

Professor Anne K. Vidaver's Abstract of her presentation, "Cross-infective microbes from plants to humans"

Microorganisms that infect and cause disease in both plants and people are uncommon but increasing in frequency of isolation. These cross-infective microorganisms are more insidious than those simply transmitted to humans by contact or consumption of plants. Currently 22 bacterial taxa and 38 fungal taxa have been reported as causing 'phytoses'. Several examples of bacterial and fungal diseases of plants and corresponding human disease will be presented. Questions that arise include accuracy of systematics analyses, role and similarity of virulence factors, genomic and pathogenicity islands and antimicrobial resistance. Newer biological techniques such as synthetic biology, illustrated by the construction of new viruses and DNA shuffling or intragenomic reconstruction, complicate oversight and regulatory action. Regulatory challenges among presumed equivalent taxa among plant and medical communities include definition and assessment of risk groups, permitting for interstate transport and differential perspective on the use and formulation of regulatory agency guidance documents. Assessment of alternatives for microbial pesticide niche markets will be presented. Potential interagency programs on cross-over pathogens will be discussed. The major challenge for agencies with regulatory responsibility for microbial biopesticides is the assessment and accuracy of taxa and scope of both natural and biological variation that may be used and their genomic stability. Management of cross-infective diseases of both plants and animals will require more interdisciplinary research and cooperative agency interactions.

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~Written Transcription of: "Cross-infective microbes from plants to humans" by Professor Anne K. Vidaver ~

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*Introduction of Professor Anne Vidaver

MODERATOR: ROBERT NOWIERSKI, USDA-CSREES:

00:00:10.2

She earned her Ph.D. in bacteriology at Indiana University of Bloomington. Her medical bacteriology was emphasized, but she was interested in plants and became a plant pathologist; specializing in bacteriology.

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Now, she currently is Professor and the head of the department of plant pathology at the University of Nebraska, Lincoln; and she's been interested in and involved in science policy issues for decades; both through the American Society of Microbiology and the American Phytopathological Society.

00:00:39.9

Anne was also Science Advisor to the National Research Initiative Program at CSREES.

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And Anne's' presentation is ... today is titled, 'Cross Infective microbes from plants to humans'.

PROFESSOR ANNE K. VIDAVER:

00:00:57.6

So, you might want to know ... why do we have this topic for this workshop?

00:01:05.9

Well, because there are some organisms that are used as microbial pesticides; or prospective microbial pesticides, and in my experience, plant pathologist don't know about some of these microbe and the medical community conversely does not.

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And it's unfortunate that with all the controlled regulatory agencies; we're missing a few, that could actually, hopefully learn from what I plan to say; namely the Food and Drug Administration and the National Institute of Health.

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I should also say that a couple of the references that I've provided with my abstract are missing. So, if you would like to know something more about what I am saying, contact me and I'll give you those.

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I'm going to talk about some illustrations of plants; of plant/human cross-infections and use those as example's.

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And then I'll talk about what this actually could mean; both to the scientific community and to the regulated community; and challenges for regulators as well. So...

MODERATOR; ROBERT NOWIERSKI, USDA-CSREES)

00:02:16.9

Let's see if we can find a mouse Anne. OK, here we go.

[Inaudible] Professor Vidaver and Robert Nowierski are speaking with each other as Professor Vidaver is setting up]

PROFESSOR ANNE K. VIDAVER:

00:02:40.7

OK.. Yes, every one of these ... ok, so what... First of all, what am I talking about?

00:02:47.6

The terms are not yet agreed upon. What this means; you can talk about organisms that are cross-infected; mainly go from plants to humans; you can call them cross-over pathogens, and you can also call them cross, or inter-kingdom pathogens.

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And Doctor Tauxe from the CDC invented the term; as far as I know, Phytoses, to of course on with zoonosis. That is organisms that go from animals to people.

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What they are not ... is they're not overlapping pathogens in the select agents list; the USDA and the NIH.

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There're other terms that are not applicable, but there are various associations of microbes and plants and humans and it's probably good to at least review those for a moment.

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Obviously, all kinds of microbes can be contaminates, and these are usually considered transient. However, you have a normal microflora on all living things and if they're in the soil they're microbiota or commensals, and generally these are considered asymptomatic.

00:04:02.2

In plants you can have organisms that live as a endophytes in plants; and generally they can be long term, or short term as well, and generally asymptomatic.

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However, you can have pathogens that can behave as endophytes before becoming symptomatic.

00:04:22.2

And then we know about symbiotic organisms that are mutually

beneficial and then we have vectors; usually insects that transmit microorganisms.

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And then we have the microbes that are transferred from animals to people; in terms that they're both pathogenic to plants ... animals and people.

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So, I will start with bacteria, then I'll transfer to fungi.

00:04:48.0

There are fewer bacteria that are cross-infective than fungi and I'll talk about those.

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Now, AGROBACTERIUM RADIOBACTER is one publicly reported of it being a pathogen as far as I know; and that is problematic.

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Nevertheless, it is the poster child for bio-control in bacteriology and plant pathology.

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And the organism K84 has been around for years now, and is also a poster child for the transgenic part of biotech; microbial release of a biocontrol agent.

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Again, for beneficial control of crown gall disease; principally on fruits of various crops. It's been extremely beneficial; and this has been the instances for many people who work in biocontrol.

00:05:44.6

However, it apparently causes opportunist diseases in people; and a variety of diseases, all the way from the blood stream to heart problems and urinary tract infections and so on.

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Now, the majority of the diseases that I'm going to talk about in humans are rare; but there will be a few that are not so rare, and I'll try to point those out when we come to those.

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And obviously, for anybody in the regulatory arena; this causes at least a plausible thought, but I'll indicate what some of the challenges are with this.

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In AGROBACTERIUM TUMEFACIENS; otherwise known as the agent of crown

gall with a very wide host range, it can cause a variety of problems as well.

00:06:36.3

On the other hand; *AGROBACTERIUM TUMEFACIENS* is, and I think most people know, has been extremely critical to the biotech industry for getting transgenic plants.

00:06:50.3

BACILLUS MEGATERIUM; a minor pathogen of a variety of plants, going from wheat to trees; but has a biocontrol agent listed to control a number of fungi.

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So while the biocontrol agent may itself be a single organism; in general, the idea is to have a wide host range, for a very important target.

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And this has been linked with oral mucosal inflammation.

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Another spore former; is a gram positive bacteria, and you know what I'm talking about; is *CLOSTRIDIUM BUTYRICUM*; causes disease of poplar and hornbeam, which I'm not sure what that is.

00:07:38.8

And apparently has been reported to cause disease in babies.

00:07:44.2

Now, *RATHAYIBACTER TOXICUS* is not known in the United States, but because it is so dramatic I'm including it here.

00:07:53.9

It causes disease in cereals, which I'll show you in a moment.

00:07:56.9

It's been a particular problem in Australia because of the death of livestock associated with the consumption of the *RATHAYIBACTER* infected in the ryegrass.

00:08:08.2

And the relationship to problems in people is still debated in terms of unexplained poisonings.

00:08:19.3

And this is what it does in cattle who consume grass that many have this yummy disease. The toxins are extremely potent and they have been characterized. Again, not in this country.

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Now when we come to BURKHOLDERIA CEPACIA; there's going to be some more presentation about BURKHOLDERIA CEPACIA, probably more than I certainly have here.

00:08:48.2

It's a minor pathogen on plants; but it can also cause disease in mushrooms...

00:08:54.3

...and it has also been used in phyto-remediation. and has occasionally been found as an endophyte.

00:09:02.9

Well, this is a disease partially known for being a problem in lung tissue and particularly in patients with Cystic Fibrosis. However, there're other diseases that it can be involved with.

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At one time there was a biocontrol agent; actually it was going to be applied for soil-borne fungi I believe, maybe we'll hear more about that later.

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It had to be taken off the market because of objections through the American Medical Association.

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This is one of the two cases I know of where you actually do have evidence; as apposed to conjecture, that the genes for plants that cause disease, and genes that can cause disease in humans, are on the same strain.

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That is not true for all strains of BURKHOLDERIA CEPACIA, but it is true for at least a few that have been so characterized.

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Very unusual and very challenging, of course if you're ready to talk about a biocontrol agent..

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Then we have BURKHOLDERIA GLADIOLI; Even a lessor problem in plant pathology, but it can cause a disease in onions and decay in bulbs of beneficial organisms and ornamentals.

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And also can cause pneumonia and diseases, generalized disease.

00:10:37.9

And recognizing ... some of my slides might be an appetite depressant for you just before lunch.

[Laughter in room]

00:10:46.9

This is sour skin of onion; you see here the rotting. It also smells terribly.

00:10:53.5

Any of you who are not pathologists don't know what you're missing ...

[Laughter in room]

...in terms of these odors, that can sometimes be very characteristic as a diagnostic agent.

00:11:07.2

And then you have the organism in lung tissue here. Not a good thing. It's very difficult to overcome.

00:11:18.6

The ENTEROBACTER CLOACAE; can cause diseases on trees and in onions and in ginger; but can also; at least in the literature, be known as a biocontrol agent. I don't believe that any have been turned over to the EPA, or anyone else yet, for actual potential commercialization.

00:11:48.9

And for those of you not familiar with bacteria; this is in the same family as E-COLI, some of the notorious E-COLI.

00:11:58.8

Can cause generalized infections; respiratory tract infections and gas gangrene.

00:12:06.2

PANTOEA AGGLOMERANS; is known by a number of different names, and in the literature, the plant pathology literature, there are a number of strains that have been proposed for biological control, usually by competitive exclusion.

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And they work very well under some conditions, but have not yet been commercialized and may not for a number of reasons. But, it is also a pathogen of Wisteria, onions and some trees and a wide variety of plants. Not the same strains of course.

00:12:40.3

You've already heard about the possibility of acquired infections; this is one of the organisms that has been reported of possible

acquired infections and can also be reported in arthritis.

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More and more bacteria by the way are being reported to cause some chronic diseases.

00:13:00.8

PSEUDOMONAS AERUGINOSA; a very minor pathogen in plant pathology, but can cause onion rot and has been used experimentally in that model plant Arabidopsis.

00:13:12.9

It is a very nasty organism if it get's into a burn ward; because it is extremely difficult to control, usually has intrinsic antibiotic resistance to a number of antibiotics. And can cause generalized bacteremia as well.

00:13:33.9

This is also one of the few cases in which a single strain has been found that does have genes that can cause a disease in plants and in humans. And so there have been a few cases where strains have been isolated from humans and then tested in plants and they have been found to be pathogenic.

00:13:52.8

The reverse of course can not been done directly, but can be done through human surrogates, such as mice; [we believe?] and that would be appropriate; and in many cases then a plant can kill mice, so that is a concern.

00:14:11.2

SERRATIA MARCESCENS; a lovely organism to look at on a petri dish usually; in terms of the red-purple color.

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It can cause disease in alfalfa and cucurbits; I'll show you this in a moment, and also a [bio?] synthetic.

00:14:27.9

It can be a nasty organism; in terms of a number of infections in the respiratory tract, urinary tract, in the eyes, in the heart and so on.

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And then we have STENOTROPHOMONAS MALTOPHILIA. It is the least plant associated; has been reported as a plant pathogen. This is contested taxonomically and it's still not decided.

00:14:51.3

In any case it can have bacteremia, generalized infection and respiratory tract infections.

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And I'll show you a couple of nasty things here.

00:15:04.9

PSEUDOMONAS AERUGINOSA infection in a burn patient here. This all gets infected and this gets particularly gruesome if you actually turn on a UV light in a burn ward you can see these people glow.

00:15:20.8

PSEUDOMONAS AERUGINOSA produces a fluorescent pigment and is also characteristic in that regard on ... even on a petri dish.

00:15:31.8

In test tubes; you can have a healthy arbidoxis and dying arbidoxis with this particular strain.

00:15:42.2

The SERRATIA MARCESCENS here; a nasty infection in the eyes.

00:15:47.8

And can kill cucurbits here, I think it's squash, but also pumpkins and plum.

00:15:56.2

It has become much more prevalent in recent years for reasons unknown.

00:16:02.1

Now, switch to fungi; and there are more of them, but even though it may sound like I'm going to talk about a lot of them, I'm not going to talk about all of them that are in the paper that I had that I was going to use as references.

[see 00:01:38.0]

"I should also say that a couple of the references that I've provided with my abstract are missing."

00:16:19.8

The prospective virtue of fungi; which I'll talk more about later, is that in some ways they are more desirable as microbial control agents; but I'll say more about why that is.

00:16:35.4

ALTERNARIA ALTERNATA; very wide host range and it starts to give you these medical terms which I actually had to look up.

00:16:47.0

Phaeohyphomycosis, which essentially as far as I can tell, means that you can actually see the hyphae and they may be ... they may be septate and have color in tissue...

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...and may even have yeast like forms and they can get into various kinds of tissues as well as on the surface of the body.

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And when the fungus gets into the brain or bone tissue; the prognosis is particularly poor, and it has been so reported.

00:17:22.4

ALTERNARIA TENUISSIMA; number of diseases on fruits and beans and blueberries.

00:17:30.3

Again, the state of health; Phaeohyphomycosis; very nasty infections and can get into the sinus cavities as well.

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ASPERGILLUS CANDIDUS; a decay.

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It can get into the brain and the heart and other organs, and bone. Very, very, very nasty.

00:17:51.1

I started reading about what these substances will do...

00:17:56.7

And here you have a very nasty infection here on a foot.

00:18:02.3

And you have here; the disease on wheat kernels.

00:18:09.4

This is why I think even if people are interested in disease; we'd would rather work with plants, rather than some of the other stuff.

[Laughter in room]

00:18:18.8

ASPERGILLUS FLAVUS; This is one that is also not only a pathogen of corn, but moldy peanuts and boll rot on cotton and is very extensive.

00:18:34.1

There is a strain for control of A. FLUVUS on cotton, and I believe it works essentially on the principle of competitive exclusion.

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And; nevertheless, it has been reported to have generalized

infection in people, and can be a problem in heart disease as well.

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ASPERGILLUS GLAUCUS; Corn ear and kernel rot...

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... And again, nasty things in terms of brain, heart, skin and even in the lungs.

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So, This is you know; another one of those appealing pictures. We can have rot in corn...

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... And then we have a real problem here with disease in the jaw; and then with the kidney infection. These are unpleasant things for anyone to experience.

00:19:34.4

AUREOBASIDIUM PULLULANS can cause russetting. And this is not particularly a serious economic disease; except that those of you that don't know plant pathology, know that even if you have a spot on anything; whether or not it's a vegetable or a fruit, it decreases the quality and even though it doesn't affect anything else, it will nevertheless decrease the economic value.

00:20:02.7

It can cause various opportunistic diseases in the lungs and all over the body.

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BIPOLARIS AUSTRALIENSIS; problem in turf grass.

00:20:16.1

Again, a whole list of diseases that it has been found in; from the outside to the inside, from the brain to the feet.

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BIPOLARIS SPICIFERA; Problem on cotton.

00:20:31.6

Problem actually in the arteries and has been reported and generalized problem in diseases throughout the body.

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These are really nice diseases here.

00:21:02.6

COLLETOTRICHUM COCCODES: A black dot of tomato and potato. Again, not a serious disease as a pathogen, but essentially a serious disease

economically, and because of appearance.

00:20:49.0

And this generalized disease of Phaeohyphomycosis in various organs.

00:21:09.4

COLLETOTRICHUM GLOEOSPORIOIDES; Anthracnose on many crops and many fruits and coffee and citrus.

00:21:19.1

It can get into the nails. And some of these pictures again are very unattractive.

00:21:25.6

CONIOTHYRUM FUCKELII; Stem Blight, dieback and canker of roses and strawberries, black root rot and cane blight of Rubus.

00:21:36.1

And again, it can cause problems in the nails and liver.

00:21:41.3

CURVULARIA BRACHYSPORA; Problem on roses.

00:21:45.4

Necrotizing cutaneous infection in the skin and your nails, and not very pleasant.

00:21:54.8

CURVULARIA CLAVATA; Leaf spot of maize.

00:21:59.0

It can get into the sinuses and the brain. It can also cause skin infections.

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CURVULARIA LUNATA; Leaf spot in rice and other plants; and melting out of turf grass.

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Can get into the brain, can be in skin and be a problem in terms of allergies.

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There's probably many more of these that can also be an allergic problem, but I didn't find those listed.

00:22:30.5

CYLINDROCARPON LICHENICOLA: Post-harvest fruit invasion, corn rot of taro.

0:22:38.4

Can be a disseminated infection, can cause diseases again in the nails.

00:22:42.8

DRECHSLERA BISEPTATA; A problem with turf-grasses and wheat.

00:22:48.2

Brain Abscess has been reported; again, not likely to be treatable.

00:22:55.3

FUSARIUM MONILIFORME; Or otherwise VERTICILLIODES in current literature. This is a pretty serious disease in many years. It can cause ear, root and stalk rot and seedling blight of corn, or maize. It can also be in sugar cane and in bananas.

00:23:15.9

Well, this can get into the disseminated infection in humans, and give you pneumonia and get in to the eyes here.

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FUSARIUM OXYSPORUM; Also blight pathogen; wilts and blights on vegetables and plantation crops and ornamentals; extremely wide host range.

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It can give you disseminated infection, pneumonia and eye infection as well.

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So, this does not go on forever, but we're getting here, and I'm not giving you all of them.

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FUSARIUM SOLANI...

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There will be a point for many of you, I hope.

00:24:02.6

[FUSARIUM SOLANI, continued]; Yellows, fruit and seedling rot on a wide range of hosts; from sweet potatoes to black walnuts, poinsettia.

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For those of you who are not a plant pathologist, I trust that you're finding, or at least hearing that there are pathogens on almost anything you can think of, and that is true.

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You can get invasive systemic infection, and problems with the eyes.

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LASIODIPLODIA THEOBROMAE; Problems on a lot of fruits and also trees...

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... and you can get subcutaneous abscess around the eyes and generalized infection.

00:24:45.0

LECYTHOPHORA HOFFMANNII; Soft rots and decay of surface layers of natural and preservative-treated timber. And I thought the whole idea of preservative-treated timber was that you had nothing happen to it; but apparently you do get [inaudible] eventually.

00:25:01.1

Chronic sinusitis can occur.

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I believe this is the last one.

00:25:11.1

PAECILOMYCES VARIOTII; Dieback and canker of pistachio.

00:25:17.9

You can get pneumonia, problems with the central nervous system, and generalized peritonitis.

00:25:24.6

PHOMA EUPYRENA; Blight of fir and pine species.

00:25:29.1

Lesions on the skin.

00:25:31.1

MUCOR CIRCINELLOIDES; Mucor rot of mango and loofa; which of I think you get sponges from, if you wash them.

00:25:42.8

And then you can have a problem in generalized infection and gangrene.

00:25:49.0

And I think this is,,, it might be the last one,

00:25:52.2

RHIZOPUS STOLONIFER; A pre and post-harvest soft rot in many fruits, vegetables and crops.

00:26:00.1

And you get a generalized infection.

00:26:03.1

So, what does all this have to do ... what does this mean in terms of recent regulatory challenges?

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Well, not the least of these challenges; it just doesn't matter, you know.

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I'll explain more; that is to refresh everybody's mind about the whole purpose is of systematics.

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When we're talking about getting a potential organism, we can't generalize about the whole main effects on ... but, we have to look at strain variation and the stability of the organism.

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And, for any agent; we have to look at what are the virulence factors and how might they be transmittable; transmitted to other organisms or not; particularly for bacteria, but not necessarily exclusively.

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People are asking questions about; "well, what do genomic islands actually mean in terms of the basic organisms since these can be differentiated genomically from the rest of the organism?"

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In many cases they carry antibiotic resistance genes or other genes not otherwise seen in that taxon.

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In bacteria particularly; pathogenicity islands have been known to have for a number of years; and these carry a number of virulence factors and may include antimicrobial resistance factors as well.

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And then; notorious for bacteria is antibiotic resistance; it may be intrinsic, that is strains that are already known to carry antibiotic resistance without any exposure to antibiotics.

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This is particularly true of those from natural systems, but certainly from artificially produced antibiotics as well.

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And then there's the question of ... for fungi, we have the emergence of, or concern about, mycocide or fungicide resistance.

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There's no shortage of challenges. But, let's talk, refresh just a moment in terms of definitions, of what ... at least what I'm talking about.

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The systematic question is to really look at the diversity and the relationships among organisms. Now, I think that's really what we've been talking about a lot already and we'll be doing it more throughout this workshop,

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One of the important questions for people in ... the more we know in the way – the less we know, is actually how do we classify organisms? I mean this is a human endeavor, but we have to do this in order to communicate.

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And so, then how we do this is still a very fluid field, and this is good; but it's a very challenging area then for anyone who is in the regulatory arena.

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This is also then true in terms of Nomenclature.

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What are you going to name an organism? How are you going to identify it? And then, how are you going to characterize any group of individuals then by rank?

00:29:24.0

And then for species; at least for the present time for bacteria, you have a species being defined with at least 70% relatedness by the DNA homology.

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Well, some microbial geneticists believe that this is; then again, inappropriate given what we know; but no one has yet come up with something that is actually being received ... received well as an alternative. So, this is still a challenge.

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What is the species? And I'm not sure even for the fungi that there is agreement amongst the species, and I don't know about some of the other organisms as well.

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And then for defining a ... that you would actually use; and that you would worry about stability, we're talking about the decedents of a

single isolation in your culture.

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Well, if you actually don't use the microorganism ... microorganism itself, but the attribute of it that would be used in a plant; that a vulturious organism, then you could have what the EPA has; namely plant incorporated protectants. And some ways this would be highly beneficial.

00:30:49.8

And this is the case for example in the papaya; where you have a gene from a virus that is protecting a papaya from the virus attack. And this is; in my view, highly desirable in many ways, that this is ... at a cost of, not just with money but other costs as well, in terms of being able to bring something like that to market.

00:31:18.8

Then there's the question of what do you do about the host responses? How do you measure the population; even of plants or of people, or animals as the case may be, because we are not in a static population in any of those categories?

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We need ... need to know a lot more about inducing the innate immunity; simply to be able to combat all these challenging organisms that are multiplying and changing at a faster rate than we are.

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OK. Area that is of particular concern to many people; and I think is a real challenge in the regulatory agency, is the emerging area of synthetic biology.

00:32:02.8

We've already seen the emergence of ... of store boughten goods being able to produce a virus that has really upset many, many people. Well, this is probably just the beginning of synthetic biology and certain people couldn't believe that it will not be very long before we can actually produce in vitro the first synthetic, small scale microorganism.

00:32:32.6

Mycoplasmas for example, I think set an example, in about less than 600 genes that are necessary for life, and this may be down the road. Again a challenge for regulators.

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DNA shuffling is going on; that is the rearrangement of the genome. And how does the ... actually seem like regulatory agency is not clear, at least it may ... that may come out in this workshop.

00:33:02.6

Are Model system analyses appropriate? In all the complexity that we are looking at in many people; that are on both sides of the fence, but in any case this is a challenge; both for the regulated community and for the regulators.

00:33:18.9

And then for everyone; all of this affects, what we do in terms of facilities design. And in terms of cost; in maintenance which are not trivial.

00:33:33.3

One place I think that there is something missing; and it is not perhaps premature to talk about, is that we could have interdisciplinary programs across agencies.

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There's certainly interagency programs already in many areas; but we do not have any, as far as I know, that incorporate USDA and NIH especially; certainly in this area of cross-infective microorganisms.

00:34:02.1

I dare say the medical community has no idea that some of these are problems in plants and the plant community has no idea that these are problems in medicine.

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Actually there ... the question really for the medical community; and even for the plant community is, Are we talking about the same organism? In many cases that's still very much the question.

00:34:29.4

In terms of looking at this issue; it could explain, perhaps in some cases, the origin of human diseases as being from sick or even asymptomatic plants.

00:34:46.0

A colleague that [Europe?] has involved has coined the term; Virulome, to talk about just a set of traits that would allow an organism to be pathogenic in particular circumstances. Whether or not it's inside a plant or human, and simply that it acquires this information and carries it around, and may be dispersed throughout the genome but, it's useful on occasions. And that may be something that will explain some things and makes things readily understood, I mean connect.

00:35:31.9

OK. We're also been talking about ... if we're talking about agents for production; production, delivery and packaging.

00:35:40.9

And we're concerned about microbial survival, spread and gene transfer, and you already heard some of that as well.

00:35:52.7

And ... We have contrast here in terms of limitation and how we even look at organisms in the medical community.

00:36:00.6

We talk about risk groups in agriculture as far as the community is concerned and the outside world. There are no risk groups, they're all people in a vat. This is just not good in science and I think that this is something that we can all work on.

00:36:14.2

Permits for the medical community is selective; not everything requires a permit.

00:36:19.2

In agriculture; it is essentially a pathogen, everything does in one form or another, although it could be ... that is improving in terms of how it is being dealt with.

00:36:31.6

Facilities are different, we have the medical community and agriculture and we won't go into that.

00:36:37.4

For antimicrobials: we have differences among agencies, some of which are required and some of which I understand are not. But, in the FDA, there is more emphasis given on the guidance documents, which are easily ... then modified as opposed to regulations in agriculture.

00:36:56.9

So these are various ... it would be... more toward examination.

00:37:06.3

There are niche markets perhaps that can be looked at.

00:37:09.1

USDA has IR-4; which almost nobody outside of the USDA has any idea what that means, and I suggested that be reexamine, if nothing else rename, so other people can understand it. And perhaps have the EPA follow with that as well.

00:37:23.9

And to take a look at other agencies efforts to have an examination account; small markets can be helped along...

00:37:36.5

... and the FDA does have an Orphan Drug Act that could act as a model.

00:37:42.3

And the take home message are several ... here.

00:37:46.4

First, that we actually recognize we have these cross-infective agents. And a big, BIG question mark; Is what is the accuracy of the medical diagnosis?

00:37:56.6

This is where we need systematics. And we need research in the regulatory agencies to promptly research 'agencies' to work in this area because a lot hinges on whether or not; in fact in some cases that I've illustrated, whether we can actually have microbial pesticides.

00:38:14.5

We're not going to have them, if in fact any of those agents really are a problem, a real problem in the medical arena.

00:38:22.1

So, we need risk assessment comparability between medical and agricultural fields.

00:38:26.8

And we've already heard we need to have vigilant monitoring and surveillance with all these organisms that are cross-infective.

00:38:35.3

And then we need to look at interagency research opportunities and regulatory challenges.

00:38:42.4

I think I'm going to be on time, so good.

00:38:48.1

So, I would be happy to talk with you more about this and I hope this will raise a lot of questions.

[Clapping in room as Moderator
Robert Nowierski approaches Professor Vidaver]

MODERATOR; Robert Nowierski, USDA-CSREES):

00:39:00.4

OK, I think we have time for a couple of quick questions for Anne.

Chris Wozniak, CSREES:

00:39:09.7

Yes, Chris Wozniak, CSREES. The question I have is basically; when you look at these various species that are implicated in the literature as infective agents, whether transfer or otherwise plant pathogens ...

00:39:21.8

... And then you look at the regulatory process; where you're really focussing on strains and the genotype of the [inaudible] strain ,

00:39:28.8

It's kind of interesting; that there's sorta the history of these species as it exists in the literature, whether that's accurate or not, and that it is suspect of that strain that's going through probable registration or whatever.

00:39:42.6

I guess I'm kinda wondering is; with the varieties that you've showed, if we're getting to this point where any report of some organism, and some instance which is considered a pathogen of livestock or on humans, is gonna basically negate this potential use of that organism and that it [inaudible] probable disease it posed.

PROFESSOR ANNE K VIDAVER:

00:40:05.8

I ... I don't think so.

00:40:08.9

As I think I indicated; the majority of these in human literature are still extremely rare. So I think basically you have one or two reports in a population of a billion or so. I don't think that's likely.

00:40:27.0

But it does still require that we need to do a better job on systematics I think.

MODERATOR; ROBERT NOWIERSKI, USDA-CSREES):

00:40:33.7

Any other questions?

00:40:35.0

DANIEL JONES, USDA, CSREES:

00:40:35.2

Daniel Jones, USDA – CSREES. Anne, do you have a rough estimate of the proportion of the kind of pathogens that are cross-over pathogens?

PROFESSOR ANNE K VIDAVER:

00:40:45.8

Very small ... very small.

00:40:48.9

Let me see.

Professor Vidaver turned to direct her continued answer to the attendees of the conference

00:40:50.0

If I remember; we have perhaps anywhere from six ... six hundred (600) to several thousand pathogens that have been described as plant pathogens and here we're talking about less than a hundred, selectively of bacteria and fungi.

Professor Vidaver then turned to DANIEL JONES, USDA, CSRES

00:41:09.2

It ... it is not a large problem, but it's not a problem that we can ignore.

00:41:14.9

And I should indicate to you one more thing.

00:41:18.2

The fungi seem to be increasing in terms of most severity and incidence; and I have seen where the medical community is puzzled by this because it is not only in terms of immunocompromised patients; maybe those with transplants and those with AIDS, but also with even otherwise healthy people. And so, the incidence is going up.

UNIDENTIFIED MALE:

00:41:46.7

My question is very touchy on this.

00:41:49.7

What is the significance of the fact that bacteria may ... the soil is an environment, and us, and bugs is [an] extension of this environment?

00:42:07.5

The ... at least one of the underlying things is; in opportunistic infections, without an immune system shock of the Embryobiota appear appearances; almost anything I gave a disease ... in some, can infect humans.

00:42:29.3

And what regulatory conclusion can be drawn from that; in the use of bio regulatory agents?

00:42:40.2

As you've pointed out; it's rather rare and under certain circumstances we're just culture idiots. And yes; that occurs, occurs very rarely.

00:42:54.1

I think the significance is; in each incidence has to be evaluated. And not just say; well it's occurred in the literature. But, I think it's these six cases I remember.

00:43:08.3

You know; if you go far enough into the realm of realization of a normal human being; and look at all your organisms and see, you're going to find a large number, especially among farm mycologists.

[Laughter in room]

00:43:23.9

Now, it's ah ... If you're going to ... we all carry these things; and I think we need to think very carefully about what that means [inaudible], I would think ... seeing the situation that I saw in CEPACIA, where the representatives; very rightly in a way, of the CYSTIC FIBROSIS SOCIETY objected to the use of CEPACIA as an insecticide.

00:43:57.7

Of a ... the reason was that they had shown that there were occasional cases of CYSTIC FIBROSIS that hadn't carried this organism. But here's the important thing, not as the major organisms. AllCYSTIC FIBROSIS tends to be infected with PSEUDOMONAS AERONOSA and carry a secondary infection as well.

00:44:29.6

So, the objection that it was found; was taken as a means for not using one of these [inaudible]

00:44:40.6

I think one out to look very carefully at theses microorganisms, that for one reason only, that one overlooks therapeutic possibilities that occur in secondary infections.

MODERATOR; Robert Nowierski, USDA-CSREES):

00:44:55.4

OK, we'll take one more quick one and that's it; unless you want to delay lunch.

UNIDENTIFIED MALE:

00:44:59.7

Well, that depends on how hungry you are.

[Laughter in room]

PROFESSOR ANNE K. VIDAVER:

00:45:03.4

Well, I just had this ... an appetite depressing [inaudible]

UNIDENTIFIED MALE:

For a weekend...

[Unidentified & inaudible speaking in room]

UNIDENTIFIED MALE:

00:45:12.4

[Inaudible] ... And uh ... I think your points are well taken, but you know, I saw these plant pathogens; some of them aren't too ... probably in the same category of the human [inaudible] or very little...

PROFESSOR ANNE K. VIDAVER:

00:45:22.1

Right

UNIDENTIFIED MALE continuing:

00:45:22.4

... and; OK, do you know any kind of strategy to avoid [inaudible]?

PROFESSOR ANNE K. VIDAVER:

00:45:33.9

Well, that's ... that's where risk assessment comes in.

00:45:36.7

And I would argue that while those of us that work with plant pathogens know that we have some so-called minor pathogens; when it comes time to explain this however to the public, you're talking about, in my view, permits for risk assessment groups; we don't have it, and I think that's long overdue.

00:45:57.0

So that we could actually say that we have; and it's clear that we have, minor pathogens, just equivalent to.. and put that back in [inaudible]

MODERATOR; Robert Nowierski, USDA-CSREES):

00:46:09.5

The very back there.

UNIDENTIFIED MALE:

00:46:10.7

Yeah, I think this about ... is kinda along the same lines on Michael [Braveman?]; [inaudible] on the four or five organizations that nobody's ever heard of.

[Laughter in room]

00:46:18.3

I think there... I think what has been missing in some of this discussion is really; is the exposure that already exists.

00:46:18.5

I think that the history of exposure to these organisms is really what ... what's telling you that the relative importance; not the fact that a report exists on the presence of an infection in human, it is the fact that there are so few reports in light of the fact that these organisms are so prevalent and that man is so being exposed to them.

PROFESSOR ANNE K. VIDAVER:

00:46:52.8

I don't disagree with that at all, but having known about; for example the BURKHOLDERIA CEPACIA situation...

00:47:03.7

... Part of my presentation is to try to minimize having that occur again; and that means that I think people know that there are these kinds of situations and to put them in the appropriate content.

00:47:16.0

If you don't even know; then you can be blind sighted and that's what I think no body wants.

MODERATOR; Robert Nowierski, USDA-CSREES):

00:47:23.1

OK, one more last question for... Rick?

GREG SIMMONS, APHIS:

00:47:24.9

Yes, Greg Simmons with APHIS.

00:47:28.1

You mentioned that there are a few cases of fungi; I think, that are increasing in some prevalence in humans.

00:47:35.1

And so just a kind of follow-up question is; Have any of the cases where information is known; is there any information about occupational risks and people that are associated with more with these sorts of organisms where you have some relationship there?

PROFESSOR ANNE K. VIDAVER:

00:47:54.0

There probably is, but right now I couldn't give you ... I ... Right now I couldn't give you a [inaudible],

00:48:00.9

But, i have come across a few.

MODERATOR; Robert Nowierski, USDA-CSREES):

00:48:04.5

OK. Would you all join me in....

[CREDITS ROLL]

~ END ~