(Patricia Thomas:) My name is Pat Thomas, and I am the Knight Chair in Health and Medical Journalism at the Grady College of Journalism and Mass Communication.

And it is my pleasure to welcome all of you once again to the Voices from the Vanguard lecture.

Sixteen times in the last four years we brought before you people who have a unique first hand perspectives on the diseases that affect neglected people throughout the world.

We have taken them as neglected diseases too often, but it is really about the people in the final analysis and we are grateful to all the students and faculty members who have come to so many of these occasions to hear these wonderful speakers who have joined us.

This is the last one for this year, but Dan Colley, my partner in this enterprise who is the Director of the Center for Tropical and Emerging Global Diseases.

Professor Colley and I want to emphasize our commitment to bringing this series back next year.

We know there are a lot of great investigators, people who have walked the walk as well
as talking the talk and we are looking forward to doing this again in 2010.

[00:01:13.496] Tonight, we are really, really pleased to have with us Dr. Jennifer Friedman,

[00:01:17.266] a pediatrician with a special interest in worms.

[00:01:20.366] Well, I guess that all doctors who treat children have probably seen their share of worms, but she is interested in it in a greater, more global sense.

[00:01:29.826] I don't know how much contacts she had with worms growing up in New Jersey and I don't think that Providence, Rhode Island is a particularly wormy place, so perhaps it is,

[00:01:34.996] but she did attend Brown University and --

[00:01:39.356] the Brown University School of Medicine.

[00:01:45.706] She couldn't seem to get away from there, except when she got a Fulbright fellowship and went to Africa and I think as she will tell you that changed her world because she has gone on to become a preeminent young researcher in the area of helminthiasis and particularly

[00:02:01.406] in what she calls polyparasitism,

[00:02:04.036] the concomitant infection with more than one type of worm.

[00:02:09.626] So, I hope there are going to be some really outstanding slides here.

[00:02:13.516] At any rate, we are thrilled to have her with us tonight.

[00:02:17.996] I want to remind you that following her talk, we will be adjourning to next door
to Demosthenian Hall where we will have refreshments

and you will have a chance to talk to her.

So, thanks for coming, and Dr. Friedman.

( Applause )

(Dr. Jennifer Friedman:) Thank you very much for that introduction.

It is really lovely to be here.

I am quite honored to follow in the footsteps of the 15 other investigators and journalists and scientists who have been here to date.

And I would like to talk to you a little bit today about our experiences in working in the Philippines, but really more broadly on the current status of geohelminths and schistosomiasis.

And I would like to begin by mentioning Dr. Norman Stoll's presidential address to the American Society of Tropical Medicine and Hygiene equivalent.

Just after World War II when many servicemen and women, probably more servicemen at that point returned with a whole host of different worms that many of which had never been seen or identified in this country before.
And it really this address
has been quoted many, many,

many a times in the parasitic disease literature
in which he said and declared that we live

in this "wormy world" and even
as recently as a few years ago,

reviews of this topic unfortunately state
that we are sort of in the same boat,

still living in quite a wormy world.

During his address, he mentioned that
probably 342 helminths have been associated

with human hosts, but about 25 of them are
of the greatest public health significance

and I want to remind you that today, I am
only going to talk to you about four of those

and the fact that many people all over
the world are co-infected with those four

and many, many others simultaneously.

I also and re-reading his address from 1947,
I wanted to take some advice and I think

that it is good advice for all of us to heed.

I think as scientists we really
live in our own sort of world.

Everyone has their favorite worm and he said
that each parasitologist just wants to live

in his thinking in one world with the
species which particularly interests him.

So, some progress has been
made since I am not him
and I am here talking to you about parasites.

But, I think that this is a common theme and I think that more and more,

we all need especially the scientists to recognize that we live in a world

with unfortunately, where children in particular are infected

with many different parasites, bacteria, viruses.

And that if we don't start to really work together to combat these diseases

and really work in our own labs, in our own field sites,

that we really won't really do our best to decrease polyparasitism in the world.

So, what I would like to talk to you a little bit about today, again really going to focus

on four worms, geohelminth, the three geohelminths,

the main three geohelminths and schistosomiasis.

We will talk about the fact that it probably is still a very wormy world

and some of the consequences of that.

We will talk a little bit about what polyparasitism means and how we are starting

to think about that and measure outcomes related to having more than one parasite or looking

at more than one parasite, some of the current interventions and hurdles,
and hopefully, some future directions.

So, I wanted to start by making this a little bit concrete for us.

This is a Trichuris worm which is just barely visible to the naked eye and I would like to remind us that this worm, and I will show you the life cycle actually,

hundreds of these worms would infect a given child and produce thousands of eggs that then contaminate the environment.

So, I would like you guys to think a little bit about a common theme as we talk about life cycles here because -- the hint is poverty and what you see with the life cycle of Trichuris and also remember that these worms are really, you know,

you sort of have to know thine enemy and respect thine enemy.

If we are battling these worms, you really still have to appreciate how well they are adapted to human hosts, how they are adapted to their and our environment, and how that makes it very, very difficult to stop the transmission cycles.

So, this worm actually, the eggs are ingested.

It actually leaves -- sorry, this worm actually stays in the colon and multiplies and within a few months of infecting, the adult female worm starts making eggs
that then contaminate the environment.

And this worm has been associated with malnutrition and its severe form a dysentery syndrome where kids have bloody stools and diarrhea and more severe malnutrition and anemia along with it.

Another worm I would like to talk to you about is Ascaris lumbricoides and Ascaris has another interesting life cycle. Ascaris actually gets ingested. So, basically eggs are contaminating the environment and basically fecally contaminated environment where eggs pass out through feces and then are basically ingested by human host after a period of development in soil usually. And then they actually leave the gut and have a whole migration through your body that ends up back in your lungs and causes an irritant cough so that you then cough up the larva, swallow it again and it ends up back in your intestine and this worm is called the giant roundworm and we'll show you why that is.

And again, this is just one worm and children can have hundreds of these worms.

So, this is a collection of worms of this.
This is Ascaris.

It looks like rubber bands, but that is Ascaris lumbricoides that were collected during a day of treatment in a Bangladesh village.

It is also important to remember that when we are talking about interventions for these diseases that this is a big issue, right, because there are many people who, especially when you are talking about treating kids that have high parasite densities and you treat someone and all of a sudden, the worms -- basically, stops the worm from being able to contract their muscles and swim and stay in the intestine, all of a sudden they are passed in the stool.

And it is a very alarming thing and a lot of people who don't think about that or talk to people that know the local populations a little bit better find the compliance is not as good as they expect.

So, this is a child, so you can imagine the child that has such a large worm at a very intense infection can have a lot of abdominal bloating, satiety.

We'll talk a little bit about how these worms probably cause malnutrition.

But basically, this is a child with
very bad Ascaris lumbricoides infection.

All right, hookworm and hookworm, I think has really always risen to its own sort of stature in the United States and worldwide partly because from a very early stage has been very closely associated with anemia. And it got a lot of publicity even in the United States at the turn of the 20th Century when the Rockefeller Sanitation Commission was out to convince Congress that hookworm was holding back the South in terms of its economic development and that hookworm had to be obliterated from the country if the South was to progress. And this is really the kind of language that was used given the concern that with the anemia associated with hookworm that work capacities would go down, that people with iron deficiency anemia that might affect their ability to think and learn, and so, this worm has always gotten a lot more attention globally. And hookworm also has a very interesting life cycle and is very well adapted to human host who walk around with no shoes on. So, when you step on the egg that has come out again in feces and is embryonating in the soil, the larvae actually walk up to the highest point they can find.
So, usually a blade of grass waiting for the innocent, unshod child to step on it and then enter your bloodstream and have a similar course to the lungs with coughing and then back down into the small intestine where they ultimately reside. And also, it can be fairly bulky, but most of the pathogenesis of this worm is really related to anemia and bleeding through the gut. So, this is an adult worm. This is a single adult worm and it basically latches on to the wall of your gut and it is not just the sort of mechanical force of this nasty-looking mouth, but also the worm releases powerful anticoagulants, so blood thinners. So, in seeding in your gut actually, it basically thins the blood along the wall here and so you basically, on a very daily basis, have blood loss in the stool and that is most likely the predominant cause of anemia in hookworm. I should also mention that all three of the worms that we just talked about are fairly good -- there is excellent therapy for them. You use Albendazole. A single dose has very good efficacy.
It is even better with two doses likely
with almost 100 percent clearance of most of these worms.
So, a single dose often clears these infections, but if you treat them in school
and they walk home without shoes on, what happens?
Right, they are immediately re-infected.
So, we have very good chemotherapeutic agents to treat geohelminths.
That is really not the problem.
So, the real problem is how to deliver them, how frequently, is that really the best,
most cost-effective approach or other approaches that we will talk about a little bit better.
Okay, the last worm that I am going to mention today is not technically a geohelminth.
It is just a helminth because it doesn't have the soil component to its life cycle,
but also a very crafty worm, also depends on humans either defecating or urinating now in freshwater.
It has an intermediate host which is a snail.
So, part of its life cycle actually occurs in a snail.
The second part of this life cycle is the cercaria is released and actually swims
to the definitive host which is humans and then migrates to a long stage all the way to either the blood vessels around the liver for two of the species or around the bladder for haematobium which is a urine species.

So, the eggs are then deposited and cause a significant pathology around the liver and then most of the eggs actually track through your body, through your bloodstream down into the gut and come out again into the environment when a definitive human host defecates in freshwater.

Okay, in case you haven't recognized the common theme here, it is sanitation, sanitation and sanitation.

And I should also mention that what's very important -- this happens to be a map of the schisto endemic areas of the world.

But, I could show you the same map, hookworm, Ascaris and Trichuris almost exactly, with a few exceptions and they would overlie in the same exact regions with Sub-Saharan Africa really bearing the brunt of disease, some South America still and a lot in Asia.

Now, figuring that I am only here talking to you about helminths today and I said we all need
to work together and not just think about our own pet parasite, right?

So, also overlay malaria and you will have a very similar look here in Africa and still large parts of Asia.

And then, if you add in the latest scourge of HIV to this, the distribution looks very similar.

So again, these are all diseases of poverty and much what we can -- we can come a very long way with economic development, sanitation, water and hygiene and it may not be that chemotherapeutic cures are the only way to go here.

So, this is a child with advanced hepatic schistosomiasis.

So, what you see here is -- what's really quite amazing about schisto worms are they actually sit in your bloodstream.

So, most of us know that our bloodstream is about the most sterile part of our body and the human host does not do well with circulating pathogens in the bloodstream.

But, this worm has done such a good job of evading itself mostly by cloaking itself with human antigens so that to a human host, for all the world looks like a self-antigen and so much less immunogenic,
and it sits right there

[00:15:45.386] in the bloodstream making thousands of eggs a day.

[00:15:50.826] Everyone's favorite story about schistosomes is that they live in permanent copulation,

[00:15:55.716] so the man and the woman live in permanent copulation in the liver, bloodstream,

[00:16:01.766] or for the urinary species in the bladder plexus and produce thousands of eggs

[00:16:09.616] which are what produces this -- mostly what produces pathology.

[00:16:12.476] Some of those eggs are swept upstream and cause really terrible liver fibrosis.

[00:16:16.936] So, these kids really look and act like an adult with really horrific hepatitis C

[00:16:22.676] or B with cirrhosis of the liver or cirrhosis of the liver due to alcoholic cirrhosis.

[00:16:30.336] And so, this is a morbidity related to schisto that is fatal and not what we call one

[00:16:36.576] of the more subtle morbidities which is how often people talk

[00:16:40.146] about helminth infections that they are there.

[00:16:42.386] We sort of co-exist with them and they cause some subtle morbidities

[00:16:45.446] and we will talk a little bit about what some of those subtle morbidities are and whether

[00:16:48.776] or not they are really all that subtle.

[00:16:50.546] I should also point out a syndrome called schistosomal dwarfism.
So, this is actually not a child.

This is someone who is about 16 years old and it is a very profound syndrome called schistosomal dwarfism.

Not the best term, but the kids with very bad liver disease with schisto have really terrible stunting of their growth, probably for a lot of different biologic reasons.

But, this is an example of the growth stunting and they enter puberty or 20 years old and have really only achieved heights on average of about four to four and a half feet.

So, how would worms that live in your gut or worm that lives in your bloodstream cause undernutrition?

And then, we will talk a little bit why we care so much about undernutrition.

A lot of these worms, we think particularly schisto which sits again right in the middle of your bloodstream and makes lots of eggs that are very immunogenic,

we found that they make a lot of these cytokines.

These cytokines are considered the cause of host of different bacterial, viral and parasitic infections and the host of (inaudible) season response.
These are very known modulators of cachexia or anorexia which cause very decreased appetite.

So, even if food is available in this context, kids have much decreased appetite and also alters muscle metabolism so that you have muscle wasting and loss of important proteins and muscle mass in the urine.

As you saw, these worms can be very bulky and a lot of them cause -- people report pain, nausea, vomiting, early satiety, and that itself may cause decreased intake which may be related to the malnutrition we know the worms caused.

And the worm bulk itself, so particularly with Ascaris, the giant roundworm probably leads to some malabsorption if the worm really blocks the host's ability to absorb nutrients which are then lost in the feces.

So, these are some of the ways we think that worms --

so all of these worms have been implicated in undernutrition particularly at higher intensities of infection and these are some of the ways that that is likely happening.

So, I am going to show you a little bit of our data from a study site in the Philippines where we treated kids for schisto, just schisto and then look at what happened
to their nutritional status after we treated them with Praziquantel, a drug of choice of schisto over 18 months.

And so, a BMI Z-score is a really nice way of assessing overall macronutrient status of a child and one thing you will notice is that overall, we treated everybody and everybody had a positive inflection here.

So, one thing I would say is a BMI Z-score -- a Z-score standardizes a nutritional status to zero, so it is really a standard -- think of it as a standard deviation from a mean.

So, your BMI Z-score, if it is 1; it means it is 1 standard deviation away from a healthy, happens to be American farm-fed boy or girl of that same age.

So, if you have a -- overall, if your BMI Z-score was minus 1, you are about minus 1 standard deviation lower from the mean of the healthy reference population of a similarly age and gender matched child.

These are now showing you a change in BMI Z-score after we treat you.

If you had gone to this village and not treated people, for the most part overtime as kids get older in this age range, they were about 7 to 18 years old you would have watched their BMI Z-score fall overtime.
because you leave kids in an environment that is not healthy over the years without treatment.

Overall, they really fall off in terms of their nutrition.

When you are comparing them to --

they are basically competing with healthy American kids when you compare them this way.

And we can talk a little bit after about the pros and cons

of using a healthy American reference standard.

But, that is what we do, that is what the WHO and CDC recommends for a lot of different complicated baseline.

But, basically what you see what happens is that overall, this is your change in BMI Z-score,

if you were wasted at the beginning of the study, overall,

your change from baseline was much greater than if you were not wasted.

But overall, everybody had a positive inflection and this is a phenomenon that is found all over the world.

So, kids who are doing worse on a lot of different measures, when you treat them for one illness, have a much better rebound effect.

And that may very well be because these were kids that were suffering more.
There is a lot of variability in terms of host immune responses to schisto, how much morbidity each host suffers so that this group may very well have been the kids that were much worse off from their schisto for whatever immunologic or other reasons and you liberate them from that disease and you basically watch their BMI Z-score go up overtime. This is a similar idea except here we are looking at treatment and your linear growth here and then your weight gain from baseline here and a group of kids that we watched for 18 months and this is their re-infection status at 18 months. So, either they were not re-infected at all, uninfected. They got re-infected, but in a low intensity, moderate or high and then, the same thing for their weight gain from baseline. So obviously, everybody is going to grow a certain number of centimeters. This is all positive and what you notice is that the low intensity re-infection, they didn't really affect their linear growth very much at 18 months, but when you get out to the moderate and the higher intensity re-infection,
these kids really had some growth stuntng from their re-infection

[00:23:01.736] and the same was true for their weight gain.

[00:23:03.656] Low intensity re-infection, not so bad.

[00:23:05.676] And then, if you get re-infected at higher intensities,

[00:23:09.666] your weight gain from baseline is significantly different than the group that gets uninfected.

[00:23:15.286] And to remind you again, all we did was treat them for one worm with this standpoint

[00:23:20.086] and so this is sort of the power of one worm in terms of its impact

[00:23:23.786] on nutritional status knowing that these are kids that I can tell you harbored almost all

[00:23:29.596] of the geohelminths at low to high intensity range.

[00:23:34.096] So why do -- you probably have heard in public health courses

[00:23:39.246] and undergraduate courses the importance of malnutrition and nutrition to child health.

[00:23:45.956] This is really considered one of the most important metrics of child health and even

[00:23:52.076] as a mere for the health of a society.

[00:23:56.596] So, the prevalence of undernutrition in a community can give you a lot of information

[00:24:02.126] about the overall health of that community and there are a lot of different reasons for that.

[00:24:07.616] One being protein energy malnutrition itself kills children.
So, many children, millions of children each year die from food scarcity and protein energy malnutrition.

Having protein energy malnutrition places children under 5 at increased risk for mortality from any cause however.

An estimate -- there is a very elegant article by Pelletier that looks at trying to estimate the number of deaths that are attributable to the potentiating effects of malnutrition and he actually estimated that that is about 56 percent of child deaths maybe preventable if that child was not malnourished when they were hit with whatever the ultimate cause of their death was.

So, I'll give you a very good example from a malaria study.

When you give children bed nets for malaria prevention, you do a pretty good job preventing their malaria-related morbidity and mortality.

But, more than one study found that you also reduce the risk of dying from measles.

So, measles is a nice indicator because it is not like a lot of other diseases.

It wasn't malaria and they just had, you know, diarrhea or was it true gastroenteritis
that really killed the child.

[00:25:25.206]
Measles is measles and bed nets reduce your mortality from measles and why is that?

[00:25:31.376]
Probably, because if you control someone's malaria, you are probably making that child that much more robust in every way and most importantly,

[00:25:42.256]
probably you are reducing their acute and chronic anemia

[00:25:45.346]
and you are reducing their undernutrition so then when they get hit with measles,

[00:25:50.126]
they are better able to survive that next insult.

[00:25:54.156]
That has also been found for gastrointestinal diseases.

[00:25:57.646]
So, deaths from severe diarrhea or dysentery also less in children that are not malnourished at the time they get that illness.

[00:26:05.186]
And given most kids in the world actually have mild to moderate malnutrition,

[00:26:12.846]
that created burden in terms of numbers and prevalence is in the mild to moderate.

[00:26:17.866]
So, if you can improve the nutritional status of kids and move them out of this range or even out of this range into well-nourished kids, when they ultimately get their measles or their malaria or their bad gastroenteritis,

[00:26:32.546]
they may very well be more likely to survive that.
And, it is one of the reasons we think that when people talk about subtle morbidities of helminth infection, so the idea that, yeah, kids co-exist with multiple helminth infections and isn't that okay.

The parasite is sort of adapted to live with us for years and years. I am not sure that it is really okay.

If we know that each worm is causing at least some malnutrition and that malnutrition in turn places them at greater risk of death, I think that it is one of the real arguments that the very least that we keep intensities of infection lower, we may do a lot in terms of decreasing particularly child mortality.

Also, malnutrition has been associated with poor cognitive performance and concentration and really may limit kids who are already very limited opportunities to take advantage of education in lesser developed countries.

And stunting, we always talk about as being related to decreased adult work capacity for a nation and also, places pregnant women at greater risk for adverse birth outcomes.

So, this is a quick look.

Now, I want to focus -- change gears a little bit and talk about anemia.
So, most of us understand that anemia is not good for us for a whole host of different reasons ranging from probably not good for our energy level or oxygen carrying capacity or work capacity.

In children in particular, we know that iron deficiency anemia in particular is not good for your cognitive function and severe iron deficiency anemia also not good for your growth.

So, this is a look at, again, S. japonicum infection and so here, I can be faulted for separating out the worms, but we were sort of interested in getting a sense of the burden that each of these worms and then, I will show you some data from the polyparasitic work.

But here, you can see, if you have heavy intensity S. japonicum, you have a significantly lower adjusted hemoglobin.

Now, if you look at just hookworm infection, moderate or heavy infection, significantly lower hemoglobin and same for Trichuris.

All of these analyses are adjusted for socioeconomic status and age and gender because you could argue back to me very easily that all of these are factors that move at poverty.
So, I am telling you that I think it is this, this is cross-sectional data,

and you may say to me, it is not that they have schisto at this intensity.

It is that they are poor and they are poor, so they are in the rice paddies,
going in freshwater, getting infected with schisto all the time instead of being in school.

So, we really do our best here to try as much as you can control for known compounders to try to really adjust for those and as you might expect, as yes, maternal education --
socioeconomic status, maternal education in particular were all very highly related to a child's hemoglobin as well.

So hopefully, we're giving you a good sense of what the worm itself does.

And again, I am showing you each of this separately.

Now, think about the fact that most of these kids are poly parasitized,

so they don't just have one worm.

They have at least two or more of them in most endemic areas.

Here is a look again at a sort of dose response by hemoglobin by intensity of S. japonicum infection and you can see the uninfected group with a nice,
juicy hemoglobin of close to 13 all the way down to the more intensity infected group of eleven and a half or so.

Again, all adjusted for the other worms and socioeconomic status in particular.

All right, and then, one final data slide, I think here to look at what happens if we treated you for your schisto with Praziquantel and then we basically look at what happen overtime if you are re-infected or not.

So, in the red, you have the group that remained uninfected, and so, this is a change from baseline, so everyone starts at about zero and if you were re-infected overtime, your hemoglobin stays below and at the very end of 18 months was significantly lower than zero, meaning that you had a significant drop in your hemoglobin.

Whereas, the group that stayed uninfected stays above that zero line, meaning that they did not have a drop in their hemoglobin.

Okay, as we have mentioned now, most of the world's children don't have just one of the parasites that we talked about.

If you look at the map that I showed you, in most part of the world, most kids have two
or more of these parasites and some have all four or three of them.

The other hard part is that many of them have them in varying degrees of intensity of infection and as I showed you, at least with schisto, if any other worms to a lesser extent,

it is probably very important the intensity of each infection that you have.

But, what happens now if you combine the data and look at the worms across low intensity even because the lower has always been, even from WHO, that well,

low intensity parasitic infections don't even cause low grade morbidity.

They probably don't cause much malnutrition, probably don't cause much anemia.

So, that is nice if you live in an area where you just have one worm at low intensity infection, but as we said, most of these kids have multiple infections.

And a very nice study done by Dr. Izzia Mamah (assumed spelling) who is a PhD student that worked with us and was very interested in this phenomenon said, "I am going to look at all the kids who have low intensity infections."

I am going to group them in one group, and I am going to compare them to a reference group that had no infections or even just one low intensity," And the kids
that had multiple infections even all at lower intensity had much higher morbidity than you would have even seen if they had one at a high intensity.

So, these kids acted like they were these -- a child who had, for example, a very high intensity single schisto infection.

Then, when you got into the kids that had higher intensity, multiple infections, these kids really, really, really look sick with hemoglobin on average of about 2 grams per deciliter lower than that reference group of uninfected or one low intensity infection.

The problem actually was you couldn't find enough kids for the reference group that had no infections so she included the low intensity in her reference group which means that probably the difference is even a little bit stronger than that.

So, even if you had two or more low intensity infections compared to uninfected or one, you had five times the chance of having anemia.

And then, she also got into some interesting work on synergy which is a very complicated topic.

But basically, what she found was having more than one worm may not necessarily be additive.
So, it may not be that hookworm plus Ascaris equals two dollars of anemia.

It is probably much more complicated than that such that there is a lot of concern that having two worms makes you look much worse than just having two worms

that they might have some negative synergistic effects that make that anemia worse.

All right, so how do you tackle this problem?

So, I am showing you a mud hut for a few different reasons.

As all of you guys can see very clearly, there is no electricity here.

I can also tell you there is no long-drop latrine here.

There are no hidden pipes with freshwater going into this house, and as I mentioned to you, these worms have adapted over thousands of years to the human host to know how we live in resource-poor settings and how to take advantage of that.

So, there is no running water in there.

There is no American standard porcelain bathroom in there, and there is not even in this particular context a long-drop.

Because I think the theme overall is that for helminth infections,
you will go a huge way to decrease transmission.

So, we recognized this in early 1920's as I mentioned, the Rockefeller Sanitary Commission to report to Congress and they designed these to distribute all over the United States and this is how they picked their design in part. They knew that hookworm larvae crawled 4 feet. The impetus for distributing these was to try to decrease hookworm infection in the United States and so, they built it 6 feet deep and it was actually a very effective intervention at reducing hookworm in the States. So this, however, is the reality in many parts of Africa and I don't mean this at all to be degrading, but this is sort of the reality. I actually think these two are very cute. They are sharing a little bit of ugali and some bean mix, but the environment is completely fecally contaminated. If you don't have a long-drop, this is where kids go, parents send to go or going outside to go either just outside in the back of a house. If they live near water source, that is commonly where people go
which is then very bad for schisto transmission, right?

Night soil is another still very commonly used fertilizer.

Does everyone know what night soil is?

So, night soil is when you take -- used as fertilizer often a mix of human and domesticated animal feces to fertilize soil.

It is apparently actually a very most excellent fertilizer,

but not good for the environment in terms of helminth infections.

And then, water.

We would go a very long way also in terms of hygiene and health if we could have better water supplies for families.

A lot of students asked me, well you know, how about you just have a potty for everybody and everybody washes their hands after they go and the truth is if you have walked miles of this much water on your head and you are picking out this water that doesn't even look so clean, you probably don't have a lot leftover to either wash your dishes, so you don't have to go into contaminated Lake Victoria or other sources with schisto and you probably aren't going to use a
lot of your water for hand hygiene either.

[00:36:59.346] Again, people need to wash their
clothes, wash their dishes, go for a swim

[00:37:03.916] and these are very common gathering
places and they are very --

[00:37:07.086] for the schisto transmission cycle as you
can imagine, this is a disaster, right?

[00:37:11.376] This is just sort of a Cercariae-feeding frenzy.

[00:37:14.646] This is a lovely habitat for the snails.

[00:37:18.456] People wade in here and they get infected.

[00:37:20.956] Many people use this as a place
to go to the bathroom and so,

[00:37:25.326] the transmission cycle continues.

[00:37:28.196] And in studies all over the world of schisto,
it is always these young teenage boys

[00:37:34.806] who have the highest intensity of
infections in almost every part of the world.

[00:37:38.816] And a lot of people think that it is the --
that young boys, I would say go for a nice swim

[00:37:43.616] in the lake and spend hours
getting themselves re-infected.

[00:37:46.526] In Egypt apparently where they have
urinary schisto where the eggs pass

[00:37:51.356] out through your urine and
blood goes along with it.

[00:37:53.506] It is a sign that you have reached manhood
when you pass your first bloody urine.

[00:37:58.466] So, it is really sort of this schisto and
these worms are really a very much a part

of the everyday fabric of life and it is
not to say that people don't recognize

that they are important,
but this is a huge problem.

And the interventions and our
armamentaria are a little bit limited

and they are limited for a
lot of different reasons.

So, snails -- so people have talked about
for schisto can you really get rid of snails?

And, getting rid of snails as you might
imagine as we found out when you try to get rid

of mosquitoes does really
horrific things to your ecosystem

and it is truly an insurmountable task.

General Mao apparently dispatched thousands
of Chinese peasants to de-snail a lot

of the Yangtze and Yellow
River valleys and years later,

he claimed that he had eradicated schisto,
which we of course know is not true

since they still have many
schisto-endemic regions of China.

Dams, creation of new dams has led to
a whole new areas endemic for schisto

because now you have a collection of freshwater
and the transmission cycle begins again.

A lot of the newer studies have looked
at school-based antihelminthic therapy
and this is really a very exciting -- an exciting approach in the sense that a lot of the burden of disease is borne by children. They are also major reservoirs for the environment so they go home and contaminate the environment.

So, targeting kids in school has become very attractive and there is a lot of very interesting modeling of prevalence of infections in schools and how frequently we need to treat kids. Dr. Colley's supported grant will hopefully help to answer a lot of these for schistosomiasis, how frequently do you have to go to school and treat based on prevalence, is that really an effective intervention, is it culturally appropriate and acceptable to different communities. Education, so hand hygiene, sanitation again, shoes, which goes under a category of both economic development and education.

And then again, I think we all really, scientists in particular and public health strategists must think both in a multidisciplinary way and across parasites. So, we all have our favorite parasite.
NIH has taught all of us that the way you keep getting money is that you study one thing

[00:40:38.746] into the greatest depth and you are the world's expert in this parasite, but I think I would

[00:40:44.846] like that we are just all not to lose sight of the fact

[00:40:47.356] that these parasites happen in a much greater context.

[00:40:51.736] We didn't talk about malaria, HIV, filaria today, all whole host of other insults
to children and particularly children and pregnant women.

[00:41:00.906] We didn't even talk about nutrition as an intervention that we have to think about

[00:41:06.956] and iron, this has come up recently in the context of malaria.

[00:41:12.326] So, people that are interested in giving iron to pregnant women

[00:41:15.526] because they have studied pregnancy and that is good for birth outcomes

[00:41:18.406] and we think in developed countries.

[00:41:22.306] So, probably we should go and do that in lesser developed countries and it turns

[00:41:28.326] out that this has raised a specter the malaria parasite may very well do much better

[00:41:33.786] if you give the human host some iron to help it grow.

[00:41:36.926] So, we have to be very careful, talk to each other,

[00:41:40.536] and really think about these interventions that,
you know, if the geohelminth people are going

to the school to give the Albendazole,

what a good idea to have Dr. Colley's core team
also know how much Praziquantel to give them

and at what frequency for their schistosomiasis.

So, we started by talking in the post World
War II era a little bit and Dr. Stoll's speech

and it is interesting, people talk a lot

about the way parasites influenced
history and the world.

And there is a very interesting history of
parasitology where there are lots of theories

that Chairman Mao may have very well
invaded Taiwan right after World War II,

but was halted at the Yangtze River Valley

when his own troops got the
acute form of schistosomiasis.

So, Katayama fever is something
that many of our troops got

in the Pacific rim during
World War II which is a disease

that basically happens probably the first time

or in a schisto naive host gets
schisto infection for the first time.

So, his troops basically entered the river,
probably, scores of them got Katayama fever

and were unable to advance on Taiwan.
And there was pretty good evidence that that was the case.

But, I think more importantly, the burden of disease really rest squarely with children in lesser developed countries and pregnant women and unfortunately, it is still a wormy world.

That said I think that we all have a lot to contribute and I think that Dr. Colley and I were talking today about really young people have to get involved with global health.

We need fresh perspectives.

I started by telling you about a speech from 1947 or '49 where we were declared to live in a wormy world and we all need to work together to combat the problem and we still live in quite a wormy world.

And we made some progress, but there is lots of progress to be made and I think young people who can get the skills in education, in economic development, in journalism, in media can really take us a long way to combating this problem because unfortunately, we do still have a long way to go.

And as always, we would like to thank our field staff in the Philippines for their hard work.

A lot of this work was done with the Research Institute of Tropical Medicine in Manila and as always we thank our study subjects.
Thank you.

(Applause)