PLOS Science Wednesday: Hi Reddit, we're Madhu and Soumya and we are both researchers and advocates for tuberculosis research, as well as editors of the new PLOS TB Channel – Ask Us Anything!

PLOSScienceWednesday [1] and r/Science AMAs[1]

[1]Affiliation not available

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the WINNOWER

REDDIT

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It has been suggested that an effective vaccine is the only hope of getting TB under control. Do you agree? How close do you think we are? What are the greatest obstacles?

wandering_wookiee

"only hope' sounds exaggerated and it is best not to look for silver bullets! Even if we can optimize the tools we have today (e.g. Xpert, new drug regimens), we will make a lot of progress. But a good vaccine can dramatically change the trajectory of decline in incidence.

The general consensus now is that we need to optimize our current tools, and work on R&D for new dx, rx and vaccines. Together, they will make a difference.

I'm an infectious disease/tropical medicine physician currently working on a TB research project in Uganda.

A few months ago, a large retrospective study was published in Emerging Infectious Diseases looking at the rate of mycobacterial disease due to *M. tuberculosis* versus *M. bovis* in the U.K., and found a higher than predicted proportion in certain populations was being caused by *M. bovis*. Have any similar studies been started but not published in North America that you're aware of?

tovarish22

We do have livestock infected with M. bovis in North America, but human cases are rare. According to CDC, M. bovis causes a relatively small proportion, less than 2%, of the total number of cases of TB disease in the United States. I am not aware of much research in this area in N America.

Hi Madhu and Soumya - thanks for taking the time to answer our questions!

I'd be interested in your thoughts about qualitative research for TB -both in terms of implementation research and the more 'political stuff' that is so well established among the HIV & MCH communities

but is still lacking for TB.

At last year's Union conference, diagnostics & drug developers voiced their concerns over the uncertainty of uptake for the R&D they were investing in. The MSF & Stop TB Partnership Out of Step reports highlight the extent to which national policymaking efforts are dangerously out of step with international standards. Recent, much celebrated innovations (GeneXpert, LPAs, bedaquiline, delamanid etc.) have had their potential impact severely hampered by uptake and implementation issues.

Are we playing a dangerous game by focussing so heavily on biomedical "magic bullets" (Xpert Omni, Vaccines, Genome Sequencing etc.) without addressing the socio-political environs in which they must be applied (locally, nationally, and globally)? How can we encourage (and fund) more of this qualitative research, and on what specific challenges do you think we should focus?

hov_hov_hov

Thanks. Yes, new tools, by themselves, can only go so far, without addressing social determinants and health systems. I think all of global health suffers from an excessive focus on tech and silver bullets! TB is reflection of this.

What are current barriers to effectively diagnosing and treating tuberculosis in high-burden countries?

mmm_toasty

Quality of TB care is suboptimal in many high TB burden countries, and there are major gaps in the cascade of TB care. Please see this review we recently published: http://www.ijidonline.com/article/S1201-9712(16)31200-0/pdf

National TB programs need to invest in Quality Improvement programs, plug gaps in the cascade, and invest in new tools.

It is quite amazing that most high burden countries are still diagnosing TB using ZN smears in 2017!

Through the increasing part of drug resistent strains like XDR-TB, do you think we stand a chance to successfully treat TB in the future ?

RoXoR987

Mathematical models project a worrisome trend with currently approaches we are using for TB care. See:

http://www.thelancet.com/journals/laninf/article/PIIS1473-3099(17)30247-5/abstract

To avert MDR and XDR-TB in future, we need to do a better job of dealing with TB today - invest more $$, improve quality of care, scale-up the best tools we have today, and be more aggressive about detecting and treating DR-TB.

Do you think there's a good possibility that I'm the foreseeable future TB with be eradicated, similar to the successes with polio?

maddogmattthomson

The End TB Strategy [http://www.who.int/tb/post2015_strategy/en/] aims to end the global TB

epidemic, with targets to reduce TB deaths by 95% and to cut new cases by 90% between 2015 and 2035, and to ensure that no family is burdened with catastrophic expenses due to TB.

This is the most ambitious goal TB has ever seen. But reaching this goal will require substantially greater investments than most countries are currently spending on TB.

So here is a question of something I've never understood.

My mom has TB. She has had it since before I was born. How it has been described to me is that it has been "Naturally sectioned off" in part of her lung. She lives like normal, and doesn't have any ailments. She can't give blood or anything, but it's still TB.

How does that happen? Is it a constant risk?

ITsPersonalIRL

There is no such thing as a naturally sectioned off part of lungs. I suspect they are referring to 'latent TB' where TB bacilli have been walled off by immune response. People with latent TB have no symptoms, and are not infectious. But there is a risk of developing active TB in future. This can be reduced with latent TB treatment.

Do you have any sense of whether CRISPR might play a role in TB treatment in the future?

data_mangler

Too early to tell, but gene sequencing, on the other hand, is already shaping to be very promising in TB. See: http://jcm.asm.org/content/55/5/1249.abstract

Hi folks! THANK YOU FOR DOING THIS AMA! I believe that many people here in the United States have no clue what a serious problem and threat tuberculosis is for populations the world over.

This NPR article states that by 2040, multi-drug resistant TB is going to become shoot up in prevalence in Russian, South Africa, the Philippines, and India by 2040. Pointedly, though, in the article, Peter Cegielski points out that lack of **airborne infection control** in some countries is a key component of this problem.

Do airborne containment protocols or practices exist that can be easily implemented in non-developed countries without requiring massive material support and/or training/retraining? Does humanity already know all it needs to about tuberculosis containment, rendering this question about containment procedures irrelevant?

Thanks for the AMA, and thank you for the work you do <3

Gamerk1d51

We know a fair bit about how to do effective airborne infection control. WHO has published guidance that is designed for LMICs. But the real issue of lack of uptake of such protocols by hospitals and health systems in many low income settings.

Do you think we are making enough progress in drug development to fight against drug resistant and extensively drug resistant tuberculosis? What is holding us back from better treatment regimens?

IBikeI

In our recent Nature Primer on TB (free access at https://www.nature.com/articles/nrdp201676), we have reviewed the current status of new TB drug and regimen development. We have made some progress with new molecules (bedaquiline and delamanid), and new regimens in late stage trials are also promising:

-Nix-TB, a Phase 3 trial testing bedaquiline, pretomanid, and linezolid (BPaL) in XDR-TB patients -NC-005, a Phase 2b trial testing bedaquiline, pretomanid, moxifloxacin, and pyrazinamide (BPaMZ) in MDR-TB patients and BPaZ in DS-TB patients

But we do need a more robust drug pipeline, since there is always a risk that promising drugs and regimens might fail, or have safety profiles that are not compatible with regulatory approvals.

What lessons can we learn from the failure of traditional DOTS programs to effective control TB in developing countries and what challenges remain to adequately fund a global TB treatment program?

Crocodile_CTC

Traditional DOTS programs have placed millions of patients on anti-TB treatment, and have saved lives. Despite this, TB incidence has not declined to the extent models predicted. We now know that merely focusing on active TB and putting patients on therapy will not necessarily reduce transmission. We need to detect TB early, and also focus on other approaches (eg. active case finding, treatment of latent TB in specific groups). The End TB Strategy by WHO does provide a more ambitious plan than the older DOTS program.

What can be the public health measures for nutrition to prevent and manage TB? Is there significant evidence to support such a program? And what would the program look like?

Coolcnt89

Undernutrition is easily one of the biggest risk factors driving the TB epidemic in many settings. India is a great example. In India, data suggest that nearly 50% of all TB can be attributed to malnutrition. See https://www.ncbi.nlm.nih.gov/pubmed/25668081

Modeling studies show that intervening on under-nutrition could have a substantial impact on TB incidence and mortality in areas with high prevalence of under-nutrition in India (see http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0128187).

India's new National Strategic Plan does include nutritional support for TB patients, but I am not sure whether it will have a population-wide impact on the epidemic, unless a serious multi-sectoral effort is made to address the widespread undernutrition problem in the country. Multiple ministries have to work together on this, not just health ministry (or national TB program).

Ultra noob question here...

I'm from India, had a case of pleural effusion about 15 years ago, completely cured now.

I was once speaking to a med student who told me that in India almost everyone is exposed to the TB bacteria, and the bacteria only kicks into action only when someone's immune system has been weakened due to some other infection. How correct/incorrect is this understanding? Thanks!

circuit_brain

Exposure to TB in India is widespread - an estimated 40% of the population is latently infected. While most people are able to contain the infection as latent TB, about 10% progress to develop active TB. This is driven by risk factors such as malnutrition, poverty, smoking, indoor air pollution.

I deployed to Iraq and came back to now having positive PPD tests. I did the INH therapy that they like to see for good measure, but am I just stuck always wondering for the rest of my life every time I get a chest infection that maybe I'm having an outbreak?

Calvertorius

If you completed your INH treatment, there is a good chance that you will never develop TB.

Hi! I am a MSGH student, mainly interested in epidemiology, particularly TB. What do you think of the TB rats used by Apopo and do you think they would be beneficial even in developed countries like the US? What advice would you give to students who want to go into research but are not able to travel out of the country? Thanks!

samosa4me

TB detection by rats is promising but a lot more work is needed to demonstrate their accuracy, reliability, and whether they can be implemented within routine national TB programs.

Research can be done anywhere - travel is not always required.

our country is notorious for abusing antibiotics. How does this help TB grow ? What steps are followed to stop this ?

heronumberwon

Antibiotic abuse is a concern in all countries! With TB, here is a nice example of how quinolone abuse can impact TB diagnosis: https://naturemicrobiologycommunity.nature.com/users/20892-madhukar-pai/posts/14067-use-of-fluoroquinolones-in-patients-with-respiratory-infections-can-delay-the-diagnosis-of-tb

As regards solutions, this is a complex problem that requires action on many fronts: better regulation of antibiotics, stewardship, provider and patient education, and R&D to continue developing better antibiotics.

Does the rise of antibiotic resistant strains of bacteria worry you at all when it comes to TB? How can we work to get rid of TB in a time where over-prescription of antibiotics is at an all-time high and is there a way to prevent this disease from becoming a superbug?

OGbootychaser

Yes, please see my responses to RoXoR987 and heronumberwon - they have asked the same question.

How much of a game-changer is bedaquiline given the concerns around side-effect profile? What's the likely impact of drugs such as pretomanid that are currently in clinical trials?

mrcchapman

The accumulating evidence on bedaquiline looks very promising. See this new multicentric study: http://erj.ersjournals.com/content/49/5/1700387

But I would be wary of calling this a 'miracle drug' - some media stories use this phrase. By itself, BQ cannot have a big impact. It needs to be integrated into effective regimens. So, we are all waiting for results of these trials:

-Nix-TB, a Phase 3 trial testing bedaquiline, pretomanid, and linezolid (BPaL) in XDR-TB patients

-NC-005, a Phase 2b trial testing bedaquiline, pretomanid, moxifloxacin, and pyrazinamide (BPaMZ) in MDR-TB patients and BPaZ in DS-TB patients

I'm a current medical student, making my first forays into cardiovascular research. What are your opinions on the resurgence of TB in London over the past few years (particularly in lower income areas) and the factors responsible?

clonegeld

I don't know much about TB in London. I hope others who know the problem can jump in and respond!

What is being done about the triple drug resistant TB that originated in India, and why is antibiotic protocol taking so long to be modified?

wandringbark

India recently released its ambitious new National Strategic Plan for TB elimination by 2025. See: http://gh.bmj.com/content/2/2/e000326

The plan is ambitious and does include scale-up of DR-TB treatment and new tools. What is essential is funding to execute the NSP!

Are there people who advocate against tuberculosis research?

DrButtstuffington

I hope not!

Hi! In the Philippines, TB is very prevalent, so much so that even with negative sputum AFBs and TB PCR, an asymptomatic person with a suspect chest xray would be assessed to have TB. What are your thoughts on this threshold for diagnosis? Are there potential novel methods of diagnosis that are both specific and affordable to the general public?

Melia25

X-rays are a great way to rapidly screen for TB, but many lung diseases can cause x-ray abnormalities. So, any abnormal x-ray needs to be followed up with microbiological tests such as smears and GeneXpert.

The best novel tool is Xpert MTB/RIF Ultra, endorsed by WHO this year. This is a more sensitive cartridge than Xpert MTB/RIF. See: http://who.int/tb/features_archive/Xpert-Ultra/en/

This should be soon available via the public TB program in Philippines.

Hello! Just the other day my mother was telling me that her mother died of TB (followed by heart attack and brain haemorrhage.) I always keep hearing about this genetic probability of rogue genes being carried down the generations.

Is this true for TB? Does the fact that her mother had TB increase my mom's chances of getting it?

I'm sorry if this is an inappropriate question for this forum!

112otipas

Only a small proportion of people infected with TB end up developing the disease. So, undoubtedly, there is a genetic susceptibility (or resistance) to TB. The problem is that we don't know enough to predict this on a case by case basis.

Do you think TB will become an issue for wild Asian elephants?

Lucythekittyslayer

I have no expertise in this area!

I don't have a question, but I do want to convey my thanks to you for advocating for TB research, and I wish you both all the best!

Mel86

Thanks!

Oh man! I know all about TB testing requirements. The CDC released their Guidelines for TB Testing in 2005. Do you know if there's going to be an update any time soon?

GryphonMane

This is the latest ATS, CDC, IDSA standards for TB diagnosis:
https://cid.oxfordjournals.org/content/early/2016/12/08/cid.ciw694.full.pdf+html

Do you know why some places used to vaccinate for Tuberculosis, and most prefer to do regular skin tests to screen those exposed? My parent's grew up in Montreal, and they both received TB vaccinations, while my local health region relies on Skin Tests.

at0lms

BCG vaccination policies vary widely across countries, and even within a country, over time. Please see our post on this: https://naturemicrobiologycommunity.nature.com/users/20892-madhukar-pai/posts/15729-tracking-tb-vaccination-policies-and-practices-through-space-and-time

What's the best way to effectively limit TB in developing countries like India which can't afford treatment

AdityaRav

Globally, the best plan we have for controlling TB is the End TB Strategy. Individual countries are developing their own National Strategic Plans. For example, India and South Africa recently released their NSPs.

I would not say that India cannot afford treatment. India recently released its ambitious new National Strategic Plan for TB elimination by 2025. See: http://gh.bmj.com/content/2/2/e000326 The plan is ambitious and does include scale-up of DR-TB treatment and new tools. What is essential is funding to execute the NSP! India is already allocating more $$ than in the past, and the new NSP needs more.

Are you familiar with the disease sarcoidosis? Given the similarities between sarcoidosis and tuberculosis, some researchers (like Dr. Wonder Drake of Vanderbilt) suspect a mycobacterial etiology. Mycobacterial genes have been found in sarcoidosis tissue specimens numerous times. Any thoughts?

Here is her webpage listing her research: https://faculty.mc.vanderbilt.edu/Faculty/Details/33871

She is currently conducting a phase 2 clinical trial using the antimycobacterial CLEAR regimen to treat sarcoidosis.

BanalOpinions

Don't know much about sarcoidosis, I am afraid.

I've had to get tested for TB a couple of times for travel and, for some reason, I always test positive for TB. So they have to switch to a chest xray to clear me. What gives? I've never had any sort of lung problem or been hospitalized with illness. Is testing really that inaccurate?

John_Barlycorn

In general, tuberculin skin test, once positive, stays positive. So, it is not very useful for repeat screening after it becomes positive. Chest x-ray, on the other hand, can be repeated. But CXR picks up only active forms of TB, not latent.

Hello guys thanks for doing AMA.

1. What is the percentage of chances of TB hitting back in future, when a person is diagnosed with TB when they were born.
2. What are the common factors or habits those are attributed to reoccurrence of TB in later stage of life.

Thanks

greenroute

Depends on the type of TB (latent or active) a person had a child, and how well it was treated.

Risk factors for future development include HIV, smoking, immunosuppresive medications, malnutrition, etc.

Is there any way to avoid the scar when applying the BCG vaccine? Have there been any changes or advancements in how you administer it?

Marshmallow4u

No way to avoid the scar. No major changes in how BCG is given.