

Hotez.txt

<time begin="00: 00: 00. 50"/><clear/>[ Music ]<br/>  
<time begin="00: 00: 16. 99"/><clear/>>> Want to thank Professor  
Colley [phonetic] and<br/>  
Professor Thomas for inviting me to this series.<br/>  
<time begin="00: 00: 22. 99"/><clear/>What's being assembled here  
in global<br/>  
health is very impressive and it's a small<br/>  
<time begin="00: 00: 27. 99"/><clear/>but very determined group of  
individuals,<br/>  
actually, not so small considering<br/>  
<time begin="00: 00: 32. 82"/><clear/>that the number of people who  
work<br/>  
on parasitic diseases and diseases<br/>  
<time begin="00: 00: 38. 08"/><clear/>of developing countries is  
dwindling in American<br/>  
-- American universities and Professor Colley<br/>  
<time begin="00: 00: 44. 39"/><clear/>and Thomas have assembled a  
very<br/>  
strong team here and this has become --<br/>  
<time begin="00: 00: 48. 59"/><clear/>this university is  
really<br/>  
being put on the map in terms<br/>  
<time begin="00: 00: 51. 62"/><clear/>of an important force in<br/>  
the area of global health.<br/>  
<time begin="00: 00: 57. 41"/><clear/>And I would like to thank  
Professors Colley and<br/>  
Thomas for two things in particular in addition<br/>  
<time begin="00: 01: 03. 51"/><clear/>to them inviting me here.  
One, I<br/>  
have to say this is probably one<br/>  
<time begin="00: 01: 06. 52"/><clear/>of the most beautiful venues  
I've ever given<br/>  
a lecture in, this is just a gorgeous place<br/>  
<time begin="00: 01: 12. 21"/><clear/>to speak and I'm very honored  
to be here for<br/>  
that and secondly, is I don't know how they got<br/>  
<time begin="00: 01: 18. 40"/><clear/>so many people to hear one of  
my lectures.<br/>  
<time begin="00: 01: 20. 95"/><clear/>The low point of my career is  
when I went to<br/>  
give a talk at the University of Pittsburgh<br/>  
<time begin="00: 01: 24. 62"/><clear/>and the only person who  
showed up was the<br/>  
person who invited me to give the talk.<br/>  
<time begin="00: 01: 29. 07"/><clear/>You see hookworm is very much  
a<br/>  
neglected disease and, of course,<br/>

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<time begin="00:01:33.29"/><clear/>who cares about hookworm in  
the United States.<br/>

<time begin="00:01:36.04"/><clear/>So I'm very<br/>  
used to speaking to crowds of five or six<br/>

<time begin="00:01:40.60"/><clear/>or seven people, so I'm  
really very grateful<br/>

that Professor Colley, Professor Thomas stood<br/>

<time begin="00:01:46.90"/><clear/>out there with their van on  
College Avenue<br/>

and Shanghaied people into the back of the van<br/>

<time begin="00:01:51.97"/><clear/>and dropped them here and  
it's<br/>

very nice of you to do that.<br/>

<time begin="00:01:55.60"/><clear/>I was asked to make my  
remarks somewhat<br/>

personal and a little bit autobiographical<br/>

<time begin="00:02:02.71"/><clear/>to give you a flavor of how  
someone like<br/>

myself who grew up in parts of Connecticut<br/>

<time begin="00:02:08.90"/><clear/>and should have been dreaming  
either of pitching<br/>

for the Yankees or pitching for the Red Sox<br/>

<time begin="00:02:14.53"/><clear/>because you're halfway in  
between the two<br/>

cities, would want to come to work on something<br/>

<time begin="00:02:19.39"/><clear/>like hookworm, and I don't  
quite know all<br/>

the reasons for it but I'm probably one<br/>

<time begin="00:02:24.62"/><clear/>of the more goal directed  
people you'll meet.<br/>

<time begin="00:02:26.54"/><clear/>When I was 13, 14 years old,  
I had a copy of<br/>

Manson's Tropical Disease on my night table<br/>

<time begin="00:02:33.73"/><clear/>and even knew back then  
that<br/>

I wanted to study parasitology<br/>

<time begin="00:02:39.87"/><clear/>and parasitic disease.

Although I probably<br/>

couldn't have predicted it would have taken the<br/>

<time begin="00:02:44.58"/><clear/>form that it did.<br/>

<time begin="00:02:45.41"/><clear/>So I can say that while, my  
friends all wanted<br/>

to pitch for the Yankees or the Red Sox,<br/>

<time begin="00:02:50.73"/><clear/>I wanted to study tropical  
diseases.<br/>

<time begin="00:02:52.57"/><clear/>So I'm a very happy

individual because<br/>

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for me this is just like pitching --<br/>  
<time begin="00:02:56.18"/><clear/>pitching for the Yankees<br/>  
and to be able to present<br/>  
<time begin="00:02:58.25"/><clear/>in this venue is particularly  
gratifying.<br/>  
<time begin="00:03:01.48"/><clear/>So along that  
autobiographical vein I want<br/>  
to take you here first and this is really<br/>  
<time begin="00:03:08.44"/><clear/>where I got started working  
on hookworm.<br/>  
<time begin="00:03:10.50"/><clear/>It's a place called the  
Rockefeller<br/>  
University and many people<br/>  
<time begin="00:03:14.12"/><clear/>in Manhattan are not even  
aware<br/>  
that this university exists.<br/>  
<time begin="00:03:18.65"/><clear/>It's on the East Side, I  
don't have a pointer<br/>  
here but that body of water that you're looking<br/>  
<time begin="00:03:22.91"/><clear/>at is the East River  
with<br/>  
Queens on the other side.<br/>  
<time begin="00:03:26.29"/><clear/>So, if you know anything  
about Manhattan<br/>  
it goes Madison Avenue, then Park Avenue,<br/>  
<time begin="00:03:31.86"/><clear/>Lexington then Third, Second,  
First and there's<br/>  
one additional avenue after you get to First<br/>  
<time begin="00:03:35.86"/><clear/>on the East Side and that's  
York Avenue<br/>  
and this is located right along York Avenue<br/>  
<time begin="00:03:40.71"/><clear/>and it's this beautiful  
swatch of green, green<br/>  
oasis in the middle of a lot of concrete.<br/>  
<time begin="00:03:46.49"/><clear/>And it's a very tiny  
university that<br/>  
has a very small graduate program<br/>  
<time begin="00:03:53.40"/><clear/>and they have this very small  
MD, PhD people<br/>  
for people like myself who have copies<br/>  
<time begin="00:03:58.73"/><clear/>of Manson's Tropical Disease  
at their<br/>  
night table, who come into school more<br/>  
<time begin="00:04:04.94"/><clear/>or less having an idea of  
what I wanted to do.<br/>  
<time begin="00:04:07.15"/><clear/>I didn't know exactly what I  
wanted to do but<br/>

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I knew I wanted to study parasitic diseases  
<time begin="00:04:11.90"/><clear/>and they bought into the idea  
that they  
would accept me and one of the great things  
<time begin="00:04:15.10"/><clear/>about this place, in  
addition  
to being so beautiful,  
<time begin="00:04:18.20"/><clear/>is that they give you a  
full  
scholarship, a full ride to medical school  
<time begin="00:04:22.34"/><clear/>and graduate school and they  
pay your stipend so that  
you don't come out of medical school  
<time begin="00:04:25.96"/><clear/>with an enormous debt and  
force you to go into  
intervention and radiology maybe you can go  
<time begin="00:04:30.56"/><clear/>into something like parasitic  
diseases.  
<time begin="00:04:32.71"/><clear/>Well, that's the upside of  
the place,  
<time begin="00:04:34.37"/><clear/>the downside of the place  
is  
it's extremely pretentious.  
<time begin="00:04:38.44"/><clear/>It's one of the most  
pretentious places  
you'll ever be and justifiably so.  
<time begin="00:04:42.72"/><clear/>What I'm showing you here is  
the  
list of the Nobel Laureates  
<time begin="00:04:47.52"/><clear/>that have gotten their Nobel  
Prize at  
this very small and tiny university.  
<time begin="00:04:54.07"/><clear/>So it probably has the  
highest Nobel  
Prize to person ratio of any university  
<time begin="00:05:00.91"/><clear/>in the United States and  
arguably in the world  
and so, when you come there as a student,  
<time begin="00:05:06.53"/><clear/>the expectations are very  
high and they  
look you straight in the eye and say, Peter,  
<time begin="00:05:12.36"/><clear/>we expect you to come out of  
this  
university and do something extraordinary.  
<time begin="00:05:15.89"/><clear/>Now the truth is most people  
my age who come  
<time begin="00:05:18.73"/><clear/>out of the university not

necessarily do  
something extraordinary but they wind up working  
<time begin="00:05:25.39"/><clear/>on what their professor  
is  
working on like any other PhD --  
<time begin="00:05:28.98"/><clear/>pretty much any other PhD  
student with  
a lot of pretense to go along with it.  
<time begin="00:05:34.63"/><clear/>But I actually took them  
literally and said, Okay.  
<time begin="00:05:36.64"/><clear/>I have to do something  
extraordinary.  
<time begin="00:05:38.79"/><clear/>And so what I would do is I  
would sit  
in the Rockefeller Library my first year  
<time begin="00:05:43.75"/><clear/>at this university, and  
the  
Rockefeller Library is very pretty.  
<time begin="00:05:46.65"/><clear/>It's right along the water  
and you're looking  
<time begin="00:05:48.14"/><clear/>out at the water having great  
thoughts  
watching the ships go by and it was during  
<time begin="00:05:52.78"/><clear/>that first year in 1980 that  
I  
read the following statement --  
<time begin="00:05:58.76"/><clear/>I was looking through some of  
the archives  
of the Rockefeller University and journals  
<time begin="00:06:06.22"/><clear/>in the university  
library  
and I came across this statement  
<time begin="00:06:10.57"/><clear/>by a man whose name is Norman  
Stoll  
and Stoll was the last person to study hookworms  
<time begin="00:06:20.20"/><clear/>in the United States in  
terms  
of a public health problem.  
<time begin="00:06:23.77"/><clear/>He did most of his work in  
the 30's, 40's,  
and 50's when he had more or less retired  
<time begin="00:06:30.14"/><clear/>and this is a speech he gave  
upon his  
retirement from the Rockefeller University,  
<time begin="00:06:35.09"/><clear/>at that time it was called  
the  
Rockefeller Institute for Medical Research,

<time begin="00:06:40.35"/><clear/>and he published this and it  
got --<br/>

<time begin="00:06:42.31"/><clear/>it was a speech that was

given as part of<br/>

the New York Academy of Tropical Medicine<br/>

<time begin="00:06:46.87"/><clear/>as it was called then and

they published it<br/>

in this journal of Experimental Parasitology.<br/>

<time begin="00:06:51.84"/><clear/>And I'm sorry the pointer is

not working,<br/>

so you'll just have to read along with me.<br/>

<time begin="00:06:57.56"/><clear/>And what he wrote the

following statements<br/>

which was something that still resonates<br/>

<time begin="00:07:01.46"/><clear/>with me today and what he

said<br/>

was: As it was when I first saw it,<br/>

<time begin="00:07:06.62"/><clear/>so it is now one of the most

evil of<br/>

infections, referring to hookworm,<br/>

<time begin="00:07:11.10"/><clear/>not with dramatic pathology

as our<br/>

filariasis or schistosomiasis<br/>

<time begin="00:07:16.16"/><clear/>which are other tropical

diseases, but<br/>

with damage, silent and insidious.<br/>

<time begin="00:07:21.74"/><clear/>Now that malaria is being

pushed back --<br/>

and that's an historically interesting point<br/>

<time begin="00:07:26.42"/><clear/>because back then they

actually thought they<br/>

were on the verge of eradicating malaria<br/>

<time begin="00:07:29.82"/><clear/>but he got that part wrong.

Now<br/>

that malaria is being pushed back,<br/>

<time begin="00:07:33.97"/><clear/>hookworm remains the great

infection of mankind.<br/>

<time begin="00:07:36.89"/><clear/>In my view it outranks all

other worm<br/>

infections of man combined in its production,<br/>

<time begin="00:07:43.28"/><clear/>frequently unrealized, of

human misery,<br/>

debility and inefficiency in the tropics.<br/>

<time begin="00:07:49.23"/><clear/>So right then and there I had

my epiphany in<br/>

the Rockefeller University library and I went<br/>

<time begin="00:07:53.86"/><clear/>around to the various

professors of Rockefeller<br/>  
and said, I'm going to work on hookworm.<br/>  
<time begin="00:07:57.88"/><clear/>And the response was, hook  
what?<br/>  
<time begin="00:08:00.24"/><clear/>And I said, I'm going to work  
on hookworm.<br/>  
<time begin="00:08:01.68"/><clear/>Well, why are you going to do  
that?<br/>  
<time begin="00:08:03.04"/><clear/>Because it's the great  
infection of mankind<br/>  
in its production frequently unrealized<br/>  
<time begin="00:08:08.08"/><clear/>of human misery, debility  
and<br/>  
inefficiency in the tropics.<br/>  
<time begin="00:08:12.12"/><clear/>And they said, well, we never  
heard of it.<br/>  
<time begin="00:08:15.72"/><clear/>And this was<br/>  
very disappointing for me because most<br/>  
<time begin="00:08:20.81"/><clear/>of the professors that I went  
to would<br/>  
not allow me to work on hookworm,<br/>  
<time begin="00:08:25.54"/><clear/>and I will never forget it  
was<br/>  
at a parasitology meeting --<br/>  
<time begin="00:08:30.62"/><clear/>it was a Gordon  
Conference<br/>  
held in New Hampshire.<br/>  
<time begin="00:08:34.57"/><clear/>This was about 1981 it was  
one of the first<br/>  
Gordon Conferences on Parasitic Diseases<br/>  
<time begin="00:08:40.13"/><clear/>because this was the  
first<br/>  
time that people were really starting<br/>  
<time begin="00:08:42.87"/><clear/>to look very seriously at  
applying molecular<br/>  
techniques to the study of parasitic diseases,<br/>  
<time begin="00:08:48.63"/><clear/>and I remember one of  
the<br/>  
professors at Rockefeller was there<br/>  
<time begin="00:08:54.13"/><clear/>and there were two men  
shouting at him<br/>  
and one was a man named John Davis,<br/>  
<time begin="00:08:58.78"/><clear/>who is now an Emeritus  
Professor<br/>  
of Tropical Medicine at Harvard,<br/>  
<time begin="00:09:02.83"/><clear/>another one was the late Ken

Warren who  
was working at the Rockefeller Foundation  
<time begin="00:09:06.70"/><clear/>and he led a program that was  
called  
the Great Neglected Diseases of mankind.  
<time begin="00:09:10.95"/><clear/>And I'll never forget  
John  
Davis shouting at my --  
<time begin="00:09:14.43"/><clear/>who ultimately became my  
thesis advisor  
saying, if he wants to work on hookworm,  
<time begin="00:09:18.90"/><clear/>let him work on hookworm and  
that's when  
it was decided at this Gordon Conference  
<time begin="00:09:22.97"/><clear/>and then that's what I  
did  
and that's how we got started.  
<time begin="00:09:26.62"/><clear/>So what is it. And this, this  
was a tough  
road to hoe because hookworms are organisms  
<time begin="00:09:34.76"/><clear/>which are difficult to  
work  
with in the laboratory.  
<time begin="00:09:37.68"/><clear/>You can't get much in the  
way  
of the organisms to work with,  
<time begin="00:09:42.18"/><clear/>so it's hard to do  
biochemistry on them.  
<time begin="00:09:44.73"/><clear/>It's hard to purify proteins  
from them,  
to even purify nucleic acids from them,  
<time begin="00:09:49.38"/><clear/>there are no genetics  
that  
one can do on hookworms.  
<time begin="00:09:53.87"/><clear/>It's impossible to do cell  
biology, so what  
I used to tell people other than the fact  
<time begin="00:09:57.58"/><clear/>that you can't do  
biochemistry, cell biology or  
genetics on them, they're really great organisms  
<time begin="00:10:04.24"/><clear/>to work with and thus the  
reason why somebody  
would work on something like this is, indeed,  
<time begin="00:10:09.99"/><clear/>their enormous burden of  
disease in the developing world  
<time begin="00:10:13.26"/><clear/>and at the time we didn't  
have  
club.med or any of the computer searches



<time begin="00: 10: 17. 43"/><clear/>that we have available today

to do look<br/>

up existing literature on a subject.<br/>

<time begin="00: 10: 21. 27"/><clear/>Back then it was something

called Index<br/>

Medicus and you would go<br/>

<time begin="00: 10: 24. 67"/><clear/>to these big volumes off the

library shelf in<br/>

1980 and look up all the current literature<br/>

<time begin="00: 10: 29. 54"/><clear/>on hookworms and no

surprise<br/>

there was really nothing on it.<br/>

<time begin="00: 10: 34. 13"/><clear/>So here was the great

infection of mankind<br/>

and there was essentially no work being done<br/>

<time begin="00: 10: 39. 06"/><clear/>at the biochemical and

molecular level.<br/>

<time begin="00: 10: 41. 50"/><clear/>So and, since I was told I

had to<br/>

do something original and great,<br/>

<time begin="00: 10: 44. 51"/><clear/>I thought well maybe this is

the one.<br/>

<time begin="00: 10: 46. 37"/><clear/>So let me tell you a little

bit about that<br/>

story and a little bit about what hookworms are<br/>

<time begin="00: 10: 51. 59"/><clear/>and why we think they're so

important<br/>

especially in the developing world.<br/>

<time begin="00: 10: 58. 52"/><clear/>

<time begin="00: 11: 00. 31"/><clear/>So first of all hookworm,

what is it?<br/>

<time begin="00: 11: 03. 57"/><clear/>It's a parasitic worm

infection.<br/>

<time begin="00: 11: 07. 19"/><clear/>In fact. It's a particular

type of parasitic<br/>

worm called a nematode spelled, n-e-m-a-t-o-d-e,<br/>

<time begin="00: 11: 14. 03"/><clear/>and together with two other

parasitic nematode<br/>

infections these comprise what we now call the<br/>

<time begin="00: 11: 21. 32"/><clear/>soil-transmitted helminth

infections<br/>

or the soil-transmitted helminthiasis.<br/>

<time begin="00: 11: 26. 48"/><clear/>They're so-called because

they<br/>

have environmental stages that live<br/>

<time begin="00: 11: 29. 91"/><clear/>in the moist warm soil of the

developing world  
and where they're practically ubiquitous. So what I'm showing you on the top are the three major soil transmitted helminth infections of humans and those are ascariasis, the large common roundworm, trichuriasis, and hookworms which are hookworms. And look at those numbers, so what is it mean that there are 1.2 billion people in the world with ascariasis? How many people are in the world? About six and change maybe 6.4, so what I'm telling you is that about a fifth or a sixth of the world's population are infected with these parasitic worms, an enormous number. I often like to say that if Carl Sagan didn't become an astronomer and go into cosmic science and decided to become a biomedical scientist this is what he would work on because what else could he talk about billions and billions being infected. So these are arguably the most common infectious agents of humankind. So I want to start out this evening giving you a sense of what it means to have a billion people infected with these worms, and we're going to go look at these kids on the left here and these are a bunch of kids who they do look a little scruffy perhaps not too

ill until we realize that they are all stunted.<br/>  
<time begin="00: 13: 05. 12"/><clear/>Their weight, they're all  
stunted,<br/>  
their heights and they're not growing<br/>  
<time begin="00: 13: 08. 26"/><clear/>and they do poorly on tests  
of IQ and cognition.<br/>  
<time begin="00: 13: 12. 56"/><clear/>These are kids that are  
growing up along the<br/>  
coffee plantations, the coffee bean goods<br/>  
<time begin="00: 13: 16. 73"/><clear/>in this case in southwestern  
Guatemala in<br/>  
this particular village of Pachalum.<br/>  
<time begin="00: 13: 23. 19"/><clear/>They're poor kids living  
in<br/>  
poor rural areas of Guatemala.<br/>  
<time begin="00: 13: 29. 43"/><clear/>Now there's an  
increasing<br/>  
body of evidence now indicates<br/>  
<time begin="00: 13: 32. 56"/><clear/>that the reason why these  
kids are stunted for<br/>  
height and weight and they do poorly on tests<br/>  
<time begin="00: 13: 38. 82"/><clear/>of IQ and tests of cognition  
is<br/>  
because they have a belly full of one<br/>  
<time begin="00: 13: 43. 49"/><clear/>or more of those three  
parasitic worms,<br/>  
ascariasis or trichuriasis or hookworm.<br/>  
<time begin="00: 13: 49. 62"/><clear/>In fact, there's an old term  
that Harold<br/>  
Brown, professor of parasitology<br/>  
<time begin="00: 13: 54. 74"/><clear/>at Columbia coined called the  
unholy trinity<br/>  
to remark on the fact that it was very common,<br/>  
<time begin="00: 14: 00. 29"/><clear/>if you have a child  
infected<br/>  
with one of these worms,<br/>  
<time begin="00: 14: 02. 98"/><clear/>they were infected  
sometimes<br/>  
with two or all three.<br/>  
<time begin="00: 14: 05. 90"/><clear/>And so how do we know  
that?<br/>  
<time begin="00: 14: 07. 25"/><clear/>How do we know that  
they're<br/>  
infected with the worms?<br/>  
<time begin="00: 14: 08. 99"/><clear/>Well, we take advantage of  
the fact that,<br/>  
when people have these parasitic worms<br/>

<time begin="00: 14: 13. 13"/><clear/>in their intestinal tract, <br/>  
they're male and female worms<br/>  
<time begin="00: 14: 16. 09"/><clear/>and they mate and they produce eggs. <br/>  
<time begin="00: 14: 18. 45"/><clear/>And so one can establish a diagnosis of the<br/>  
unholy trinity by looking in their stool, <br/>  
<time begin="00: 14: 24. 30"/><clear/>Looking in their feces under a microscope<br/>  
and looking for the characteristic egg, <br/>  
<time begin="00: 14: 28. 89"/><clear/>each of the worm produces an egg<br/>  
that has a characteristic morphology. <br/>  
<time begin="00: 14: 32. 97"/><clear/>So we're going to do that now in this village of<br/>  
Pachalum in Guatemala and here you see age class, <br/>  
<time begin="00: 14: 39. 50"/><clear/>age class on the X-axis you<br/>  
see 0 to 3, 4 to 7, 8 to 12, <br/>  
<time begin="00: 14: 44. 37"/><clear/>and on the Y-axis you see prevalent the percent<br/>  
-- percentage of these kids that are in infected<br/>  
<time begin="00: 14: 50. 09"/><clear/>with either ascariasis, in the white, <br/>  
trichuriasis, in the dark green, <br/>  
<time begin="00: 14: 54. 27"/><clear/>and hookworm in the, I<br/>  
guess that's a teal color. <br/>  
<time begin="00: 14: 58. 08"/><clear/>So what percentage of the kids in<br/>  
this villages harbor ascariasis worms?<br/>  
<time begin="00: 15: 03. 53"/><clear/>  
<time begin="00: 15: 07. 93"/><clear/>It means that they all do, right. <br/>  
<time begin="00: 15: 09. 32"/><clear/>80, 90 close to 100 percent, <br/>  
they all harbor ascariasis. <br/>  
<time begin="00: 15: 12. 77"/><clear/>Almost as many harbor trichuriasis<br/>  
and almost again as many harbor hookworm. <br/>  
<time begin="00: 15: 17. 19"/><clear/>Now what we're going to do is we're going<br/>  
to go to the next village over from Pachalum<br/>  
<time begin="00: 15: 22. 43"/><clear/>in Guatemala, I don't even know what<br/>  
the name is, but I can promise you<br/>  
<time begin="00: 15: 25. 71"/><clear/>that this is exactly what

you'll find.<br/>  
<time begin="00: 15: 27. 89"/><clear/>In fact, you go to any  
rural<br/>  
village in Guatemala<br/>  
<time begin="00: 15: 31. 10"/><clear/>and you will see the same  
recurring theme that<br/>  
there are a 100 percent of the kids infected<br/>  
<time begin="00: 15: 37. 87"/><clear/>with ascariasis, almost as  
many again<br/>  
with trichuriasis, the whipworm,<br/>  
<time begin="00: 15: 41. 04"/><clear/>almost as many again with  
hookworm.<br/>  
<time begin="00: 15: 42. 85"/><clear/>In fact, you go to any rural  
village<br/>  
in Central America, in Nicaragua,<br/>  
<time begin="00: 15: 47. 69"/><clear/>Honduras, Panama this is what  
you'll find.<br/>  
<time begin="00: 15: 50. 64"/><clear/>You go to any rural village  
in tropical<br/>  
regions of the Americas: Venezuela,<br/>  
<time begin="00: 15: 55. 71"/><clear/>Brazil, Peru this is what  
you'll find.<br/>  
<time begin="00: 15: 58. 25"/><clear/>If you do this exercise in  
southeast Asia, in<br/>  
Thailand, Vietnam, Laos, Cambodia, South China,<br/>  
<time begin="00: 16: 06. 81"/><clear/>in sub-Saharan Africa  
where<br/>  
there's probably more infections<br/>  
<time begin="00: 16: 09. 50"/><clear/>than anywhere else, this is  
what you'll find.<br/>  
<time begin="00: 16: 11. 44"/><clear/>So then you start getting the  
sense that,<br/>  
gee, maybe there really could be a billion people<br/>  
<time begin="00: 16: 16. 47"/><clear/>in the world with this many  
parasites.<br/>  
<time begin="00: 16: 19. 42"/><clear/>Now we do a fair amount of  
work in China<br/>  
and my Chinese colleagues have completed a study<br/>  
<time begin="00: 16: 26. 85"/><clear/>in the early 1990's that I  
like to think all<br/>  
of the Chinese could do which is they needed<br/>  
<time begin="00: 16: 31. 72"/><clear/>to know who had parasites in  
their country,<br/>  
and they set out and collected fecal exams<br/>  
<time begin="00: 16: 37. 00"/><clear/>on 1,477,742 individuals, one  
of the<br/>

largest health surveys ever done. <br/>  
<time begin="00:16:44.94"/><clear/>They found 45 percent of  
their <br/>  
population infected with ascariasis. <br/>  
<time begin="00:16:49.64"/><clear/>Well, what's the population  
of China? <br/>  
<time begin="00:16:51.67"/><clear/>It's at least a billion, <br/>  
right, 1.2 billion at the time. <br/>  
<time begin="00:16:56.51"/><clear/>So we're talking about almost  
half a -- <br/>  
<time begin="00:17:01.83"/><clear/>half a billion people  
infected with <br/>  
ascariasis just in China alone. <br/>  
<time begin="00:17:05.62"/><clear/>And if you add India to that  
you almost get up to be <br/>  
a billion right then and there, so this gives you a sense <br/>  
<time begin="00:17:10.14"/><clear/>of the enormous,  
enormous <br/>  
numbers of people infected. <br/>  
<time begin="00:17:16.16"/><clear/>So the first part of this  
talk: <br/>  
It's a very wormy world out there. <br/>  
<time begin="00:17:20.73"/><clear/>And, in fact, Norman Stoll  
once wrote a paper <br/>  
called: It's a Wormy World and he's right. <br/>  
<time begin="00:17:26.69"/><clear/>The next point is there's not  
only a <br/>  
lot of worm infections in the world <br/>  
<time begin="00:17:30.89"/><clear/>but they're a particular  
problem <br/>  
among children and why is that? <br/>  
<time begin="00:17:34.41"/><clear/>I don't know how well that  
shows up in the <br/>  
back with the color scheme and the lights, <br/>  
<time begin="00:17:38.55"/><clear/>but what it shows is on the  
X-axis, age, and <br/>  
the Y-axis, number of worms per individual, <br/>  
<time begin="00:17:46.51"/><clear/>and what you see is that  
there is, this <br/>  
is a composite study done by a number <br/>  
<time begin="00:17:52.16"/><clear/>of groups including ours but  
there's <br/>  
many other groups that have been able <br/>  
<time begin="00:17:56.71"/><clear/>to replicate this pattern,  
and <br/>  
it shows that there is a period <br/>  
<time begin="00:18:01.53"/><clear/>in one's life when we're

wormier than others.<br/>  
<time begin="00: 18: 04. 93"/><clear/>Because remember these worms  
are not like<br/>  
other infectious agents you hear about.<br/>  
<time begin="00: 18: 09. 98"/><clear/>They're not like bacteria or  
protozoa that are<br/>  
multiplying inside your body, in other words,<br/>  
<time begin="00: 18: 16. 79"/><clear/>the more worms you have the  
sicker<br/>  
<time begin="00: 18: 20. 49"/><clear/>you get because they're  
animals<br/>  
inside an animal, animals inside people.<br/>  
<time begin="00: 18: 25. 36"/><clear/>So the worms are mating and  
producing eggs<br/>  
but they're not doubling in their numbers,<br/>  
<time begin="00: 18: 30. 03"/><clear/>and so what this is showing  
is that for<br/>  
reasons which are still not entirely clear<br/>  
<time begin="00: 18: 36. 44"/><clear/>because these parasites are  
so neglected in<br/>  
terms of their study that there is a peak period<br/>  
<time begin="00: 18: 41. 56"/><clear/>of worminess in the life of  
an individual<br/>  
and when is that peak period of worminess?<br/>  
<time begin="00: 18: 46. 87"/><clear/>  
<time begin="00: 18: 48. 48"/><clear/>Starts going up around age 3  
or 4 and then<br/>  
continues until around age 15, so<br/>  
<time begin="00: 18: 55. 65"/><clear/>you have a situation now  
where you have<br/>  
children, essentially, school age children,<br/>  
<time begin="00: 19: 01. 52"/><clear/>age 5 to 15 is when they're  
running around<br/>  
with their highest worm burden and the fact<br/>  
<time begin="00: 19: 06. 95"/><clear/>that they're in school is  
very important<br/>  
because, as I said, worms are stunting height,<br/>  
<time begin="00: 19: 11. 44"/><clear/>they're stunting weight and  
they're<br/>  
stunting your ability to learn in school<br/>  
<time begin="00: 19: 16. 10"/><clear/>by suppressing IQ and  
suppressing cognition.<br/>  
<time begin="00: 19: 19. 24"/><clear/>So this is why even though  
worm infections are<br/>  
<time begin="00: 19: 22. 34"/><clear/>so common world-wide they're  
a particular<br/>  
problem among school age children,<br/>

<time begin="00: 19: 26. 56"/><clear/>and so they're not only a  
medical problem<br/>  
but they're also an educational problem.<br/>  
<time begin="00: 19: 32. 24"/><clear/>So what does it mean to have  
these high worm<br/>  
burdens as we stated, large numbers of worms<br/>  
<time begin="00: 19: 38. 66"/><clear/>in children as opposed to  
other populations?<br/>  
<time begin="00: 19: 41. 50"/><clear/>And to give you a sense of  
that, let's go here.<br/>  
<time begin="00: 19: 43. 77"/><clear/>What I'm showing you are some  
pictures of some<br/>  
kids, this is a child from Haiti on the left,<br/>  
<time begin="00: 19: 48. 93"/><clear/>and a child who -- that one  
of my students<br/>  
took of a kid in Paraguay on the right.<br/>  
<time begin="00: 19: 56. 28"/><clear/>And what do you notice about  
them?<br/>  
<time begin="00: 19: 58. 98"/><clear/>  
<time begin="00: 20: 02. 23"/><clear/>They have a kind of big  
distended<br/>  
abdomen, don't they?<br/>  
<time begin="00: 20: 05. 38"/><clear/>In fact, if you were to run  
your hand<br/>  
over the surface of their abdomen,<br/>  
<time begin="00: 20: 10. 25"/><clear/>you would actually palpate  
the outline of worms<br/>  
<time begin="00: 20: 12. 66"/><clear/>in their intestinal  
tract<br/>  
because there are so many worms.<br/>  
<time begin="00: 20: 15. 32"/><clear/>Now how do we know that?<br/>  
<time begin="00: 20: 16. 76"/><clear/>Well, we actually have drugs  
that<br/>  
are available to expel the worms<br/>  
<time begin="00: 20: 21. 50"/><clear/>and the two major drugs used  
are known<br/>  
benzimidazole anthelmintics,<br/>  
<time begin="00: 20: 26. 42"/><clear/>one's called mebendazole  
and<br/>  
the other one is called albendazole.<br/>  
<time begin="00: 20: 30. 99"/><clear/>And what we're going to do is  
we're going<br/>  
to take this little girl on the right here<br/>  
<time begin="00: 20: 34. 43"/><clear/>and give her one of those  
drugs, and<br/>  
these are the worms from that one child.<br/>  
<time begin="00: 20: 41. 26"/><clear/>Those enormous ascariasis



worms, <br/>  
and it's pretty obvious. <br/>  
<time begin="00: 20: 45. 10"/><clear/>That's actually my student  
holding up<br/>  
the worms with a big smile on her face. <br/>  
<time begin="00: 20: 48. 32"/><clear/>I cut off her smile, being  
that she has<br/>  
a nice smile it seemed inappropriate. <br/>  
<time begin="00: 20: 51. 95"/><clear/>She was so delighted to see  
all these worms out, <br/>  
so it's pretty obvious why this child is going<br/>  
<time begin="00: 20: 56. 89"/><clear/>to get into trouble, right,  
these<br/>  
worms are going to get entangled<br/>  
<time begin="00: 21: 00. 44"/><clear/>in a Medusa-like writhing  
mass, you<br/>  
know, cause acute intestinal obstruction. <br/>  
<time begin="00: 21: 05. 03"/><clear/>So, if you go visit a  
hospital <br/>  
in a developing country, <br/>  
<time begin="00: 21: 08. 17"/><clear/>it's very common to see a  
child<br/>  
who's recently been operated<br/>  
<time begin="00: 21: 10. 82"/><clear/>on for this acute intestinal  
obstruction. <br/>  
<time begin="00: 21: 14. 44"/><clear/>They're going to wander. <br/>  
<time begin="00: 21: 15. 64"/><clear/>They'll sometimes wander  
into<br/>  
the pancreas and into the liver<br/>  
<time begin="00: 21: 19. 70"/><clear/>to cause a number of problems  
there. <br/>  
<time begin="00: 21: 22. 75"/><clear/>They will sometimes migrate  
up<br/>  
out the nose or down out the anus, <br/>  
<time begin="00: 21: 26. 72"/><clear/>and it's obviously very  
concerning to parents<br/>  
when they see something like that, but<br/>  
<time begin="00: 21: 33. 74"/><clear/>it's clear that having these  
kinds of worms are<br/>  
going to get you into serious trouble because, <br/>  
<time begin="00: 21: 39. 04"/><clear/>if for no other reason than  
you're<br/>  
feeding a child in a developing child, <br/>  
<time begin="00: 21: 43. 33"/><clear/>you're essentially feeding  
the worms<br/>  
first before you're feeding the child. <br/>  
<time begin="00: 21: 48. 27"/><clear/>So this is a very

dramatic<br/>  
consequence of worminess<br/>  
<time begin="00: 21: 52. 49"/><clear/>in school -age children in a  
developing country.<br/>  
<time begin="00: 21: 56. 50"/><clear/>But there's something  
more<br/>  
subtle that I think is even --<br/>  
<time begin="00: 21: 59. 98"/><clear/>something more subtle but  
it's something<br/>  
which I think is very important.<br/>  
<time begin="00: 22: 05. 20"/><clear/>What I'm showing you here on  
the left<br/>  
is what looks like a growth chart<br/>  
<time begin="00: 22: 10. 90"/><clear/>that you might see in any  
pediatrician's office.<br/>  
<time begin="00: 22: 12. 85"/><clear/>So those of you who have  
taken your kids to<br/>  
the pediatrician, you've seen him or her mark<br/>  
<time begin="00: 22: 17. 74"/><clear/>down your child's weight on  
the growth<br/>  
chart and it usually goes along with,<br/>  
<time begin="00: 22: 21. 72"/><clear/>I'm sorry, I don't have the  
pointer here,<br/>  
but it goes along with different percentiles.<br/>  
<time begin="00: 22: 25. 20"/><clear/>You see age on the X-axis, in  
terms<br/>  
of months and weight, on the Y-axis,<br/>  
<time begin="00: 22: 31. 38"/><clear/>in terms of weight gain, and  
you look for<br/>  
children to grow along different percentiles<br/>  
<time begin="00: 22: 35. 97"/><clear/>of weight versus age, and  
this is, you see the<br/>  
third percentile, the 10th, the 25th, the 50th,<br/>  
<time begin="00: 22: 42. 02"/><clear/>the 70th all the way up to  
the 97th percentile.<br/>  
<time begin="00: 22: 46. 71"/><clear/>But now I'm showing you a  
child who's plodding<br/>  
along in the red there and what's happened<br/>  
<time begin="00: 22: 51. 79"/><clear/>to this child is his growth  
is flat.<br/>  
<time begin="00: 22: 53. 91"/><clear/>He's not growing at all until  
we intervene.<br/>  
<time begin="00: 22: 56. 92"/><clear/>And now we're going to  
intervene by<br/>  
giving a dose of drugs to expel the worms.<br/>  
<time begin="00: 23: 02. 84"/><clear/>And what happens after

we<br/>  
give that dose of drugs?<br/>  
<time begin="00: 23: 05. 85"/><clear/>  
<time begin="00: 23: 06. 94"/><clear/>You see this very impressive  
catch-up growth,<br/>  
all of a sudden now the child can grow.<br/>  
<time begin="00: 23: 11. 80"/><clear/>So what I like to tell my  
medical students<br/>  
who are interested in the endocrine system,<br/>  
<time begin="00: 23: 16. 25"/><clear/>here's the world's  
leading<br/>  
endocrinopathy, it's parasitic worms.<br/>  
<time begin="00: 23: 19. 79"/><clear/>Here's the world's  
leading<br/>  
cause of growth suppression.<br/>  
<time begin="00: 23: 23. 02"/><clear/>What's the mechanism?<br/>  
<time begin="00: 23: 23. 87"/><clear/>How do worms suppress  
growth?<br/>  
<time begin="00: 23: 25. 99"/><clear/>Anybody have an idea?<br/>  
<time begin="00: 23: 27. 99"/><clear/>  
<time begin="00: 23: 33. 00"/><clear/>So intuitively you would  
guess, right,<br/>  
intuitively you would guess there's some type<br/>  
<time begin="00: 23: 36. 39"/><clear/>of competition between  
parasite<br/>  
and host for nutrients.<br/>  
<time begin="00: 23: 41. 80"/><clear/>But the sad truth is nobody  
knows, why?<br/>  
<time begin="00: 23: 45. 41"/><clear/>Because nobody studies  
this.<br/>  
<time begin="00: 23: 46. 89"/><clear/>So here's the world's leading  
cause<br/>  
of growth retardation in the world<br/>  
<time begin="00: 23: 50. 93"/><clear/>and you cannot find a single  
paper in the<br/>  
scientific literature on the mechanism<br/>  
<time begin="00: 23: 56. 14"/><clear/>by which worms stunt growth,  
why is that?<br/>  
<time begin="00: 23: 59. 46"/><clear/>  
<time begin="00: 24: 02. 76"/><clear/>Well, the problem is who<br/>  
funds this kind of research?<br/>  
<time begin="00: 24: 08. 58"/><clear/>This is not a problem in the  
United States.<br/>  
<time begin="00: 24: 12. 93"/><clear/>It's the leading cause of  
growth retardation<br/>  
not in Georgia, but it's the leading cause<br/>  
<time begin="00: 24: 17. 36"/><clear/>of growth retardation perhaps

in Central<br/>

America and there are no agencies<br/>

<time begin="00:24:23.04"/><clear/>that are specifically

directed to funding basic<br/>

mechanism problems in the developing world.<br/>

<time begin="00:24:30.57"/><clear/>There's a term that those of

you who attended<br/>

Victoria Hale's talk she probably<br/>

<time begin="00:24:35.56"/><clear/>used the term, the 10/90 gap

to refer<br/>

to the fact that less than ten percent<br/>

<time begin="00:24:40.96"/><clear/>of the world's resources go

for the research on<br/>

problems that afflict 90 percent of the diseases<br/>

<time begin="00:24:46.83"/><clear/>in the world and those

diseases are those<br/>

represented by those in developing countries.<br/>

<time begin="00:24:50.50"/><clear/>It's astonishing, the world's

leading cause<br/>

of growth retardation and there's<br/>

<time begin="00:24:53.82"/><clear/>no scientific literature on

the topic.<br/>

<time begin="00:24:57.14"/><clear/>Now as to that I'm going to

direct<br/>

you to the right-hand panel,<br/>

<time begin="00:25:02.17"/><clear/>this issue of Parasitology

Today which I know<br/>

most of you get at home and this is to show<br/>

<time begin="00:25:10.24"/><clear/>that these worms not only

suppress growth<br/>

and physical development but they<br/>

<time begin="00:25:15.38"/><clear/>also inhibit the ability of

kids to learn.<br/>

<time begin="00:25:19.02"/><clear/>So there are good studies

to<br/>

show that the more worms you have<br/>

<time begin="00:25:24.76"/><clear/>in your intestine, the lower

your IQ is.<br/>

<time begin="00:25:28.01"/><clear/>So they have a direct,

there's some type of<br/>

almost direct effect of impairing IQ and tests<br/>

<time begin="00:25:34.19"/><clear/>of cognition and tests of

school performance.<br/>

<time begin="00:25:37.47"/><clear/>So just like worms are a

leading cause<br/>

<time begin="00:25:38.90"/><clear/>of physical growth

retardation<br/>

they're also the leading cause<br/>

<time begin="00:25:41.74"/><clear/>of more psychiatric

disturbance<br/>

in developing world.<br/>

<time begin="00:25:45.12"/><clear/>What's the mechanism?<br/>

<time begin="00:25:47.63"/><clear/>Who knows.<br/>

<time begin="00:25:49.19"/><clear/>But a very important problem

and, so this is<br/>

one of the reasons why these worm infections are<br/>

<time begin="00:25:53.73"/><clear/>so important is because their

ability to cause<br/>

physical and intellectual growth retardation<br/>

<time begin="00:26:01.62"/><clear/>and physical and intellectual

development.<br/>

<time begin="00:26:04.15"/><clear/>Now the problem though

is<br/>

-- as important as that<br/>

<time begin="00:26:08.79"/><clear/>is, the worms generally

speaking are not killing.<br/>

<time begin="00:26:13.29"/><clear/>So you might have heard about

malaria as one of<br/>

the leading killers of children in the world,<br/>

<time begin="00:26:17.82"/><clear/>2 million deaths annually,

but what worms are<br/>

doing is something a little bit different.<br/>

<time begin="00:26:23.13"/><clear/>They're not so much

killing<br/>

kids in the developing world,<br/>

<time begin="00:26:26.54"/><clear/>there's about 100,000

deaths<br/>

a year from<br/>

<time begin="00:26:30.28"/><clear/>these types of parasitic

worms, a few more<br/>

from the kinds of worms that Dan Colley studies,<br/>

<time begin="00:26:36.83"/><clear/>schistosomiasis which causes

about<br/>

200 maybe 1,000 deaths per year,<br/>

<time begin="00:26:40.37"/><clear/>but rather they're destroying

quality of life.<br/>

<time begin="00:26:43.32"/><clear/>And we've only developed a

metric for<br/>

measuring that over the last two decades<br/>

<time begin="00:26:49.28"/><clear/>and the metric that we use to

focus on<br/>

the ability of something to cause disease<br/>

<time begin="00:26:54.76"/><clear/>and cause disability but not

necessarily<br/>  
death is a metric known as the DALY,<br/>  
<time begin="00:27:00.29"/><clear/>it stands for the Disability  
Adjusted Life Year.<br/>  
<time begin="00:27:03.59"/><clear/>It refers to the number of  
life years<br/>  
lost either from premature death,<br/>  
<time begin="00:27:09.35"/><clear/>something that might kill you  
in childhood,<br/>  
or premature disability such as worms.<br/>  
<time begin="00:27:14.70"/><clear/>And when we use this metric  
of DALYs,<br/>  
<time begin="00:27:18.09"/><clear/>what we find is that these  
worm infections these<br/>  
helminth infections are enormously important.<br/>  
<time begin="00:27:24.15"/><clear/>So not using deaths but using  
DALYs look at<br/>  
where helminth infections stack up compared<br/>  
<time begin="00:27:29.93"/><clear/>to what we sometimes refer to  
as the<br/>  
big three, H.I.V. AIDS, TB or malaria.<br/>  
<time begin="00:27:36.04"/><clear/>So helminth infections are  
right up there,<br/>  
<time begin="00:27:38.51"/><clear/>with hookworm infections  
among the most<br/>  
important of all the different helminths.<br/>  
<time begin="00:27:44.23"/><clear/>The problem for someone  
like<br/>  
myself is we have Bono beating the drum<br/>  
<time begin="00:27:51.22"/><clear/>about AIDS, malaria and TB,  
you have<br/>  
Angelina Jolie beating her drum about AIDS,<br/>  
<time begin="00:27:56.71"/><clear/>malaria and TB but we don't  
have<br/>  
myself who gets about four people coming<br/>  
<time begin="00:28:02.25"/><clear/>to a lecture, and Dan Colley  
who does a<br/>  
little better gets about ten people coming<br/>  
<time begin="00:28:06.45"/><clear/>to his lecture to talk about  
parasitic worms.<br/>  
<time begin="00:28:09.48"/><clear/>And so there's this great  
disparity in advocacy,<br/>  
<time begin="00:28:12.88"/><clear/>but having said that the  
World Health<br/>  
Organization is very effective in trying<br/>  
<time begin="00:28:19.05"/><clear/>to do their best to persuade

ministers<br/>  
of health throughout the developing world<br/>  
<time begin="00:28:24.26"/><clear/>to adopt procedures by which  
children, <br/>  
especially school-age children, <br/>  
<time begin="00:28:30.24"/><clear/>would start receiving  
these<br/>  
what we call anthelmintic drugs, <br/>  
<time begin="00:28:35.39"/><clear/>these anti-worm drugs on a  
large scale. <br/>  
<time begin="00:28:38.62"/><clear/>And in 2001 at the 54th World  
Health<br/>  
Assembly, see the World Health Assemblies are<br/>  
<time begin="00:28:43.94"/><clear/>where major health decisions  
are made, are<br/>  
actually passed on an international scale, <br/>  
<time begin="00:28:50.86"/><clear/>the following resolution was  
proposed<br/>  
and it was known as Resolution 54.19, <br/>  
<time begin="00:28:58.05"/><clear/>With a goal of attaining a  
minimum target<br/>  
of regular administration of anthelmintic, <br/>  
<time begin="00:29:04.21"/><clear/>anti-worm chemotherapy which  
was comprised of<br/>  
a benzimidazole anthelmintic, either albendazole<br/>  
<time begin="00:29:10.67"/><clear/>or mebendazole, the one that  
put all<br/>  
those worms in the pan that you just saw, <br/>  
<time begin="00:29:15.02"/><clear/>for the soil-transmitted  
helminths, <br/>  
plus a second drug known as praziquantel <br/>  
<time begin="00:29:20.13"/><clear/>which treats another very  
important<br/>  
helminth infection known as schistosomiasis<br/>  
<time begin="00:29:24.43"/><clear/>which Professor Colley  
studies, to at<br/>  
least 75 percent and up to 100 percent<br/>  
<time begin="00:29:30.59"/><clear/>of all school-age children at  
risk<br/>  
for morbidity by the year 2010. <br/>  
<time begin="00:29:38.00"/><clear/>That's a big program, in  
fact, the estimates<br/>  
are we're talking about the regular treatment<br/>  
<time begin="00:29:42.63"/><clear/>of 500 million school  
children<br/>  
on an annual basis. <br/>  
<time begin="00:29:46.04"/><clear/>So, if implemented, this

would become one of  
the largest health programs ever attempted  
<time begin="00: 29: 53. 03"/><clear/>but for a good reason because  
of the enormous  
impact that these worms have on child health  
<time begin="00: 29: 59. 13"/><clear/>in terms of physical growth  
as well  
as education vis-a-vis intellectual  
<time begin="00: 30: 04. 25"/><clear/>and cognitive  
development.   
<time begin="00: 30: 05. 60"/><clear/>So this was a very exciting  
resolution,   
however, it's not as rosy as you might think  
<time begin="00: 30: 11. 44"/><clear/>and the reason we're  
particularly  
concerned about it has to do with this.   
<time begin="00: 30: 17. 58"/><clear/>This is a graph of a study  
that Marco  
Albonico and his colleagues at WHO did  
<time begin="00: 30: 24. 82"/><clear/>in Pemba Island off the coast  
of  
Tanzania and what I'm showing you  
<time begin="00: 30: 29. 66"/><clear/>on the Y-axis is our  
measurement of number of  
worms per individual and on the X-axis is days.   
<time begin="00: 30: 39. 55"/><clear/>And what they did is they  
went into two  
villages, they went into Village A or Village B  
<time begin="00: 30: 43. 46"/><clear/>or the red village or the  
blue  
village and they went in armed  
<time begin="00: 30: 47. 66"/><clear/>with an anthelmintic  
drug,   
in this case mebendazole.   
<time begin="00: 30: 50. 34"/><clear/>Now it turns out mebendazole  
doesn't  
always work as well as advertised.   
<time begin="00: 30: 53. 69"/><clear/>In some regions the efficacy,  
the ability  
of them to cure these worm infections,   
<time begin="00: 30: 58. 67"/><clear/>is only around 21 percent but  
in this case they  
did pretty well, and they brought the number  
<time begin="00: 31: 03. 21"/><clear/>of worms on the left-hand  
side of that  
graph pretty much down close to zero.   
<time begin="00: 31: 07. 52"/><clear/>And now what they're going



to, what these<br/>

guys did in Pemba Island is they walked<br/>

<time begin="00:31:13.82"/><clear/>away after anthelmintic

deworming.<br/>

<time begin="00:31:16.68"/><clear/>Deworming is a term that we

sometimes<br/>

use to deal with these worms.<br/>

<time begin="00:31:18.94"/><clear/>And now we're going to walk

away for<br/>

120 to 180 days, four to six months.<br/>

<time begin="00:31:25.60"/><clear/>What's happened?<br/>

<time begin="00:31:27.18"/><clear/>

<time begin="00:31:30.88"/><clear/>They're back.<br/>

<time begin="00:31:32.55"/><clear/>They came back because

one<br/>

of the unusual features<br/>

<time begin="00:31:35.09"/><clear/>about these worms is

they<br/>

do not have the ability<br/>

<time begin="00:31:38.27"/><clear/>to stimulate naturally

protective immunity.<br/>

<time begin="00:31:41.50"/><clear/>And so what the studies show

is that and<br/>

this is particularly true of all the worms<br/>

<time begin="00:31:47.46"/><clear/>that we're talking about

today but it's<br/>

particularly important for hookworm<br/>

<time begin="00:31:52.04"/><clear/>but what it means is that

hookworm<br/>

infected patients will reacquire hookworms<br/>

<time begin="00:31:56.38"/><clear/>to pretreatment levels within

four<br/>

<time begin="00:31:58.71"/><clear/>to twelve months following

a<br/>

dose of anthelmintic chemotherapy.<br/>

<time begin="00:32:02.71"/><clear/>What this means is

practically speaking, unless<br/>

you're prepared to go back into these villages<br/>

<time begin="00:32:09.77"/><clear/>with your dose of anthelmintic

drugs every<br/>

four to six months for the life of this child<br/>

<time begin="00:32:15.45"/><clear/>or for the time these

children are in<br/>

school, the kids are going to remain wormy<br/>

<time begin="00:32:19.38"/><clear/>because the worms come right

back.<br/>

<time begin="00:32:22.09"/><clear/>So is one of the reasons

why  
even though we have drugs available to deworm,  
<time begin="00:32:27.94"/><clear/>they're often not effective  
for  
purposes of public health control  
<time begin="00:32:31.13"/><clear/>because of this unique  
feature  
of the worms to come back.  
<time begin="00:32:34.07"/><clear/>And now there's good data to  
indicate that the  
efficacy of these BZAs, these benzimidazoles,  
<time begin="00:32:40.41"/><clear/>as I said, this is point  
number 3,  
will diminish with increasing use.  
<time begin="00:32:44.57"/><clear/>In other words, what starts  
to happen, if  
you keep on repeating this exercise over  
<time begin="00:32:48.55"/><clear/>and over again, the drugs  
stop  
working as well as they used to.  
<time begin="00:32:52.17"/><clear/>And there is concern that  
this might  
be the beginning of what we're seeing  
<time begin="00:32:56.04"/><clear/>as anthelmintic drug  
resistance that the worms  
are becoming resistant to the drugs and it turns  
<time begin="00:33:01.10"/><clear/>out it only takes a point  
mutation in one of  
the nematode tubular alleles to confer this type  
<time begin="00:33:06.86"/><clear/>of resistance and so  
Professor Kaplan in the vet  
school is actually studying this phenomena not  
<time begin="00:33:11.60"/><clear/>for human worms but for  
veterinary worms  
but it's a similar type of phenomena.  
<time begin="00:33:16.02"/><clear/>So this business of the worms  
coming back and  
the fact that now maybe we're seeing the tip  
<time begin="00:33:23.00"/><clear/>of resistance occurring makes  
us  
think well we might have to come  
<time begin="00:33:26.41"/><clear/>up with something better,  
that in  
the long run for these drugs.  
<time begin="00:33:32.36"/><clear/>And this is particularly true  
for hookworm  
and let me tell you a few specifics  
<time begin="00:33:37.34"/><clear/>about hookworm before we

go<br/>  
<time begin="00: 33: 39. 89"/><clear/>into what we're actually  
going<br/>  
to propose to do about it.<br/>  
<time begin="00: 33: 42. 84"/><clear/>So I don't know how well it  
shows up here.<br/>  
<time begin="00: 33: 44. 49"/><clear/>Is there any way we can get  
the<br/>  
lights down just for this one slide?<br/>  
<time begin="00: 33: 47. 49"/><clear/>If it's not possible, don't  
sweat it.<br/>  
<time begin="00: 33: 50. 91"/><clear/>But what I'm showing you is a  
scanning electron<br/>  
micrograph of a hookworm on the left-hand side<br/>  
<time begin="00: 33: 58. 70"/><clear/>and it's armed with these  
very ferocious looking<br/>  
teeth or cutting plates that allows it to adhere<br/>  
<time begin="00: 34: 05. 93"/><clear/>to the inside layer of the  
small intestine.<br/>  
<time begin="00: 34: 09. 34"/><clear/>And in the middle panel  
what<br/>  
I'm showing you is a longitudinal section<br/>  
<time begin="00: 34: 13. 79"/><clear/>of hookworm intestine with  
the worm attached<br/>  
and you can see how deeply embedded the worm is<br/>  
<time begin="00: 34: 19. 87"/><clear/>in the intestinal tract.  
What<br/>  
they have the ability to do,<br/>  
<time begin="00: 34: 23. 09"/><clear/>well, that's getting a little  
better,<br/>  
<time begin="00: 34: 24. 81"/><clear/>is they have the ability to  
attach<br/>  
onto the inside of the small intestine.<br/>  
<time begin="00: 34: 29. 94"/><clear/>They tear away at small blood  
vessels in<br/>  
the intestine and then they almost look<br/>  
<time begin="00: 34: 34. 13"/><clear/>like little internal leeches  
and<br/>  
they're actually feeding on blood,<br/>  
<time begin="00: 34: 36. 87"/><clear/>and what you're seeing on the  
right-hand side is<br/>  
blood pouring out of the other end of the worm,<br/>  
<time begin="00: 34: 42. 46"/><clear/>so that a person who has  
large numbers of<br/>  
hookworms is essentially losing blood.<br/>  
<time begin="00: 34: 47. 02"/><clear/>He's hemorrhaging through his

intestinal tract and the result is that an individual who is so affected with large numbers of hookworm is losing enough blood to cause iron loss sufficient to cause iron deficiency because blood is rich in iron and protein loss because blood is very rich in protein. So it's causing iron deficiency and protein malnutrition and here's a major cause of it. So 40 hookworms will cause about 1.0 mLs of blood loss per day so here is a kid walking around in developing country with 40 worms losing 1.0 mLs of blood per day, may not seem like a huge amount but it's about .6 milligrams of iron but that's their daily iron requirement. So these worms are robbing kids of their daily iron requirements and the consequences then are, there's some good epidemiologic studies to show that 37 percent of the iron deficiency anemia in Brazil is due to hookworm, in Zanzibar 35 percent and up to 73 percent of severe anemia in Africa is due to hookworms. We saw that many parts of Africa hookworm is as important as a cause of anemia, the consequence of the anemia has a lot to do, the chronic anemia in kids, with child growth retardation, child intellectual and cognitive impairments and then very important

it's  
also a problem in pregnant women.  
<time begin="00:36:08.23"/><clear/>So pregnant women are another  
very vulnerable  
population and now there's good studies to show  
<time begin="00:36:14.12"/><clear/>that hookworm results in  
adverse maternal  
fetal outcomes, increased maternal mortality,  
<time begin="00:36:19.62"/><clear/>low birthrate and increased  
infant mortality.  
<time begin="00:36:29.91"/><clear/>All right.  
<time begin="00:36:30.16"/><clear/>I did something bad.  
<time begin="00:36:32.06"/><clear/>  
<time begin="00:36:33.95"/><clear/>So, now the question is  
well,  
what -- what can we do about this.  
<time begin="00:36:38.06"/><clear/>Well, I wonder if you can  
take  
me one step back, one slide back.  
<time begin="00:36:45.21"/><clear/>We looked at this and said  
well,  
<time begin="00:36:47.92"/><clear/>and this is how I really  
got  
started in the hookworm business.  
<time begin="00:36:50.83"/><clear/>I said well, the problem if  
the hookworms keep  
coming back, what can we do that's preventive.  
<time begin="00:36:56.44"/><clear/>What can we do to prevent  
the  
hookworms from coming back?  
<time begin="00:36:58.70"/><clear/>And the answer is can you  
make a vaccine,  
can you make an anti-worm vaccine?  
<time begin="00:37:04.47"/><clear/>And the answer turns out is  
yes we think we can.  
<time begin="00:37:07.99"/><clear/>And let me tell you how  
we  
think we can go about doing that.  
<time begin="00:37:11.47"/><clear/>So I'm going to start you at  
the bottom  
of this chart where you see worms.  
<time begin="00:37:15.97"/><clear/>And I'm sorry, I don't have  
the pointer.  
<time begin="00:37:17.15"/><clear/>Worms are attached to the  
inside of  
an intestine they're feeding on blood,  
<time begin="00:37:21.72"/><clear/>what happens is the worms are

mating, <br/>  
and they're producing eggs and, <br/>  
<time begin="00: 37: 25. 03"/><clear/>when eggs exit the body in  
feces, those<br/>  
feces get deposited on ground that has lots<br/>  
<time begin="00: 37: 31. 15"/><clear/>of moisture and shade in  
the<br/>  
absence of sanitation and this, <br/>  
<time begin="00: 37: 35. 37"/><clear/>these will allow the eggs to  
hatch and will<br/>  
give rise to small larvae stages which will feed<br/>  
<time begin="00: 37: 41. 85"/><clear/>on organic debris and  
bacteria in the ground<br/>  
<time begin="00: 37: 44. 80"/><clear/>and then what they'll do is  
they'll undergo a<br/>  
spontaneous molt to which is sometimes known<br/>  
<time begin="00: 37: 50. 12"/><clear/>as the L3 or the third  
stage<br/>  
infected larvae stage and that's shown<br/>  
<time begin="00: 37: 54. 60"/><clear/>on the upper left-hand panel  
where I'm trying<br/>  
to show you blades of grass and clusters<br/>  
<time begin="00: 37: 58. 85"/><clear/>of worms are standing on the  
blades of grass<br/>  
and they're waving like this and it's a behavior<br/>  
<time begin="00: 38: 06. 61"/><clear/>that called questing and  
you<br/>  
know what they're questing for?<br/>  
<time begin="00: 38: 10. 89"/><clear/>They're questing for you,  
of<br/>  
course, to come into contact with them<br/>  
<time begin="00: 38: 14. 29"/><clear/>and these larvae have the  
ability<br/>  
to directly penetrate human skin<br/>  
<time begin="00: 38: 17. 80"/><clear/>and they can also be  
swallowed in the<br/>  
case of another species of hookworm. <br/>  
<time begin="00: 38: 23. 36"/><clear/>These worms will go through a  
one- to<br/>  
two-month sojourn through the body. <br/>  
<time begin="00: 38: 27. 98"/><clear/>They'll go through the lungs  
and eventually<br/>  
make their way to the intestinal tract<br/>  
<time begin="00: 38: 32. 30"/><clear/>where they'll grow up to be  
adult worms that<br/>  
are about a centimeter long and feed on blood. <br/>  
<time begin="00: 38: 37. 31"/><clear/>So what is it that makes

anything about this<br/>  
that makes me think we can make a vaccine?<br/>  
<time begin="00:38:41.45"/><clear/>Well, it turns out that a  
group at<br/>  
Johns Hopkins School of Public Health<br/>  
<time begin="00:38:45.65"/><clear/>in the 1930's actually did  
make a vaccine.<br/>  
<time begin="00:38:48.27"/><clear/>And what they showed is that  
they took<br/>  
those L3, those third stage infected larvae,<br/>  
<time begin="00:38:54.02"/><clear/>and started taking small  
doses of that and<br/>  
immunized, taking laboratory animals,<br/>  
<time begin="00:38:59.91"/><clear/>they could immunize  
laboratory animals<br/>  
using small inocula of those L3<br/>  
<time begin="00:39:04.49"/><clear/>of those third stage larvae  
and so that's<br/>  
what I mean by at the top there success<br/>  
<time begin="00:39:09.58"/><clear/>vaccinating dogs against  
canine dog<br/>  
hookworm infection using the dog hookworm,<br/>  
<time begin="00:39:14.91"/><clear/>ancylostoma caninum with L3,  
and it was<br/>  
taken one step further in the 1960's so that<br/>  
<time begin="00:39:21.86"/><clear/>by 1970 you could buy a  
bottle of dog hookworm<br/>  
vaccine, and you could buy it in Florida in 1973<br/>  
<time begin="00:39:29.02"/><clear/>and the eastern half of  
United States by 1974,<br/>  
and it was comprised of living larvae,<br/>  
<time begin="00:39:36.68"/><clear/>they're about 600 microns  
in<br/>  
size, so about a little less<br/>  
<time begin="00:39:40.01"/><clear/>than half a millimeter,  
zapped with x-rays.<br/>  
<time begin="00:39:43.16"/><clear/>And you need to zap them with  
x-rays just enough<br/>  
so that they would stay alive but not so much<br/>  
<time begin="00:39:48.84"/><clear/>that they would develop  
after<br/>  
you gave them to the animal.<br/>  
<time begin="00:39:51.36"/><clear/>So you could march in with  
your dog in Florida<br/>  
in 1973, say I want to immunize the dog<br/>  
<time begin="00:39:56.01"/><clear/>against hookworm, your

Hotez.txt

veterinarian would take  
those x-ray zapped larvae, he'd have a bottle  
<time begin="00: 40: 00. 32"/><clear/>on the shelf of x-ray zapped  
larvae and  
then he would inject your dog and,  
<time begin="00: 40: 06. 23"/><clear/>twice, and you'd get a  
pretty  
good immune response  
<time begin="00: 40: 08. 79"/><clear/>that protected your animal  
against infection.  
<time begin="00: 40: 10. 69"/><clear/>The problem was, there  
were  
multiple problems, one of them was,  
<time begin="00: 40: 14. 03"/><clear/>when those x-ray zapped  
larvae started  
to die, they stopped secreting something  
<time begin="00: 40: 19. 85"/><clear/>that they needed to  
stimulate  
a protective immunity.  
<time begin="00: 40: 23. 01"/><clear/>There was something the  
larvae were  
secreting, they were actually spitting out,  
<time begin="00: 40: 28. 24"/><clear/>that was stimulating the  
protective immune response.  
<time begin="00: 40: 31. 77"/><clear/>So although the vaccine  
worked,  
commercially it was a failure  
<time begin="00: 40: 34. 63"/><clear/>because the poor veterinarian  
couldn't  
keep the stuff on the shelf long enough.  
<time begin="00: 40: 38. 48"/><clear/>Once he let it go for more  
than a few weeks,  
the larvae started to die on the shelf  
<time begin="00: 40: 42. 69"/><clear/>and they were no longer  
secreting  
something that was protective.  
<time begin="00: 40: 47. 72"/><clear/>So we came up with the idea,  
well,  
what if we don't do the larvae,  
<time begin="00: 40: 52. 08"/><clear/>we just collect enough worm  
spit from the larvae  
in order to elicit a protective immune response?  
<time begin="00: 40: 57. 33"/><clear/>The problem was you can't get  
enough hookworms,  
<time begin="00: 40: 58. 96"/><clear/>so we have to make it  
ultimately  
by genetic engineering.  
<time begin="00: 41: 03. 17"/><clear/>And so we went on this very



arduous<br/>  
journey in the late '80's and early 1990's<br/>  
<time begin="00: 41: 09. 50"/><clear/>to undertake the worm spit  
program to actually<br/>  
identify what these larvae were making<br/>  
<time begin="00: 41: 16. 53"/><clear/>that were stimulating  
the<br/>  
protective immune response.<br/>  
<time begin="00: 41: 18. 84"/><clear/>And so I had gotten my first  
NIH grant in<br/>  
the late 1980's to start looking at this<br/>  
<time begin="00: 41: 26. 03"/><clear/>and it was very distressing  
to me<br/>  
because, after getting my grant,<br/>  
<time begin="00: 41: 31. 26"/><clear/>I realized that they weren't  
making anything.<br/>  
<time begin="00: 41: 34. 66"/><clear/>This was not good, this was  
my first NIH grant.<br/>  
<time begin="00: 41: 36. 27"/><clear/>I told the NIH what I was  
going to do.<br/>  
<time begin="00: 41: 37. 80"/><clear/>I was going to identify what  
the worms<br/>  
spit and use it to make a vaccine<br/>  
<time begin="00: 41: 41. 33"/><clear/>and there was really nothing  
in the spit.<br/>  
<time begin="00: 41: 45. 46"/><clear/>So this was of great concern  
to me until I had<br/>  
recruited a postdoc to my lab named John Hardin<br/>  
<time begin="00: 41: 51. 89"/><clear/>who had an interest in worm  
physiology and<br/>  
he had found that, if you take larval stages<br/>  
<time begin="00: 41: 59. 76"/><clear/>of worms and incubate them  
with serum from<br/>  
a laboratory animal something in the blood<br/>  
<time begin="00: 42: 06. 61"/><clear/>from a laboratory animal,  
that you can trick<br/>  
them into thinking they were in people.<br/>  
<time begin="00: 42: 11. 44"/><clear/>And that was, so I said  
well,<br/>  
maybe that's what we need to do.<br/>  
<time begin="00: 42: 15. 99"/><clear/>We need to first trick the  
larvae<br/>  
into thinking they're in the person<br/>  
<time begin="00: 42: 19. 06"/><clear/>and that's what will cause  
them<br/>  
to start spitting out something<br/>

<time begin="00: 42: 22. 85"/><clear/>that is protective and indeed  
that was the case.<br/>  
<time begin="00: 42: 25. 55"/><clear/>So our strategy became<br/>  
then to reproduce the effect<br/>  
<time begin="00: 42: 30. 96"/><clear/>of what we call an attenuated  
larval L3 vaccine<br/>  
<time begin="00: 42: 34. 62"/><clear/>by substituting a  
genetically<br/>  
engineered recombinant antigen<br/>  
<time begin="00: 42: 38. 35"/><clear/>because you would never get  
enough of the<br/>  
molecules in the spit to make it yourself.<br/>  
<time begin="00: 42: 41. 85"/><clear/>You had to make it by genetic  
engineering and<br/>  
this one slide took us almost a decade to get<br/>  
<time begin="00: 42: 47. 67"/><clear/>this slide because it's  
hard<br/>  
to get enough of the material in an abundance<br/>  
<time begin="00: 42: 55. 05"/><clear/>in order to identify the  
molecules that<br/>  
the worms are secreting number one,<br/>  
<time begin="00: 43: 00. 23"/><clear/>and then you have to go  
through the arduous<br/>  
task of making what are known as [inaudible]<br/>  
<time begin="00: 43: 06. 09"/><clear/>from the parasites in order  
to clone the genes<br/>  
for these and then genetically engineer them<br/>  
<time begin="00: 43: 10. 71"/><clear/>into something else like a  
bacteria or a yeast.<br/>  
<time begin="00: 43: 14. 15"/><clear/>And so these are the three  
major proteins<br/>  
that we identified from<br/>  
<time begin="00: 43: 21. 43"/><clear/>those larvae and one of them  
is<br/>  
called ancylostoma secreted protein one,<br/>  
<time begin="00: 43: 26. 28"/><clear/>ancylostoma secreted protein  
two and<br/>  
astacin metalloprotease 1, so ASP1, ASP2 and ASP3,<br/>  
<time begin="00: 43: 34. 30"/><clear/>and this was a decade of work  
that<br/>  
John Hawdon, H-a-w-d-o-n, and I came up with<br/>  
<time begin="00: 43: 42. 93"/><clear/>and we decided that these  
were the vaccine<br/>  
candidates we were going to pursue.<br/>  
<time begin="00: 43: 47. 70"/><clear/>Now I don't have time to,  
unfortunately, go<br/>  
into the science and the science is kind of fun<br/>

<time begin="00: 43: 51. 62"/><clear/>and quirky and interesting  
but<br/>  
to make a long story short,<br/>  
<time begin="00: 43: 56. 22"/><clear/>we identified of those three  
molecules one of<br/>  
them in particular looked particularly promising<br/>  
<time begin="00: 44: 03. 40"/><clear/>as a vaccine candidate and it  
became the<br/>  
protein in the middle there known as ASP2.<br/>  
<time begin="00: 44: 09. 42"/><clear/>This is a crystal structure  
of the protein<br/>  
which we ultimately solved in collaboration<br/>  
<time begin="00: 44: 17. 55"/><clear/>with [inaudible] Sojo at the  
University<br/>  
of Nebraska and I'm sorry to say<br/>  
<time begin="00: 44: 23. 05"/><clear/>to this day we know  
everything about this<br/>  
protein except what it does for the parasite.<br/>  
<time begin="00: 44: 28. 03"/><clear/>But what we have shown is a  
number of important<br/>  
things, one of them is first of all that the,<br/>  
<time begin="00: 44: 37. 25"/><clear/>if you take antibodies to  
this protein,<br/>  
it blocks the ability of larvae to move.<br/>  
<time begin="00: 44: 43. 41"/><clear/>It impairs their ability to  
migrate.<br/>  
<time begin="00: 44: 45. 33"/><clear/>It impairs their ability to  
go from<br/>  
A to B. So it's doing something,<br/>  
<time begin="00: 44: 49. 64"/><clear/>so an antibody response, so  
the<br/>  
proteins needed for the larvae to<br/>  
<time begin="00: 44: 54. 20"/><clear/>know where it's going in the  
world and<br/>  
secondly, we found that, if you go into regions<br/>  
<time begin="00: 45: 02. 21"/><clear/>of Brazil or China where  
there is endemic<br/>  
hookworm and we found that same result<br/>  
<time begin="00: 45: 06. 91"/><clear/>in two countries, that there  
is a subset of the<br/>  
population that naturally seems to learn how<br/>  
<time begin="00: 45: 13. 20"/><clear/>to make the antibodies to  
this<br/>  
protein which is very unusual.<br/>  
<time begin="00: 45: 16. 84"/><clear/>So about a fifth, so if you  
go<br/>  
into any hookworm endemic area,<br/>

<time begin="00: 45: 19. 42"/><clear/>you'll find about 15 percent  
of the population<br/>  
naturally has antibodies to this protein<br/>  
<time begin="00: 45: 25. 08"/><clear/>and that 15 percent is  
protected from<br/>  
getting heavy hookworm infection. <br/>  
<time begin="00: 45: 29. 19"/><clear/>So we have this interesting  
laboratory<br/>  
observation on antibody inhibiting the ability<br/>  
<time begin="00: 45: 33. 31"/><clear/>of the larvae to migrate with  
human<br/>  
immunoepidemiological evaluation and then, <br/>  
<time begin="00: 45: 39. 67"/><clear/>when we tested it as a  
protected vaccine<br/>  
in laboratory animals, it worked. <br/>  
<time begin="00: 45: 44. 05"/><clear/>It elicited an immune  
response that inhibited, <br/>  
<time begin="00: 45: 47. 16"/><clear/>that would greatly reduce the  
number<br/>  
<time begin="00: 45: 48. 82"/><clear/>of adult hookworms  
compared<br/>  
to laboratory control animals. <br/>  
<time begin="00: 45: 53. 81"/><clear/>As I say, I don't have time  
to go into it today<br/>  
but the mechanism then is that these antibodies<br/>  
<time begin="00: 46: 00. 47"/><clear/>to this ASP2 protein inhibit  
the ability<br/>  
of the L3s to migrate through the tissues. <br/>  
<time begin="00: 46: 06. 04"/><clear/>It reduces the number of  
adult hookworms<br/>  
and then this will then reduce the amount<br/>  
<time begin="00: 46: 10. 57"/><clear/>of intestinal blood  
loss, <br/>  
reduce the number of egg counts<br/>  
<time begin="00: 46: 13. 99"/><clear/>and ultimately reduce  
malnutrition and anemia. <br/>  
<time begin="00: 46: 17. 14"/><clear/>So after almost 25 years of  
work, we had come<br/>  
<time begin="00: 46: 20. 75"/><clear/>up with what we thought was a  
viable<br/>  
strategy for making a vaccine. <br/>  
<time begin="00: 46: 26. 12"/><clear/>The problem came when I  
realized<br/>  
that we had just done the easy part. <br/>  
<time begin="00: 46: 30. 49"/><clear/>Why do I say that?<br/>  
<time begin="00: 46: 31. 37"/><clear/>Well, because hookworm is,

it  
belongs to a group of what are known  
<time begin="00:46:35.73"/><clear/>as 13 neglected tropical  
diseases, so what do  
I mean by these neglected tropical diseases,  
<time begin="00:46:42.38"/><clear/>these are, at least 13  
infections  
which include things like river blindness  
<time begin="00:46:47.14"/><clear/>which is caused by  
onchocerca  
volvulus on the left,  
<time begin="00:46:50.91"/><clear/>Guinea worm in the middle  
lymphatic  
filariasis on the right, leprosy is another one  
<time begin="00:46:55.34"/><clear/>of these neglected diseases  
represent a group  
of that parasitic and bacterial infections  
<time begin="00:47:02.74"/><clear/>that occur in rural areas  
of  
low-income countries almost exclusively.  
<time begin="00:47:07.75"/><clear/>So they are diseases that  
have the  
exclusive purview of the estimated 2  
<time begin="00:47:12.43"/><clear/>to 3 billion people who  
live  
on less than \$2 a day.  
<time begin="00:47:16.35"/><clear/>They not only occur in a  
setting of  
poverty but they also promote poverty  
<time begin="00:47:20.70"/><clear/>and another interesting  
feature about them is  
you've heard of things like emerging infection,  
<time begin="00:47:24.87"/><clear/>like Avian Flu or West Nile  
or SARS,  
these are diseases which we never knew  
<time begin="00:47:29.79"/><clear/>where a problem before  
but  
suddenly they kind of appear,  
<time begin="00:47:32.20"/><clear/>well, they don't just appear  
but they appear  
over a period of years, and maybe you read  
<time begin="00:47:36.82"/><clear/>about them in the newspaper  
and  
they're diseases of great concern.  
<time begin="00:47:40.44"/><clear/>Well, these are just the  
opposite, these are not  
emerging at all, these have burdened humanity  
<time begin="00:47:44.47"/><clear/>for centuries so much so that

you can find  
vivid descriptions of these in ancient text  
<time begin="00: 47: 49. 21"/><clear/>and you can pick up the Bible  
or the Talmud  
or the Bible by Giza or the writings  
<time begin="00: 47: 52. 64"/><clear/>of Hippocrates or the  
Egyptian papyrus and find  
references, very clear cut vivid references  
<time begin="00: 47: 59. 42"/><clear/>to these diseases and one of  
the reasons  
is they have notoriety being deforming  
<time begin="00: 48: 03. 87"/><clear/>and disabling and, therefore,  
they have an  
intense stigma associated with them, and then of course,  
<time begin="00: 48: 10. 03"/><clear/>they don't receive the  
attention  
of the Bonos, the Angelina Jolies,  
<time begin="00: 48: 13. 83"/><clear/>not to mention the attention  
of the  
United States public health community  
<time begin="00: 48: 18. 55"/><clear/>and as you can imagine you  
make  
products for these things you can.  
<time begin="00: 48: 22. 69"/><clear/>What's the commercial market  
for them?  
<time begin="00: 48: 26. 15"/><clear/>This is bad, this is viral  
that's,  
imagine I'm going to make a hookworm  
<time begin="00: 48: 31. 29"/><clear/><br/>  
vaccine for the 3 billion people  
<time begin="00: 48: 35. 33"/><clear/>in the world who live on less  
than \$2 a day.  
<time begin="00: 48: 38. 35"/><clear/>I mean, this is the  
biomedical  
equivalent of the Producers.  
<time begin="00: 48: 41. 27"/><clear/>You know the movie The  
Producers, they make  
a Broadway show that deliberately flops,  
<time begin="00: 48: 45. 52"/><clear/>well this, for this you  
basically have to convince people  
<time begin="00: 48: 49. 61"/><clear/>to back your guaranteed  
money-losing company.  
<time begin="00: 48: 52. 66"/><clear/>So that was of great concern  
for us but we  
took great inspiration from the work of Gandhi  
<time begin="00: 48: 58. 84"/><clear/>who once said: My experience  
has taught me

Hotez.txt

<time begin="00: 49: 01. 63"/><clear/>that no movement ever stops  
or<br/>  
languishes for want of funds.<br/>  
<time begin="00: 49: 05. 76"/><clear/>This does not mean that any  
movement<br/>  
can go on without money but it does mean<br/>  
<time begin="00: 49: 09. 96"/><clear/>that wherever it has good men  
and all of<br/>  
that and good women and true at its helm,<br/>  
<time begin="00: 49: 14. 07"/><clear/>it is bound to attract  
to<br/>  
itself the requisite funds.<br/>  
<time begin="00: 49: 16. 72"/><clear/>So we figured we had that  
going for us.<br/>  
<time begin="00: 49: 20. 04"/><clear/>So what did we do?<br/>  
<time begin="00: 49: 21. 25"/><clear/>Well, what we did was, we  
realized<br/>  
that we were never going to make a,<br/>  
<time begin="00: 49: 26. 78"/><clear/>get a pharmaceutical company  
interested<br/>  
and we decided we're just going<br/>  
<time begin="00: 49: 29. 64"/><clear/>to have to do the damn thing  
ourselves.<br/>  
<time begin="00: 49: 32. 24"/><clear/>So what we did was set-up in  
association<br/>  
<time begin="00: 49: 36. 85"/><clear/>with a non-governmental  
organization called the<br/>  
Sabine Vaccine Institute with the logo on the right<br/>  
<time begin="00: 49: 41. 40"/><clear/>and that's named after Albert  
Sabine<br/>  
who discovered the polio vaccine, joined<br/>  
<time begin="00: 49: 45. 38"/><clear/>with the laboratory at GW, we  
would set-up what<br/>  
we called our guaranteed money-losing company,<br/>  
<time begin="00: 49: 51. 50"/><clear/>and if you go to the seventh  
floor of our<br/>  
building, it looks just like a bio-tech company.<br/>  
<time begin="00: 49: 56. 30"/><clear/>It has fermenters  
whirring.<br/>  
<time begin="00: 49: 58. 16"/><clear/>It has quality control  
units,<br/>  
quality assurance units, it's just,<br/>  
<time begin="00: 50: 02. 24"/><clear/>I can promise you we're never  
going to turn a<br/>  
profit and the reason we're going to do this,<br/>  
<time begin="00: 50: 07. 76"/><clear/>of course, is because of the

backing of the  
Bill and Melinda Gates Foundation that gave us  
<time begin="00: 50: 12. 11"/><clear/>that funding in order to take  
this all the way  
through from the laboratory observation such as  
<time begin="00: 50: 17. 08"/><clear/>what I just presented, to the  
point where  
we're going to make a bottle of vaccines.  
<time begin="00: 50: 22. 18"/><clear/>So the hookworm vaccine that  
was manufactured  
is a recombinant protein expressed in yeast  
<time begin="00: 50: 29. 65"/><clear/>and then absorbed to an  
aluminum  
compound known as a hydrogel  
<time begin="00: 50: 34. 00"/><clear/>to help it stimulate an  
immune response  
and these are the list of the milestones.  
<time begin="00: 50: 38. 15"/><clear/>And it's getting late so  
I  
want to finish up and there  
<time begin="00: 50: 41. 14"/><clear/>at the bottom right is our  
first  
bottle of hookworm vaccine.  
<time begin="00: 50: 46. 55"/><clear/>One of the problems for doing  
this is we  
thought it was very important early  
<time begin="00: 50: 52. 59"/><clear/>on that even though this  
vaccine would never  
be licensed in the United States we wanted  
<time begin="00: 50: 58. 72"/><clear/>to not bypass the usual  
routes of drug  
development that one would have to do let's say  
<time begin="00: 51: 05. 25"/><clear/>if you were a Merck or a  
Pfizer so we wanted to  
go through the U. S. Food and Drug Administration  
<time begin="00: 51: 10. 92"/><clear/>which means filing what's  
known as an  
investigational or a new drug application.  
<time begin="00: 51: 15. 31"/><clear/>The problem there is FDA  
doesn't  
really care if you're Merck or Pfizer  
<time begin="00: 51: 19. 25"/><clear/>or whether you're a  
guaranteed money-losing  
company called the Human Hookworm Vaccine  
<time begin="00: 51: 23. 31"/><clear/>Initiative and Sabine  
Vaccine  
Institute, you still have the same,  
<time begin="00: 51: 25. 89"/><clear/>pass the same amount of



rigorous tests  
and that's why you need something  
<time begin="00: 51: 29. 64"/><clear/>I like a large scale Gates  
funding  
because it is very expensive.  
<time begin="00: 51: 31. 99"/><clear/>You have to bring in quality  
control  
experts, quality assurance experts and people  
<time begin="00: 51: 35. 54"/><clear/>with industrial experience  
and that  
requires a fairly high salary so we chose  
<time begin="00: 51: 41. 42"/><clear/>to do instead is we took  
faculty  
members, research faculty members,  
<time begin="00: 51: 45. 12"/><clear/>research assistant  
professors, research  
associate professors and got them trained  
<time begin="00: 51: 49. 39"/><clear/>in industry practices so it's  
kind of a  
hybrid culture of academia and industry  
<time begin="00: 51: 56. 68"/><clear/>and we were greatly helped by  
a group of  
consultants from an organization known  
<time begin="00: 52: 00. 61"/><clear/>as Science Applications  
International  
Corporation, SAIC, that was very helpful  
<time begin="00: 52: 05. 44"/><clear/>in teaching us how to go  
about  
doing those industry practices.  
<time begin="00: 52: 09. 72"/><clear/>So we've now completed our  
phase one study  
in 36 adult healthy human volunteers.  
<time begin="00: 52: 15. 92"/><clear/>We give doses of ten 1500  
micrograms of  
doses of zero, two and four months for safety  
<time begin="00: 52: 20. 58"/><clear/>and immunogenicity, and I'm  
not yet supposed  
to disclose the results of that study other  
<time begin="00: 52: 26. 27"/><clear/>than the fact that it's  
safe  
and immunogenic and so,  
<time begin="00: 52: 30. 12"/><clear/>and now what we're doing is  
based on the results  
of this which we hope to reveal fairly soon,  
<time begin="00: 52: 38. 10"/><clear/>we want to now see if the  
thing works.  
<time begin="00: 52: 40. 67"/><clear/>So where are we going to do

that?  
<time begin="00: 52: 43. 04"/><clear/>What you need to do  
clinical  
trials in a developing country,  
<time begin="00: 52: 45. 71"/><clear/>you can't just march  
into  
villages in a developing country.  
<time begin="00: 52: 48. 27"/><clear/>You really have to go where  
there's  
a good scientific infrastructure,  
<time begin="00: 52: 52. 99"/><clear/>and we really searched for a  
long time before  
we found the right mix where there's both a lot  
<time begin="00: 53: 00. 53"/><clear/>of endemic hookworm infection  
and yet at  
the same time there was the capacity to,  
<time begin="00: 53: 05. 81"/><clear/>there was a scientific  
expertise and capacity  
to help pull off a clinical trial of a product  
<time begin="00: 53: 13. 42"/><clear/>under what they call GCP,  
Good Clinical  
Practices, that is you will adhere  
<time begin="00: 53: 17. 05"/><clear/>to all the standards that you  
would want to  
use in the United States and the reason I was  
<time begin="00: 53: 22. 14"/><clear/>so thrilled to come down here  
to the University  
of Georgia is to publicly thank Dan Colley  
<time begin="00: 53: 28. 02"/><clear/>because one of the things  
that Dan's been doing  
<time begin="00: 53: 29. 67"/><clear/>over the last 20 years is he  
has  
done all the hard work that saved us  
<time begin="00: 53: 34. 88"/><clear/>from all doing all the hard  
work by establishing  
this extraordinary infrastructure in the State  
<time begin="00: 53: 39. 44"/><clear/>of Brazil called Minas  
Gerais  
by over years and years going  
<time begin="00: 53: 43. 38"/><clear/>to this laboratory called  
Rene  
Rachou Research Center which is part  
<time begin="00: 53: 47. 09"/><clear/>of the Oswaldo Cruz  
Foundation building up  
the capacity that made it possible for us  
<time begin="00: 53: 52. 15"/><clear/>to then walk in and then

work<br/>  
with this very well-trained team,<br/>  
<time begin="00: 53: 56. 58"/><clear/>this team that Dan had  
trained to go in<br/>  
and now see if it works against hookworm.<br/>  
<time begin="00: 54: 00. 75"/><clear/>And that's where we're at  
right now which is now<br/>  
that we've shown that it's safe and immunogenic,<br/>  
<time begin="00: 54: 05. 41"/><clear/>meaning it will elicit some  
immune<br/>  
response, we're at the point now to see<br/>  
<time begin="00: 54: 09. 03"/><clear/>over the next few years  
whether it actually<br/>  
protects against human hookworm infection<br/>  
<time begin="00: 54: 14. 90"/><clear/>and so the idea is, I don't  
know<br/>  
how well it shows up here but rather<br/>  
<time begin="00: 54: 17. 85"/><clear/>than getting  
re-infection,<br/>  
we'd have that flat line.<br/>  
<time begin="00: 54: 20. 52"/><clear/>I don't think it will remain  
flat.<br/>  
<time begin="00: 54: 21. 86"/><clear/>I think there will be some  
re-infection and<br/>  
that's why we think we're ultimately going<br/>  
<time begin="00: 54: 26. 27"/><clear/>to have to add a second  
component to<br/>  
the vaccine which we're now working<br/>  
<time begin="00: 54: 30. 03"/><clear/>on which is not just the L3  
antigen<br/>  
ASP2 but an adult antigen as well<br/>  
<time begin="00: 54: 35. 89"/><clear/>to further reduce the blood  
loss.<br/>  
<time begin="00: 54: 38. 10"/><clear/>And I know it's late but  
I'll<br/>  
just show you a couple of slides.<br/>  
<time begin="00: 54: 41. 00"/><clear/>Can I get the lights  
down<br/>  
again, is that possible?<br/>  
<time begin="00: 54: 46. 13"/><clear/>We've also found another very  
interesting<br/>  
class of protein from the adult parasite<br/>  
<time begin="00: 54: 51. 53"/><clear/>and as the adult parasite is  
feeding on blood<br/>  
what happens is it starts swallowing blood,<br/>  
<time begin="00: 54: 56. 75"/><clear/>then blood gets digested, the  
hemoglobin that's<br/>

inside red cells gets digested allowing the  
<time begin="00:55:03.07"/><clear/>parasite to feed on that  
digested  
blood as a source of nutrition.  
<time begin="00:55:07.63"/><clear/>Well, Alex Lucas in our group  
found this very  
interesting class of enzymes that the worm uses  
<time begin="00:55:13.85"/><clear/>to degrade blood as it feeds  
and what we  
found was that if we immunize an animal  
<time begin="00:55:19.19"/><clear/>with those enzymes, it  
elicits  
an antibody response  
<time begin="00:55:23.42"/><clear/>to these proteins these  
enzymes  
that line the gut of the worm.  
<time begin="00:55:27.32"/><clear/>So as the worm is feeding on  
the blood  
the antibodies localize to it almost  
<time begin="00:55:30.51"/><clear/>Like a Trojan Horse and grind  
up the gut  
of the worm and make it unable to use  
<time begin="00:55:35.07"/><clear/>that blood effectively so the  
two  
proteins together we think are going  
<time begin="00:55:38.65"/><clear/>to be additive in terms of  
their effect.  
<time begin="00:55:43.38"/><clear/>Now, as I said, so  
that's  
still the easy part so making the vaccine,  
<time begin="00:55:49.54"/><clear/>as hard as it was, is the  
easy part.  
<time begin="00:55:51.80"/><clear/>Now clinically testing it as  
hard as  
that's going to be that's still going  
<time begin="00:55:54.62"/><clear/>to be the easy part and why  
do I say that?  
<time begin="00:55:56.81"/><clear/>Well, it's based on our  
experience  
that we've  
<time begin="00:55:58.94"/><clear/>had with other high-tech  
recombinant  
vaccines such as the Hepatitis B vaccine.  
<time begin="00:56:04.69"/><clear/>So this is a vaccine  
that  
many of us have gotten.  
<time begin="00:56:07.54"/><clear/>I would argue that most

of  
us have gotten in this room.  
<time begin="00: 56: 10. 07"/><clear/>It's the only licensed  
recombinant vaccine and  
so for all that 40 years of genetic engineering  
<time begin="00: 56: 16. 22"/><clear/>and biotechnology we still  
only have one  
licensed recombinant vaccine and that's  
<time begin="00: 56: 20. 03"/><clear/>for Hepatitis B. So there was  
a 20  
<time begin="00: 56: 22. 31"/><clear/>to 30 year period before  
wide  
scale availability was achieved  
<time begin="00: 56: 27. 38"/><clear/>with that Hepatitis B  
following proof of  
principle that the vaccine actually works,  
<time begin="00: 56: 32. 18"/><clear/>and it was 10 to 15  
years  
from the time of licensure.  
<time begin="00: 56: 35. 58"/><clear/>So what the Gates Foundation  
is very concerned  
about this and they've asked us to say, well,  
<time begin="00: 56: 40. 23"/><clear/>Peter, it's great that  
you're  
doing this but give us a plan.  
<time begin="00: 56: 42. 62"/><clear/>We don't want to wait 20, 30  
years  
before this vaccine is widely used,  
<time begin="00: 56: 47. 04"/><clear/>and we're not the only  
ones  
they're telling this to.  
<time begin="00: 56: 50. 06"/><clear/>Their telling this to  
some  
of their other grantees.  
<time begin="00: 56: 52. 14"/><clear/>We now have to come up  
with  
a plan to shorten that 20  
<time begin="00: 56: 54. 49"/><clear/>to 30 years time horizon to  
say to five to ten.  
<time begin="00: 56: 58. 26"/><clear/>And I will end by telling you  
a couple  
of interesting things that we have done.  
<time begin="00: 57: 02. 46"/><clear/>First of all there's a lot of  
challenges to  
what the term that we use is global access  
<time begin="00: 57: 08. 20"/><clear/>for this vaccine, the

enormous magnitude<br/>  
of scale of the human hookworm problem, <br/>  
<time begin="00: 57: 13. 34"/><clear/>the 740 million people  
infected with<br/>  
hookworm, insuring that it's used<br/>  
<time begin="00: 57: 17. 50"/><clear/>in high transmission  
communities which tend<br/>  
to be occurring in remote and rural areas<br/>  
<time begin="00: 57: 23. 14"/><clear/>of the developing world, it's  
neglected disease<br/>  
status meaning impoverished people are the<br/>  
<time begin="00: 57: 27. 66"/><clear/>lowest priority commercial  
markets, there's<br/>  
no market for travelers or for the military<br/>  
<time begin="00: 57: 33. 02"/><clear/>and all of the current  
massive funding<br/>  
schemes are all focused on the big three. <br/>  
<time begin="00: 57: 37. 64"/><clear/>We have, worms have not, <br/>  
have yet to hit the radar screen<br/>  
<time begin="00: 57: 40. 45"/><clear/>and we also don't have  
good<br/>  
health delivery systems. <br/>  
<time begin="00: 57: 43. 08"/><clear/>We want to make this a  
school-based vaccine<br/>  
<time begin="00: 57: 45. 19"/><clear/>because that's the target  
population<br/>  
almost all the vaccines given<br/>  
<time begin="00: 57: 48. 91"/><clear/>in developing countries  
are<br/>  
used in the infant period. <br/>  
<time begin="00: 57: 51. 72"/><clear/>So that's going to be a  
standing<br/>  
program of immunization. <br/>  
<time begin="00: 57: 54. 79"/><clear/>Well, one of the ways<br/>  
we want to overcome this is first<br/>  
<time begin="00: 57: 59. 57"/><clear/>of all not have all the  
vaccine made in<br/>  
Washington D.C. What we're trying to do is build<br/>  
<time begin="00: 58: 06. 07"/><clear/>in sustainability so that  
the<br/>  
vaccine can be made overseas. <br/>  
<time begin="00: 58: 08. 91"/><clear/>So what I'm showing you is a  
list, a<br/>  
ranking of countries, 1 through 25, <br/>  
<time begin="00: 58: 13. 72"/><clear/>and ranked by very unusual  
metric which is<br/>  
not just looking at the number of patents<br/>  
<time begin="00: 58: 18. 27"/><clear/>that they've produced or

going on the  
top right, the number of U.S. patents,  
<time begin="00:58:23.97"/><clear/>or the GDP per capita by  
looking at the  
number of U.S. patents per GDP per capita.  
<time begin="00:58:29.81"/><clear/>What do I mean by that?  
<time begin="00:58:30.78"/><clear/>What it means is I'm  
interested  
in countries that have high output  
<time begin="00:58:37.11"/><clear/>in intellectual property  
based on,  
divided by the wealth of the country.  
<time begin="00:58:44.60"/><clear/>So we look at countries like  
the United States  
and Japan, they're very wealthy countries  
<time begin="00:58:48.65"/><clear/>and they produce a lot of  
patents and they're  
at the top of the list, no surprise there.  
<time begin="00:58:52.86"/><clear/>But there's a group of  
countries in the gray  
such as India, China, Brazil, South Africa,  
<time begin="00:58:58.03"/><clear/>Thailand, Malaysia,  
Indonesia, Argentina,  
which do very poorly economically but  
<time begin="00:59:03.35"/><clear/>yet are overachievers in  
terms of their  
ability to make patents and other metrics  
<time begin="00:59:09.03"/><clear/>of high innovations such as  
peer reviewed  
papers and making health products, drugs,  
<time begin="00:59:15.20"/><clear/>vaccines and diagnostics, and  
when you look at  
the metric of U.S. patents per GDP per capita,  
<time begin="00:59:21.46"/><clear/>some of those countries come  
up  
unexpectedly high such as India, China,  
<time begin="00:59:25.31"/><clear/>Brazil and the terms used for  
these countries  
are IDC or Innovative Developing Countries.  
<time begin="00:59:30.73"/><clear/>They've somehow learned to  
do  
something very extraordinary in terms  
<time begin="00:59:33.98"/><clear/>of their ability to handle  
biotechnology.  
<time begin="00:59:36.87"/><clear/>So a key part of our global  
access now is we're  
going to these countries and teaching them how  
<time begin="00:59:41.46"/><clear/>to make the NAASP2, as

it's  
called, hookworm vaccine.  
<time begin="00:59:46.09"/><clear/>And the first one we started  
out with  
is called Instituto Butantan  
<time begin="00:59:49.75"/><clear/>on the upper left is their  
symbol there  
which has a snake and the reason is  
<time begin="00:59:53.41"/><clear/>because it started out as a  
snake farm.  
<time begin="00:59:55.45"/><clear/>It used to collect snakes  
from all over Latin  
America and take the venom from the snake  
<time begin="01:00:01.32"/><clear/>and inject them into horses  
after  
detoxifying it to make snake  
<time begin="01:00:04.51"/><clear/>antivenoms for all the  
Americas.  
<time begin="01:00:06.75"/><clear/>Now starting in the 1980's  
they put in  
a national program for self-sufficiency  
<time begin="01:00:12.23"/><clear/>immunobiologists, now they  
produce  
<time begin="01:00:14.85"/><clear/>at this snake farm 86  
percent  
of the vaccines for Brazil.  
<time begin="01:00:18.69"/><clear/>So they made 400, in 2005  
they made 483  
million doses of vaccines such as DPGBTCG  
<time begin="01:00:26.18"/><clear/>and they make their own  
recombinant  
Hepatitis B vaccine.  
<time begin="01:00:29.35"/><clear/>Now we're working on a  
process of technology  
transfer, so they are going to make the vaccine  
<time begin="01:00:33.24"/><clear/>for the Americas and the idea  
will be the  
same in India and China and elsewhere.  
<time begin="01:00:37.67"/><clear/>And then, lastly, we're  
very  
concerned about the fact that we want  
<time begin="01:00:42.98"/><clear/>to make this a school age  
vaccine.  
<time begin="01:00:44.65"/><clear/>It turns out from the lessons  
I learned  
from Hepatitis B you want to be able



<time begin="01:00:48.66"/><clear/>to use the vaccine in a  
program<br/>  
<time begin="01:00:52.17"/><clear/>that's actually that involves  
a health<br/>  
delivery mechanism that will actually be used.<br/>  
<time begin="01:00:57.97"/><clear/>And so now we have this  
great<br/>  
instruction process by which we're working<br/>  
<time begin="01:01:04.64"/><clear/>with developing countries to  
buy into the idea<br/>  
that we're going to use this hookworm vaccine<br/>  
<time begin="01:01:09.47"/><clear/>in the schools possibly even  
administered<br/>  
by nonhealth care professionals<br/>  
<time begin="01:01:14.17"/><clear/>which is still a little  
bit<br/>  
controversial and we're trying to build<br/>  
<time begin="01:01:19.05"/><clear/>on some other school-based  
vaccine programs<br/>  
<time begin="01:01:21.28"/><clear/>that are being considered  
including this<br/>  
very interesting cervical cancer vaccine<br/>  
<time begin="01:01:26.67"/><clear/>for human papillomavirus that  
was developed<br/>  
recently by Merck and Glaxo-SmithKline.<br/>  
<time begin="01:01:32.21"/><clear/>They're also looking at  
a<br/>  
school-based vaccine program<br/>  
<time begin="01:01:36.51"/><clear/>to immunize school-age girls  
before they<br/>  
become sexually active and get exposed<br/>  
<time begin="01:01:41.06"/><clear/>to human papillomavirus, so  
maybe there<br/>  
will be some tie-in between hookworm vaccine<br/>  
<time begin="01:01:45.76"/><clear/>and human papillomavirus  
vaccine program.<br/>  
<time begin="01:01:48.83"/><clear/>These are kind of some of the  
things<br/>  
that we're trying to do to shorten<br/>  
<time begin="01:01:51.85"/><clear/>that timeframe from 30 years  
down to 5 or 10.<br/>  
<time begin="01:01:55.99"/><clear/>So it takes more than a  
village<br/>  
to make a hookworm vaccine.<br/>  
<time begin="01:01:59.22"/><clear/>It takes quite a group of  
scientists in order<br/>

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to create our guaranteed money losing company. <br/>  
<time begin="01:02:06.18"/><clear/>Maria Elena Bottazzi at the  
top<br/>  
left is our project manager. <br/>  
<time begin="01:02:09.78"/><clear/>We get a lot of advice from  
the Sabine Vaccine<br/>  
Institute especially Phil Russell who's a former<br/>  
<time begin="01:02:15.76"/><clear/>major general in the  
army. <br/>  
<time begin="01:02:17.43"/><clear/>Turns out Walter Reed Army  
researchers, <br/>  
enormous amount of expertise<br/>  
<time begin="01:02:21.34"/><clear/>that they've acquired in  
vaccine development. <br/>  
<time begin="01:02:23.45"/><clear/>They have a team of  
mathematical <br/>  
modelers from the London School of Hygiene<br/>  
<time begin="01:02:26.76"/><clear/>and Tropical Medicine  
and<br/>  
experts in clinical trials. <br/>  
<time begin="01:02:29.65"/><clear/>FIOCRUZ we're working with  
extensively and that's a<br/>  
group headed by Rodrigo Correa-Oliveira<br/>  
<time begin="01:02:35.41"/><clear/>as well as these two  
Butantan<br/>  
which is headed by Isisias Raw, <br/>  
<time begin="01:02:39.86"/><clear/>the Australian QIMR<br/>  
Queensland Institute of Medical Research<br/>  
<time begin="01:02:43.40"/><clear/>and finally Science  
Application<br/>  
International Corporation<br/>  
<time begin="01:02:46.27"/><clear/>that provides some of the  
consultant advice. <br/>  
<time begin="01:02:50.60"/><clear/>NIH funded some of the early  
part of this work, <br/>  
<time begin="01:02:52.57"/><clear/>the March of Dimes Birth  
Defects Foundation<br/>  
was also helpful but it was really the Bill<br/>  
<time begin="01:02:56.48"/><clear/>and Melinda Gates Foundation  
that<br/>  
provided that big, big dollars that we need<br/>  
<time begin="01:03:00.96"/><clear/>to actually fashion something  
in<br/>  
the laboratory into a product. <br/>  
<time begin="01:03:04.25"/><clear/>So I'll stop there. <br/>  
<time begin="01:03:05.03"/><clear/>I don't know if there are any  
questions. <br/>

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<time begin="01:03:06.49"/><clear/>I really appreciate your  
patience<br/>  
in listening to me this evening.<br/>  
<time begin="01:03:10.81"/><clear/>Thank you.<br/>  
<time begin="01:03:12.51"/><clear/>[ Applause ]<br/>  
<time begin="01:03:18.01"/><clear/>[ Music ]<br/>