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INDONESIA RESEARCH PARTNERSHIP ON INFECTIOUS DISEASE

KEMENTERIAN KESEHATAN REPUBLIK INDONESIA

NEWSLETTER

January 2020

FROM OUR Sponsor:

To The Unknown: Discovering New Pathogens in The Laboratory

Lifestyle and Sports Exercise and Upper Respiratory Tract Infection

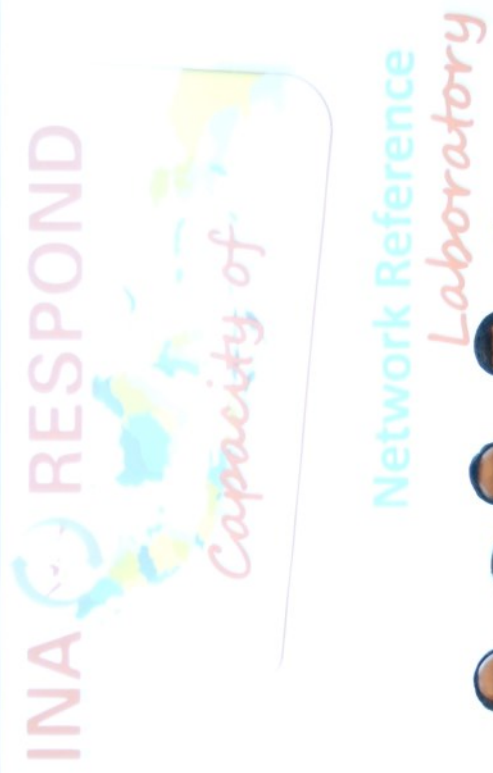Comic Corner Put Rewards in Place for a New Habit to Begin

TRIPOD and INA-PROACTIVE Studies' Updates

NATIONAL INSTITUTE OF HEALTH RESEARCH AND DEVELOPMENT
MINISTRY OF HEALTH REPUBLIC OF INDONESIA
2020

INA-RESPOND Laboratory Capacity Meeting,
7 January 2020, Jakarta

INA-RESPOND
newsletter

content

January 2020 Edition | issue #76

MASTHEAD

FEATURES

INA-RESPOND Newsletter

TRIPOD & INA-PROACTIVE Study Updates

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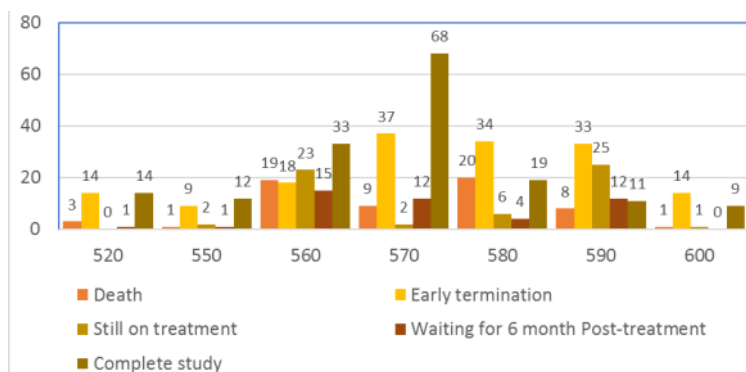

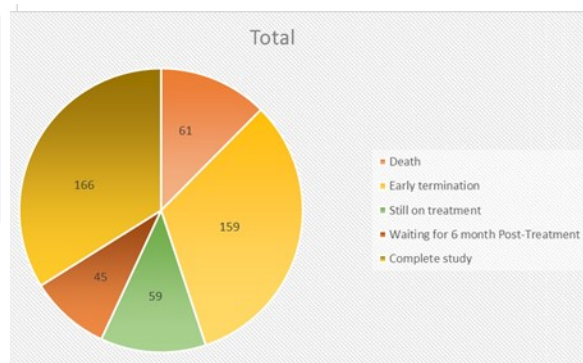Figure 1.Participant status per site based on uploaded CRF per 5 Jan 2020

Figure 2. Total Participants Status based on uploaded CRF per 5 Jan 2020

STUDY UPDATES

INA102

PARTICIPANT STATUS

Per 5 January 2020, the total ongoing participants in TRIPOD study are 104 out of the 490 enrolled participants. From those 104 current participants, 59 are still on TB treatment while 45 are waiting for the 6-month post-treatment visit. One hundred sixty-six participants have completed the study while 220 participants are terminated early (including death). Therefore, there are still 21.2 % of participants from the total enrolled participants in the follow-up status. From the uploaded CRFs, there are 1 participant from site 520 (RS Sanglah Denpasar) who still need to be followed up, 3 participants from site 550 (RSUP dr. Wahidin Sudirohusodo Makassar), 38 participants from site 560 (RSUP dr. Kariadi Semarang), 14 participants from site 570 (RSUD dr. Soetomo Surabaya), 10 participants from site 580 (RSUP dr. Sardjito Jogjakarta), 37 participants from site 590 (RSUP Persahabatan Jakarta), and 1 participant from site 600 (RSUP dr. Adam Malik Medan).

AWAITING CULTURE AND DST RESULT

The results for baseline culture and DST from all sites are complete. However, we are still waiting for the DST line 2 and/or the culture isolate date from 9 subjects.

| 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	Complete (still waiting for DST line 2 result and culture isolate date from 9 subjects)
570 (n=128)	Complete	Complete
580 (n=83)	Complete	Complete
590 (n=89)	Complete	Complete
600 (n=25)	Complete	Complete

Figure 3.Culture and DST results up to 5 Jan 2020

INA104

Four sites, namely Site 510 (Hasan Sadikin Hospital), Site 540 (Sulianti Saroso Hospital), Site 670 (Zainoel Abidin Hospital), and Site 680 (Soedarso Hospital) ended their screening and enrollment activities on 31 December 31 2019. Therefore, screening and enrollment have now ended in 16 sites. These sites are now focusing on subjects' follow-up. The remaining three sites, i.e. Site 700 (T.C. Hillers Hospital in Maumere), Site 690 (Abepura Hospital in Papua), and Site 520 (Sanglah Hospital in Bali) will continue its screening and enrollment until 30 June 2020. Per 5 January 2020, a total of 4,109 subjects had been enrolled which consist of 3,930 adults and 179 pediatrics from a total of 7,011 subjects screened from 19 study sites. Total of screened and enrolled subject from each Site shown in the figure below:

From a total of 4,109 subjects had been enrolled per 5 January 2020, there are 81 end-of-study subjects due to dead cases, withdrawn consent, and change of domicile. Details of end-of-study distribution per site is shown in Figure 2. As followings:

The Statistical Analysis Plan (SAP) meeting will be conducted on 23 – 24 January 2020. Core-Protocol Team and INA104 Secretariat Team will attend this meeting. The purposes of the meeting are to give Protocol overview and current data analysis and to discuss the statistical analysis plan for the INA-PROACTIVE study.

All Site Number Screened vs Enrolled
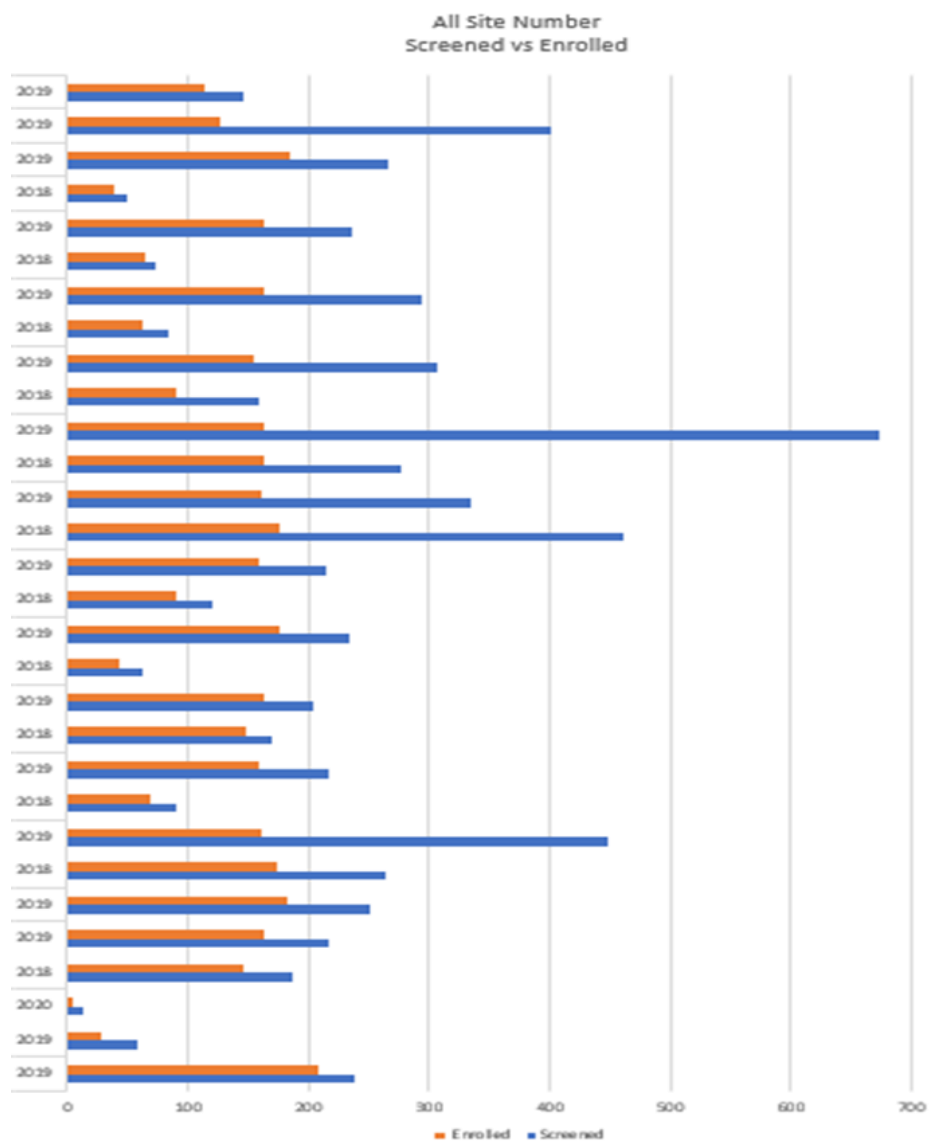
Site Number	Subject		Total End Of Study	Total Existing Subject
	Total Screened	Total Enrolled		
510	238	208	0	208
520	72	34	0	34
530	403	310	6	304
540	251	182	0	182
550	712	337	13	324
560	306	230	7	223
570	372	313	4	309
580	295	220	0	220
590	336	249	18	231
600	795	338	11	327
610	950	327	12	315
630	466	245	2	243
640	380	225	0	225
650	310	229	4	225
660	317	222	1	221
670	401	126	0	126
680	147	115	0	115
690	130	86	2	84
700	130	113	1	112
Grand Total	7011	4109	81	4028

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SITE 550: RS. DR. WAHIDIN SUDIROHUSODO, MAKASSAR

By: Fatmawaty Ahmad

From left to right: Munawir, A. Tessioja, Dewi Sriyanti, Kartini, Asvin Nurulita, Mansyur Arif, Sudirman Katu, Ninny Meutia Pelupessy, Dhiny Reskita Ayu, Fatmawaty Ahmad, Yusran Adi Fitrah

Who does not know Makassar? Known as the City of Sailor, Anging Mamiri City, or Daeng City; Makassar is one of the largest cities in Eastern Indonesia and a popular tourist destination for its history, culture, and culinary delights. If you are a food junkie, you definitely must try Makassar's *coto, pallubasa, "pisang ijo,"* and seafood. Sunset at Losari Beach is one of the tourist destinations that is hard to miss.

Wahidin Sudirohusodo Hospital, Makassar, a.k.a site 550, is a regional referral hospital in Eastern Indonesia. Site 550 became one of the first sites to join INA-RESPOND research in 2013. This site has participated in four studies: AFIRE, Sepsis, TRIPOD, and PROACTIVE studies.

Prof. dr. Mansyur Arif, , Sp.PK (K), MARS is a Steering Committee member of INA-RESPOND network. Currently, he also serves as the Director of Medical, Nursing, and Support Services of Wahidin Sudirohusodo Hospital, Makassar.

He has just completed his Hospital Administration Magister Study Program. Charismatic, intelligent, innovative, and revolutionary are some traits that we use to describe him. His hobbies are playing badminton and cycling.

dr. Sudirman Katu, Sp.PD-KPTI was a Principal Investigator of the Sepsis study, and he is again trusted to lead the PROACTIVE study. He is friendly and humorous, which makes it easier for us to communicate and discuss study-related issues with him.

dr. Ninny Meutia Pelupessy, Sp.A., our Co-Principal Investigator, is one of the leading pediatricians in Makassar. Because of her caring and friendly nature, children are comfortable and not afraid to be approached by her. She is still completing her doctoral study in Medical Sciences at *Universitas Indonesia*. Dr. Ninny loves traveling; Russia is one of her dream tourist destinations.

dr. Asvin Nurulita, M. Kes, Sp.PK (K), our other Co-Principal Investigator, is our front liner for consulting laboratory problems. She currently serves as the Head of Clinical Pathology Laboratory Installation of Wahidin Sudirohusodo Hospital, Makassar. Being decisive and disciplined are the keys to her success. Pop music entertained her in free time. Her 2020 resolution is to be more patient and consistent.

We have several Research Assistants (RAs) for the PROACTIVE study. A couple of them (Muh. Khaerul Muqsith and Yusran Adi Fitrah) have left their post to pursue their education and other passions. Our current RAs are Fatmawaty Ahmad, Munawir, Dhiny Reskita Ayu, Andi Q. Syahrezo, and Kartika Paramita.

Fatmawaty Ahmad joined the INA-RESPOND network during the AFIRE Study. She has just completed her study as a Clinical Pathologist. We often go to her to confide and discuss problems because she is our wise senior "sister." Food and movies are some of her many favorite things.

Munawir is one of the best Research Assistant at site 550. His commitment and loyalty are unquestionable. His dream is to become a Microbiologist. Whenever he has some spare time, he uses it to play badminton.

Dhiny Reskita Ayu, who was a Research Assistant for the TRIPOD study, joined The PROACTIVE study in March 2019. Her inquisitive nature and talk activeness often make our days more fun and colorful. She is a big fan of Korean pop music (K-Pop), and since she joined our little family, you would most likely hear K-Pop songs playing in the background of our office when you come to visit.

Kartika Paramita was involved in INA-RESPOND's SEPSIS and TRIPOD studies. She recently completed her education in Clinical Pathology. Watching Korean dramas and reading novels are her hobbies in her spare time.

Andi Qautsar Syahrezo joined in August 2019. We call him "little brother," not only because of his young age but also because of his calm and shy personality. Naruto, One Piece are some of the comics he likes. He hopes to be an internist in the future.

Dewi Sriyanti is one of the most reliable Medical Laboratory Technology Specialists at Wahidin Sudirohusodo Hospital. She has been with the network since the AFIRE study. We love her excellent performance, capability, and energy! This year is rather exciting for her as she is trying to get pregnant.

Kartini is our other Laboratory Technician. She is neat, organized, and coordinated. She is also very friendly to patients and always ready whenever we need her. Her expertise in handling logistics is highly valued. In her spare time, she sings and cooks. Her *Nasu Alikku* (name of traditional food) is the best.

Andi Tessioja is a Research Nurse for PROACTIVE study. She is like a walking Medical Record; whenever we ask for some information, she can give us a full, detailed answer. We love her dedication to her work. In her free time, she goes shopping and jogging. Car Free Day on Sunday is a suitable place to fulfill her hobbies.

Since joining the INA-RESPOND network, our site has experienced many ups and downs. With the start and the end of a study, each Research Assistant replaced, every rejection of informed consent or the death of our patient, we become stronger and wiser. From INA-RESPOND, we have learned a lot about how to carry out the good clinical practice. It sounds easy in theory, but it turns out quite challenging to apply. However, we always try to be better according to our motto "*Sekali layar terkembang, pantang biduk surut ke pantai.*" *Ewako Makassar*!

Kartika Paramita and Andi Qautsar Syahrezo
Research Assistants at Site 550

PROACTIVE Team @Site 550

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THE 24TH CONGRESS OF THE ASIAN PACIFIC SOCIETY OF RESPIROLOGY (APSR 2019)

By: Ika Fajarwati and Diah Handayani

REPORT

Worldwide, Tuberculosis is one of the top ten causes of death and the leading cause of a single infectious agent. In 2017, TB caused an estimated 1.3 million deaths (range 1.2-1.4 million) among HIV-negative people and an additional 300,000 deaths (range 266,000-335,000) among HIV-positive people. It is estimated that 10 million people developed TB in 2017. 58% of them were men, and 10% of them were children. About two-thirds of the infected people were in eight countries: India (27%), China ((%), Indonesia (8%), the Philippines (6%), Pakistan (5%), Nigeria (4%), Bangladesh (4%) and South Africa (3%). Only 6% were in Europe and 3% in America. Meanwhile, drug-resistant TB continues to increase. About 558,000 people developed TB resistant to rifampicin (RR-TB) and 82% of this had multidrug-resistant TB (MDR-TB). WHO has reported that the disease burden caused by TB is falling globally. Worldwide, the TB incidence rate is falling about 2% per year, but it is not fast enough to reach the first milestones of the End TB Strategy. This target cannot be met without research and development.

The Asian Pacific Society of Respirology (APSR) was established in 1986 with the objectives of advancement and promotion of knowledge of the respiratory system in health and disease. It strives to encourage research, improve clinical practice through teaching, increase awareness of health problems in the area, and promote the exchange of knowledge among respirologists in the Asia-Pacific region. The specific aims of the Society are:

- Promoting and coordinating activities in the field of respiratory medicine

- Fostering research activities in the field of respiratory medicine

- Organizing and coordinating regular congresses and occasional meetings

- Producing regular publications, including a Newsletter, the APSR Respiratory Updates and Respirology, a journal of international repute.

The 24th Congress of Asian-Pacific Society of Respirology (APSR 2019) was held by the Vietnamese Society of Respirology (VNRS) from 14 – 17 November 2019 in Hanoi Capital, Vietnam. It attracted more than 2,100 delegates, 82 keynote speakers, along with 300 oral and more than 500 poster presentations covering all aspects of respiratory medicine. This year dr. Ika Fajarwati and dr. Diah Handayani, two representatives of INA-RESPOND from site 590 (*Persahabatan Hospital*), had the opportunity to attend APSR 2019 Congress.

The first day of congress started with a pre-congress workshop. Pulmonology experts from United States, France, Australia, and Korea delivered new updates on pulmonary function and testing; oxygen therapy and mechanical ventilation; imaging studies for respiratory disease and asthma diagnosis, treatment, monitoring, and practical skill. The opening ceremony was held on 14 November 2019.

In an oral session about tuberculosis, a scientist from Vietnam presented the prevalence of latent tuberculosis among household contacts of patients with MDR-TB in Vietnam. The prevalence of latent tuberculosis infection (LTBI) among household contacts of patients with MDR TB was high (1.9%). From Indonesia, a study about the treatment success rate of MDR-TB in HIV patients still remains low (25,4%) and it is related to employment and marital status.

The presenter from Japan came up with a case report about high-dose steroid re-addition to anti-tuberculous therapy in a patient with refractory tuberculous meningitis. A 54-year-old man in an unconscious state was admitted to the hospital due to TBM associated with miliary tuberculosis. Several tuberculomas were found on brain MRI. Four anti-tuberculous drugs combined with dexamethasone at 0.4 mg/kg/day were started, and dexamethasone was tapered weekly in accordance with the guideline. He regained consciousness, and acid-fast bacilli disappeared from the cerebrospinal fluid within two weeks. However, cerebral tuberculomas continued to progress, which caused cerebral infarction five months after admission. Therefore, the initial high-dose dexamethasone was again added to

INA-RESPOND Newsletter

TO THE UNKNOWN: DISCOVERING NEW PATHOGENS IN THE LAB

By: Aaron Neal, D.Phil

The start of a new year is an exciting time full of possibilities. It is a time to look back at the accomplishments and challenges of the past year while looking forward to new opportunities for personal and professional growth and success in the coming months. For many of us in the U.S., this time provides a fresh start at work following time away from the office to enjoy family and holiday celebrations.

While the first few days of a new year are generally calm, 2020 started with alarm in Wuhan, Hubei Province, China. An unexplained cluster of atypical, severe pneumonia cases immediately raised concerns of a potential pandemic, possibly driven by a feared pathogen like H1N1, SARS, or MERS. Epidemiological methods connected all of the known cases to a local seafood market that also sold animals and animal organs, but surprisingly, pneumonia did not seem to spread from person-to-person. Standard laboratory tests ruled out most known respiratory pathogens, including influenza and known coronaviruses, so public health response teams were left with an increasingly common question: Could this disease be caused by a new human pathogen?

Chinese scientists now suspect that the Wuhan outbreak was caused by a novel betacoronavirus, the same coronavirus family that includes the zoonoses SARS and MERS. But how did they arrive at this conclusion? Discovering a new pathogenic virus, bacteria, or parasite, is an exciting prospect, but when is searching appropriate, and how exactly can we do this? Thanks to significant advancements in genome sequencing technology over the past few years, the answers to these questions can be found in the laboratory.

Before beginning the search for a new pathogen, it is important to consider all of the circumstances surrounding an unexplained illness. As infectious disease specialists in INA-RESPOND and NIAID, we naturally want to jump to the conclusion that an illness is caused by a pathogen. This thinking can be unintentionally supported by genome sequencing technology due to the high sensitivity of the methods. Put simply, unbiased sequencing can be so sensitive that if we look for microbes in patient samples, we will usually find them without knowing if they are the cause of the illness or not. In Wuhan, the lack of human-to-human transmission and the negative lab tests suggested that the illnesses could be caused by environmental exposure, such as chemical poisoning, and not an infectious new virus or bacteria. However, after

evaluating the patient characteristics and available evidence, including the known pattern of viruses spilling over from animal reservoirs to humans at traditional markets, Chinese authorities moved forward with the suspicion that the pneumonia cases were indeed caused by a pathogen.

What happened at this point in Wuhan remains somewhat unclear since all of the data is not yet available to the international community. What is clear, though are the general steps that must have been followed to connect the pneumonia cases to a new betacoronavirus through unbiased sequencing. We all know that in a typical outbreak, where there is a high clinical suspicion of the disease, routine laboratory tests such as blood culture, microscopy, PCR, and ELISA are sufficient enough to identify pathogens. In these situations where the pathogen target is known or highly suspected, traditional

Aaron Neal, D.Phil.

International Health Scientist

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National Institutes of Health

U.S. Department of Health and Human Services

Sanger sequencing remains a simple yet powerful technique for obtaining highly accurate sequences and confirmatory evidence of infection. However, this "biased" approach of searching for a causal pathogen is unsuccessful when the target is unknown or substantially different from the clinically-suspected microbe. In Wuhan, all of the standard lab assays were negative, including for coronaviruses, but this only meant that the cause of the pneumonia was not yet known to science.

To overcome the search bias inherent in most laboratory techniques, next generation sequencing (NGS) has emerged as a successful alternative to traditional diagnostics [1]. Deep sequencing, massively parallel sequencing, and high-throughput sequencing are all similar terms for the same technology of amplifying all nucleic acid in a given sample, regardless of source, quantity, or complexity. This means that pathogen nucleic acid, as well as host nucleic acid, commensal flora nucleic acid, and any contaminating nucleic acid, will be amplified in an "unbiased" manner. This has the advantage of detecting any unknown pathogens present, or signal, but the disadvantage of detecting many unwanted sequences, or noise. The concept of next generation sequencing is quite simple in theory, but how is it practically used in a situation like the Wuhan outbreak?

Assuming that an outbreak is caused by a new pathogen, like in Wuhan, and assuming that the correct patient sample type has been collected, such as throat swabs for a respiratory disease, the first step is to extract nucleic acid for testing. Most outbreak pathogens are viruses, so extracting RNA generally leads to greater success than DNA, but either or both nucleic acids can be used for NGS. Since nucleic acid extraction methods extract all RNA and/or DNA from a sample, it becomes important to carefully select samples with low host noise RNA/DNA and/or enrich extracts for pathogen signal RNA/DNA. Samples like tissue biopsies will contain significantly more host nucleic acid compared to blood or CSF, so selecting this type of sample may generate so much noise in the results that the signal is lost. Alternatively, methods like VirCapSeq/BacCapSeq [2] and spiked primer enrichment [3] selectively enrich extracts for pathogen nucleic acid by either binding signal RNA/DNA and washing away noise RNA/DNA or by specifically amplifying signal RNA/DNA over noise RNA/DNA so that more signal RNA/DNA is sequenced.

Once enriched nucleic acid extracts have been obtained, they are processed and sequenced on one of three types of NGS machines: Illumina, Ion Torrent, or Nanopore. Illumina machines, which rely on detecting fluorescent signals incorporated into DNA during sequencing, are the most widely-used instruments in the NGS field. Ion Torrent machines, which rely on detecting ions released when a base is incorporated into DNA during sequencing, are slightly cheaper but more error-prone than Illumina instruments. Nanopore devices, which directly detect DNA bases as they pass through charged pores in a chip, are the newest and most promising class of NGS instruments. Though all three technologies generate useful sequence data, Illumina and Ion Torrent machines produce short (<300 bp) sequence fragments that must be over-

laid to form long sequence "contigs," while Nanopore devices are capable of sequencing fragments that are thousands of base pairs long.

Scientists in Wuhan likely used Illumina instruments to obtain their sequence data, but no matter what technique and instrument were used, the final step in the NGS pipeline is bioinformatics. A typical sequencing run can produce over 100 million sequences, most of which are noise, so it is critical to identify which sequences, if any, belong to a potentially causal pathogen. To do this, bioinformatics analysis programs systematically compare sequencing results to the known sequences available through the NCBI database at the NIH. By comparing results to the human genome, host noise sequences can be easily removed, leaving potential pathogen sequences behind. These sequences can then be systematically compared to known pathogens or pathogen families to identify any known or new pathogens present in the sample.

Since Chinese scientists identified a novel betacoronavirus in Wuhan, their sequencing results must have contained sequences that partially-matched the family Coronaviridae, the genus Betacoronavirus, SARS, and/or MERS when compared with the NCBI database. Additionally, phylogenetic analyses and other computational methods most likely provided greater insight into the origins and similarities of the new betacoronavirus to its known pathogenic neighbors. Depending on the sample processing techniques used, officials could also relate the number of new betacoronovirus sequences in the samples to how heavily infected the patients are since a high viremia will result in more RNA and more sequences in the results. Though we do not know how long it took to go from sample to final result in Wuhan, many NGS workflows are capable of generating results in 24-48 hours from sample collection.

The rapid and successful identification of a novel betacoronavirus is a scientific feat that should be celebrated, but like most laboratory tests, the results from NGS should be considered carefully and confirmed by additional testing. In Wuhan, this means obtaining more samples from all known infected individuals and screening them for the new pathogen by PCR and Sanger sequencing. It will also be important to isolate and culture the virus from samples positive for the betacoronavirus so that in vitro, in vivo, and antibody screening/production experiments can be completed. After their unexpected and painful experience with SARS, Chinese officials were thankfully prepared to mobilize quickly and efficiently to address the similar Wuhan outbreak. We can be sure that outbreaks caused by new pathogens will continue to occur in the future, so it is critical that we understand and add new diagnostic technologies like NGS to our toolkit for fighting infectious diseases.

Reference

[1]   https://www.nature.com/subjects/next-generation-sequencing

[2] https://mbio.asm.org/content/6/5/e01491-15

[3] https://www.nature.com/articles/s41564-019-0637-9

the multiple anti-tuberculous drugs. As a result, extended cerebral tuberculoma lesions have since reduced. High-dose steroid re-addition to multiple anti-tuberculous drugs should be considered as a treatment option for progressive TBM.

A researcher from Malaysia presented clinical characteristics and treatment outcomes of multidrug-resistant tuberculosis in a tertiary center in Malaysia. Of the 63 MDR-TB patients, 33% of them were foreigners, and the highest were Indonesians. About 49.2% of MDR TB patients completed the treatment, but unfortunately, 41.3% of them had poor outcomes. Male gender and smokers were associated with poor treatment outcomes.

On the third day, TRIPOD national principal investigator, dr. Erlina Burhan, delivered a presentation about tuberculosis contact investigation in high tuberculosis burden settings. There was a study located in Padang, West Sumatera about contact investigation in children whose parents were diagnosed with tuberculosis. It was concluded that the high number of LTBI in children was caused because treatment of LTBI did not become a priority. Not only children, health workers in hospital settings who face tuberculosis patients every day have high-risk exposure to LTBI. Comprehensive and periodically screening are required to protect them from becoming an active TB patient.

A speaker from Australia presented about the diagnosis of non-tuberculosis mycobacterium (NTM). It is vital to diagnose NTM correctly. This is done because the clinical manifestation of NTM is almost similar to tuberculosis. The next speaker from India talked about an update of NTM treatment. Not only were macrolids used to treat this disease, but the inhalation of Amikasin was also added into the treatment.

From assembly meeting, dr. Erlina Burhan as chair and dr. Diah Handayani as a mentor gained a lot of case reports from many countries. This meeting purpose was to give an opportunity for

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RELATIONSHIP OF EXERCISE AND UPPER RESPIRATORY TRACT INFECTION

By: Septi Mandala Putra

LIFESTYLE & SPORT

Introduction

Influenza is one of the common etiologies for the upper respiratory tract infection (URTI). However, the influenza virus only contributes about 20 percent of influenza-like illness patients. Adam K[1] et al. found from the 334 samples, 266 samples (78%) were positive at least one virus, and influenza virus was the most detected virus. Socioeconomic expense in the United States costing about five billion dollars annually, because of truancy from work and school, doctor's expense and over the counter medications[2].

Respiratory viral infections represent the most prevalent and pathogenic form of infectious disease. Infection occurs when a host comes in contact with infected aerosolized droplets or contaminated surfaces. The virus then invades and infects the host's upper or lower respiratory mucosal tissues. Illness duration typically lasts for 7–14 days, and the usual symptoms include cough, nasal congestion, fever, body aches, malaise, and in severe cases, death.

Cross-sectional and longitudinal data suggest persons who engage in regular moderate intensity exercise maintain a reduced risk of self-reported respiratory symptoms[3]. Moderate exercise intensity may decrease the risk of URTI, but too little or too much may increase the risk. Research has shown that exercise in moderately fit and active people with a URTI does not prolong or intensify the illness. This finding is important for fitness enthusiasts who are interested in enjoying exercise and maintaining their fitness levels during a URTI.

### Exercise and viral infection in humans

A recent study found a low-to-moderate frequency of exercise reduced the risk of influenza-associated mortality in adults, while a high frequency of exercise (>4d/week) failed to reduce the risk of essential when compared to the sedentary referent group[4]. Matthews et al. found a 29% decrease in an incidence rate of URTI symptoms in adult men and women who engaged in moderate-to-vigorous physical activity of at least 11.96 MET·h·d−1 when compared with those individuals who were less physically-active[5]. These studies support the hypothesis that moderate exercise is protective against URTI symptoms and that there may be a differential dose-response effect such that in-

tense, prolonged exercise or overtraining increases disease risk or symptom severity.

A pair of studies from the laboratory of David Nieman examined the incidence of URTI in athletes who participated in a variety of running races. A comparison of runners competing in a 5 km, 10 km, or 21.1 km race found athletes who ran over 21 km per week had reduced incidence of respiratory symptoms when compared with athletes training at a lesser volume, and that runners training for the 21.1 km race had fewer infections than their shorter-distance counterparts in the two months before the race. A second study examined more than 2000 athletes competing in the Los Angeles Marathon[6]. Runners who trained >97 km per week had twice the risk of the development of URTI symptoms when compared to the referent group which trained <32 km per week. Furthermore, runners who completed the marathon increased their risk for URTI nearly 6-fold during the week following the race when compared with similarly-trained controls that registered, but did not participate in the marathon.

Nieman et al.[7] also examined the effect of 15 weeks of moderate-intensity exercise training on symptoms of URTI. Exercising subjects demonstrated shorter infectious episodes compared to their sedentary controls as measured by the number of symptom-days per infectious episode.
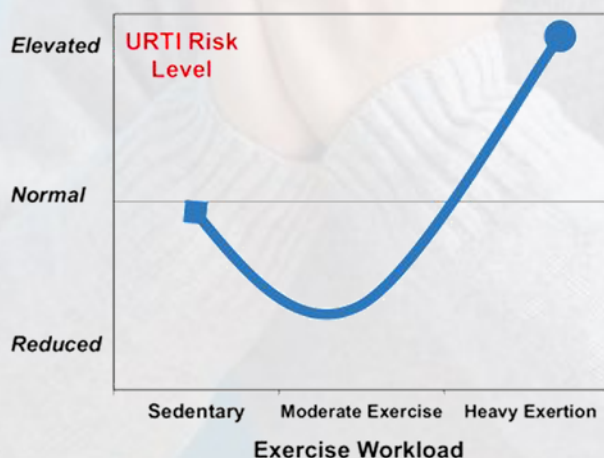
Picture downloaded from :

https://journals.humankinetics.com/view/journals/ijsnem/29/2/article-p181.xml\

Relationship between salivary IgA and URTI

Concentrations of salivary IgA (s-IgA) have been examined as a means of explaining the incidence rates of URTI in athletes because s-IgA binds to and opsonizes foreign organisms including respiratory viruses. Salivary IgA is considered the first line of defense in subjects that have been previously exposed to specific pathogens. It appears that long dura-

tion and high-intensity exercise, in both an acute and chronic fashion, decreases salivary IgA and is associated with increased respiratory symptoms[8].

Nieman et al.[9] examined 155 ultramarathoners who had qualified to run the 160-km and found that nearly 1 – 4 runners reported URTI episode during the two weeks following a 160 km race, and the decrease in salivary IgA secretion rate was significantly greater.

In contrast, limited research suggests both acute and chronic moderate-intensity exercise increases s-IgA levels providing protection against respiratory symptoms. Klentrou et al.[10] found 12 weeks of moderate exercise training reduced self-reported infections and decreased URTI symptoms, which were correlated with increased s-IgA.

Conclusion

This article support that moderate-intensity exercise reduces inflammation and improves the immune response to respiratory viral infections.

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INA-RESPOND Newsletter

PUT REWARDS IN PLACE FOR A NEW HABIT TO BEGIN

By: Aly Diana

It's New Year again, and for most people, it is time to think about New Year's resolutions. And most of the time, the resolution involves changing our lousy habits. We believe that we know what habit is and the best way to change it, but let's peek on the 'scientific' perspective of it (just in brief, of course).

To my surprise, there are a lot of definitions for habit, from a simple one to a very complicated one. Some behavioral scientists define a habit as a learned sequence of acts that have become automatic, unconscious responses to specific cues or triggers around us. Others explain habits as behaviors that are performed repeatedly and with little preceding forethought, which might be understood as impulses toward behaviors that are generated automatically in response to an environmental cue from a context in which that behavior has previously been executed repeatedly.

In general, three primary 'ingredients' have been proposed to be associated with habit formation: contextual stability (cue/trigger), behavioral frequency (repetition/routine), and rewards. The brief explanations as follow:

Cue/trigger: Habits are always triggered by a cue, typically in a context that is stable and consistent in our lives. The cue triggers our memory of doing the same action or routine previously and helps to initiate it again. When such an environment is stable and consistent – when we are in the same place at the same time of day - we are more likely to carry out a particular behavior, deeply embedding a habit.

Repetition: For a behavior to become a true habit, it needs to be performed frequently and repeated many times over. Exact figures for how long it takes to build a habit vary, depending on the complexity of the behavior. Rewards: We can be motivated to repeat behaviour if we believe we will reap some reward. It is this element that can fix a behaviour in place, so it becomes a habit – to the extent that we might not even need the reward once the behavior has become automatic.

Charles Duhigg then introduced a simple model of habits called "The Habit Loop Model", consists of trigger, routine, and reward; and suggested ways to break an old and build a new habit. By recognizing the elements of the habit loop, we can break an old habit by removing the trigger or replacing positive reward with negative association. However, instead of removing a bad routine, it is suggested that the best way to break a bad habit is by replacing it with a new good routine in an existing habit loop. We can use the same cue to start a new habit and then assign an appropriate positive reward associate with it.

The role of reward as a reinforcer of cue-response associations has been extensively studied within the behaviorist literature.

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Where performance is highly rewarded, the likelihood that behavior would be repeated was high, and, traditionally, habits were thought to develop only when rewards were received for each repetition of the behavior. One thing with rewards, sometimes it is hiding in a plain side, and we don't really know. For example, when we eat a cake in a cafeteria, the rewards can be the cake itself or a change in scenery, a temporary distraction, an opportunity to socialize with friends, sugar blast, or else. We need to learn what it is that we are really craving for. In case we only need a distraction as a reward, we can change cake with something less 'dangerous'.

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YEAR OF THE RAT

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Happy Chinese New Year

INA-RESPOND Newsletter

The Indonesia Research Partnership on Infectious Disease newsletter is an internal bulletin of INA-RESPOND research network intended to disseminate information related to the network's studies, activities, and interests to all members of the network as well as its sponsors and related parties.

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