't think we need to go into climate change or... I think the other matters are all trivial by comparison.

S: So does that have any evolutionary.....

L: ... their rather poorly-regulated mechanisms for adaptation and above all the immense population numbers, even with very low mutation rates. When you've got a mole's worth of bugs, that's a lot of opportunity for variants. So the issue is, then, do they find their host and once having found them, will they have a good opportunity to spread.

S: Yeah, exactly.

L: The human population, first the total numbers of the population and then the hosts that are available and the way they stratify. And these convocations of very large numbers of people live in very crowded conditions, very poor hygiene; you couldn't design a better setup for new outbreaks to expose. I think, I'm certain that will happen.

S: I'm asking for a little biology lesson here which is about the notion of virulence. As I understand it, in the 1918-19 pandemic, one of the reasons at least that people are giving in the 1990s in reconstructing those events for the increased virulence was

the frequency by which this virus could be transmitted because of the trench warfare, because of people going back to their towns and villages, that this is going to have an evolutionary impact on the organism itself, using a sort of game theory to account for...

L: When there are fresh hosts readily available, there's likely to be selection for enhanced virulence as it goes along. Just as in standard Darwinian theory... as long as the hosts are there and as long as the first host doesn't die too quickly but there's a nice balance on that score, you can expect selection for more rapid replication. The virulence is sort of a side effect. For a viral pathogen it's sort of indifferent whether the host lives or dies. In fact, it's to its disadvantage if the host dies as opposed to a bacterium, by the way. Bacteria can multiply in putrefying flesh; viruses cannot. That's a severe limitation.

S: What does virulence mean?

L: Virulence is an operational term; it's a black box. Virus in, disease/death out. And just think of all the considerations involved.

S: I see. Okay, so does it mean...

L: It's everything involved. Ease of transmission, rapidity of replication, side effects of formation of toxins, disabling of the host's defenses -- you have to include drug resistance plus the de facto situation of that black box is that drugs are going to be thrown at it. So you think what are all the defense mechanisms and what are all the things that keep the organism capable of coping with the virus. So you really have to think of it in those operational terms.

S: Okay.

L: It's generally correlated with rapid multiplication. A virus that multiplies slowly is not likely to be virulent just because there would be less of it around.

S: Right. So can I assume, then, logically that with the speeding up of the transmission of viruses that you were speaking about a moment ago with a million people crossing borders per day that we would then be enhancing a virulence of viruses?

L: It's a second order effect, but it provides the setting in which that evolution is more likely to occur. Where you will start

limiting those selective forces is if you run out of hosts. Then there's no new place for a virus to go, there can be no selected drive for it to enhance its virulence. Then those viruses which last longer than the host of origin are the ones that are going to survive, and that's less virulence. The ones that don't kill their hosts -- and this is what we see with AIDS -- the virus is going to be there ten years later. The ones that kill their host promptly -- the host is dead, the virus is dead. So that's why there's a paradox in the evolutionary trends. The short run will tend to favor rapid multiplication and what goes along with it; the long run would tend to favor a more symbiotic/mutualistic relationship.

S: A classic dilemma.

S: Let's go to 1988, then. In '88 you're talking about what, the AIDS pandemic; there is new cholera; there's lots of emerging new viruses. What do you people do? Is that what you...

L: Okay. Again, you're asking that at a sort of personal level. I didn't publish it. I was one of the very first people... when the initial report about HIV and I had this conversation with Igor Tamm in biology. He said "It's gotta be a virus". There was a lot of skepticism about it at that time; we even thought [amyl] nitrite would help it and so on. I remember talking about this with a number of people and saying, "What would happen in its further evolution" and so forth. But I don't recall my having gone public with it right then.

S: Public with what?

L: My concerns about the further evolution of AIDS. Then I was invited to appear at a symposium that was organized by the New School for Social Research on plagues. And I think I sent you a copy of this. If not, do you have "Pandemic as a Natural Evolutionary Phenomenon"?

S: No.

L: I'll get that for you right now.

S: What year are we talking about?

L: Let me look at it. How I came to be invited.

S: What was January '88?

L: That was the conference at the New School on plagues. And I

talked just to that title; I gave that ecological genetic evolutionary picture.

But AIDS was the central aspect of it. I don't recall if I had written anything ... this issue of Social Research has several other very interesting papers in it.

S: May I have a copy of this?

L: Yeah. Oh, but there's a place which could confuse you if I don't correct your copy. There's a typo with "antibodies" instead of "antibiotics". I refer here to some of the columns that I'd written on the same things, but I'd been fairly quiet about it for about twenty years on this particular topic. And it was AIDS that sort of brought it back to me. It was sort of "Okay, it's happened". I hadn't guessed that it would be as insidious, the high latency kind of aspects in this multi transmission. But new bug had come out of Africa and it was devastating".

But I sort of left it at that. But then Elie Wiesel organized a conference of Nobel laureates; I think that was also in 1988 in December.

S: What is this person's name?

L: Elie Wiesel, the poet of the Holocaust. That's when I got to know him and I've gotten to know him very well since then. And he had the illusions that the Nobel laureates, of which he is one, were all such wise and human people. And he wanted to collect them to make some statements about how the world might be better through good thinking at the time that some of them might have to offer. I cautioned him that it wasn't going to work out quite that way.

S: About what?

L: No, about Nobel laureates. But he was committed to it. There was certainly a lot of hoopla. Francois Mitterand who was co-sponsor with the Majesty of the French state was -- part of it was held at the Elysee. I sort of wondered, "Well, what could my contribution to that be?" I said, "Okay, I'll pick up this and I'll talk about it". And I wrote a somewhat more passionate version of this paper which in the end was published in JAMA. A medico, a close friend of mine who is a physician, made that suggestion -- an inspired one. And it was more of a column. I read it and I said, "You know, Josh, it's time to make an issue of this again. This is serious business. Nobody was paying much

attention to you twenty years earlier, but they will now". And that's sort of the genesis of my own current involvement.

I ran into Steve Morse at one of the cocktail parties at the President's House, found out he was interested in similar matters and told him I would back him up very strongly if he wanted to organize a conference on it. So he talked to some of the folks at NIH and did organize that first conference in Washington on this. We got some virologists in the country and a few biologists from elsewhere.

S: What is the theme?

L: Is there a problem with emerging infections. I think that's where he started.

S: And what to do?

L: Not quite.

S: So is there a problem? What does that mean? Are we speeding up the process of infections, or are there going to be more of them?

L: Well, just what's there. A threat analysis. Some discussion about the ecological historical background of it, but I needed to get some credibility that AIDS was not just *suigeneris*, that there were people in a wide range of other areas of virus research who felt equally troubled. And I found plenty of them. The only rhetorical exception was Howard Temin. (I'll explain that in a minute); they all spoke up very strongly and the gist of it was, "Yeah, the bugs I've worked on really trouble me a great deal. I'm really interested and impressed that all of you other specialists and all of your other favorite bugs have exactly the same feeling. The aggregate is something we really ought to be concerned about". I've never gotten that kind of scientific consensus because the mood until then was roughly, "Yeah, we take the terrible vaccines, antibiotics and so forth" and there are many quotes from the 1960s that infectious disease had been conquered. So this was the counter manifesto -- "No, we have lots of problems". But there had never been an aggregation of those kinds of scientific interests.

S: So what are they? There's not just the viral outbreaks; there's also bacterial plasticity, which antibiotics aren't working.

L: Yeah. The major element of virulence in bacteria to be concerned

about is antibiotic resistance. The selective pressures there are enormous, and I think we see that happening but not nearly as obviously and overtly. We only see these new cholera strains coming along, in the Shigella toxin showing up in E. coli, strains like the so-called E. coli 0157; we have other instances of it. But antibiotic resistance is just happening all over the place.

S: So '88's just taking inventory. So now there's something called "germs are back again" in the sense that it's a _____ term, and the question is taking inventory of how many of these kinds of problems do we have.

L: The first conference in Washington was "Is there a scientific base of concern" and the answer was a resounding "Yes" with a lot of detail about individual areas. Howard Temin was the only one who spoke up and said (well you interpret his terms) "Well, maybe there's a problem but we oughtn't to put it this way. We're gonna get very inhumane treatment of people who are carrying HIV if they are pictured as being threats to the rest of the community, so let's play that down entirely.

S: Play what down -- play AIDS down?

L: The possibility of further evolution of HIV. I was just raising an issue for analytic inquiry -- what could happen in its mode of transmission, could it become more rampant and contagious pariah. They're close enough to being that already. And I said, "Look, I know the empirical evidence as well as anybody. I feel greatly relieved about it, but I think there ought to be more research on what are the barriers to person-to-person transmission by aerosol", and that's never been satisfactorily answered. There is still, I would say, a flimsy empirical basis of confidence it's not spread that way.

S: What about ebola? When was ebola outbreak in Zaire, the first one?

L: In '67. I don't know if I brought up ebola in my columns. I did Lassa and Marburg which were the analogues.

S: Why I mentioned ebola in that note is that with ebola, you have quarantine; in AIDS there's never a quarantine. And if you use AIDS as your benchmark of what's politically correct but sensitive and so on, it could be very dangerous to.....

L: Well, we knew about person-to-person transmission with ebola

although with the most recent outbreak you wonder how much of that was contaminated needles that would have been the same with HIV. But the overall epidemiology of ebola does suggest that isolation precautions will make a big difference in transmission whereas with AIDS, we talk ourselves into the view that if you avoid needles and if you avoid unsafe sex that you're perfectly safe. And to a reasonable approximation that's turned out to be correct. But there is more that we don't know than we do about ebola, we don't really understand how readily it is transmitted but it does look as if infection control procedures have worked so quarantine has been justified. So it's an isolated outbreak. If we knew that there were twenty people suffering from AIDS and that was all there were, I'd have no hesitation about quarantining them. I'd say, if that's the way to contain them, even if it's only a question of sexual behavior that is involved. Of course, when you have tens of thousands/hundreds of thousands....

S: And worse still, isn't there the period of incubation when a virus is latent.

L: Yeah.

S: whereas you're not going to tell whether or not they're infected until after...

L: and conversely, it has to go on forever, so saying "We're going to isolate people for three weeks and if they're still healthy and well, we are going to let them go at that time.

S: No, but wouldn't it effect the virulence of the AIDS virus through quarantine? Isn't the virus gonna mutate and say "Okay, this is a bad strategy to kill these organisms"?

L: If I deprive it of new hosts, it can't get very far.

S: Right. But will it change substantially the structure of the DNA in the virus by doing that eventually in any ecological time?

L: The structure of the DNA will change to the extent that it's able to proliferate.

S: But what time frame do you think of when you think of that?

L: We must be talking about something other....

S: No, no. When you talk about the mutation rate or the increase of virus through quarantine or through lack of quarantine, what kind of time frame does one think about when you think about the plasticity of viruses?

L: The purpose of quarantine is not to first order, to modify the evolution of virulence; it's to keep it from getting out from those people who have been infected and spreading into the wider herd.

S: Correct.

L: If you had substantial spreading into the wider herd, that by itself is likely to provide selective factories that will enhance virulence, so it has to do with how many passages are there. So at the end of ten or twenty passages of one individual to another to another to another, I would expect there would have been enough selective pressure...

S: That's what I'm asking.

L: ...to be surprised that there is no enhancement of virulence.

S: That's what I'm asking. So ten. I didn't realize that; that's fast, isn't it?

L: Well, it's only ten passages, but think how many generations there are within a given host. Twenty generations in that host...thirty.

S: Now, in '88 you mentioned the sensitivity of the AIDS issue. What about Cassandra? Was there talk about "What do we do, how do we behave once we determine that maybe, okay, there is a problem. How do we speak to the public about this, how do we speak to agencies and..."?

L: Well, I was loath to talk to the public about theories of AIDS changing its mode of transmission. My message was to the research community, saying, "it's important to rely on shallow empiricism as the basis of our conclusions". I didn't want to entangle public reaction. I'm still a little more cautious about that, but on a very narrow balance if you want to get some sort of action you have to talk to the public. But I sympathize with a lot of what Howard had to say. I wanted any action to be effective action and not hysterical.

S: But did you have effective action?

L: It's only just beginning, but I'll give you the latest on that. Here, you can take that. It was just issued yesterday.

So anyway, after that first Washington conference, I then thought, "Okay, that was much more successful than I anticipated it was going to be. We've now gotta move towards what are we going to do about it". I wanted to see this done in stages; I wanted to have absolute certainty about the credibility of the threat before going any further. And even with Howard's caveats that it didn't apply to other viruses and so on, I was very gratified. And had a lot of bolstering from my colleagues there and so on, so I didn't feel...

S: How many people there?

L: About fifty.

S: And did you pay your own way to go there? Or any agent sponsoring the committee?

L: I think the NIAID took on the expenses of it and so on. Now if there's a political agenda, this has to do with the justification for that particular agency. People like Tony Fauci worry that nobody cares about infectious disease any more; we'd have all the microbiologists in the world worrying about the rice bowls, so I can't deny those kinds of factions.

S: Sure. Everybody's got to win here in order for it to work.

L: But I don't think it contaminated their scientific judgment on this point because say, you know, ten years earlier they weren't thinking that way.

S: But it would certainly give them some motivation to attend and to

L: Right. So the next step then was to try the Health Sciences Policy Committee of IOM and I brought up a whole policy orientation.

S: What's IOM?

L: The Institute of Medicine. That's the principle organ for health policy pronouncements of the National Academy of Sciences. I'm one of the founding members of that. In fact, a little story on that. I have to dig up my files (I can't find them), but I think I invented it and I did so when I was on President Kennedy's

health transition team when he was first appointed. At that time, The AMA was the only organized vehicle for professional expression on health policy matters, and it was totally dominated by practitioners; and academic physicians sometimes had very different views; before Medicare and things of that sort had come into place, really had no place to go, and I said "Let's have a national academy of medicine as part of the NAS complex", so that we'd have an authoritative group that could talk about health science policy and so on.

I don't know if there's a direct continuity. That was in the report we gave to Kennedy. Wilbur was to be Secretary of Health; he was the chairman of this task force, and there were a lot of conversations. And a few years later the Institute of Medicine was born at the Academy to do exactly what I was proposing and has been fairly effective in that role. The AMA's come a long way since it's inception. It had monopolized the lobby on health issues and they had done a lot to hold things back.

S: So this another politic. That's right: whose jurisdiction is this?

L: Correct. That was as political as I ever got when I worked with Kennedy during that month or two, on the transition team. So I am reminded I wasn't totally insulated in those things.

S: Is infectious diseases normally the domain of the AMA or NIH?

L: Well, NIH is the research aspect of it. This wasn't an issue for the AMA at that time. At that time health policy had to do with government role in insurance, Medicare in particular and things of that sort.

So back again here, so to explain the IOM -- the IOM was the constituted body. I knew I could get authenticity through that. I was named chairman of the Task Force, but I insisted on having a co-chair, someone who already had an established reputation as a virologist which I'm not. And that was Bob Shope; that was a splendid choice. So he and I co-chaired it. He was head of the Virology Unit at Yale at that time and knew more about all the viruses than the rest of the world put together and that actually.

S: What's his name again?

L: Bob Shope who had an impeccable scientific reputation. So we

labored for a couple/few years and came out with this little turquoise book on emerging infections report. Have you got one? I hope your library has it. It's deemed to be a scarce collector's item at this point, but I'll show you what it looks like. Information on specific organisms and how to find out more about them and so on. That's become...

S: The way you describe this, Josh, it's very, very rudimentary. All you can say is what you do so far -- correct me if I'm wrong -- in the late '80s and '90s is taking inventory of what we've got out there.

L: This is a set of policy recommendations, step by step, and I still held back the way I guided the committee and said "Let's be very careful about assigning tasks to specific government agencies. Let's drive this to what are the things that need to be done but don't tell people in government how to go about it because then you get into all their turf fights". I wanted to have an absolutely solid ground, that there's something we've got to pull together and agree on that there's a threat or a few measures to be taken and "then we'll work on the organization of it". And I think that was sound advice, as a matter of fact. This nailed it down for sure, and this has been cited over and over and over again. You'll find it repeatedly cited in this document, for example.

S: Okay.

L: So the next stage (Let me get one more document).

S: Emerging Infections Book: Microbial Threats to Health in the U.S. Institute of Medicine published by the National Academy press in 1992 and Lederberg and Shope are the editors.

L: Ultimately it starts getting out of my own hands as it had to do, and this is the first government agency to respond. And this picks up immediately on the IOM report. It's an outline of what are they going to do about it. Now, that's only a piece of the problem. This has to do with public health measures, surveillance, diagnosis, monitoring; it doesn't cover the vaccines, doesn't cover the health care aspects of it. It's very limited in the international side of it. But the background of that is the astonishing degree to which that kind of public health activity has deteriorated over the last twenty or thirty years.

Basically what's happened is the budgets are flat, states are

poorer and so those are going down. And then the special problems of AIDS and TB have gobbled up what's there, so about 60% of their budgets are devoted for monitoring and surveillance are devoted to those two diseases. There's nothing left over for a systematic inquiry of things like "flesh eating streptococci" and so forth. Basically no good statistics on things like that. We don't know if that's an emerging disease or not.

S: Fascinating. So how do you do benchmarks" Is there long-term monitoring for other kinds of....

L: Well, they're trying to set up systems to do that, and it takes a little money; not a lot, but CDC may have gotten --I'm never clear how much is gonna be taken back overnight -- another \$6 million to set up more comprehensive monitoring for a wider range of infectious disease conditions.

S: Worldwide monitoring?

L: No. Mostly U.S. We actually heard yesterday. Here's an extra copy of that; that shows you the current status of these activities. That's in the U.S. alone. So the next stage is the report I just gave you - that's as I said - this is now elevated to a broader federal inter-agency activity, and I've played some role in knocking on doors and trying to provoke some further action and interest. And that report has just come out. And now the agencies have gotten together and they decided on a division of labor and what things they would like to do, so I didn't have to get into the turf fights. They argue it out by themselves.

S: Okay. In terms of base lines and monitoring, in your first meeting in '88 -- as you described it to me at least -- the quick and dirty was that it was very easy to do in effect of this polemic with people in the '70s who said, "Look, we've eradicated all these diseases". And so if your base line is zero in that sense of ... then you can talk about, "Well, look. We now have a serious problem". Is that right?

L: No, I don't understand what you're saying.

S: Well, how do you know if you have emerging viruses? How do you know if there's increase in epidemics?

L: Well, some things are so spectacular you can't avoid it; some things you discover by happenstance, like what happened with

hanta virus in the southwest. It's been going around for a long time and you didn't know that this was emerging as a distinctive entity, but a very shrewd internist remembered that there had been another case just like it and guess what? It was the fiance of the person he was treating right now and he said "Oh, we've got something alarming on our hands. A very sudden progression of disease in young people. They come into the hospital, acute respiratory distress and twenty-four hours later they're dead." So then you get into all the machinery: okay, what's the agent; you pull in the PCR stuff and you identify the virus. It's called Hantavirus but there's a new syndrome connected with it. So now suddenly we have a new emerging entity, but that's by recognition of something that had been going on for some time before.

S: I see.

L: But it's by happenstance. And so you say, "How many of these things are going on? We don't filter the amount of the noise. And we need to do that if we're going to advise people. Now the CDC issues an advisory to people living in suburbia, because we now realize this virus is in total of the United States. You be very careful how you handle rodent droppings. They might well be contagious and there have been at least a couple of cases that have been clearly identified - one here in New York -- from that kind of a source. So where is Hanta going to go, I haven't got the foggiest idea. It's all over the mice, all over the continent. You ought to be thinking about that in Canada too, by the way; no respect of that boundary. So far nothing observed in the natural history of the mice that they get any disease from it. And quite sporadically it's showing up in people who have been in contact with them. It's obviously readily transmissible from mouse droppings to people. What about human droppings to people and other effluvia things? We don't know anything about that. There's no known example of secondary transmission person to person, but we don't know why not.

It has the favorable aspect that it's a rapidly-fulminating disease so these people don't stay menaces very long. There's a very short interval of potential of transmission.

S: So what does monitoring mean in this context? Does monitoring mean once you've set up long-term monitoring, does it mean measuring increased numbers of different kinds of outbreaks?

L: Basically that's correct. And then if you don't really know

for sure what's causing them is to do the not so logical work so you can figure that out, so you can provide a proper taxonomy. That's not just to make tidy pigeonholes. I suppose different disease entities.

We could institute quarantine; a legal base does exist. Peggy Hamburg has invoked it. She's the Commissioner of Health Care. By the way, that's David Hamburg's daughter and that's David Hamburg over there.

S: She's invoked quarantine?

L: For people suffering from TB who are not compliant with medication and who therefore remain infectious. She's locked up a dozen of those folks and keeps them in an isolation ward and pumps medication down their throat until they are no longer infectious and then lets them go out and they're essentially on parole at that stage. For TB, the legal authority for that has existed, and she could call an emergency for any other disease that would warrant it. And could actually get by even the civil rights advocates and so on. I mean, they do recognize a threat to the community. The difference with AIDS was that with AIDS, you couldn't do anything to help them and it was very ambiguous whether quarantine would make any difference. I mean, as long as sexual transmission was the only issue and we don't at this stage use quarantine to control sexual behavior.

S: Right. Now, you've never - especially in terms of your advocacy in political roles -- been someone to shy away from public controversy and political action. In most outbreak stories what I've been noticing is a trend, especially as I interview scientists who, (in fact I can document this) have been very reluctant to get involved in doing outbreak research because of it's political nature. That is to say, especially when governments get involved, is it a natural occurrence? Is it anthropogenic? Or, as I could imagine in the case of AIDS, is it....

L: That's not my experience. I know any number of people who would be more than happy to do the research. Getting funding for it has been more the issue, getting support for it to happen. And there are other political obstacles, getting across those boundaries.

S: I'm thinking of Cassandra. I'm thinking of what happens to you.

L: I think we've passed that at this stage. I think that's one of

the advantages. I mean, you can't talk Cassandra when you've had this group coming out with that conclusion. That was the whole purpose of doing that.

S: You did mention to me on email once that you indeed experienced Cassandra.

L: Yeah, that was in the '60s.

S: Oh, it was in the '60s. So in the '80s there was no..

L: In the '80s when I brought up the possibility of airborne transmission, I had a few folks decrying it saying, "Why do you want to invoke public hysteria and so on", I reminded them I wasn't talking to the public. It did spill over. I couldn't totally exclude reporters picking that up. Whenever I had the opportunity I would say, "Look, that's a research agenda. There's no evidence for airborne transmission. It's a hypothetical thing to worry about in the future" and I did try to lower the profile on that. It's a tightrope -- trying to say anything about it addressing one community without fuelling the kinds of things that Howard Temin was worried about. He was willing to go much further, and I think suppose what I think he actually believed of because of what he thought were social distortions that would come from scientifically-accurate statements.

S: Can I raise one other conceptual issue? I know you've got other things to do, but this is something I see pervasive in the outbreak stories I've looked at that which is this anthropogenic versus natural argument. And that, it seems to me, seems to exist against a backdrop of something called The Balance of Nature. That is, if there is...

L: Yeah.

S: So does that play out, does that have any meaning with respect to viral outbreaks, is balance of nature -- checks and balances -- and somehow if there's an outbreak we've caused it; therefore (that's what anthropogenic means)..... does that paradigm work?

L: Well, I think different communities take a different view of the matter. I have a lot of environmentalists begging me to come along with them and say, "Well, one of the hazards of climate change is going to be viral outbreaks".

S: Yes, yes.

L: and I can't go along with that.

S: Are you serious? When did they come up to you and say this to you?

L: There are a couple of conferences being organized on it, there have been in the past. I was down at the Smithsonian a few weeks ago.

S: This is fascinating.

L: So everybody in the climate change area is eager to recruit this, and there is going to be health impacts with another change coming up in a couple of months. It also came up -- I was on a climate change review group when climate change is the center of activity. I wrote a section about infectious disease impact. I said it's unpredictable. I said there'll be changes in precipitation, there'll be changes in vector distribution. Some places may dry up and have fewer; other places may get wetter and will have more. But that all of these effects in my view were quite small relative to the dominant ecological change which is happening over that time scale, and that's the human population.

S: I see. And transportation.

L: And I continue to hold that view. I can't deny there'll be some effect there, but it will be really second order. And over the time scale we're talking about, we should have the technology of vector control. So it's not high on my list of either the source of worries for infection or why we worry about climate control.

S: It seems to me that it's a more generic argument.

L: Yeah.

S: Against why be so concerned about global warming. There are more immediate things that are going to get us before that which is over population.

L: Now, there are anthropogenic diseases well known. I guess the snails in the Aswan Dam (and Schistosomiasis) is the outstanding example, so we know those kinds of things can happen. I'm probably more conservative on this than most of

the people who have working on this issue with me, but you'll see Argentina arena-virus when you have agriculture moving into forested areas, those sort of zones. Jungle yellow fever is an outstanding example of that. So those things happen. But I don't think they begin to compare with the sheer issues of travel and density, even there.

S: Okay. You took my question in a different direction than I wanted to go, but I'm glad you went that way. What I was thinking was that if you talk about something anthropogenic in terms of outbreaks, you've got to have a baseline. Is the baseline no epidemics? Is the baseline the world is now balanced and that somehow when humans knowingly screw up that balance? Does that model work for viruses?

L: Well, I don't believe it for a minute. I don't think nature is benign. In that regard I think nature has a lot of warring constituencies. Balance may be the ultimate outcome, but balance may be the disappearance of some species as a part of that outcome, and I can't guarantee that won't include us. I used exactly that expression. So I think that's totally unpredictable.

S: When you say that, is that a polemic?

L: Yeah.

S: Why? I know coral reefs are a beautiful place to look for this because in coral reefs you think of them as checks and balances that have evolved over ions; therefore when you see an outbreak you say "Oh, anthropogenic".

L: Okay, I'll epitomize it. I think I may have asked you already. I've been very struck with the phrase that man is a man-made species, and I think that probably captures most of the rest of it. Of course we're out of balance; we're intrinsically out of balance. Population more than 5 Million Homo sapiens on this planet generates an enormous imbalance, and we'll never recapture it.

S: Okay, I understand that. And that's in a different sense of what we're talking about, though. In respect to coral reefs in the '70s, people wake up and they dragged Darwin's book out and said "Guess what? Coral reefs have never had a complete "balance of nature". And the whole polemic against something being natural, something that's anthropogenic is "First let's get rid of the paradigm - a balance of nature -- because that's garbage.

There never was this balance of nature". This is the myth upon which you...

L: I wouldn't go so far, but I don't want to mix a balance of nature with a preferred status of Homo sapiens. A balance of nature might exclude Homo sapiens.

S: And the balance of nature may be over a period of time, that is geologic.

L: That's back to the man-made species again.

S: What do you mean by that? It resonates in my mind in a different way. What do you mean when you keep saying that "Man is a man-made species"?

L: The current status of the human condition is much less a consequence of natural evolution than it is a cultural change.

S: In that sense, we're controlling our own evolution to an extent.

L: Well, control may be too strong a term. We're unwitting pawns of social and cultural evolutionary processes as much as an actual but biological evolution plays a relatively small role at this stage. And there's as much difference between homo sapiens of 20,000 years ago and homo sapiens today as there is between other homo species.

S: When studying outbreaks, I understand when debates are what is anthropogenic and what's natural, people usually try to find a pristine system in which humans haven't intervened and say, "Okay, that's the baseline upon which we can monitor?"

L: I don't believe for a minute those pristine circumstances rendered those people immune from pandemic crises.

S: That's my question.

L: Of course not.

S: Okay. So there's no, I mean, these viral outbreaks, in your mind, are working consistently in evolution. And what are we doing - enhancing the frequency of outbreaks?

L: The density of the human population more than any other factor is doing that.

S: Okay. You mentioned to me one time about four years ago.

L: We do other things as well. We invade the forests, we expose ourselves to the Zoonoses and the vector borne diseases and from those sources as well. There are people who point to antibiotic resistance and say, "Well, we shouldn't use antibiotics". Of course, that's crazy. You're going to deny yourself the advantage of it? It won't make any difference whether they're resistant or not, under those circumstances let's try and find a balance - the most effective compromises that you can make to optimize whatever measures we can take that will protect our health.

S: And that's good for the individual, maybe bad for the species and vice versa.

L: That's right. There's the commons problem very seriously.

S: What do you call it?

L: The problem in the commons.

S: Exactly. Tragedy of the Commons. You mentioned to me and this is something that preyed on my mind since I last saw you -- which was when you were talking about viruses as modes of evolutionary change and you said to me that you thought the chances of a virus doing something that may be adaptable to the organism would be equivalent to throwing a dart into a computer.

L: Yeah. I would have said that about mutation. It's the same paradigm. I guess that's right. I think I have to temper that a little bit; I've learned a few things since then. Above all, I've taken Kimura very seriously about drift in evolution. Most darts that we throw into our computers don't do anything -- change nucleotides with no consequence whatever. The other as a lot of evolutionary change involves systems a little bit more highly integrated than just random short circuits, that we have modules. The individual exons to be even more precise about it -- being tried out in various experimental configurations. So a lot of genetic experiments are a little bit more structured than that, I think.

S: Okay. When you talk about the ecology of viruses -- this is again, give me a quick biology lesson here -- what is the predator of a virus? Can you talk about predator relationships

in terms of viruses?

L: Nobody keeps viruses to their advantage. They don't have that much flesh on them. So to that extent, it's more a question of defending yourself against them rather than getting any positive advantage from them. So there really is no predator.

S: Does that make them unique among....

L: Pretty much.

S: It takes them into...

L: There's an iota. There's a little bit of DNA in a cell that manages somehow to defeat that viral DNA maybe incorporated _____ a few nucleotides, but it's just so trivial. The selective factors involved in relationships with viruses really have to do with defense. That's why there is... selfish DNA show that's the case. If that DNA can get past the point where it's either a threat to the host ... a lot of the DNA that we have in our genome is living there essentially as innocuous passengers. It isn't costing very much.

S: But where does it put them in ecology? At the top of the food chain?

L: That's a good question, yeah. The answer is yes. In fact, I wrote a little piece called "Crowded at the Summit".

S: Are you serious?

L: Yeah. I'll get that out for you.

S: Please.

L: And it is the food chain. They're not anybody's food in any significant fashion and the....

S: So it's hard to play. I'm thinking of an insight that has been used now to understand outbreaks, mathematical models for catastrophe theory that are based on predator relationships. These kinds of modelling then, well, when I think of outbreaks from a metascientific point of view, I'm looking at the structure of the controversy, the problems that scientists have in conceptualizing what counts as evidence-- is this just new techniques for measuring for something or

is there really a new phenomenon here -- all those kinds of of methodological and meta problems. So I can see them as being very similar. But if I look at the modelling aspect of viruses, I'm wondering why (in the same problem with symbionts) and if viruses have to be considered differently than, say, understanding zebra mussels in the Great Lakes, understanding the invasion of plants and animals that Elton was talking in his '57 book which was a brilliant book on how each species....

L: Well, they are different in detail, and I think you and I are very familiar with those differences on they're not food, and two they can enter into intense symbiotic relationships. And I startle people by telling the story of the mitochondria, the parasitic bacteria that ended up in us. It goes back to another paradigm. I said it comes from Van Neil, but I can't verify that. People who hate microbes will learn about them than people who respect them and may even love them.

S: Sure.

L: And that again is learning to live with them, I guess.

S: But -- and this goes back to the paradigm business -- and I'll keep looking at it -- it's something that you see is much more continuous with understanding viral evolution, viral ecology.

L: Well, maybe I remember texts that other people have forgotten. Theobald Smith had pretty much said it all, and then Dubos followed it up.

S: But this is all autobiographical; this is your continuity.

L: Yeah.

S: There may not be a continuity in a population sense of the visibility of the problem, the way in which one thinks about the problem.

L: Oh, I think that's absolutely right. But I think the public perceptions were that we had taken care of infectious disease and there was a twenty-year gap and now suddenly they're back again. How come? Some mistrust of science, and we must have messed it up with the anthropogenic ideas and so forth.

S: Well, I was looking through and twenty years ago an expression

like "viral ecology" was an oxymoron. I mean, it seemed like virus.

L: I can't buy that.

S: No? Okay.

L: On a technical level, I think Burnet had come in very readily - the Natural History of Infectious Disease.

S: Well, there you go.

L: There wasn't enough of that. A lot of gut feelings were not being well informed by those kinds of discussions, but there was certainly a level of discourse that tended to operate there.

But I'll go back to another point that almost contradicts it. In the public health community, bugs were products of special creation.

S: Exactly, exactly.

L: They were not thinking about evolution.

S: So what's new here? What's new here may be the actors who are in the front line making policy such as yourself as opposed to this.

L: Reviving an evolutionary perspective.

S: Correct. And maybe putting this evolutionary/ecological perspective in the face of medicine and saying "Now deal with it".

L: That's correct. The people who study infectious disease in departments of medicine have very little by way of evolutionary background. In their thinking they've learned a little bit about it. They had to with drug resistance and plasmids and so on, but yeah, I gave a talk on the future of infectious disease, and I have given out what I would regard as the most simplistic discussion of these evolutionary considerations. I did this for the Infectious Disease Society of America. It got raves -- "Innovation, illumination, insight". I was giving what I regarded as baby talk. It's what they needed.

S: Who are these people -- the infectious disease people?

L: The people who manage infectious disease at the hospital you go to.

S: Right. And when you talk about them thinking in terms of special creation, you're talking about that every virus is a new virus.

L: Mm huh.

S: They don't think of continuity.

L: No.

S: And they don't think of all those things that we were talking about.

L: That's right.

S: So this is what I'm saying -- so that when you come into this domain with these new books of emerging infectious and emerging viruses, it's new for me and I remember when I picked up Morse's book and a whole series came out on the evolution of viruses -- not the Coming Plague. I think that is more just a....

L: That's journalistic.

S: Yeah, exactly. But the others say "No, there's something new here and it's literature". There's something new in terms of maybe what I'm detecting is who's speaking. And also this sounds like evolutionary biology now, it reads like biology, finally this is what Dubos had argued long ago in the '60s with the virology people, "your poor cousins in the mansion of pathology." Why don't we get some biology of these things and study the natural history of these things.

And this is something that needs to be studied, then, is how people that do get the power to come in and not end up in a turf battle with these people in hospitals and saying

Do have the legitimacy to speak about this and why this wins in the '80s and perhaps didn't win in the '60s"?

L: Look, let's go back to the '40s; the idea of a bacterial genetics was a nullity and especially in the medical community. Medical bacteriology had evolved without the benefit of any evolutionary thinking whatsoever with the notable exception of Theobald Smith. His book on parasitism is really a very special

perspective through there, but it did not get into medical teaching. If you go through textbooks of medical bacteriology, I mean, that's the place to find these kinds of transitions. A few of them give some lip service, you know, new findings in genetics and so on. But there's a twenty or thirty year lag in that kind of teaching.

S: Yeah. And something else by way of conclusion. It seems to be that I think needs to be explored from a historical point of view is your medical training. And this seems to me to be something that I think needs to be explored more for many people in the twentieth century across disciplines and then study their paradigms. I can understand your 1952 paradigm a lot better once I know the medical training. And I realize that both now. And I noticed in my interview with Jean Brachet and then some other things that Brachet mentioned afterwards that he was trained in medicine, had a certain approach to doing biology. And it seemed that those people like yourselves who come in - and you were obviously a lot younger but you'd been doing the work in the same period - that there seems to be something that needs to be explored there, that you're crossing over and you essentially as an individual, constantly crossing over in the turf of policy, of medicine, of hospital practice, AI in Australia and so on with, what was it, associated with diagnostic treatments and things of that nature? Weren't you involved with McFarlan Burnet? Okay. That's another talk, another interview.

L: Well, I was in some ways predisposed, but I was also in the right place? Here I was an undergraduate in a department that Dobzhansky headed and then going on to medical school and getting the basic medical sciences part of it which is cross-disciplinarian in the other ways and a great educational advantage over the graduate student who focuses on microbiology or biochemistry or whatever. So it just all fell in on it.

S: And also taking microbes and treating them as a biological entity and I think this may be...

L: If there's any figure that I could compare myself with it's Rene Dubos who I guess is not medically trained, as a matter of fact.

S: And is a microbiologist. Did you know him?

L: Yeah. The answer is yes. His books influenced me much more than the personality. Well, this is helpful to me, Jan, if you

want to continue this some time.

S: I would indeed. Thank you.