# Avoiding Infectious Diseases as an LMT



Take the Test

Face it, licensed acupuncturists make a living by putting their hands on people, and it's easy to get exposed that way to infectious diseases. This course provides an overview of the world of bacteria and viruses and how they spread. It is more for your benefit than your patients'. **The purpose of this course is to provide you as a licensed acupuncturists with some perspective on the interplay between microbes and humans and the pressing need to prevent infections in a clinical setting, "a burgeoning problem of ever increasing intensity" as the speaker in the accompanying lecture points out.**

Basic to Yin Yang theory is the notion that everything is continually changing.
We do not live in a static universe. This is especially true in the microbial world, where the interval between generations can be 15 to 20 minutes or less versus three to four times in a century for humans. This capability of microbes to replicate and mutate rapidly has enormous implications for human health, especially in the realm of nosocomial or clinic originated infections.

Presently 5% of all hospital patients leave with microbial infections they did not have when they entered. This results in more than 20,000 deaths annually. Patients who do recover spend an average of ten extra days in the hospital and $5 billion to $10 billion per year in additional medical related expenses.

Perhaps better than anyone else, Dr. Joshua Lederberg understood and eloquently expressed the fragile, symbiotic, and interdependent relationship between man and microbes. His appreciation of the threat which plagues pose to our human species was both profound and humbling. Dr. Lederberg was the 1958 Nobel Laureate in Physiology and Medicine, and his research into how bacteria mutate led to the discovery of DNA by Crick and Watson.

Before his death in 2008, Dr. Lederberg had served as Chairman of the Department of Genetics at the University of Wisconsin and at Stanford University, as President of the Rockefeller University, and as a scientific adviser to WHO's Advisory Health Research Council.

He received the US National Medal of Science in 1989, where his consultative role was specifically cited. Dr. Ledeberg had been a member of the National Academy of Sciences since 1957, and a charter member of its Institute of Medicine, had served as Chairman of the President's Cancer Panel and of the Congress' Technology Assessment Advisory Council, as well as on numerous other consultative panels.

In this lecture, presented courtesy of American Nutriceuticals at the Rockefeller University, Dr. Ledeberg clearly pointed out the vast disparity between the amounts expended for incredibly expensive hospital stays and the paltry sums spent on even the most elementary of public health safeguards, such as the collection of statistics and intelligence about what is going on in the domain of infectious disease.

Take the Test

Dr. Lederberg went on to discuss the following:

**a.** the great plagues in human history;
**b.** trends in American infectious disease mortality between 1900-92;
**c.** diseases which have emerged in the past twenty years for which we did not know the causal agents before such as Lyme disease, Hairy cell leukemia, and cat scratch disease;
**d.** the reemergence of old diseases such as drug resistant strains of malaria and tuberculosis;
**e.** the impact of modern technologies on the increased transmissibility of infectious diseases;
**f.** the huge library of genetic information which is freely exchanged between microbial species and kingdoms of life;
**g.** the co-evolutionary aspects of microbial infection;
**h.** vectors of disease transmission and the impact of transmissibility on pathogenicity;
**i.** examples of microbial infections with varying levels of lethality;
**j.** factors affecting the rate and lethality of nosocomial infections; and
**k.** what can be done to prevent nosocomial infections?

As licensed acupuncturists, we would all do well to heed his words.

Dr. Harvey Kaltsas, A.P.

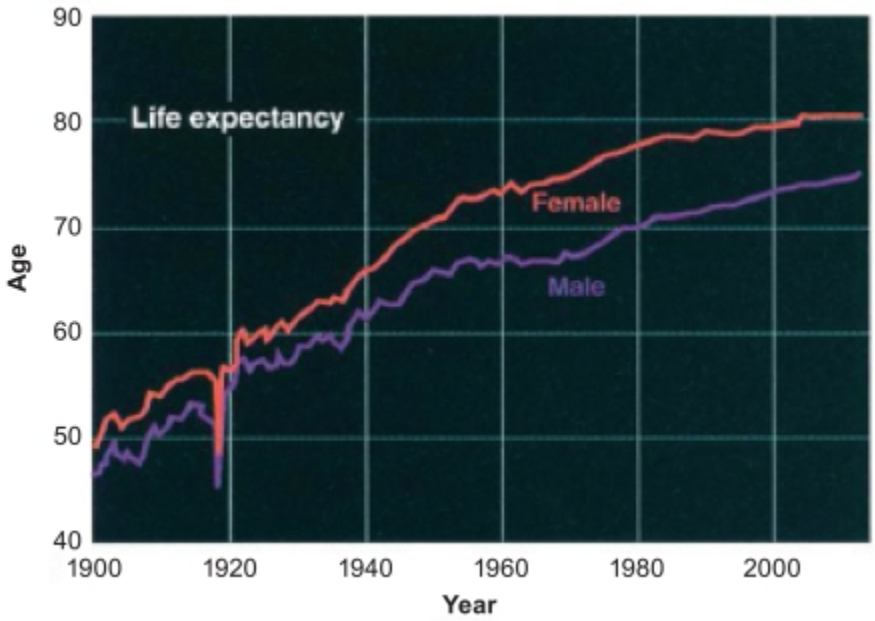
***The following lecture was given in 2000 by Nobel Laureate Dr. Joshua Lederberg, M.D. at the Rockefeller University in New York City to a group hosted by American Nutriceuticals of Sarasota, Florida.***

What I'd like to emphasize is the co-evolutionary relationship of the human species with its would be predators. And the only predators today of any significance are the micro-predators. We are at the top of the food chain, or so we would like to say. We are nevertheless meat for the bugs, and in the long run dust into dust, as you well know; and it's their job in an evolutionary sense to accelerate that process, which is what we call disease, or premature putrefaction might be another grim way to look at it.

If you don't understand that that is the contest, then you don't really understand the nature, really, of civilized life. We no longer live in the Garden of Eden. Things are not simply provided for us. We have gone out over the world and grabbed what we could get and multiplied our populations enormously. We live in an artificially constructed environment in many ways. The human species is in fact a man-made species. It's an artifact. It's been created as a result of human culture with some legacy of the genetic and evolutionary background to draw upon, but totally transformed by our own institutions. There's good news and bad news. The bad news is pretty obvious. In our own multiplication we're that much more meat for the bugs, but if we use our intelligence and our social organization and the traditions which we can accumulate, perhaps we have a chance to continue to compete as we have done, but with remarkable fluctuations over many, many centuries.

This chart is something that should be so widely, recognized displayed, and discussed. I really marvel how many people ask me for copies of it. Although it's… they're the very generally available vital statistics. This is life expectancy in the U.S. during the century. The most important factor of it is the difference between the beginning and the end. An enormous increase,

improvement in life expectancy which is an indicator of health, of freedom from death, and to some degree freedom from illness.




**Source:** Social Security Office of the Chief Actuary

Most of that rise is the first 50 years, and that's almost entirely attributable to the decline of infectious disease as a cause of mortality. Since that time infectious disease has played a declining role in the total, and there's been creeping progress in dealing with the constitutional ills of human kind - of which heart disease, cardiovascular disease, and cancer still remain the most important ingredients.

The first half of the curve is very jagged, and that's mainly attributable to episodic epidemics of one kind and another. [There's been] a smoother interval since then with halting progress. Some plateaus, some acceleration.

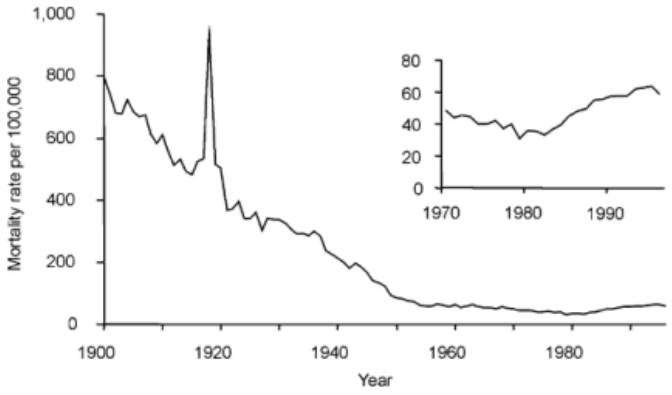
The period between 1950 and 1970 can be described as the evidence of coronary disease and other cardiovascular disease – stroke- which has been in a remarkable degree abated since that time. We don't truly know the causes of it, although post war affluence may be the most important consideration. Subsequent to that time; self-consciousness about lifestyle, diet, smoking, and the use of aspirin may be some of the positive contributors, as well as gradually improving medical management of heart disease and so forth. Even coronary bypass does play some sort of part in that, but probably the least of all the interventions that I've just indicated.

But there's one other way very striking feature of that our history, and that's the enormous dip in 1918. That was the pandemic influenza of that interval - it was called the Spanish Flu, which is almost a guarantee that is started somewhere else. Probably Kansas was the original site of origin, an army contingent being the first recognized point of outbreak, as those troops went overseas were certainly part of the movement, not all of it, of transmitting that flu to Europe. [It] came back in even more aggravated form in the following spring.

And the result was the most catastrophic event in human demography in the United States in the 20th century. It was ½ a million deaths; 25 million deaths around the world, which is a good match for the number of combat casualties that we had in World War I with all the slaughter that there was in the trenches and so on. It's a forgotten episode. Most folks if reminded will say "my grand uncle died of it" or something of that kind, but it is astonishing how little attention has been paid to it until recently.

The resurgence of fowl influenza in Hong Kong and the small handful of deaths we have seen there has been a reminder of that previous event. Also, one has to say the public health establishment - to some degree the public - has been sensitized by discussions of that history, because 1998 Hong Kong Flu might have been a precursor to a new pandemic of different seriotypic form, a new assortment that had the potentiality of matching what was in 1918. And we're not sure at this moment we've seen the end of it, although there've been no new cases of the bird flu for the last two, three weeks which is a very good sign, an indication that human to human transmission has not accelerated. We don't see the chain reaction which would be the signature of a burgeoning epidemic, and I have to say the world has responded appropriately to this epidemic circumstance in a way which is unprecedented in history. There's no other example I can recall where there's been so well informed and so energetic a response so as to nip an epidemic in the bud.

There are wild geese as well as fowl that are involved in the world wide transmission of this influenza. We may or may not have seen the end of it as far as transmission of bird flu to the human is concerned; and if this continues to happen, there's always the problematic question as to whether there'll continue to be human to human transmission. Now if we look a little bit more closely at the statistics on infectious disease mortality that have been collected from the CDC, this is mostly a success story. The only problem with success is complacency - when you drop your guard, and then things may start to happen that are really rather ugly. So it is the same historical picture, but expressed in terms of mortality from infectious disease and the proportion of total mortality which is attributed **(Trends in Infectious Disease Mortality 1900-1992 - CDC**) to infectious disease.




**Deaths resulting from infectious diseases decreased markedly in the United States during most of the twentieth century**

Take the Test

However, between 1980 and 1992, the death rate from infectious diseases increased 58 percent. The sharp increase in infectious disease deaths in 1918 and 1919 was caused by an influenza pandemic, which killed more than 20 million people.

**SOURCE:** Hughes (2001)

I think the scales are really quite clear. I don't think I need to elaborate them any further, but the important thing to note is the modest rising tail as we come up to contemporary time – there's a real flattening out - but the beginning of a rise in the last few years. About half of that is attributable to this decade's plague, the HIV, which has been going on around the world - with which we did everything wrong in the terms of trying to nip it in the bud, but we didn't have the scientific basis to proceed much further.

There was even some confusion at the early appearance of this disease whether it was a viral infection. It was a brand new category of infections as far as human disease was concerned – the retroviruses - although I'm proud to say that right here [at the Rockefeller University] in 1911 Peyton Rouse had discovered the first retrovirus in the form of the Rouse Sarcoma Virus, [a] cancer carrying virus in fowl. It took 50 years for full recognition, and he eventually did win a Nobel Prize for that work - a tribute as much to his longevity as it was to the very important quality of his research and the very long time it took for that work to have real impact in cancer research and virology.

It's really only the fortuitous happenstance of a tradition of research on the Rouse Sarcoma Virus (Dr. Kanafusa here at Rockefeller University played an important role in maintaining that tradition since Dr. Rouse retired and died and then [it was] picked up by Gallo and others at the National Career Institute) that there was a precedent to examine HIV, recognizing that it belonged to the category of retroviruses and so on.

We're in a stage right now of temporary improvement, almost stalemate, in the treatment of HIV with the pro tease inhibitors, but there's very little doubt that resistance will continue to occur and will accumulate in those categories of viruses. The story is far from over, and these drugs are simply impossibly expensive for distribution throughout the rest of the world. We're certainly going to have to find other approaches in order to deal with the global pandemic. But the HIV is only about ½ of that recent rise. A large part of the rest of it is nosocomial infection, and it really does attract our attention as a burgeoning problem of ever increasing gravity, and I'll come back to that again in a little while.

Just by way of general background, I've superimposed the cover of one of the several government agency reports that have appeared during the last 5 or 6 years on the emerging infections threat. This is a production of a Committee an International Science and Technology out of the Office of Science and Technology Policy – and it attempted to lay a ground work for federal policy in dealing with this area. It was a great document. It says all the right things. It collects a lot of the relevant statistics and information about why global health should be high on the priority list of US policy. The only trouble is it has a little caveat on the back page from the Office of Management and the Budget that in effect said: "Don't take this seriously. None of this has been approved for budgetary purposes."

And the miracle is that they allowed this to be published in the first place! Bit by bit there's been a kind of creeping recognition and some money is starting to flow. I'd say since the beginning of a campaign to reintroduce infection into the professional consciousness, that I'm proud to have a part in through the Institute of Medicine and some other institutions, perhaps a total of $100,000,000 in additional expenditures have been piled on to our research and public health budgets to try t deal with them [infectious diseases].

I reckon that's about a week's worth of the increment in health care expenditures from one year to the next that has been sort of diverted into this arena. The disproportion of expenditure on health care which everybody demands once they're ill, knocking on the doors, incredibly expensive stays in hospitals, especially treatments, and so on and so forth - versus elementary public health safeguards, even just the collection of statistics and intelligence - is absolutely shocking.

It seems incomprehensive to me, but it's the victory of personal wants against public policy, because most individuals think it's somebody else's business to worry about the long term picture, and [and then they] scream like bloody murder - one can understand that - if they don't have prompt access to every bit of high tech medicine as soon as they have any medical problems at all, and too many people are still looking for that kind of access - and inequities also drive the picture.

But I've also indicated some of the great plagues of history that accent the gravity of these events of which there are occasional signals in the sporadic outbreaks that you're all acquainted with. They appear in the press all the time these days – very appropriately and very well covered. When we have people like Larry Altman, writing as he does for medical pages for the *New York Times*, we really have a potential avenue for media enlightenment of these issues that really is a high point. Anyhow in the Committee on International Science and Technology study we have some very interesting charts – it's time to start updating them- that's three or four years ago but here's an example of newly recognized infectious diseases in the last 20 years.

These are not just new outbreaks; these are outbreaks for which we did not know the causal agents until this recent interval. So the notion that we had conquered infectious disease by the 1950s, you know, falls flat on its face. There's a whole panoply of agents of which we were totally unaware, and there are still plenty others to come, and new ones keep cropping up all the time.

Almost none of these are brand new in the terms of being novel biological entities. Almost all of these have existed in the disease background but were not differentiated or have not reached a scale of recognition till fairly recently. Probably the outstanding exception to that is HIV. We don't know the time it entered the human population, but it reached significant epidemic proportions outside of Africa only about 20 years ago. How long it had been smoldering in human populations when it emerged from the vast panoply, the zoo of Simian viruses, we really don't know very, very clearly.

In addition to our new co-inhabitants, we have the reemergence of the diseases that for the most part we thought had been kept under control, for which there had been remedies, [that] then start reappearing from time to time in a wide variety of places. Malaria has always been with us in one area or another, but it in some countries had been all but eradicated through vector abatement campaigns. It reached essentially zero in Sri Lanka at about the beginning of this period of time. Then a relaxation of effort and the emergence of pesticide resistance on the part of mosquitoes (and essentially the abandonment of new pesticide development in the face of all the anxieties about chemical pollution that have been derivative of the overuse of pesticides) have led to a resurgence of this disease; and then, in addition, the accumulation of drug resistant varieties of malaria have now made this a very serious problem.

There are many parts of the world in which there are either zero or one medication available for the strains of malaria prevalent. Stay away from Northwest Thailand, please; it's a very dangerous place to be from that perspective, with strains of *plasmodia falciperum* which have high case fatality rates as well as the devastating effects of disease. So I have two, three friends who just can't travel anymore because they're personally sensitive to the anti-malarial agents; and if they were to acquire malaria, they would be untreatable. But there are also locales where everybody is untreatable, and especially if you come into the situation without a carryover of maternal immunity or earlier exposure to these parasites, you'll be in for a really serious battle with disease. Well that's just one … out of a long list.

Multi-drug resistant tuberculosis here in New York City is potentially another example of that. I really congratulate Dr Margaret Hamburg who was Health Commissioner during both the Dinkins and until recently the Giuliani Administrations for having gotten on top of that one, and I think [she] nipped that one in the bud as far as New York City is concerned with quite draconian measures of enforced drug treatment and whatever. So there are things that can be done, but they require alert and energetic public health policy. So what's going on? Why are all these things happening? There is a combination of two divergent kinds of phenomena. One is the ecological setting, the man made environment that we have generated for ourselves, and the other are the evolutionary potentials of the bugs. Human evolution plays a negligible role in recent history. There just isn't enough time, and we protect ourselves from evolutionary change by the invocation of medical and hygienic interventions.

The last thing in the world we want is for natural selection to be our savior, by weeding out those who are susceptible to a disease and leaving only those who are resistant survivors. On a species level that might be our response to a pandemic flu. I don't doubt that there are – although we don't know there are in a human – there are polymorphisms that would protect in some measure. There are against every other disease, but that's not an acceptable answer to our confrontation to disease. So let's get Darwin out of it please as far as we're concerned.

It's a very important aspect of microbial duplication that they continue evolving – another word about that in a moment. But even if there were no significant variations in microbial genetics, if they were not evolving, but they are – but even if they weren't, we'd still be seeing fresh outbreaks as we alter the ecological settings in which we operate.

Here I've tried to give some ordered indication of what I think the main factors are in vulnerability. We have the paradox that the very technology which has given us the principle weapons, the principle armor against microbial attack, that technology has also allowed for and encouraged as part and parcel – what should I call it – the growth of civilization, but I don't mean that in the positive cultural sense. I mean the enormous multiplication of cities; the condensation of people – huge population densities, conurbations, stratification in social, economic, political, hygienic terms - and it doesn't take much imagination to see how if you were to continue to do it, you couldn't get a more appropriate set up for providing sea beds for the taking hold of microbial attack, for the spreading of infection, and then getting out of control. And then right next to the establishment of these foci of infection and of emergence, we have the fact that every one of us is a jet setter, and travel on 12 hours to 24 hour notice from any point on the globe to another is today a commonplace. A million people today board and land in another national destination, crossing national borders. That's a brand new phenomenon in human history, as is the density of human populations altogether.

So while I guess HIV is the prime example of a disease that has certainly been disseminated in that fashion and would not have spread throughout the world as rapidly as it has without these exigencies of transport by a variety of media, as well as the densities of human population, there can be no doubt there will be many others… and is one reason to worry about a Hong Kong Flu.

If a Hong Kong Flu were to become easily transmissible between human to human the way garden variety flues are at the present time, it wouldn't stay in Hong Kong for three days. I mean it would be around the world. I think there are a hundred thousand people a week traveling from Hong Kong to other international destinations. And there is no way to stop it. There's no point in even talking about quarantine on that scale. It would be evaded overnight by every imaginable medium; and transit time of people from one point to another is so much shorter than the incubation time of disease. Most folks will have no idea whatever that they were ill, as they indeed become the carriers going around the world.

Well….I've indicated a number of other features and ecological settings they're also contributory to the setup that while we have the technology to counter it, we're beginning to develop the global as well as national public health organizations to try and deal with it. In other respects we're more vulnerable that we ever have been in history, so we have a greater need for that social intelligence to combat it. But then we also look at the evolutionary side. It's just a very brief summary chart. I've already indicated some of the limitations in human evolution. It's a no-win as our answer, although we can get very important lessons.

Quite recently a polymorphism has been discovered – very sluggish prior investigation for polymorphisms affecting HIV – in fact there was a Chemokine receptor which seems to be necessary for invasion of cells by the HIV virus. Individuals having a deletion of this receptor seem to be perfectly healthy. What it's doing there in the normal isn't quite clear, but they are protected very substantially against the disease. That opens the door to many new therapeutic inventions, and that knowledge is the more important aspect of it. I don't think we can continue waiting for the Darwinian increase of CCR5 negative individuals as being the human answer to HIV, but the knowledge of those polymorphisms gives us insight into how we might have other humane interventions that might make an important difference.

On the microbial side the picture is exactly the opposite. They live by their evolutionary adaptability. They undergo vast fluctuations of population size. They multiply every 15 to 20 minutes. If we're talking about bacterium, they grow much faster than that. If we're talking about viruses, they reach population sizes that are truly astronomical in their dimensions. A billion infectious organisms in one infected human being would be a commonplace. You can multiply that by a hundred or a thousand, and if they go up and down, oscillate from billions to one or a few and then reinfect new susceptible hosts or have resistance mutations so they can recur, that's commonplace in the life history of bacteria. And we don't regard it as inhumane, and they don't have the wit to realize what sacrifices are undergoing in the name of the continuation of their own species.

I mean it's not a symmetrical game of any kind whatsoever. But even apart from the numbers that are involved, the mutagenic mechanisms in microbes give them an intrinsically higher degree of viability. There are two other features. Many, many bacteria carry reservoirs of their past experience in genetic segments that remain unexpressed until the organisms face an adaptive stress. And then, through DNA inversions or DNA transpositions, we can have the expressions of old history.

We can see this, for example in malaria, where the existing epitotes may result in the invocation of immunity but new epitotes are unmasked by the transposition of DNA segments within the malarial parasite so that the old immunity does no good because there's a new coating on the malaria, and they will then multiply unchecked; and this is a cycle that can be repeated hundreds of times, not just one or two as alternative past history, different pages in the archives that can be re-invoked, regularly occurring programmed changes in the intrinsic DNA of these organisms.

There is a huge library of genetic information freely exchanged among microbial species. This is plasmid transfer, the most notable examples to us today are those plasmids that carry drug resistance, but plasmids carrying other virulence factors are also known to have been around since time immemorial. We wouldn't have a problem with E -coli 0-157 if it were not for the fact that a plasmid caring the shigella viratoxin had moved into an E-coli strain, and that's what causes the damage with this newly recognized pathogen.

Cholera toxin plays, has a very similar kind of history in which phage -mediated transfer has resulted in the formation of new toxigenic strains. But for our present discussion the point to remember is the vast reservoir for drug resistance which has accumulated in the microbial population in a wide number of different species and which is readily transmitted to pathogenic species by plasmid transfer from numerous range s of sources. Just to remind you of processes, there are several mechanisms of gene transfer from bacterium to bacterium; one bacterium may conjugate with another one and you have the passage of DNA of the host. This is what we call the sexual mode of genetic interaction.

You can have bacteria phages carrying material into a bacterium from another species; you have a raw DNA doing that. In this case, this is the plasmid transfer; you can see whole chromosome transfer from bacterium to bacterium. Anyhow, there really is a world wide web of genetic information freely communicable among species in the bacterial world, and there are documented examples of this kind of exchange through vast kingdoms of different kinds of

microbial species (plants – *agrobacterium* – yeasts – conjugative gram negative) so that you can have factors moving step wise from yeast to gram negative bacteria to gram positive bacteria to the newly recognized kingdom of archaea.

Plasmids can be moved into the ancient categories. Plasmid transfer is part and parcel of the crown gall bacterial disease in plants. This is used for genetic engineering purposes. We have these kinds of movements. So anyhow it's an integrated web. In fact, you might even think of the microbial world being a single complex genome with its parts in communication with one another, and to that degree highly adaptable, looking for every avenue of finding economic riches in which it can occupy different habitats. That sounds innocuous, but a bacterium's habitat is our disease when that includes our own body.

So that versatility is of the utmost importance in terms of how we think about our relationship with bugs. I'll just say a word or two about the co-evolutionary aspects of this relationship. And I just want to concentrate on this part of this chart. The parasite - will it pursue a short term or a long term strategy? Well look at how our entrepreneurs act in contemporary society and guess what tends to win out. A short term strategy for a microbe – and this is not a matter of fore-thought or choice; this is the consequence of biological events and of natural selection then operating.

The short term strategy is to proliferate as quickly as possible. After all, if you have within a single infected individual, the bug that divides the most rapidly gets there the firstest and the mostest because there are more of them, and inevitably natural selection with the single infected host will favor the most virulent, the most rapidly multiplying components, That can be a dead end.

If you had instant death of the host that had been infected with a new virus, that would be the end of it as far as that virus was concerned, particularly for viruses; but for most bacteria it takes a living host to transmit the disease to another living host. There are hardly any exceptions to that - anthrax in a moderate degree and botulinum which is really a toxin rather than an infectious disease- are the only exceptions that I can think of where what I would call carrion, where an infected dead host plays a significant role in the further transmission of the disease.

But essentially every other infection I can think of – you might be able to remind me of one or two others – requires the live host for effective transmission. If nothing else, then, to be able to be walking around or sneezing, coughing, excreting, shaking hands, engaging in sexual activity, takes a live being and by and large a healthy one, in order to be an effective transmitter. So the bug that incapacitates or kills its hosts is really working against its own long term interests, because otherwise it may be breaking down its channel of transmission.

But within the host the bug doesn't know that. The fastest ones are the ones who are selected the most avidly. So the long term interests of any infective agent are to mute its pathogenicity, to multiply at moderate speed, to do so in ways that only mildly compromise the health of the host or induce the host to avoid health seeking behaviors of one kind or another and then promote its own transmission.

And indeed we find many, many diseases that do exactly that. The common cold would be a wonderful example: highly contagious, not severely debilitating, barely reducing the host's mobility, inducing sneezing, coughing, the emission of the infective agents, and just at the margin of disease so you sort of tend to avoid somebody with a cold, but you don't avoid them like the plague, because it isn't bad enough to invoke those kinds of defensive measures.

So that sort of a virus is really the most successfully adaptive of all, and the fact that we tolerate it and don't think we have to do too much about it is an example of it. Those viruses are going to be around a very, very long time. The ones that kill promptly have a very short future. Hanta virus, if it were not for the maintenance of the murine reservoir, would be a dead end. No known case, maybe one known case of a human to human transmission in the United States. There may have been an outbreak in Argentina where there had been some others under fairly careless precautions about transmission. Well one might then expect, and here we are always dealing with pretty theoretical concepts - it's very hard to test these propositions in practice, that there would be a correlation between lethality of infection and the ease of transmissibility [in] circumstances where there is a guaranteed vector. If you're in a highly mosquitoes rich environment where you're pretty sure that an infected individual is going to get his bug into a mosquito that will then bite somebody else, very lethal forms of parasites will be tolerated. That's what we're seeing with *plasmodium falciperum* in North West Thailand for example where it's typical to get a hundred bites a day from the ambient mosquito - typical, not unusual, amid population.

In those conditions there's virtually no constraint from the transmissibility on the lethality of the infection. And I want to put it to you that that's a good model for nosocomial infection, and one of the reasons why the hospital is such a hazardous place to be is that there are guaranteed carriers, and that highly lethal forms of disease are going to have unhindered transmission in that setting; and one has to say that the health care providers as well as some of the patients are the mosquitoes of that scenario. Until we start thinking about the problem in those terms, we're not going to come to grips with it appropriately. So the fact that the odds of infection are increased is a double whammy. It's also associated with the odds of that same infection being of highly lethal capacity.

Well, let me turn just a little bit more immediately to the nosocomial infection issue. I'm going to quote now from the " Emerging Infections": probably should have this as a handout but it's just a page and a half out of the book that I was just showing to you a moment ago… At least 5% of the hospital admissions patients come out with a disease they didn't have when they went in. **Twenty thousand (20,000) deaths annually!** I think that number's gone up since this report was written. Patients recovering - an extra 10 days of hospital care. Hospitals acquired infections account for an extra 5 to 10 billion dollars a year in additional medical related expenses. And then you can find some of the specific categories in which this occurs. Many factors which increase nosocomial infection in a hospital are inherent in any health care setting; not only are persons with serious infections frequently admitted to hospitals, providing an intra-hospital source of pathogenic organisms, but these people also tend to be immune compromised. What's not mentioned in this chart is that a hospital is also a place of very concentrated use of antibiotics; therefore no surprise that you're going to see the emergence of and continued selection of antibiotic resistant organisms in that kind of setting.

In addition, there are invasive procedures, especially the use of catheters, which gravely enhance the risk of nosocomial infection in the very process. So a whole constellation of factors. What can be done about it? Probably the most comprehensive statement appeared in the January 17, 1946 issue of *JAMA*, which is an issue devoted to emergent infections, and you get a lot of the further statistics and recommendations; but first of all there needs to be a system. There needs to be a systematic approach, a recognition that this is a problem, that the angels of mercy are also angels of death and disease willy nilly. The system for rapid detection and reporting of resistant micro -organisms, when we'll get to the point of routine screening of health care workers for nasal carriage of infectious disease, I'm not sure, but I think it's in the cards: I think the next major scandal that can be attributed and then the lawsuits that will follow. So it's a rather unpleasant prospect. It may mean severe dislocations in employment and employability, but I don't see how this can be eventually avoided.

I think in the meantime the best way to forefend it is to institute the strictest of hygiene regimes in order to limit the gravity of these conditions during the interval: facilities for hand washing, isolation, environmental hygiene, managerial goals and accountability for reductions of colonization of infection resistant organisms.

Not indicated on this chart is that this system cannot be confined to the individual hospital. It has to be accepted a responsibility of the hospital community, and I think it will be scandalous if there are examples of hospitals withholding information about their own experience when it's important that that be shared with the rest of the professional community in order to anticipate emergent resistance, specific kinds of problems, [and] what needs to be done to clean it up.

I suspect this will be mandated by government authorities. Before very long there'll be systematic reporting of the incidence of nosocomial infection. There will be injustice. There will be hospitals, because they accept a higher proportion of compromised patients and practice invasive procedures more frequently, out of necessity will appear to get a black eye because they'll have an unhealthier outcome; and there'll have to be an important educational program to have and evaluate such statistics. That's still being worked out at the present time, how to achieve that without doing undue injury. But the lessons really plain in the meantime, and that is much more aggressive steps are needed in the intra-hospital setting in order to control these kinds of problems. And although in the case of multiple resistant staph aureus, nasal carriage is probably the main reservoir, several authorities indicate that transient colonization of hands of the providers is the most important medium of that transmission.

So many hospitals don't even have decent facilities for hand washing at the right locations, or there's the myth that if you put on a glove, that's going to be protection. It may protect you, but it may be the medium of transmission to the very next patient. So on and off, on and off, would be the only imaginable way – there have been surveys of practice on the part of practitioners and providers that indicate 40 -50% of physicians don't wash their hands between patients. Now this probably includes patients who have a very low likelihood of carrying infectious agents and so on, but it's certainly not a routinely ingrained habit from point to point. That's got to be looked after.

So those are the remedial measures that we have to think about. Well, it's a problem to some degree that's been swept under the rug; but it's not going to stay there, I think, associated with what's going on in the evolution of pathogenicity and of drug resistance, which after all is a component of pathogenicity. It behooves us to take a very close look at what we can all do to prevent this piece of the problem.

Thank you very much.

# An Infectious Disease Timeline

## 1300s

**1346** Black Death begins spreading in Europe.

## 1400s

**1492** Christopher Columbus initiates European-American contact, which leads to transmission of European diseases to the Americas and vice versa.

## 1500s

**1530** Girolamo Fracastoro puts forward an early version of the germ theory of disease.

## 1600s

**1627** Cinchona bark (quinine) is brought to Europe to treat malaria.

**1683** Anton van Leeuwenhoek uses his microscopes to observe tiny animalcules (later known as bacteria) in tooth plaque.

## 1700s

**1796** Edward Jenner develops technique of vaccination, at first against smallpox.

## 1800s

**1848** Ignaz Semmelweis introduces antiseptic methods.

**1854** John Snow recognizes link between the spread of cholera and drinking water supplies.

**1860s** Louis Pasteur concludes that infectious diseases are caused by living organisms called “germs.” An early practical consequence was Joseph Lister’s development of antisepsis by using carbolic acid to disinfect wounds.

**1876** Robert Koch validates germ theory of disease and helps initiate the science of bacteriology with a paper pinpointing a bacterium as the cause of anthrax.

**1880** Louis Pasteur develops method of attenuating a virulent pathogen (for chicken cholera) so that it immunizes but does not infect; in 1881 he devises an anthrax vaccine and in 1885, a rabies vaccine. Charles Laveran finds malarial parasites in erythrocytes of infected people and shows that the parasite replicates in the host.

**1890** Emil von Behring and Shibasaburo Kitasato discover diphtheria antitoxin serum, the first rational approach to therapy for infectious disease.

**1891** Paul Ehrlich proposes that antibodies are responsible for immunity.

**1892** The field of virology begins when Dmitri Ivanowski discovers exquisitely small

pathogenic agents, later known as viruses, while searching for the cause of tobacco mosaic disease.

**1899** Organizing meeting of the Society of American Bacteriologists—later to be known as the American Society for Microbiology—is held at Yale University.

## 1900s

**1900** Based on work by Walter Reed, a commission of researchers shows that yellow fever is caused by a virus from mosquitoes; mosquito-eradication programs are begun.

**1905** Fritz Schaudinn and Erich Hoffmann discover bacterial cause of syphilis—*Treponema pallidum.*

**1911** Francis Rous reports on a viral etiology of a cancer (Rous sarcoma virus).

**1918–1919** Epidemic of "Spanish" flu causes at least 25 million deaths

**1928** Frederick Griffith discovers genetic transformation phenomenon in pneumococci, thereby establishing a foundation of molecular genetics.

**1929** Alexander Fleming reports discovering penicillin in mold.

**1935** Gerhard Domagk synthesizes the antimetabolite Prontosil, which kills *Streptococcus* in mice.

**1937** Ernst Ruska uses an electron microscope to obtain first pictures of a virus.

**1941** Selman Waksman suggests the word "antibiotic" for compounds and preparations that have antimicrobial properties; 2 years later, he and colleagues discover streptomycin, the first antibiotic effective against tuberculosis, in a soil fungus.

**1944** Oswald Avery, Colin MacLeod, and Maclyn McCarty identify DNA as the genetically active material in the pneumococcus transformation.

**1946** Edward Tatum and Joshua Lederberg discover "sexual" conjugation in bacteria.

**1948** The World Health Organization (WHO) is formed within the United Nations.

**1952** Renato Dulbecco shows that a single virus particle can produce plaques.

**1953** James Watson and Francis Crick reveal the double helical structure of DNA.

**Late 1950s** Frank Burnet enunciates clonal selection theory of the immune response.

**1960** Arthur Kornberg demonstrates DNA synthesis in cell-free bacterial extract. François Jacob and Jacques Monod report work on genetic control of enzyme and virus synthesis.

**1970** Howard Temin and David Baltimore independently discover that certain RNA viruses use reverse transcription (RNA to reconstitute DNA) as part of their replication cycle.

**1975** Asilomar conference sets standards for the containment of possible biohazards from recombinant DNA experiments with microbes.

**1979** Smallpox eradication program of WHO is completed; the world is declared free of smallpox.

**1981** AIDS first identified as a new infectious disease by U.S. Centers for Disease Control and Prevention.

**1982** Stanley Prusiner finds evidence that a class of infectious proteins, which he calls prions, cause scrapie in sheep.

**1983** Luc Montagnier and Robert Gallo announce their discovery of the human immunodeficiency virus that is believed to cause AIDS.

**1984** Barry Marshall shows that isolates from ulcer patients contain the bacterium later known as *Helicobacter pylori*. The discovery ultimately leads to a new pathogen-based etiology of ulcers.

**1985** Robert Gallo, Dani Bolognesi, Sam Broder, and others show that AZT inhibits HIV action in vitro.

**1988** Kary Mullis reports basis of polymerase chain reaction (PCR) for detection of even single DNA molecules.

**1995** J. Craig Venter, Hamilton Smith, Claire Fraser, and colleagues at The Institute for Genomic Research elucidate the first complete genome sequence of a microorganism: *Haemophilus influenzae*.

**1996** Implied link between bovine spongiform encephalopathy ("mad cow disease") and human disease syndrome leads to large-scale controls on British cattle.

**1999** New York experiences outbreak of West Nile encephalopathy transmitted by birds and mosquitoes.

## 2000s

**c. 2000** Antibiotic-resistant pathogens are spreading in many environments.

**NOTE:** For more extensive chronological listings, see "Microbiology's fifty most significant events during the past 125 years," poster supplement to *ASM News* 65(5), 1999.

Take the Test