INA-RESPOND

INDONESIA RESEARCH PARTNERSHIP ON INFECTIOUS DISEASE

KEMENTERIAN KESEHATAN REPUBLIK INDONESIA

NEWSLETTER

July 2019

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Studies' Updates

NATIONAL INSTITUTE OF HEALTH RESEARCH AND DEVELOPMENT
MINISTRY OF HEALTH REPUBLIC OF INDONESIA
2019

D2EFT INVESTIGATOR MEETING

Jakarta, 18—19 June 2019

INA-RESPOND newsletter

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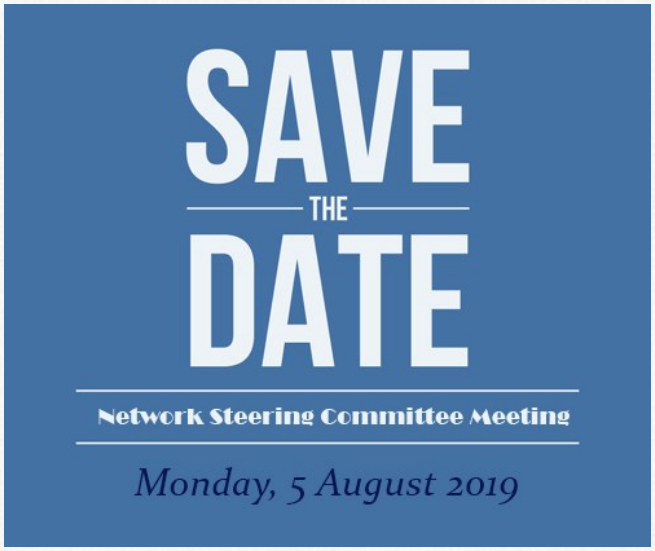
FEATURES



MASTHEAD

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INA-RESPOND Newsletter

TRIPOD & INA-PROACTIVE Study Updates

By: Eka Windari R., Lois E. Bang, Maria Intan Josi, M. Ikhsan Jufri, Venty Muliana Sari

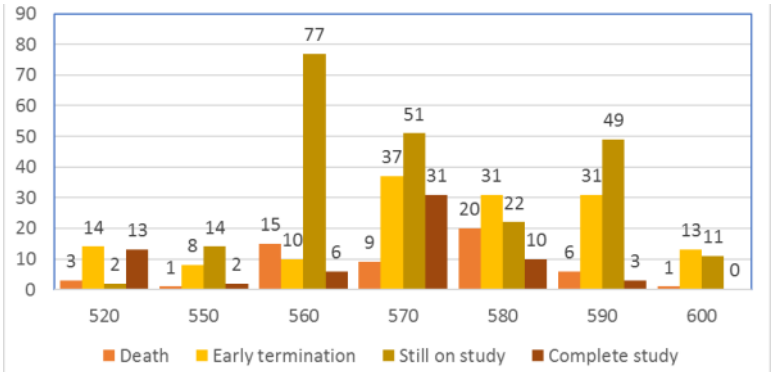

Figure 1.Participant status per site based on uploaded CRF per 30 June 2019

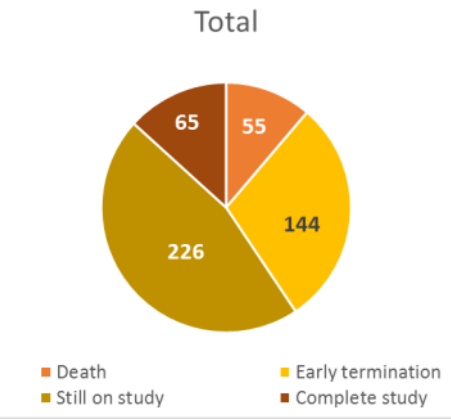

Figure 2. Total Participants Status based on uploaded CRF per 30 June 2019

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PARTICIPANT STATUS

Per 31 June 2019, the total ongoing participants in TRIPOD study are 226 out of 490 enrolled participants. Sixty-five participants have completed the study while 199 participants are terminated early (including death). Therefore, there are still 46,1% of participants from the total enrolled participants in the follow-up status. From the uploaded CRFs, there are 2 participants from site 520 (RS Sanglah Denpasar) who still need to be followed up, 14 participants from site 550 (RSUP dr. Wahidin Sudirohusodo Makassar), 77 participants from site 560 (RSUP dr. Kariadi Semarang), 51 participants from site 570 (RSUD dr. Soetomo Surabaya), 22 participants from site 580 (RSUP dr. Sardjito Jogjakarta), 49 participants from site 590 (RSUP Persahabatan Jakarta), and 11 participants from site 600 (RSUP dr. Adam Malik Medan).

Results for baseline culture and DST from all sites are ongoing. The three sites that have all the full result for culture and DST are site 520, site 550, and site 600. All culture and DST result will be on hold until further result information from the reference lab.

Site	Waiting for Baseline Study Culture Result	Waiting for Baseline DST Result
520 (n=32)	Complete	Complete
550 (n=25)	Complete	Complete
560 (n=108)	Complete	3
570 (n=128)	Complete	9
580 (n=83)	4	5
590 (n=89)	1	1
600 (n=25)	Complete	Complete

Figure 3.Culture and DST results up to 30 June 2019

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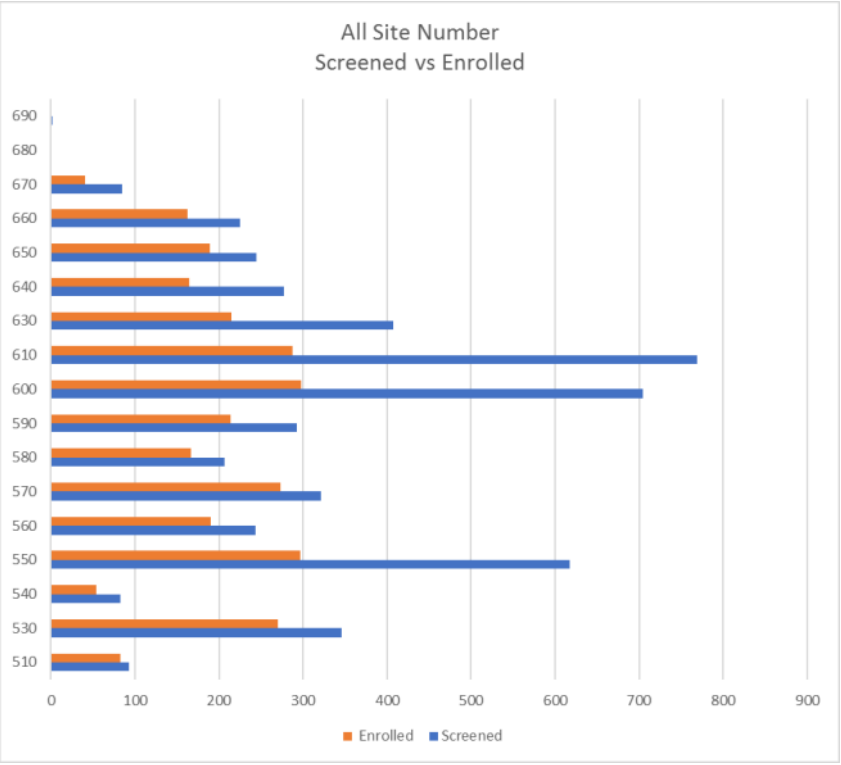
INA-PROACTIVE study currently has 18 active recruiting sites since it was first activated on 10 January 2018. By 7 July 2019 (data from 17 sites), a total of 2,907 subjects, consisting of 126 pediatrics and 2,781 adults, out of 4,917 screened patients had been enrolled. The enrollment rate was 59.12% of the total screening. Details are shown in Figure 1 on the right.



The enrollment failure rate was 40.88% from total screening. Details on the reason for failures are shown in Figure 2 below:

In the last NSC meeting, it was agreed that INA104 study would stop activating sites after 18 sites covering from the west to the east part of Indonesia join the study. We currently have 15 active sites, and three more sites are going to follow by the end of July 2019, making the total number of active sites 18. The last three sites to join our INA-PROACTIVE study are:

1. Site 680, RSUD dr. Sodarso, Pontianak with dr. Ivan Lumban Toruan, Sp.PD as the PI. The site activation was on 3 July, and the first enrolment subject was on 4 July 2019.
2. Site 690, RSUD Abepura, Jayapura with dr. I Made Gede Darmaja, Sp.PD., FINASIM as the PI. The site activation was on 27 June, and the first enrolment subject was on 2 July 2019.
3. Site 700, RSUD Dr. TC Hillers, Maumere with dr. Asep Purnama, Sp.PD, FINASIM as the PI. The site activation was on 5 July, and the first enrolment subject was on 8 July 2019.

Another good news came from Site 680, RSUD Dr. H. Moch Ansari Saleh Banjarmasin. The site PI, dr. Hj. Wiwit Agung SNC, Sp.PD,K-Ger, was selected for a poster presentation at National Congress XXIV PETRI in Batu, Malang on 4-6 July 2019. She presented INA104 cases from Site 630 through her poster entitled "The Characteristics of Patients with Antiretroviral Treatment Initiation in Moch Ansari Saleh Hospital in the Last 5 Years". Congratulation to site 630 for the achievement, and may it motivate us to do our best for other many accomplishments to come.

Reason for failures	510	530	540	550	560	570	580	590	600	610	630	640	650	660	670	680	690	Total
1. Suspect HIV	0	2	1	1	0	3	8	0	0	19	6	0	0	0	0	0	0	40
2. Refuse to consent	0	0	0	11	0	0	0	0	1	9	9	0	0	7	8	0	0	45
3. Unwilling to comply with the study procedures	1	6	2	4	8	0	0	7	1	4	0	0	7	2	1	0	0	43
4. Plans to move away	0	25	3	2	18	4	9	0	28	25	0	17	6	2	0	0	0	139
A. No show	1	10	1	11	7	0	4	8	13	6	13	12	4	3	2	0	0	95
B. Busy (in a hurry)	4	28	15	98	4	11	1	20	336	274	76	25	4	11	16	0	0	923
C. Has been enrolled	1	5	7	35	6	13	8	5	8	30	6	51	22	26	9	0	0	232
D. Participated in other CT	3	0	0	150	10	17	0	37	19	114	82	7	12	12	8	0	1	472
E. Hospitalized or unwell	0	0	0	0	0	0	10	0	0	0	0	0	0	0	0	0	0	10
F. Others (e.g. no referral letter from other health facility, equipment trouble)	0	0	0	8	0	0	0	2	0	1	0	0	0	0	0	0	0	11
Grand Total	10	76	29	320	53	48	40	79	406	482	192	112	55	63	44	0	1	2010

INA-RESPOND Newsletter

SITE PROFILE: DR. SOETOMO GENERAL HOSPITAL, SURABAYA

By: dr. Yufi Aulia Azmi

SITE PROFILE

Dr. Soetomo General Hospital in Surabaya, the capital city of East Java province, is one of INA-RESPOND network's study sites. The site, led by Prof. Usman Hadi, dr., Ph. D., Sp. PD-KPTI, as the Network Steering Committee member at site, has participated in several of our network's studies such as AFIRE and TRIPOD since 2011. Currently, the site is participating in INA-PROACTIVE study and will join in D2EFT research shortly. The hospital's active and continuous participation in the network's studies shows excellent commitment to research collaboration, particularly related to infectious diseases.

Prof. Usman Hadi, dr., Ph. D., Sp. PD-KPTI

We want to introduce our INA-PROACTIVE study team members from site 570, RS. Dr. Soetomo, Surabaya.

PI:

Prof. Usman Hadi, dr., Ph. D., Sp. PD-KPTI

He is a Professor in the Department of Internal Medicine Faculty of Medicine, *Universitas Airlangga*. He is a role model for the entire site team due to his dedication and discipline. He is very competent and an expert in research, mainly in tropical infection. His many scientific journals have been published and benefitted the health research community.

Co-PI:

M. Vitanata Arifijanto, dr., Sp. PD-KPTI., FINASIM

Dr. Vitanata is a Staff in the Department of Internal Medicine, Dr. Soetomo General Hospital. He is also a Lecturer in the Faculty of Medicine, *Universitas Airlangga.* He has good networking and has a great interest in the field of research.

Bramantono, dr., Sp. PD-KPTI., FINASIM

Dr. Bramantono is a Senior Staff in the Department of Internal Medicine, Dr. Soetomo General Hospital. He has excellent observation skills and very creative. His insights always provide solutions if the team face obstacles in the study.

From left to right: M. Vitanata Arifijanto, dr., Sp. PD-KPTI., FINASIM, Bramantono, dr., Sp. PD-KPTI., FINASIM, Musofa Rusli, dr. Sp. PD., FINASIM, Munawaroh Fitriah, dr., Sp. PK

Musofa Rusli, dr. Sp. PD., FINASIM

The youngest staff in the Division of Tropical Infectious Disease, Department of Internal Medicine Dr. Soetomo General Hospital, very interested in the research, energetic, careful decision-maker and problem solver. He is currently taking a tropical infectious disease consultant degree.

Dwiyanti Puspitasari, dr., Sp. A (K)., MCTM, DTM & H

A pediatrician in pediatric tropical infection division of Dr. Soetomo General Hospital. She is active in the division, department, and national levels research. Dr. Dwiyanti is a very patient person. She is currently taking a doctoral program at the Faculty of Medicine, *Universitas Airlangga*.

Munawaroh Fitriah, dr., Sp. PK

Dr. Munawaroh is a young staff at the Clinical Pathology Laboratory Installation of Dr. Soetomo General Hospital. She loves sharing her knowledge with her junior colleague and actively guides the residents. She is enthusiastic in the research, especially in HIV infection.

Research Assistants:

Yufi Aulia Azmi, dr

Dr. Yufi is one of the Research Assistants of site 570. He is a graduate from the Faculty of Medicine, University Airlangga, who is very interested in research. He joined the INA-RESPOND site team at the end of 2017 when the site was preparing itself for the INA-PROACTIVE study.

Rinta Prasetiyanti, dr

Dr. Rinta is the only woman Research Assistant of site 570. She joined the team and has actively participated in the PROACTIVE study together with dr. Yufi from the beginning.

Rahmat Sayyid Zharfan, dr

Dr. Rahmat is the youngest RA at the site 570. Although he is the youngest, he has a lot of scientific experiences and has obtained the title of an outstanding student of the Faculty of Medicine, *Universitas Airlangga* and became a participant in a research exchange program to Groningen.

Dandy Hertriwibowo, dr

The most recently RA at the site 570, calm in dealing with various situations, a problem solver person.

Lab. Technicians

Ms. Yuanita Bahar, Amd. Kes and Ms. Diah Wahyuni, Amd. Kes are the two Lab Technicians at site 570. They are both very experienced in handling the study because they have been members of the research and development division at Clinical Pathology Laboratory of Dr. Soetomo General Hospital for more than five years.

From left to right: Yufi Aulia Azmi, dr, Rinta Prasetiyanti, dr, Rahmat Sayyid Zharfan, dr, Dandy Hertriwibowo, dr, Ms. Yuanita Bahar, Amd. Kes

INA-RESPOND Newsletter

WORKING COMMITMENT: A JEWEL NOT SO HIDDEN

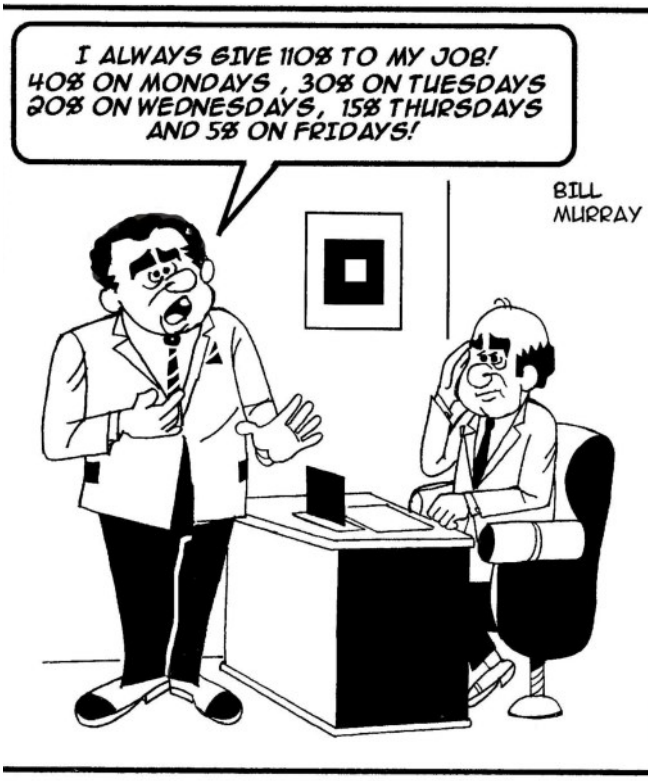
By: Aly Diana

Much like any relationship, commitment is at the heart of a healthy partnership. When employees are committed to their work and place of business, they are more likely to be happy and productive. Dedicated employees take ownership of their work and are ambassadors for their company, both inside and outside of office doors.

However, it is common to feel that our commitment to work is waning, and we are probably dealing with a lack of motivation. Without personal motivation, we don't have the drive to commit to anything - not even our essential job functions. As we can feel it, lack of commitment and motivation is not a good sign for any relationships. We need to be proactive in our attempts to regain our commitment, improve our productivity, and get our momentum back.

There are some suggestions out there about how to get back to our feet and turn things over: 1) Admit to ourselves that we are having commitment issues. By insisting that we are not in a slump, we prevent ourselves from getting out of it; 2) Set goals, both large and small. Setting a big-picture goal requires us to commit over a period of time while distracting us from minor problems and frustrations. Minor goals, like finishing a minor report by the end of the day, give us both a sense of urgency and the immediate satisfaction of a job well done; 3) Make a public commitment. When we keep goals to ourselves, there is little sense of accountability. However, if we promise our employees that something will be finished by a specific time, our commitment to that goal increases; 4) Congratulate ourselves. Positive thinking has a powerful effect on commitment, so encourage ourselves when we meet our goals, and 5) Take breaks. Exhausting ourselves is a sure way to burn out and lose our sense of commitment, so take frequent breaks to keep our head clear and our spirit strong.

Like every other relationship, it takes two to Tango. Here are some of the things that organizations can incorporate to bring in changes: 1) Build a strong team as teamwork does wonder! Achieving targets together may make difficult tasks look easily achievable; 2) Let employees know what the organizations expect from them. Most employees want to be a part of a success story of the organization they are associated with. Therefore, it is vital to communicate the goals, vision, and mission clearly to the employees; 3) Culture of trust, as trust is an essential factor that brings exceptional results in any relationships. Trust is earned by putting in constant efforts in actions and deeds; 4) Help the employees grow by providing learning opportunities, cross-training and any other methods that support their overall development; and 5) Celebrate success together, tell the employees they have made a difference, encourage them to do better. Even the slightest gesture will lead them to do better with each passing day. This will lead to a better commitment at work.



COMIC CORNER

References:

Bhat A. 2019. "Commitment to work: definition and tips to improve work commitment." QuestionPro.com, https://www.questionpro.com/blog/commitment-to-work/

Hanasya J. 2016. Testing the effects of employee engagement, work environment, and organizational learning on organizational commitment. Procedia - Social and Behavioral Sciences 229; 289 – 297.

Mercurio ZA. 2015. Affective commitment as a core essence of organizational commitment: An integrative literature review. Human Resource Development Review; 14(4) 389–414.

Marzullo D. 2019. "What is the value of employee commitment?" Zenefits.com, https://www.zenefits.com/blog/the-value-of-employee-commitment/

INA-RESPOND Newsletter

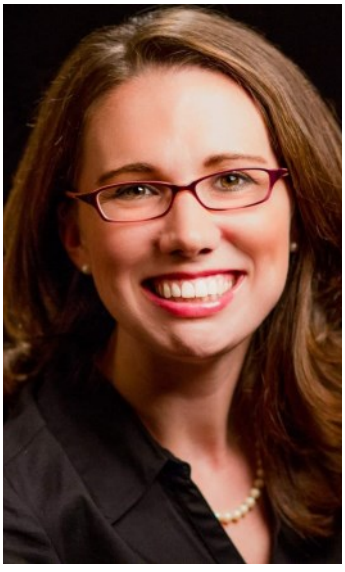
MEET THE TEAMS OF LEIDOS BIOMED

By: Katie Watkins, MPH, PMP [C]

Leidos Biomedical Research, Inc. (LBR) holds prime operations and technical support contract with the Frederick National Laboratory for Cancer Research (FNLCR), the only US federally-funded laboratory focused solely on biomedical research1. Via direct contracts with PT Ganesha and PT Prodia, LBR provides project and technical management expertise to the National Institute of Allergy and Infectious Diseases (NIAID) to facilitate the effective execution of the INA-RESPOND project. Although our colleagues across the expansive INA-RESPOND network may be most familiar with the Leidos Clinical Project Managers (PMs), several other LBR functional groups collaborate closely with the PMs each day to fulfill our mission. Please note that the below descriptions are not intended to be an exhaustive list of the many responsibilities fulfilled by each respective team, but a snapshot of how the teams collaborate to contribute to overall INA-RESPOND project success.

Research Subcontracts

As the name suggests, the Research Subcontracts group executes and manages the contracts held by LBR, including ongoing oversight of agreements, identification and adoption of new contractual requirements/regulations, and management of agreement modifications. Our colleagues also review every subcontract invoice for alignment with the period of performance and the type of contract. In addition, this group tracks the subcontract-purchased Government Furnished Equipment (GFE), which is the property procured using US federal funds.



Katie Watkins, MPH, PMP [C]

Clinical Project Manager I

Clinical Monitoring Research Program Directorate (CMRPD)

Frederick National Laboratory

Leidos Biomedical Research, Inc.

Support to NIAID DCR

Finance

Our finance group works on developing and tracking our Leidos budgets each year, inputting them into financial systems, analyzing projected costs, and working closely with LBR's government customer, NIAID. Within the financial Accounts Payable group, our Subcontract Invoice Processors (SIP) review invoices upon receipt from the vendor. SIP reviews focus on cost allowability within the approved project budget, as well as US Federal Travel Regulations2 (e.g., per diem).

Compliance, Control, and Audit Department

In addition to conducting ongoing internal company audits, as well as audits of research subcontracts, the LBR audit team reviews project-related travels for allowability in accordance with US Federal Travel Regulations2.

Property Compliance Department

The Property Compliance Department maintains a database of GFE purchased with US government funding through the LBR prime contract, in accordance with US Federal Acquisition Regulations3. When requested, this team provides decals for each piece of Sensitive or Capital Equipment purchased. When subcontracts are closed out, a collaborative process between PMs, Property, Finance, and Research Subcontracts groups ensures reconciliation of the property database to the equipment on-the-ground.

In summary, our colleagues in each group are crucial to our mission at LBR! My hope is for this overview to provide a sense of the various teams working, frequently behind-the-scenes, to provide support to the many projects ongoing at LBR.

References

https://www.leidos.com/company/subsidiaries/leidos-biomedical-research

US Federal Travel Regulations (FTR): https://www.gsa.gov/policy-regulations/regulations/federal-travel-regulation-ftr

US Federal Acquisition Regulations (FAR): https://www.acquisition.gov/browse/index/far

INA-RESPOND Newsletter

SCIENCE CORNER

TUBERCULOSIS EVOLUTION THROUGHOUT HUMAN HISTORY

By: Lidya Chaidir

Tuberculosis is an ancient scourge. It has plagued humankind throughout known history and human prehistory. The literature is full of tuberculosis descriptions. This frequent disease was named as schachepheth in the Old Testament, phthisis in ancient Greece, "tabes" in ancient Rome, and "schachepheth" in ancient Hebrew. In the 1700s, TB was called "the white plague" due to the paleness of the patients and "consumption" in the 1800s. Johann Lukas Schönlein eventually unified the nosology and proposed the name 'tuberculosis' in 1834 due to the presence of tubercles in all forms of the disease. During this time, TB was also called the "Captain of all these men of death." The history was changed dramatically on March 24, 1882, when Robert Koch made his justly famous presentation, Die Aetiologie der Tuberculose, to the Berlin Physiological Society. He named the microorganism as Tuberkelvirus. The tuberculosis agent was named as Mycobacterium tuberculosis in 1883. [1]

The TB bacterium is older than was once believed. Using molecular genetics and genome sequencing, Gutierrez and her colleagues concluded that an early progenitor of M. tuberculosis was present in East Africa as early as 3 million years ago. East Africa was, then, the ancestral home of both tubercle bacilli and its human hosts. Through detailed genetic analysis of 259 samples of TB bacteria collected from different parts of the world, Gagneux and colleagues created a "family tree" of the germ, marking its evolution throughout human history with the genetic mutations they observed. As reported in the journal Nature Genetics, their findings indicate that TB mycobacterium emerged some 70,000 years ago among humans in Africa. It then migrated with them, spreading around the world as the population expanded during the Neolithic revolution. [2]

It reveals that some 20,000 to 30,000 years ago, TB bacteria developed the ability to go dormant in its hosts, then re-emerged decades later (latent TB). This ability may have developed as a survival strategy in the age of small, widely dispersed populations of hunter-gatherers, when TB might otherwise have killed off its isolated hosts quietly and died out itself, without gaining the opportunity to spread. This latency is what makes TB so hard to control, as the bacteria can hide out for extended periods among human hosts and breakthrough in new environments. However, over millennia, humans might even have benefited from their relationship with TB, as latent infection with the germ might have provided immunity against more lethal pathogens that existed in new human environments, or among archaic human populations. [2, 3]

Of all the M. bacterium strains circulating today, few strike more fear in public-health officials than the 'Beijing lineage.' First identified in greater Beijing in the mid-1990s, this lineage now circulates throughout the world, and many strains are resistant to drugs that vanquish other types of TB. Consistent with its name, the Beijing lineage did indeed

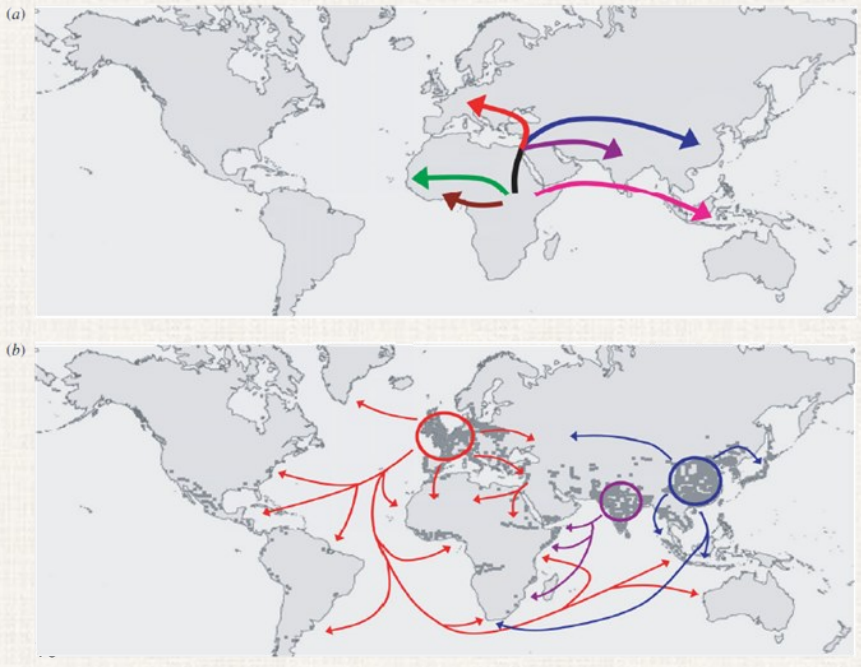


Figure 1. 'Out-of-and-back-to-Africa' scenario for the evolutionary history of human TB. (a) M. tuberculosis originated in Africa and some lineages accompanied the Out-of-Africa migrations of modern humans. (b) The three evolutionary 'modern' M. tuberculosis lineages seeded Europe, India and China, respectively, and expanded as a consequence of the sharp increases in human populations in these regions starting a few centuries ago (each dark grey dot corresponds to 1 million people). These lineages then spread throughout the world via exploration, trade and conquest. Red lines correspond to Euro American lineage, Blue lines: East Asia lineage, Purple and pink lines: Indo Oceanic lineage, Green: West Africa,

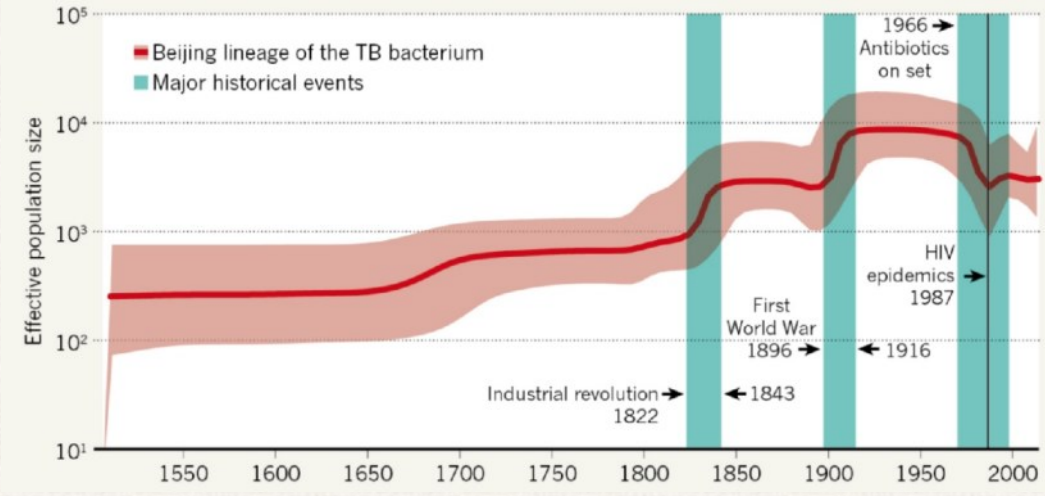


Figure 2. Several ups and downs in the prevalence of a family of TB bacterium strains that originated in Beijing followed major social and economic events.

emerge near north-eastern China, Wirth's team report in Nature Genetics. And it did so around 6,600 years ago, the researchers found, which coincides with archaeological evidence for the beginnings of rice farming in China's upper Yangtze River valley. [4]

Through their genome analysis of 4,987 samples of the Beijing lineage from 99 countries, Wirth's team used the sequencing information to date the expansion of the lineage and showed how the strains are related. They show that this lineage initially originated in the Far East, from where it radiated worldwide in several waves. They detected successive increases in population size for this pathogen over the last 200 years, practically coinciding with the Industrial Revolution, the First World War, and HIV epidemics. Two MDR clones of this lineage started to spread throughout central Asia and Russia concomitantly with the collapse of the public health system in the former Soviet Union (Fig 2). [4]

Figure 2. Several ups and downs in the prevalence of a family of TB bacterium strains that originated in Beijing followed major social and economic events.

In Indonesia, although TB is endemic throughout the archipelago, disparities in prevalence and strain distribution have been shown. Beijing genotype (corresponds to modern lineage 2-East Asian) was predominant in Java, but not in the eastern part of Indonesia, where the ancient lineage 1 (Indo Oceanic) was the most prevalent. We hypothesize that the difference in genotype distribution is related to the history of human migration in Indonesia. It is likely that Beijing strains were recently introduced to East Indonesia (Papua) and mostly introduced by large scale migration of people from West Indonesia following the Indonesian control over Papua starting in 1963. [5]

But if we compare this situation with our neighboring country, Papua New Guinea (PNG), modern strains like Beijing were present in much higher proportion than that in Indonesian Papua. This might indicate that those strains have been well established in PNG for a longer time. PNG and Papua have a similar historical background with regard to the first human migration to Papua from Africa 40,000-60,000 years ago, given the fact that Australia and Papua formed one continent, called Sahul. Following this, the second migration of Austronesians occurred approximately 3,500 years ago. We hypothesize that the difference began to appear when the Europeans arrived and later divided the island administratively in the 1880s: West Papua region was ruled as Netherlands New Guinea while the Eastern part of the island as German- and British New Guinea. This may have influenced how TB spread through PNG and Papua; Papua developed more connections to other parts of Indonesia and parts of Southeast Asia (like the Philippines), while PNG connected with the Pacific regions and Australia. However, the high genetic diversity among M. tuberculosis isolates observed in Papua may also be the result of recent transmission in combination with heterogeneity due to endogenous reactivation of latent infection. [5, 6]

What does this complex evolutionary history mean for efforts to control TB in the modern world? No effective vaccine against the disease exists. New antibiotic drugs are urgently needed in regions where the disease is widespread, yet bacteria will always be quick to evolve resistance. A better understanding of the relationship between humans and TB–and its complicated history–will help find a way to fight the disease and break its long, devastating pattern.

References

I. Barberis, N.L. Bragazzi, L. Galluzzo, M. Martini. The history of tuberculosis: from the first historical records to the isolation of Koch's bacillus. Journal of Preventive Medicine and Hygine. 2017 Mar; 58(1): E9–E12.

Comas I., Coscolla M., Luo T., Borrel S., Holt KE., et al. Out-of-Africa migration and Neolithic coexpansion of Mycobacterium tuberculosis with modern humans. Nature Genetics 2013; 45: 1176

Levy S. The Evolution of tuberculosis: genetic analysis offers new insight on the spread of an ancient disease. BioScience 2012; 62(7): 625

Merker M., Blin C., Mona S., Duforet-Frebourg N., Lecher S., et al. Evolutionary history and global spread of the Mycobacterium tuberculosis Beijing lineage. Nature Genetics 2015; 47: 242

Chaidir L., Sengstake S., de Beer J., Oktavian A., Krismawati H., et al. Predominance of modern Mycobacterium tuberculosis strains and active transmission of Beijing sublineage in Jayapura, Indonesia Papua. Infection, Genetics, Evolution 2016; 39: 187

Ley SD., Riley I., Beck HP. Tuberculosis in Papua New Guinea: from yesterday until today. Microbes and Infection 2014; 16(8): 607

INA-RESPOND Newsletter

THE ROLE OF EXERCISE IN IMMUNE FUNCTION

By: dr. Septia Mandala Putra

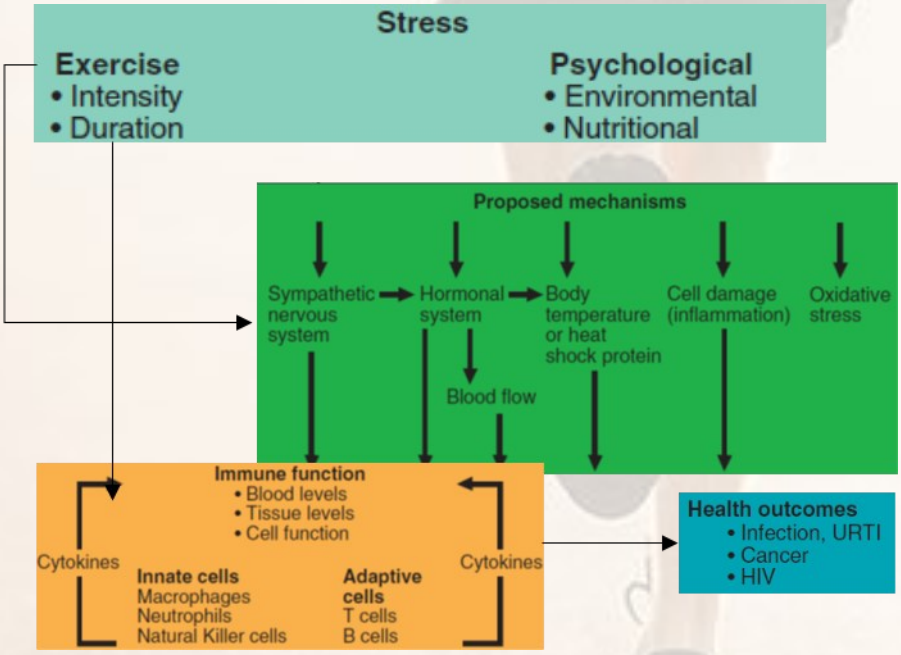
Introduction

Humans are regularly exposed to bacteria, viruses, and parasites capable of causing mild to severe disease. The fact that most of the time, these foreign invaders do not overcome us is a testimony to the importance and efficiency of the body's defense mechanisms, comprised primarily of the immune system.1 Exercises proved to have extensive benefits as active individuals claim they feel better and healthier than sedentary individuals. They have colds, flu, sore throats, and common illnesses less often.

Epidemiological evidence indicates that regular physical activities and frequent structured exercise reduce the incidence of many chronic diseases, including infectious disease such as viral and bacterial infections.2 Almost all immune cell populations in the bloodstream is altered in some way during and after exercise

The immune response to exercise

An acute bout of exercise causes an immune response. Figure 1 depicts the complexities involved in trying to address this relationship.



Exercise may alter immune function directly or through any combination of the mechanism listed below:

1. Directly stimulating immune function
2. Stimulating the sympathetic nervous system
3. Altering hormones (epinephrine, norepinephrine, cortisol, growth hormone, prolactin, and thyroxin)
4. Increasing body temperature
5. Exercise-induced cell damage (release of acute phase proteins)
6. Increasing oxidative stress

An important factor that must be considered when describing the effect of exercise on the immune system is the recovery period from exercise. Upper respiratory tract infection (URTI) was found in high volume, endurance-trained athletes (Mackinnon et al.,1987; Nieman, 1997b; Tomasi et al., 1982), this can be caused of a strenuous bout of exercise that suppresses the immune cells.

Strenuous training or overtraining is associated with a suppression of several immune variables. Most notable among changed immune functions following severe training is suppression of leukocyte numbers, a decrease in neutrophil function, a reduction of the natural killer cell (NCKA), and a reduction in lymphocytes

Running at high intensity, serum cortisol concentrations are significantly elevated above control levels for several hours (Nieman et al., 1995). Cortisol has been related to many of the immunosuppressive changes experienced during recovery

Latest evidence on the relationship between exercise and the immune system

Regular exercise can enhance vaccination response, increase T-cells, and boost the function of the natural killer cells in the immune system. Exercise also lowers levels of the inflammatory cytokines that cause the 'inflamm-ageing' that is thought to play a role in conditions including cardiovascular disease; type 2 diabetes; Alzheimer's disease; osteoporosis and some cancers.3

Moderate intensity exercise reduces inflammation and improves the immune response to respiratory viral infections. Acute and chronic moderate exercise induces a level of stress hormones that down-regulates excessive inflammation within the respiratory tract and aids in activating innate anti-viral immunity shifting the immune response.4

Regular exercise training is a countermeasure against a persistent systemic inflammatory state, which is a typical feature of cardiovascular and metabolic diseases is by lowering levels of pro-inflammatory cytokines. It is supposed that these effects are mediated by a modification of metabolic signals and innate immune regulation, the release of anti-inflammatory cytokines from muscle, the release of stress hormones, and a process known as browning of adipose tissue.5

Moderate activity (cycling) of 1-hour duration has been shown to increase the capacity of blood neutrophils (phagocytic cells) to respond to both receptor independent and receptor-dependent in vitro stimulation.

Regular moderate activity in both populations (sedentary and active) is considered to promote an anti-inflammatory environment. This is an essential underlying mechanism in the protection against chronic inflammatory conditions (e.g., cardiovascular disease, type 2 diabetes, obesity) gained from physical activity in older populations.6

Higher levels of physical activity are associated with a lower relative risk (RR) of colon cancer (in both males and females), breast cancer in women, and prostate cancer in men.1

Practical application for exercise prescription

Nonetheless, in light of available data, it is prudent to advise the general public that exercise bouts of low-to-moderate intensity (< 60% VO2max) and duration (< 60 minutes/bout) exert less stress on the immune system than do prolonged sessions (> 90 minutes) of heavy exertion (> 75% O2max). Moderate- versus high-intensity exercise results in a reduced stress hormone response, which has been associated with a more favorable immune response.

Guideline for postponing training due to upper tract respiratory infection (URTI)1s

One of the challenges facing exercise enthusiasts, athletes, and occupational workers is knowing when exercise can be safely and effectively performed during an illness. The following guidelines suggest when exercise training is and is not appropriate

Maintain training if the URTI is only minor and systemic infection is lacking (no fever, aching muscles, extreme fatigue, or swollen glands); or stop for a couple of days. Consider using decongestants during the day and antihistamines at night.

2. If the URTI causes positive signs of systemic infection (fever, aching muscles, extreme fatigue, and swollen glands), stop training for 2–4 weeks. If training is not stopped, viral cardiomyopathy or severe viral infection may result.

3. If symptoms occur above the neck (runny or stuffy nose, scratchy throat), begin sessions with a short or light activity. If symptoms worsen, stop; if symptoms lessen, continue. If symptoms are below the neck (muscle ache, vomiting, diarrhea, and fever), stop training until the symptoms go away.

Reference

1. Plowman SA, Smith DL. Exercise physiology for health, fitness, and performance. 3rd ed. Philadelphia: Lippincot. William& Willkins; 2011.

2. Campbell JP, Turner JE. Debunking the myth of exercise-induced immune suppression: Redefining the impact of exercise on immunological health across the lifespan. Front Immunol. 2018;9(apr):1–21.

3. Sander R. Exercise boost immune response. Nurs Older People. 2012. Jun 29;24(6):11

4. Martin SA, Pence BD, Woods JA. Exercise and respiratory tract viral infections. Exerc Sport Sci Rev. 2009;37(4):157–164.

5. Kruger K, Mooren FC, Pilat C. The immunodulatory effects of physical activity. Curr Pharm Des. 2016;22(24):3730-48.

6. Davison G, Kehaya C, Wyn Jones A. Nutritional and Physical Activity Interventions to Improve Immunity. Am J Lifestyle Med. 2014;10(3):152–169.

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