INA-RESPOND

INDONESIA RESEARCH PARTNERSHIP ON INFECTIOUS DISEASE

KEMENTERIAN KESEHATAN REPUBLIK INDONESIA

NEWSLETTER

October 2018

The Sitting Disease:
The Risk of I'll-Do-It-Tomorrow Attitude

The 4th Annual RePORT International Meeting in Suzhou

Pre-Print: Good News for Authors?

Clostridium Difficile : A Short Review

NATIONAL INSTITUTE OF HEALTH RESEARCH AND DEVELOPMENT
MINISTRY OF HEALTH REPUBLIC OF INDONESIA
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INA-RESPOND TRIPOD Study Team
@The Hermitage Hotel
Jakarta

INA-RESPOND newsletter

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FEATURES

INA-RESPOND Newsletter

TRIPOD & INA-PROACTIVE Study Updates

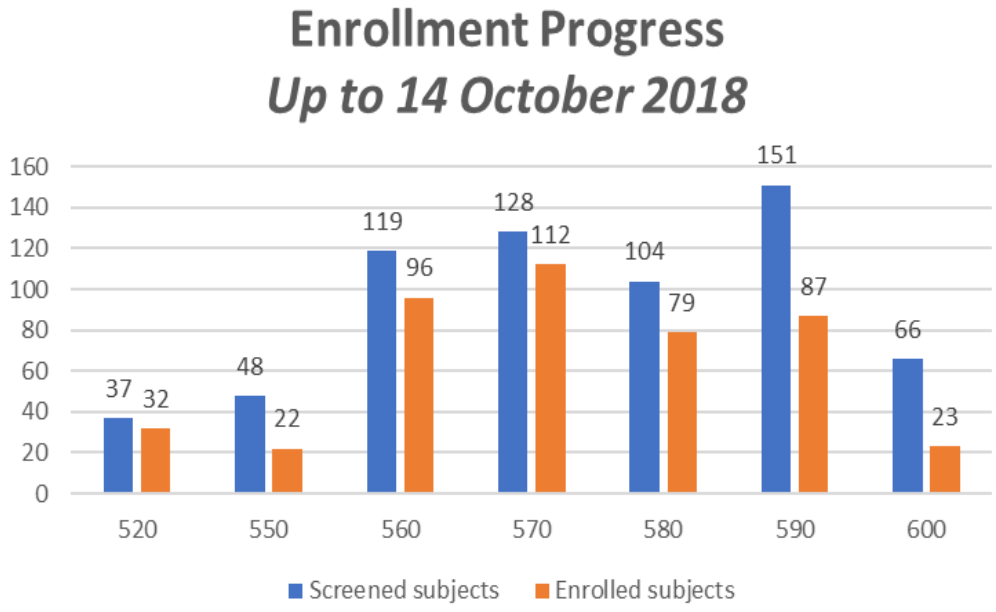
By: ANANDIKA PAWITRI, EKA WINDARI R., LOIS E. BANG, MARIA INTAN JOSI, M. IKHSAN JUFRI, VENTY MULIANA SARI

STUDY UPDATES

INA102

Screening and Enrolment

Up to 14 October 2018, sites had enrolled a total of 451 subjects. The sites enrolled 69% of the screened patients (451 enrolled subjects from 653 screened patients).



Interim Analysis Meeting

On 17 – 18 October 2018, TRIPOD study team gathered in Jakarta for an interim analysis meeting. Representatives from each site and protocol core team discussed some points, such as enrolment progress, diversity of TB subject's categories, chest X-ray interpretations, manuscript ideas, etc. As the highlight of this meeting, the protocol specialist and statistical consultant presented preliminary results of TRIPOD study. It was shown that, based on study data per September 2018, the study had successfully answered the primary objective and several secondary objectives. These results will influence the continuation of subject recruitment, which after a thorough discussion, protocol core team and all site team decide to permanently halt the participants enrolment per 1 December 2018. Necessarily follow up will be performed as usual.

Manuscript Writing of TRIPOD Study Result

Since the primary objective has been answered by current TRIPOD study data, the team can now focus on preparing the publication manuscript. The main manuscript will certainly talk about the primary result of TRIPOD study from all sites. Moreover, in the previous interim analysis meeting, each site team gave their ideas on what topics will be written, apart from the main article. They have developed a manuscript outline for their each proposed idea. Some ideas were also raised by reference lab team, specifically for further investigation of TRIPOD study specimens. Afterwards, the protocol core team will summarize and analyse the ideas, and afterwards, the study teams will be divided into groups based on the feasible manuscript ideas.

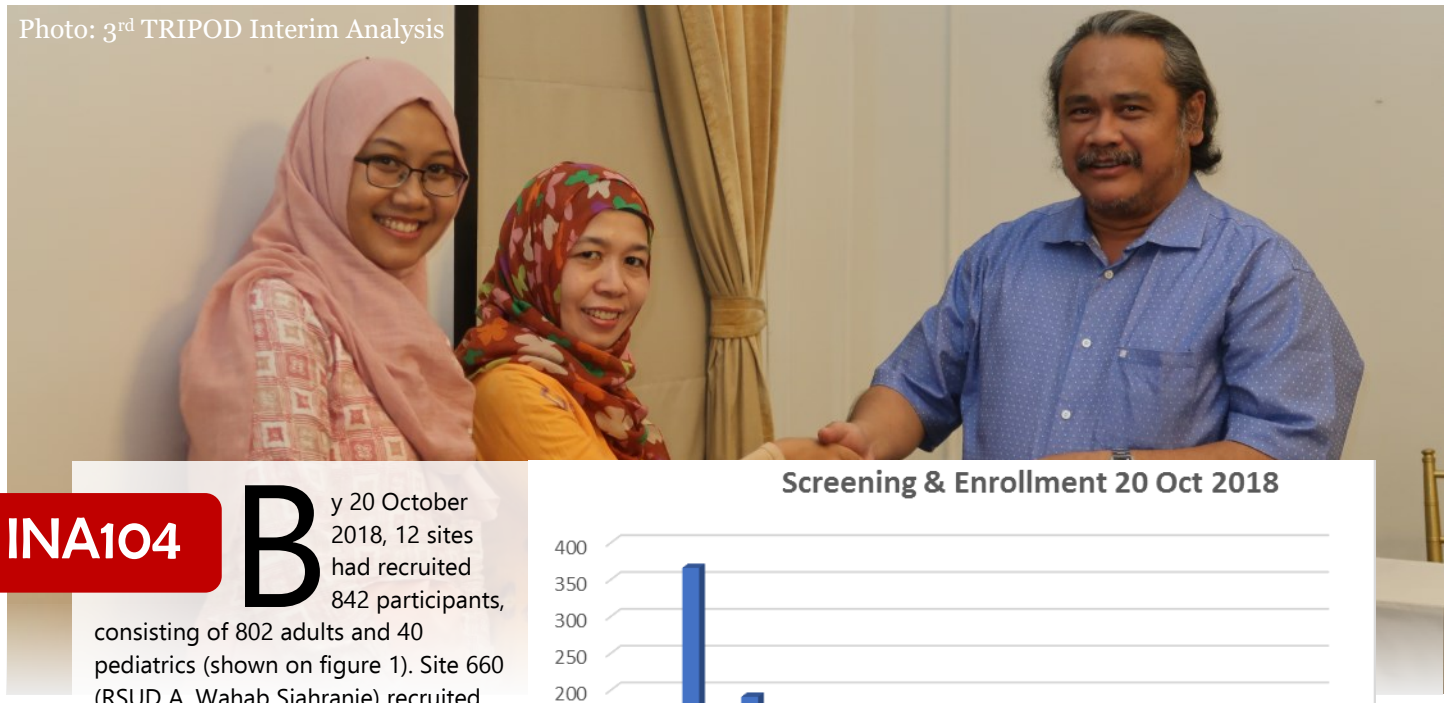


Photo: 3rd TRIPOD Interim Analysis

INA104

By 20 October 2018, 12 sites had recruited 842 participants, consisting of 802 adults and 40 pediatrics (shown on figure 1). Site 660 (RSUD A. Wahab Sjahranie) recruited its first participant on 3 Oct 2018. Enrolment failure rate was 34,9% from total screenings due to the reasons mentioned in table 1.

2nd Site Monitoring Visit (SMV) to site 550/ RS Dr. Wahidin Makassar was conducted on 24-27 Sep 2018, and 1st SMV to site 580/ RSUP Dr. Sardjito Yogyakarta was done on 22-23 Oct 2018. We are planning to do the 3rd SMV to site 610/ RSU Kabupaten Tangerang on 29 -31 Oct 2018.

Currently, we are also preparing for the Site Preparation Visit to site 520/ RSUP Sanglah, Denpasar and Site 540/ RSPI Sulianti Saroso, Jakarta. Hopefully, we can conduct the Site Preparation Visit to both sites by November 2018. In addition, we are working on the site assessment of RSUD Jayapura, RSUD Merauke, and RSUD Zainoel Abidin.

Reason	610	600	550	530	570	630	590	650	640	560	580	660	Total
HIV negative	-	-	1	-	-	1	-	-	-	-	-		2
Refuse to consent	2	-	2	2	4	-	2	-	-	-	-		12
Unwilling to comply with the study procedures	1	16	-	3	3	-	-	-	-	7	3		33
Plans to move away	-	7	4	6	-	1	2	-	2	2	-		24
Others:	18	207	45	20	8	37	10	2	7	1	15	4	374
A. No show	6	205	11	12	4	23	10	-	2	1	2	2	278
B. Busy (in a hurry)	12	2	20	7	4	3	-	2	5	-	10	2	67
C. Not cooperative	-	-	1	-	-	-	-	-	-	-	-		1
D. Has been enrolled	-	-	10	-	-	5	-	-	-	-	-		15
E. Unwell	-	-	1	-	-	-	-	-	-	-	-		1
F. No referral letter from others health facilities	-	-	-	1	-	-	-	-	-	-	-		1
G. Equipment trouble	-	-	-	-	-	6	-	-	-	-	-		6
H. Participated in other CT											3		3
I. Hospitalized	-	-	2	-	-	-	-	-	-	-	-		2

Table 1. Enrollment Failure Reasons

INA-RESPOND Newsletter

Site Profile: RSUD Dr. H. Moch. Ansari Saleh, Banjarmasin

By: ARINI MULIANA

From left to right : dr. Maimunah (Treasury), Hj.Lutfia Rahimah,SKM (LT), Irma Meilyana FU,S.Kep,Ns (Nurse), dr. Astri Pratiwi (RA), dr. Dwiana Savitri, SpKK (CoPI), dr. Priyanti Kisworini,Sp.A (CoPI), Dr. dr. Anna MA, Sp.PK, MPH-MMR (NSC), Ieda S.Hayati,SKM, M.Kes (Kabid Diklitbang), dr. Hj. Wiwit Agung Sri NC, Sp.PD, K-Ger (PI), dr. Rahmawati,Sp.PK (CoPI), Silvia Rahmi A,A.MD,AK (LT), Setiawati,AMK (Nurse), dr. Arini Muliana (RA)

SITE PROFILE

We are from Dr. H. Moch Ansari Saleh Hospital in Banjarmasin, South Kalimantan (site 630). Dr. H. Moch Ansari Saleh Hospital is the first referral hospital in Banjarmasin. Working with INA-RESPOND in this HIV research (INA-PROACTIVE / INA104) is our first experience working in a network. Site 630 is the 6th site activated by INA-RESPOND. The activation of our site started on 10 July 2018, followed by subject enrolment on 17 July 2018. The term "superwomen" is probably perfect to describe our team because all members of our team are women. Here is a brief introduction of our members.

Dr. dr. Anna Martiana Afida, Sp.PK, MPH-MMR.

She is the head of "*Pelayanan Medik*" in Dr. H. Moch Ansari Saleh Hospital, Banjarmasin. Her presence in every meeting is always worth the wait because she is funny. She likes travelling, and food is what turns her on; she is a big foodie. Even though she has already had so many titles, she keeps learning and studying. Fun fact: she has finished her study in the law field!

dr. Hj. Wiwit Agung SNC, Sp.PD, K-Ger.

She is a specialist consultant for the Geriatric department. Her hobby is drinking coffee; No single day goes by without her sipping a cup of coffee. She is energetic and high-spirited. Even though she is very busy, her dedication for this research is honourable. She always spares time to have a discussion with the team (especially with the RAs) about the development of this research. Her motherly attitude and kindness make everyone feels comfortable during a consultation with her.

dr. Dwiana Savitri, Sp.KK FINSDV

This beautiful doctor is a consultant and counsellor in VCT Polyclinic. She is the founder and is responsible for the VCT Polyclinic. In addition, she is also a responsible person for *Poliklinik Kulit & Kelamin*.

dr. Priyanti Kisworini,Sp.A, M.Kes.

Composed and coolheaded are probably the best traits attributed to this romantic and creative woman. She loves reading and writing poems.

dr. Rahmawati, Sp.PK.

She is the Head of Laboratory Installation. She loves eating, watching movies, and sightseeing. Watching movies or shows, like *Upin & Ipin*, with her children makes her really happy.

dr. Astri Pratiwi.

Not only does she work in VCT Polyclinic, but she also works in *Poliklinik Kulit & Kelamin* everyday, which makes her very busy. Moreover, she works as a Research Assistant in INA104. Kind-hearted, compassionate, and humble are the perfect words to describe her.

Clock-wise: enrollment process; INA-RESPOND room at site; Laboratory work; Taking participant's specimen at laboratory

dr. Arini Muliana

She is the youngest and smallest person among the team members. Her hobbies are eating and sightseeing. She finished her internship program at the hospital in February 2018. Being a part of this team as a RA is her first official professional experience.

Hj. Lutfia Rahimah, SKM

She is one of the seniors in Clinical Pathology Laboratory. In addition to being patient and deft at work, she is also very skilful in the kitchen. Her hobby is cooking!

Silvia Rahmi Astuti, A.MD.AK

She is a very careful and fun person. Did you know she has neat and beautiful hand writing? Her hobby is shopping and sightseeing at the malls.

Setiawati, AMK

She is the only nurse in VCT Polyclinic. It is not an exaggeration when I say HIV patients at our hospital know her. Her hobbies are shopping and travelling.

SITE 630 TEAM MEMBERS:

NSC at site

Dr. dr. Anna Martiana Afida, Sp.PK, MPH-MMR

PI

dr. Hj. Wiwit Agung SNC, Sp.PD, K-Ger

Co-PI

dr. Dwiana Savitri, Sp.KK FINSDV

dr. Priyanti Kisworini,Sp.A, M.Kes

dr. Rahmawati, Sp.PK

Research Assistants

dr. Astri Pratiwi

dr. Arini Muliana

Lab Technicians

Hj. Lutfia Rahimah, SKM

Silvia Rahmi Astuti, A.MD.AK

Nurses

Setiawati, AMK

Irma Meilyana Fajar Utami, S.Kep.Ns

INA-RESPOND Newsletter

A Story from "The Venice of China"; The 4th Annual RePORT International Meeting

By: RETNA INDAH, KANTI LARAS, GUSTIANI SALIM, ADHELLA NAYSILLA, HERMAN KOSASIH

Millions of people continue to fall sick with tuberculosis (TB) each year, until now. Although The number of new cases has been falling by 2% per year since 2013, countries are not doing enough to end TB by 2030. In 2017, approximately 10 million people developed TB, and 558,000 of them were diagnosed with drug-resistant TB. Two-thirds of the affected people were in eight countries: India (27%), China (9%), Indonesia (8%), the Philippines (6%), Pakistan (5%), Nigeria (4%), Bangladesh (4%), and South Africa (3%). Efforts to halt the spread of TB domestically and globally are critical to reducing TB-related morbidity and mortality. To address the global health emergency that TB represents, the World Health Organization (WHO) End TB Strategy sets ambitious goals for 2035 to reduce TB deaths by 95 percent and to reduce TB disease incidence by 90 percent (relative to 2015 levels).

In support of this goal, research must extend from basic research to identify biomarkers that accurately predict outcomes of active and latent TB to clinical research to measure efficacy and effectiveness of new tools and strategies for TB. The Regional Prospective Observational Research in Tuberculosis (RePORT) consortia developed a common protocol for data and specimen collection to be implemented by any TB studies. Each RePORT network is designed to support local, in-country TB-specific data and specimen biorepositories and associated research. Since its beginning in 2012, this collaboration has involved 6 countries with high burden TB: Brazil, India, South Africa, Indonesia, China, and the Philippines. This year INA-RESPOND as the RePORT Consortium in Indonesia sent 5 representatives (Herman Kosasih, Retna Indah, Kanti Laras, Gustiani Salim, and Adhella Naysilla) to attend the 4th annual RePORT international meet-

ing on 12–14 September 2018 in Suzhou, China. In this meeting, some of the country members presented the preliminary results of their studies. Some country members had also done more advance research using the collected specimens.

The meeting began with welcome speech and opening remarks from Director of Innovation Alliance on Tuberculosis Diagnosis and Treatment (IATB), Suzhou Health Commission, and representative from National Institute of Allergy and Infectious Diseases, NIH. The meeting continued with the presentations from China consortium, consisting of members who were responsible for basic research, translational platform, clinical hospitals, and disease control. They presented the huge workload of diagnosing TB using many methods. The speaker from Institute of Biophysics of Chinese Academy of Science presented their work on Mycobacterium tuberculosis (MTB) vaccine research and talked about the challenges to find a new technique to obtain a global picture of MTB's 4000+ proteins that can provoke host humoral and cellular immune response. Another speaker from China Clinical Center on TB presented their study about profiling the N-Acetyltransferase 2 (NAT2) gene in China TB patients. Polymorphisms in this gene are responsible for the N-acetylation differences in human populations which are segregated into rapid, intermediate, and slow acetylator phenotypes. Patients who belong to the slow acetylator group are known to be at risk from most drug-induced toxicity, whereas those in rapid acetylator group may experience treatment failure. This step is important in the term of personalized medicine of TB disease specially to prevent Isoniazid (INH)-induced hepatitis. Another attractive presentation was the use of smart application for TB patient management system that can be accessed by both clinician and patient of TB. The feature of drug and visit schedule reminder in this application increases patients' compliance and reduces lost-to-follow-up numbers.

India reported the results from the National Drug Resistance Survey in 2017. This survey revealed that approximately 20% of patients with any-resistance to anti-tuberculosis drugs were new cases. India's representative also talked about the health system delay in anti-TB initiation in DOTS setting. The overall treatment delay among 880 participants, in which 65% sought private health facilities as their first point of care, was on average 21 days.

People who are in close contact with TB patients (house hold contacts) were also targeted participants in REPORT consortia studies. Unfortunately, RePORT Indonesia has not been able to conduct this study protocol. One of the focuses in house hold contact research was the latent TB infection (LTBI), in particular several biomarkers that can be used to distinguish between latent and active TB, as presented by the Indian representative.

In this meeting, each consortium also shared their experiences in Material Transfer Agreement (MTA) procedures in each country. China and Indonesia have the same problem in transferring specimens across the country. Some countries such as India, Brazil, and south Africa had already gone through the specimen transfer procedure, and they have been working together to find some potential biomarkers including biomarkers in TB patients with diabetes, extrapulmonary TB, and HIV patients with TB. Regarding the biomarkers study, participants in the small group discussion agreed that REPORT consortia needs a standardized procedure for specimens' quality assurance and the laboratory methods used in the study. This Standard Operating Procedures (SOPs), as living documents, should be applied in all laboratories to minimize the lab-to-lab variations.

The discussion in data management session, led by FHI 360 Data Director for RePORT study - Lisa, was interesting and fruitful. Several interesting ideas came from the presentations of these following topics: RePORT International RICC Data Elements Bank Issues, Transferring RePORT Data to the RePORT International Coordinating Center (RICC), DMs Role in Risk-based Quality Management Efforts, and Basic Concepts and Application of De-Identification and Anonymization Techniques for Health Data. Lisa also demonstrated the Data Transfer process and the group discussed elements of the data transfer protocol. During the discussion on the basic concepts of data de-identification and data anonymization, there was a discussion on how these techniques possibly and should be applied to the pooled RePORT International data. Kanti Laras, as TRIPOD Lead Data Manager, represented Indonesia in this session.

Before the meeting was closed, young investigators from South Africa, China, India, and Indonesia had the opportunity to present their studies. These young investigators went through several selection and elimination process and were selected by RePORT international reviewers to receive a travel award to the 4th annual RePORT International meeting. This year, dr. Adhella Naysilla from INA-RESPOND Site 560 (Dr. Kariadi Hospital, Semarang) represented Indonesia with her abstract entitled "Factors related to BMI changes in intensive phase among DS TB patients in Indonesia". Hopefully, her experiences in the meeting will motivate other doctors to become more involved in research activities, especially in TB.

We give our sincerest appreciation to RePORT China consortium for the excellent organization of this meeting. See you in Manila next year!

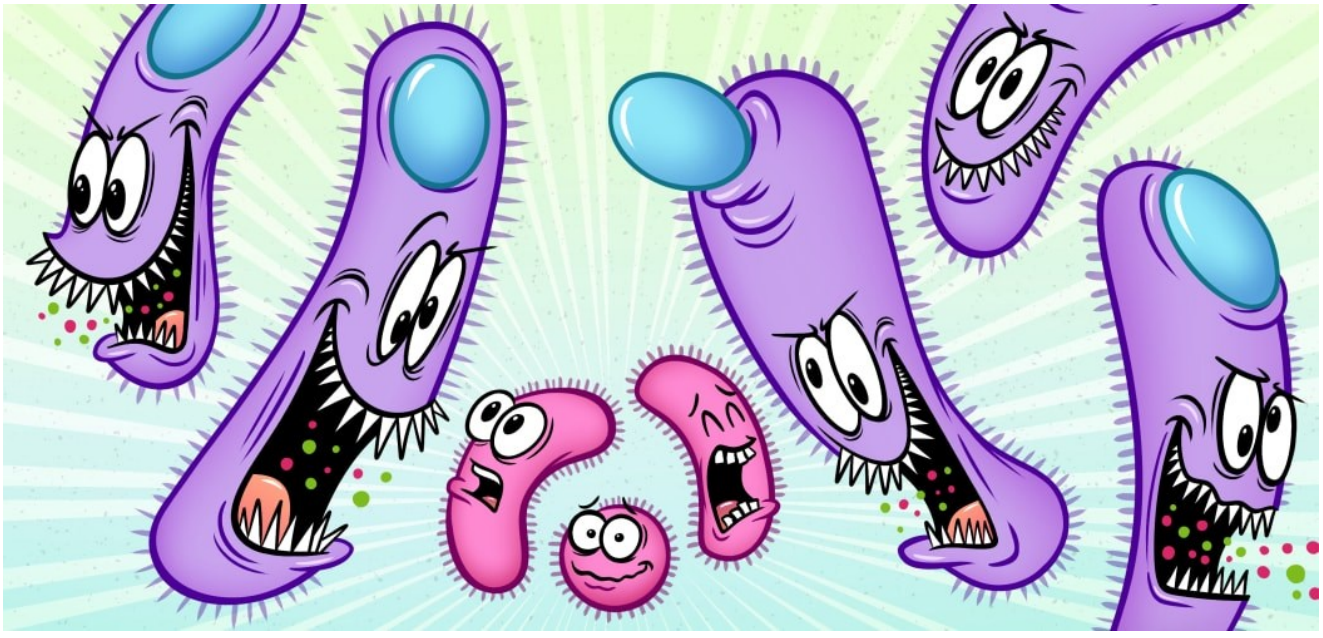
The 4th Annual Regional Prospective Observational Research in Tuberculosis (RePORT) International Meeting 2018

— Suzhou, China —

INA-RESPOND Newsletter

Clostridium Difficile – A Short Review

By: M.HELMI AZIZ



Have you ever taken antibiotics for your infection, but you ended up with diarrhea? Diarrhea is a common adverse effect of antibiotics administration and can occur in 5–30% patients who are taking antibiotics shortly after treatment or up to two months after the end of the treatment. Antibiotic-associated diarrhea results from disruption of normal microflora which enables an overgrowth of "bad" microorganism that induces diarrhea such as Clostridium difficile (C. difficile). This month's article will focus on C. difficile, the most well-known pathogen to cause antibiotic-associated diarrhea.

MICROBIOLOGY

C. difficile is a Gram-positive, anaerobic, spore-forming, toxin-producing bacillus that is transmitted via fecal-oral route [1-4]. C. difficile was first discovered in the stool of neonates in 1935 by Halland O'Toole, and it has been shown to colonize in 60–70% of infants [1]. In addition, some people carry the bacteria in their intestines as carriers and able to spread the infection to others [1]. Although C. difficile was considered as commensal bacteria, nowadays, C. difficile is considered as the most important healthcare-associated pathogen worldwide [1, 2].

C. difficile spores can be found anywhere and persist in aerobic environments [1]. The spores are resistant to gastric acid and commonly-used hand decontaminants (alcohol rub), making it easily transmitted via fecal-oral route [1]. After the disruption of gut microbiota (the colonization barrier) C. difficile spores germinate sufficiently on intestinal epithelial cells [1]. Furthermore, after the colonization on intestinal epithelial cells, C. difficile can produce two protein exotoxins: TcdA (toxin A - enterotoxin) and TcdB (toxin B - cytotoxin) [1, 3, 4]. Both toxins trig-

ger various intracellular signaling which leads to inflammation, cell death, clinical manifestation of C. difficile associated diarrhea, and mucosal inflammation [1, 3].

EPIDEMIOLOGY

C. difficile was first recognized as the antibiotic-associated diarrhea pathogen in late 1970 [3]. In the early 2000s there was an emergence of a hypervirulent strain called North American pulsed-field gel electrophoresis type 1 (NAP1) which has more production of toxins (A, B, and binary toxin), more adherence to intestinal epithelium, more antibiotic resistant, more spore production than the previous strain, and higher mortality rate than the previous strain [1-4].

Due to changes in the virulence and the usage of antibiotic, there has been a marked increase of C. difficile morbidity and mortality. In Europe, seven C. difficile infections occur for every 10,000-overnight hospital patient [3]. In addition, in the past decade, C. difficile infection has also been reported in the community outside the hospital setting which accounts for up to a third of new cases [2, 3].

DIAGNOSIS

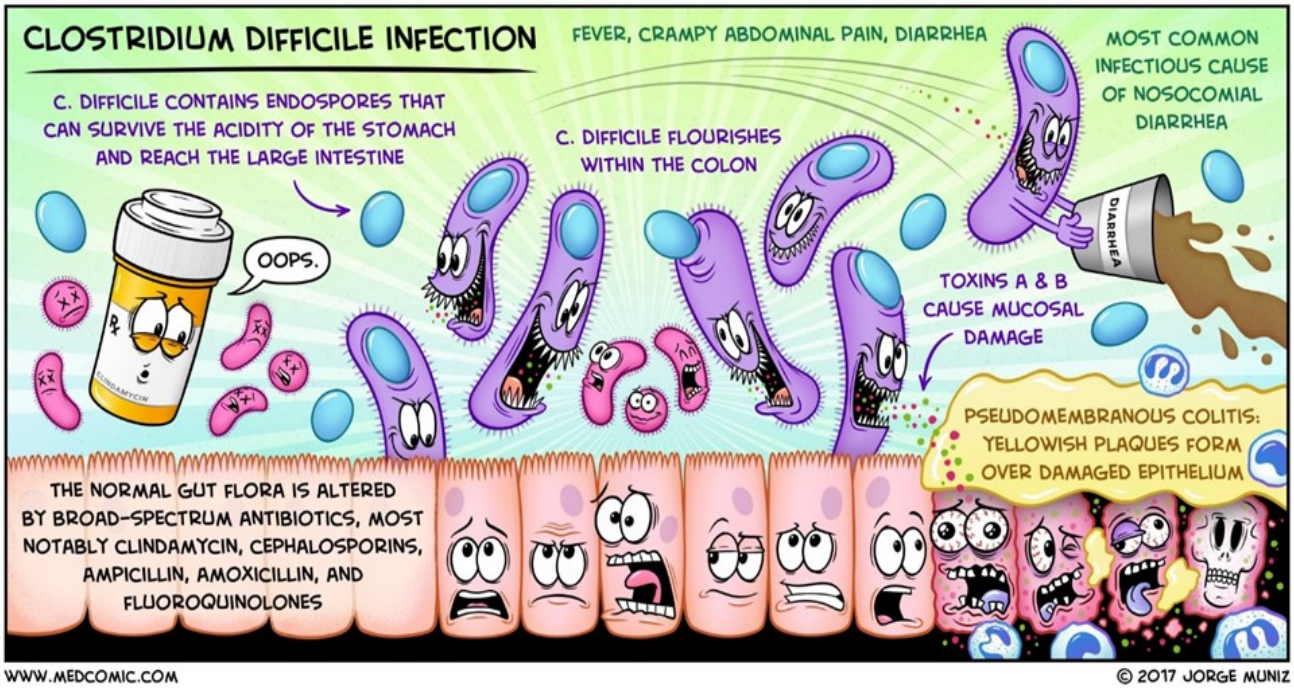
The clinical presentation of C. difficile infection ranges from asymptomatic, mild-moderate diarrhea, pseudomembranous colitis, fulminant colitis, and toxic megacolon [1, 4]. Diagnosis of C. difficile infection is based on the clinical presentation with confirmed microbiological evidence of the pathogenic strain of C. difficile in stools.

Due to the nature of C. difficile which has genetically-diverse species, including pathogenic (toxin-producing) and non-pathogenic strains, bacterial culture becomes less specific to differentiate both strains [1, 3]. In addition, C. difficile culture requires anaerobic culture which not widely available [2]. Therefore, C. difficile is currently diagnosed either by enzyme immunoassay (EIA) for toxin in stool or EIA for C. difficile glutamate dehydrogenase (GDH) or DNA-based tests targeting the microbial toxin genes in unformed stool [2, 4]. Radiographic findings can be used to detect abnormalities in the mucosa of the colon [1, 4]. Endoscopy is indicated to rule out other colonic diseases and to visualize the presence of pseudomembranous colitis [1, 4].

TREATMENT/MANAGEMENT

The first steps to treat C. difficile infection is to stop antibiotics that disrupt the gut normal flora [4]. In the meantime, supportive treatment such as fluids and electrolyte management should be carefully observed [4]. All healthcare providers and visitors should do hand hygiene with soap and water instead alcohol-based sanitizers to prevent C. difficile spore's transmission [4].

Since its recognition in 1970, metronidazole and vancomycin have been used for C. difficile infection [2]. For mild-to-moderate infection metronidazole (500 mg t.i.d. for 10−14 days p.o./i.v.) or vancomycin (125 mg q.i.d. for 10−14 days p.o.) have been considered to



have equivalent effect [2, 4]. However, in severe or complicated C. difficile infection vancomycin p.o. is better than metronidazole [2, 4].

A novel therapy, fidaxomicin (a poorly absorbed, bactericidal, macrocyclic antibiotic), was approved by the FDA for C. difficile infection [1, 2, 4]. Fidaxomicin (200 mg b.i.d. for 10 days p.o.) and vancomycin have similar cure rates, but fidaxomicin has a lower recurrence rate than vancomycin [1, 2, 4]. The use of anion-binding resins (to neutralize the toxin), human monoclonal antibodies (against toxin A and B), other antibiotics (Rifaximin and Nitazoxanide), and other emerging therapies (CRS3123 and Cadazolid) are promising for future therapy of C. difficile infection [4].

About 10–20% of C. difficile infections recur after the acute episode. However, when the patient already had one recurrence, the rate increases to 40–65% [2, 4]. The first recurrence may be treated using the previously mentioned antibiotics [2, 4]. The second and subsequent recurrences can be difficult to cure, but fidaxomicin or tapered-pulsed vancomycin regimen may be used to treat this case [2, 4]. Fecal microbiota transplantation and probiotics administration may be used to reestablish the normal composition of gut flora [1, 2, 4]. However, the data are too retrospective although both treatment have been considered safe and effective [1, 2, 4].

PREVENTION

Antibiotic stewardship by minimizing the routine use of ceftriaxone and ciprofloxacin could reduce the rate of C. difficile infection by 77% [1, 2]. Hand hygiene using soap and water than using alcohol-based hand sanitizers is proven to be more effective to reduce the number of viable C. difficile spores [1, 2]. Meanwhile, the use of probiotics to prevent C. difficile colonization has an uncertain effect and not recommended although it is safe and easily adoptable [2].

In the past decade, the number of C. difficile infection cases has increased. In Indonesia, the prevalence of C. difficile is relatively higher than the neighboring countries [5]. Moreover, inappropriate antibiotic usage in Indonesia could contribute more of C. difficile cases in the future. However, there is a lack of surveillance of this pathogen in Indonesia and worldwide. resulting in the lack of recognition of C. difficile as a major health problem.

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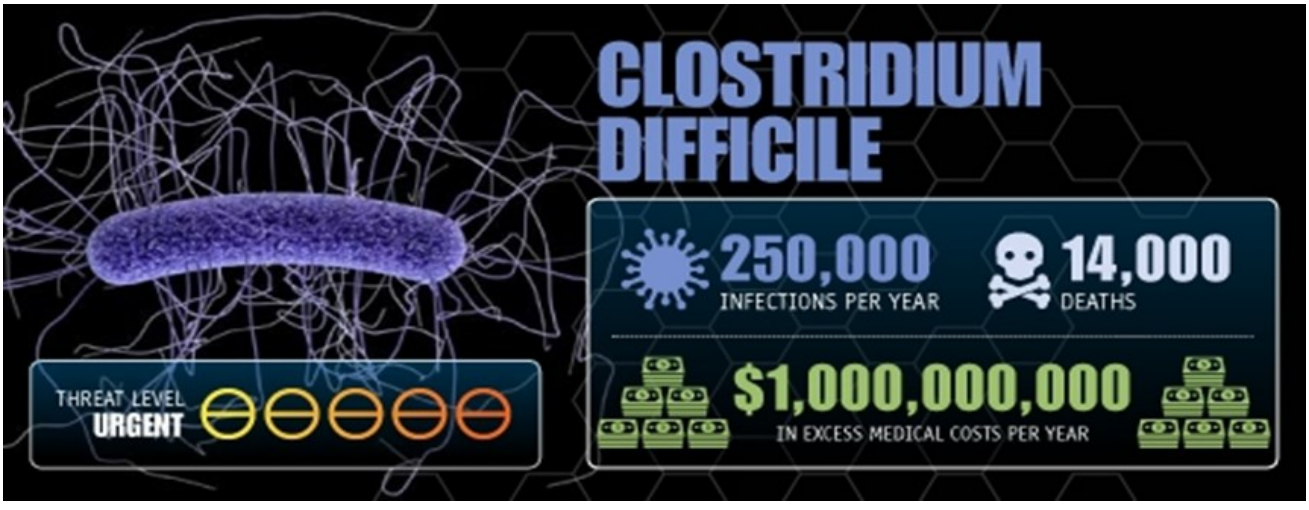


INA-RESPOND Newsletter

The Sitting Disease: The Risks of I'll-do-it-tomorrow Attitude

By: RIA LESTARI

Name : dr. Ria Lestari, BMedSc, PGDipSEM

Address : L'Avenue Apartment, North Tower, Unit N21IJ

Occupation : resident doctor at University of Indonesia (Sports Medicine Program)

We commonly use the term "sedentary behaviour" or "the sitting disease phenomenon" in the contexts of TV viewing, computer and game console use, sitting in our workplace, and the large amount of time spent in vehicles. Your favourite television shows can make you laugh, cry, or even scream; and if you watch them often enough, they could even shorten your life! According to the Exercise and Sport Sciences study [1] from Australia, 80% people who watched more than four hours per day were more likely to die over the 14-year study period than those who watched less or none.

In 2010, 23% of adults aged >18 years were barely active globally, and physical inactivity had been identified as the fourth leading risk factor for global mortality, according to the World Health Organization [2]. Furthermore, according to a study from the American Journal of Clinical Nutrition [3], physical inactivity has been associated with an increased risk of diseases like heart disease and cancer, also a larger risk of early death in people. However, the connection with early death is independent of each people's BMI. Because of that, one of the worst things you can do to your body is doing nothing at all. Sluggishness or inactivity can make you prone to such deadly conditions. The advice is simple: *get off your butt a.k.a. get moving!*

There's no need to have a second thought: Prolonged inactivity is not healthy. Read on to learn more – these alarming side effects of living a sedentary life will make you jump out of your seat.

It leads you to emotional imbalance

A recent Singaporean study [4] indicated that people who reported having 10 hour/day of sedentary behaviour were 29% more likely to have psychological distress—say, feeling tired, anxious, restless, or hopeless—than those who were active. A study from BMC Public Health [5] stated that physical activity may be helpful to improve mental health, relieve stress, and increase sleep satisfaction in adolescents.

Since exercise has mood-boosting effects, it does sound important. When you work up a sweat, your body will produce endorphins—a happy hormone—and it is just as efficiently as prescribed antidepressants according to a study by British Journal of Pharmacology [6].

It raises your risk of cancer

Physical inactivity can be really sinister: an American meta-analysis study [7] concluded that inactive people were associated with a greater risk for cancer (breast, colon, colorectal, endometrial, and epithelial ovarian). Moreover, another meta-analysis study [8] from Germany found that the cancer risk increases with each 2-hour

Rank	Cause of Death	Percent of Deaths
1	High Blood Pressure	12.8%
2	Tobacco Use	8.7%
3	High Blood Glucose	5.8%
4	**Physical Inactivity**	**5.5%**
5	Overweight & Obesity	4.8%
6	High Cholesterol	4.5%
7	Unsafe Sex	4.0%
8	Alcohol Use	3.8%
9	Childhood Underweight	3.8%
10	Indoor Smoke Solid Fuels	3.3%
	Source: WHO World Health Organization	

increase in sitting time: 8% for colon cancer, 10% for endometrial cancer, and 6% for lung cancer.

In addition, the researchers wrote that the risks almost doubled for individuals who regularly spend their butt parked in the front of the screen, probably because they tend to snack on junk foods and drink sweetened beverages when they are glued to their TV-watching routine.

This will open the way for obesity. Because when you sit, you do not involve in light-intensity physical activities (such as standing, walking, or even eating) that escalate calorie burn. A research about cancer from New York [9] stated that physical inactivity can contribute to obesity, which has been linked to the progress of cancer growth.

It spikes your blood sugar and cholesterol higher

Even if you're at a healthy weight, your blood sugar level can increase if you sit on the chair for too long, according to a recent University of Florida study [11]. This is important because uncontrollable blood sugar is associated with increased risk of developing diabetes, the researchers added.

Fascinatingly, another study from Australia [12] stated that too much mindless eating in front of the TV may finally lead to the elevation of blood glucose, free fatty acids and triglycerides. While they are people who maintain a healthy weight, apparently, they also have a higher ratio of fat to muscle, with an average of 25 percent body fat or more for men. This "skinny fat" condition leads to various metabolic issues, like higher blood pressure, blood sugar, and cholesterol levels, the researchers said.

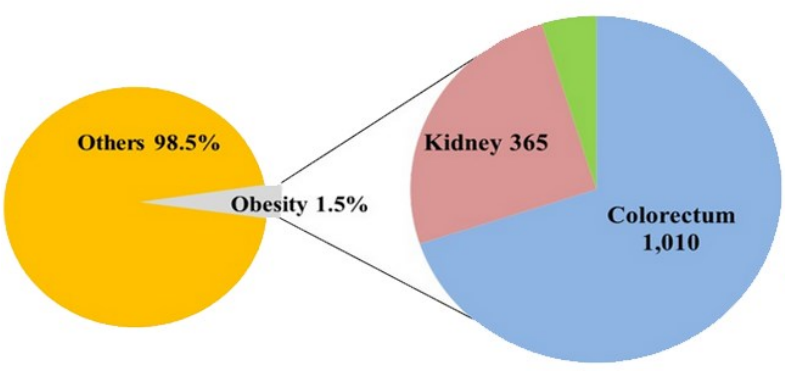
It can slow down your sex life

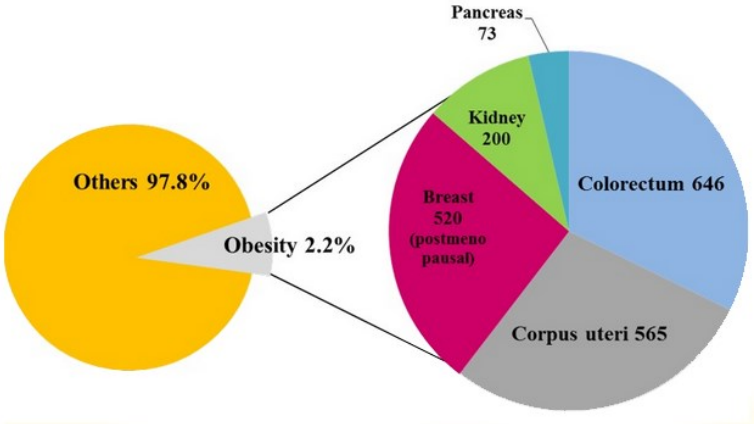
Your inactive behaviour can lead you to a bigger belly and have an erectile dysfunction (ED). One study from Harvard [13] stated that men with waists more than 102 centimetres are more than twice to develop the ED than those with waists below 80 centimetres. It can also affect your sperm, according to a recent Danish research [14], men who sit more than 5 hours a day have 29% lower sperm concentration than men who do not sit for that long.

It can deteriorate your bone health

When referring to the bones in the body, the catchphrase "use it or lose it" really does apply. In fact, sedentary behaviour accelerates changes in muscle power, strength, and power, according to a research from University of Missouri [15].

Physical inactivity is a primary cause of bone loss and might be associated to the aging process of your bone suggested by one [16] of the studies from National Institute of Health. Another study from the Canadian Medical Association Journal [17] explained that routine physical





activity helps strengthen the bones and prevent osteoporosis from developing. The benefits clearly outweigh the potential risks, particularly in older people.

How do We Fight the Sitting Disease?

Considering the recent findings, it has become obvious that most people face two barriers: too little exercise and too much sitting. Especially in children, the American Academy of Pediatrics gives advise parents to limit their children's screen time – televisions, DVDs, iPads, and video games – to no more than 2 hours per day [18]. Parents must encourage their children to get off the sofa, go out, and play.

However, recent evidence is irresistible that adults also benefit from similar advice by their doctors. Patients need to get out of their comfortable chair and start to move frequently, both at work and at home. Suggesting patients to reduce extended sitting can be combined with up-to-date recommendations on exercise and weight management, according to Mayo Clinic researchers [19].

Start slowly, then add your exercise gradually. Try not to feel beaten or overwhelmed. Do what you can. Getting some exercise or moving is always better than getting none. For example, take your dog for a walk, stand up when talking on a phone, do your chores around the house or the garden, take the stairs instead of the elevator at your workplace, and park your car further so you can walk more.

If you want to do some exercise but you don't know how to start, you can visit a sports medicine physician to tailor you some appropriate and accurate exercises (an exercise prescription) which will be made only for you and your specific conditions and goals.

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INA-RESPOND Newsletter

Pre-Print: Good News for Authors?

By: ALY DIANA

COMIC CORNER

Recently, we may or may not have heard about a new term in our scientific world, a pre-print. Because this is a new trend, including for me, I will start with its definition, benefits of posting a pre-print, and a main consideration before we publish our pre-print. A general definition of pre-print is a version of a scientific manuscript posted on a public server prior to formal peer review. So, as soon it's posted, our pre-print becomes a permanent part of the scientific record, citable with its own unique digital object identifier (DOI), and available for critiques and suggestions by the whole world.

Many journals encourage authors to publish the pre-print, including Nature, Lancet, and PLOS. Journals see pre-print as an important step toward a more open and transparent peer-review process which will bring good effects for both individual authors and the broader scientific community. Pre-print allows us to share our results when we are ready, before our paper has been officially published in our targeted journal. We must admit, sometimes/most of the times, publishing process may take a very long time. As the scientific world is buzzing faster than it was before, even finding suitable reviewers for our paper can take forever. Sometimes we have a series of papers, which should cite the previous paper (for the methods or the results), but delayed publication of the first paper will delay other papers to be published as well, as many journals do not accept citation to a 'non-published' article. In this sense, pre-print sounds like a perfect solution because it is a published material (again, with its own unique DOI), and many journals accept it to be cited. Pre-print also enables us to showcase our latest work for applying for a grant, a scholarship, or a job. A link to a publicly posted preprint is more illustrative and compelling than a title on a CV with the annotation "in development" or "under review."

A lot of groups in this world are interested in the same discovery, and it is common for researchers to report the same findings at around the same time. Unfortunately, peer-review process may artificially delay one paper in favour of another. Posting a pre-print allows researchers to publicly date stamp their discoveries. The sooner a research becomes available, the sooner it can begin to receive views and citations. In general, public posting increases the number of times paper is viewed and cited. Preliminary feedbacks also help authors to improve the manuscript, public may pick up things that slips from our or the reviewers' mind. Collegial discussion can lead to new ideas, follow-up studies, or collaborations with other research groups. It opens opportunities to many good things sooner than later. Another good news is from the moment a pre-print appears online to the day that the article is published in a peer reviewed journal, we can make as many updates as we want or need. Each version is numbered and incorporated into the pre-print record.

When we submit an article to a journal, most journals these days will ask whether we have already published a pre-print, and several journals also offer whether we want to publish our pre-print through their existing pre-print server. When our article is accepted for publication, the peer-review version will be automatically linked to our pre-print. One main consideration, although most journals are happy about pre-print, NOT ALL journals are, especially journals which have a strict embargo policy. Some also has a rule for us to publish an open access article once we published our pre-print. Open access is good, but it means that we must prepare more funding. So, please read the policy of our target journal carefully before we decided whether we want to publish our pre-print or not.

So, I will ask the same question as PLOS: Will you post tour next manuscript as a pre-print?

References:

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