

INA-RESPOND

INDONESIA RESEARCH PARTNERSHIP ON INFECTIOUS DISEASE



NEWSLETTER

June 2018

The Association of
**CLINICAL RESEARCH
PROFESSIONALS**

*COVER LETTER:
A Cover People Judge*

Eid Mubarak

**NIPAH VIRUS:
SHOULD WE BE
PREPARED FOR IT?**

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

2018

Eid-Mubarak



INA-RESPOND newsletter

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SENIOR WRITERS

Aly Diana, Dona Arlinda, M. Helmi
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Dedy Hidayat, Lois E. Bang, Louis
Grue, Maria Intan, M. Ikhsan Jufri,
Neneng Aini, Nurhayati, Ungke
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INA-RESPOND Secretariat

Badan Penelitian dan Pengembangan
Kesehatan, RI Gedung 4, Lantai 5.
Jl. Percetakan Negara no.29,
Jakarta, 10560
www.ina-respond.net

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TRIPOD & INA-PROACTIVE Study Updates

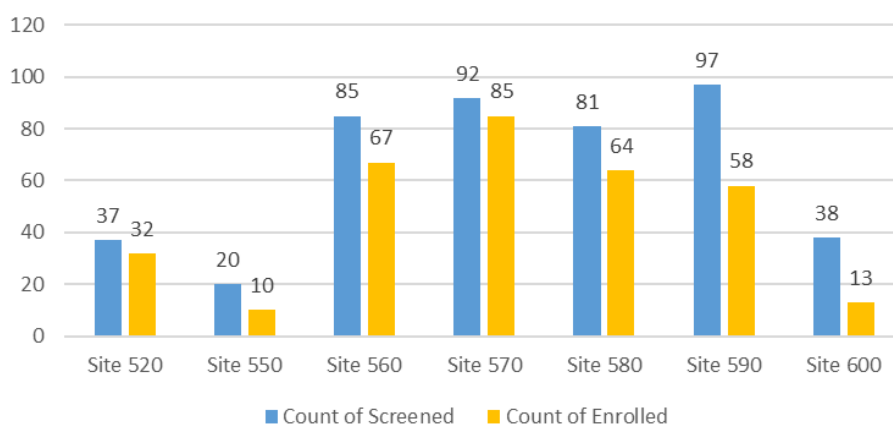
By: ANANDIKA PAWITRI, CALEB L. HALIM, LOIS E. BANG, M. IKHSAN JUFRI, VENTY MULIANA SARI

Screening and Enrolment

INA102

By 3 June 2018, sites had enrolled 329 subjects. Sites enrolled 73% of screened patients (450 screened patients). Total subjects enrolled based on our enrolment target is 57% (329 from 576). Enrolment progress until 3 June 2018 can be seen in the graphic on the right.

Screening and Enrollment in Each Site



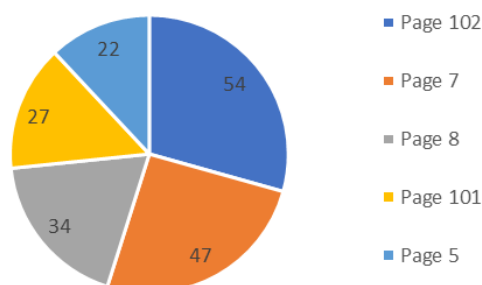
Data Evaluation

In the last couple of months, INA-RESPOND Secretariat has been trying to sum up findings at sites related to data documentation. Accurate data record plays a key role in clinical research for valuable publication.

The most frequent 'missing' answer in Data Clarification Form (DCF)

All complete CRFs submitted by sites are under scrutiny by the Data Management. If Data Manager finds discrepancy or incomplete items in the CRF, Data Clarification Form (DCF) or On-site Data Clarification Form (ODCF) will be sent / requested to get clarification.

Most 'Missing' Data in DCF (%)



DCF Descriptions			
Page 102	Missing AFB result At least 1 row in the specimen collection table is not filled in Missing Sputum collection method Missing date of specimen collection	Page 8	Missing sputum type for Xpert At least 1 row in the specimen collection table is not filled in Missing Sputum collection method
Page 7	At least 1 row in the chest x-ray table is not filled in (% lung affected, location) Missing lab evaluation result (HIV, Ureum) Missing date of specimen collection	Page 101	Compliance (missing number of medication left, receiving injection or not)
		Page 5	At least 1 row in the treatment seeking behavior table is not filled in



INA104

Six months have passed since INA-PROACTIVE study enrolled its first subject. Up to now, a total of 219 subjects have been enrolled.

Tangerang Hospital has enrolled 70 participants for INA-PROACTIVE study while Adam Malik Hospital, Wahidin Hospital, and Soetomo Hospital have enrolled 127 participants (50, 53, and 24 participants respectively). Our newest activated site, RS Cipto Mangunkusumo, has enrolled 22 subjects. The study participants comprises 208 adult subjects and 11 pediatric subjects.

12 sites have signed the INA-PROACTIVE study contract and agreement. The latest site that signed the contract is site 660 (RSUD Abdul Wahab Sjahranie, Samarinda). Site 560 and site 580 are still waiting for hospital's permission.

Site 630 (Moh. Ansari Saleh Hospital, Banjarmasin) will be activated in the first week of July. Site 640 (St. Carolus Hospital, Jakarta) and site 650 (Budi Kemuliaan Hospital, Batam) will have their Site Initiation Visit on 28-29 June. As for site 660, Site Preparation Visit will be conducted after the site has appointed their Research Assistants. INA-RESPOND Secretariat is waiting for site 670's Hospital Director (Kandou Hospital, Manado) to sign the contract.

INA-PROACTIVE Study Protocol version 2.0 was approved by NIHRD Ethical Committee

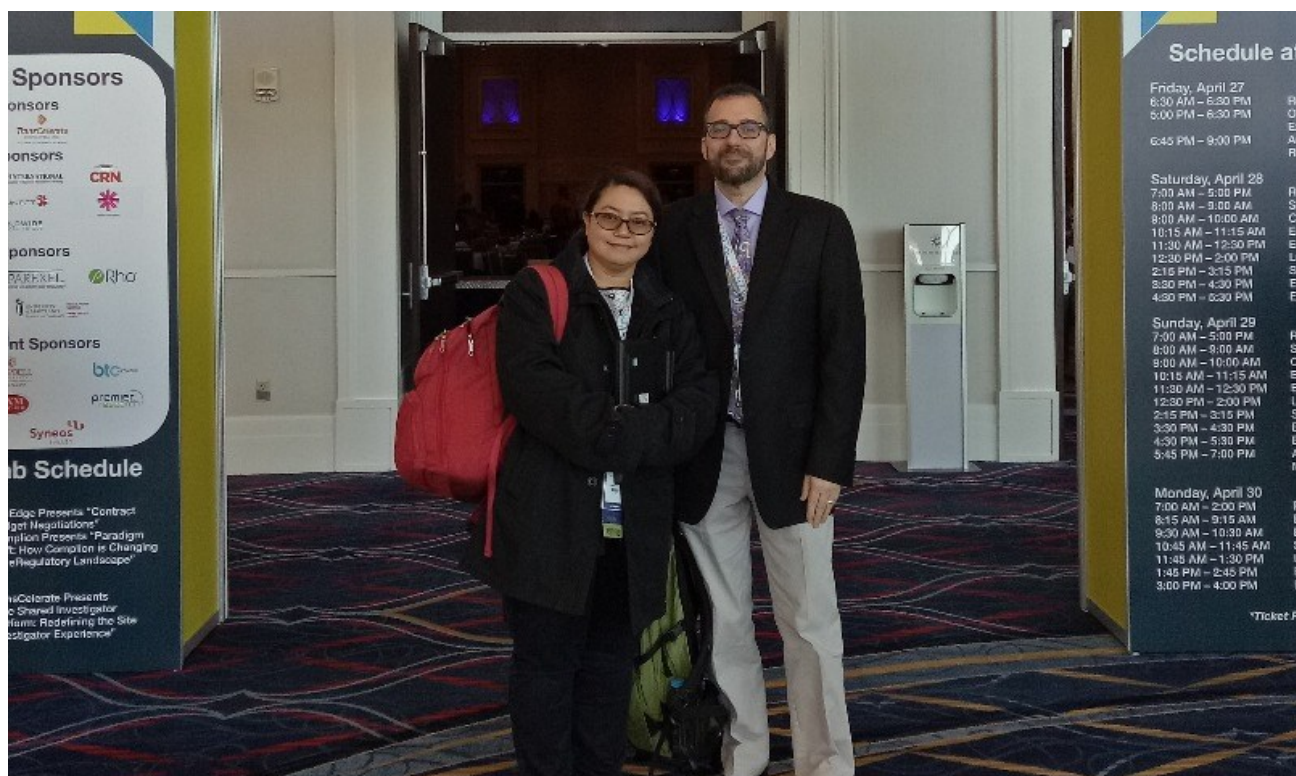
on 7 June 2018. The Secretariat is preparing all necessary laboratory supplies according to the changes made in version 2.0. (Cartridge CD4 (PIMA), Single syphilis Rapid Test, Rapid HIV antibody test Oncoprobe). Operational call for protocol Version 2.0 training updates will be conducted to sites through Ops Call Teleconference.

Site	SPV	SIV	Activa- tion	Enrolled Subjects
Site 610 (Tangerang Hospital)	19-20 Dec 2017	22 & 27 Dec 2017	09 Jan 2018	70
Site 600 (Adam Malik Hospital)	7-8 Feb 2018	12-13 Feb 2018	12 Mar 2018	50
Site 550 (Wahidin Hospital)	13-14 Feb 2018	19-20 Feb 2018	13 Mar 2018	53
Site 530 (Cipto Hos- pital)	21-22 Feb 2018	13-14 Mar 2018	3 May 2018	22
Site 570 (Soetomo Hospital)	20-21 Mar 2018	4-5 Apr 2018	26 Apr 2018	24
Site 560 (Kariadi Hospital)	11-13 Apr 2018	23-24 Apr 2018	-	-
Site 580 (Sardjito Hospital)	18-20 Apr 2018	17-18 May 2018	-	-

INA-RESPOND Newsletter

ACRP 2018 Meeting & Visit to NIH

By: Mila Erastuti and Neneng Aini



ACRP 2018 Meeting

The Association of Clinical Research Professionals (ACRP) held its annual expo on 27-30 April 2018 at the Gaylord National Resort & Convention Center, National Harbor, Maryland. This is a premier education and networking event for clinical research professionals. ACRP 2018 is the place to learn practical strategies, best practices, and creative solutions needed to improve clinical trial quality.

Each year ACRP brings clinical research community together to learn, connect, and explore opportunities to drive excellence in clinical research, which involve a broad spectrum of clinical research professionals reflective of the diverse nature of the clinical research enterprise. ACRP 2018 attendees' roles and organizations may vary, but they share one thing in common: a passion to improve public health through quality clinical research.

All types of Clinical Research Professionals such as Clinical Research Coordinators (CRCs), Monitors (CRAs), Project and Site Managers, executives and decision makers attended this event. Mila and Aini from INA-RESPOND Secretariat along with Susan Vogel and Louis Grue from NIAID had the opportunity to attend this event.

Several interesting topics of workshop were discussed in this expo such as e-Consent: Improving the Consent Process



through Innovative Technology, which was presented by Leigh J. Marck. He presented the e-consent process by using video or the internet. The subject electronically signs the Informed Consent Form (ICF) in pdf format by using the e-signature, and the ICF is sent by email. The study team will record the ICF process (voice and video). The whole process need to abide to the regulations stated in 21 CFR part 11 about electronic records, electronic signatures (score and application). We need to consider whether the subject is willing to be recorded in video and to ensure we have separate secure server to save the back-up ICF.

Another interesting topics is navigating SMART central IRB (CIRB) startup on the CT Superhighway. During the discussion, we learned about innovative CIRB workflows developed by working groups of the National Institutes of Health-funded

Trial Innovation Center (TIC). The speakers outlined how they approached local context review and study site activation under the SMART reliance agreement for multi-center trials. These innovative workflows pave a new way for future research and plays an integral role in accelerating the translation of research.

Dr. Jodi Black, Deputy Director of the Office of Extramural Research at the National Institutes of Health (NIH) and Ms. Rebecca Williams, Assistant Director of ClinicalTrials.gov are the panelists for "Signature Series: Inside NIH: Turning Discovery into Health" at the ACRP 2018 meeting. They said that NIH had been working diligently over the past decade to try and tear down silos and ensure clinical trial information is shared as widely as reasonably possible.

Enhancing transparency and public dissemination of data

will reinforce public trust in clinical trials. Currently, NIH can withhold trial funds from academic medical institutions that don't properly report results on ClinicalTrials.gov. In the months ahead, NIH could go to the U.S. Food and Drug Administration (FDA) to seek financial penalties for recalcitrant trial practitioners. Since its launch in February 2008, ClinicalTrials.gov has housed more than 30,000 studies with summary results. It contains more than 270,000 records of interventional and observational studies and unlimited information access. Updated nightly, it receives 200 million-page views per month with 93,000 unique visitors per day.

NIH Visit

After joining the ACRP meeting, we had the opportunity to visit the National Institute of Allergy and Infectious Diseases (NIAID) office and National Institutes of Health Clinical



Center (NIH CC) in Bethesda, Maryland from 1-3 May 2018. Mr. Louis Grue arranged the visit schedule.

On the 1st day, we had a meeting with Ms. Susan Vogel, Clinical Research Oversight Manager, and Ms. Shelly M. Simpson, Clinical Trials Director, Clinical Monitoring Research Program, Frederick National Laboratory for Cancer Research, Leidos Biomedical Research, Inc. In this meeting, we discussed our monitoring strategy for INA-RESPOND studies and related issues, implementation of risk-based monitoring that incorporates quality by design and risk management principles during the protocol development and implementation of INA-PROACTIVE and Schistosomiasis study, and the opportunities and challenges using electronic technologies such as e-consent and electronic case report form (e-CRF) or electronic data capture (EDC). A pilot phase needs to be implemented for Schistosomiasis Study to ensure that everything is in place, and we can identify potential problems prior to the study implementation.

NIH Clinical Center

During the visit, we had an opportunity to visit NIH CC in Building 10 and see its facilities. We, accompanied by Dr. Chun Yen as our guide, visited the isolation ward which hospitalize Ebola patients and joined a discussion of microbiology results in the microbiology laboratory. During the discussion, all laboratory results were discussed with all participating investigators, and the microbiologists shared/presented all new theories or information related to the laboratory results. It helps the investigator ensure high reliability in the safe delivery of patient-centric care in a clinical research environment.

We also met the pharmacists at the Pharmacy Department and discussed their services, the Research Services and Scientific Activities. In this service, the pharmacists act as Clinical Pharmacokinetic Research Laboratory (CPRL) staff. The CPRL assists clinical investigators in the design, analysis, and interpretation of pharmacokinetic studies. The CPRL supports NIH scientists in several major areas of pharmacokinetic research, including drug interaction studies and characterization of drugs with non-linear disposition.

We had the chance to meet their CRA and discussed the source document verification process using the Electronic Health Record, which they call the Clinical Research Information System (CRIS).

This system is used to support patients' care, research, and administrative activities in the NIH Clinical Center.

Facts at a Glance of NIH CC

The National Institutes of Health (NIH) Clinical Center is a hospital solely dedicated to clinical research at the NIH campus in Bethesda, Maryland. The Clinical Center, known as Building 10, consists of the original part of the hospital, the Warren Grant Magnuson Clinical Center, and the newest addition, the Mark O. Hatfield Clinical Research Center. The two parts are connected to form one large building.

Since the hospital's opening in 1953, NIH scientists have worked with volunteer patients to create medical innovations. Clinical Center successes include pioneering the cure of cancerous solid tumors with chemotherapy; the use of nitroglycerin to treat heart attacks; identifying a genetic component in schizophrenia; conducting the first successful replacement of a mitral valve to treat heart disease; and the creation of blood tests to identify both Acquired Immune Deficiency Syndrome (AIDS) and hepatitis. In October 2014, Clinical Center staff successfully treated one of the first few Ebola virus cases in the United States.

The Clinical Center has been a leader in the "bench-to-bedside" concept. Its specialized hospital design places patient care units in close proximity to research laboratories. This model supports interaction and collaboration among clinical researchers.

The NIH Clinical Center also offers an extensive range of clinical research training to help prepare the next generation of clinician-scientists. The innovative curriculum includes courses in pharmacology, principles and practice of clinical research and bioethics.

National Library of Medicine

On the last day of our visit, we went to NIH National Library of Medicine (NLM) on the campus of the National Institutes of Health in Bethesda, Maryland. NLM has been a center of information innovation since its founding in 1836. The world's largest biomedical library, NLM maintains and makes available a vast print collection and produces electronic information resources on a wide range of topics that are searched billions of times each year by millions of people around the globe. It also supports and conducts research, development, and training in biomedical informatics and health information tech-



nology. In addition, the Library coordinates a 6,500-member National Network of Libraries of Medicine that promotes and provides access to health information in communities across the United States. Here are some of the NLM services:

PubMed, citation for biomedical literature

Open i , Open Access Biomedical Image Search Engine

MeSH, a hierarchically-organized terminology for indexing and cataloging of biomedical information such as MEDLINE/PUBmed and other NLM databases

ClinicalTrials.gov, a database of clinical studies worldwide provides information on publicly and privately supported clinical studies on a wide range of diseases and conditions.

MedlinePlus, reliable, up-to-date health information for patients and their families and friends.

TOXNET, search databases on hazardous chemicals

The Visitor Center staff offer tours of the Library daily. The one-hour tour, which originates in the

NLM Visitor Center (Room 127, Building 38A), includes an 8-minute video providing an overview of NLM programs and services; brief demonstrations of the library's online information resources; and a walking tour that includes the computer room, reading room, exhibition area, and the History of Medicine Division.

We would like to thank INA-RESPOND and partners for the opportunity to visit the ACRP Expo and NIH. It was a very interesting and valuable experience. We hope this experience can help to increase our contribution to INA-RESPOND network. We thank INA-RESPOND Secretariat, especially dr. M. Karyana, M.Kes, NIH-NIAID for the support. We would also like to thank Mr. Louis Grue and dr. Chun Yen for arranging the schedule and accompanying us during our visit.

"Anyone who stops learning is old, whether at twenty or eighty. Anyone who keeps learning stays young" - Henry Ford.

Reference:

<https://www.acrpnet.org/about/news-events/>

INA-RESPOND *Newsletter*

Travel Report: National Cancer Institute

By: WAHYU NAWANG WULAN, GUSTIANI, UNGKE ANTON JAYA



REPORT

To support the objectives of INA-PROACTIVE Study, a team from the INARESPOND reference laboratory learnt the techniques that will be adopted as methods to assess the medical characteristics of HIV/AIDS patients of PROACTIVE. Complying with INA104 protocol, the tests include, but are not limited to: a) existing diagnostic methods that may have not been accessible at the time of the collection of specimens, b) standard of research tests to identify drug resistance, c) testing to study immune markers that

might enable better management or prediction of outcomes for participants, d) to be used to study pathogenicity, and e) genetic/genomic testing upon consent of the participant. As such, the techniques learnt include: diagnostics of HIV infection (antigen/antibody/biomarker detection), CD4 and plasma HIV RNA level (viral load/VL) testing, subtype and resistance/genotype profiling. The training was done on 19-30 March 2018 in two separate locations: diagnostics of HIV-1 infection at Virus Isolation

and Serology Laboratory (VISL) and AIDS Monitoring Laboratory (AML) of the Frederick National Laboratory at the National Cancer Institute (NCI) at Fort Detrick, Frederick, Maryland; and resistance/genotyping profile at the RTT Headquarter, Buford, Atlanta, Georgia.

At the NCI, we learnt the two diagnostics stages of HIV-1 in plasma-EDTA specimen. The first line of HIV detection is identifying the presence of p24 antigen (Ag) and antibody (Ab) to HIV-1 and HIV-2 using

an immunochromatographic test called Alere Determine™ HIV-1/2 Ag/Ab Combo. When positive results come up, they are confirmed using a second line of detection, which is a choice of either the Cambridge Biotech HIV-1 Western Blot Kit or the Geenius HIV-1/2 Supplemental Assay. The Cambridge Biotech HIV-1 Western Blot Kit is a qualitative detection and identification of antibodies to HIV-1 proteins (p17, p24, p31, gp41, p51, p55, p66, gp120, gp160). The Geenius™ HIV 1/2 Supplemental Assay is another immunochromatographic test that identifies antibodies to HIV-1 and HIV-2, consisting of gp36 and gp140 (HIV-2 envelope peptides), p31 (HIV-1 polymerase peptide), gp160 (HIV-1 envelope recombinant protein), p24 (HIV-1 core recombinant protein), and gp41 (Group M and O) (HIV-1 envelope peptides).

Samples that are confirmed positive, and information on VL is not known, were then tested for VL using the m2000rt system (Abbott Realtime HIV-1 Assay), which is a real-time reverse transcription polymerase chain reaction (real-time RT-PCR) that amplifies a segment in the integrase gene of HIV-1. Results are reported in copies/ml. The limit of detection (LOD) is 40 cp/ml with 1.0 ml input volume, 75 cp/ml with 0.5 ml input volume, and 150 cp/ml with 0.2 ml input volume. To overcome the low concentration (<1000 cp/ml), the VISL concentrates the sample by 17000 RPM (23000x g) centrifugation for 1 h, 40 C, and resuspend the sample in 0.4 ml volume.

The HIV-1 genotyping (drug resistance) profile is checked on samples with >1000 cp/ml VL. There are two genotyping methods employed by the NCI: the GeneTHINK CoreSEQ HIV-1 PR/RT Genotyping Kit with Thin Slab Acrylamide Sequencing

System (TSASS) (RTT MolecularDx, USA) and next generation sequencing (NGS) using MiSeq Dx (Illumina). The GeneTHINK system is used for routine screening of resistance-associated substitutions (RAS) in protease and reverse transcriptase genes (observe resistance against protease and RT-inhibitor), and has a cut off level of 15-20% mutation in virus population. NGS is also optimized to detect mutation in the similar gene. However, it is more for research purpose, having ability to detect up to 5% mutation, which probably does not have clinical importance at time of observation. In addition, data analysis using the GeneTHINK system is already set using the VISGEN software; while the NGS is in-house optimized, using a self-developed bioinformatics pipeline. The lab technologist also specially learnt the GeneTHINK HIV-1 genotyping protocol at the RTT Headquarter in Buford, Georgia.

In NCI, we also visited the AIDS Monitoring Laboratory (AML). All facilities in this department are BSL2* level. Here we learnt specimen processing and serial laboratory tests after blood is collected from patients. Firstly, lab personnel match all information on tube with sample information sheet. Then a code called "P number" is assigned to substitute the patient's name or identity and other data related to the patient or patient's blood. The information in "P number" can be retrieved from the database by laboratory staff who has access. The blood is then aliquoted and processed to separate the plasma/sera and peripheral blood mononuclear cells (PBMCs) for subsequent serial laboratory tests and repository.

The serial laboratory tests consist of hematology, flowcytometry, and cytokine measurements. For hematology, the test performed is a com-

plete blood count to measure the number of red blood cells, white blood cells and platelets using automated hematology instrument. Peripheral blood smear, a thin layer of blood spread onto the glass slide, is also made to observe whether there are abnormalities of the blood cell components under the microscope. In flowcytometry section, blood was processed to measure and investigate certain leukocytes subsets and other immune system cells or markers that play important role in AIDS. Flowcytometry instrument available at AML lab are the six-color and eight-color panel of FACS Canto© (BD company). The six-color panel is used to measure T cells (CD3), T cells subsets (CD4 and CD8), B cells (CD19) and Natural Killer / NK cells (CD 16, CD56) in one tube. The eight-color panel simultaneously measure eight different cell subsets or other markers, such as HLA DR, CD3, CD4, CD8, CD25, CD27, CD38, and 45RQ. Cytokine measurement was done at the serology lab. The lab has employed an updated technology of cytokine measurement named Ella Cytokine© (R&D Systems). Ella Cytokine is much easier to operate, less hands-on and time consuming, reproducible and no cross reactivity compared to ELISA (Enzyme Linked immunoassay), which used to be a preferred method to quantify cytokine level in blood. Ella Cytokine also uses only small amount plasma EDTA and the result is available in just one hour. Until March 2018, Ella Cytokine has been equipped with several panels required to observe AIDS-related study, such as interleukin 6 (IL6), tumor necrosis factor alpha (TNFα), and C-reactive protein (CRP). Another important panel, D-dimer, is planned to be launched in near future.

We thank INA-RESPOND and partners for this learning opportunity. It was truly a valuable experience.

INA-RESPOND Newsletter

Nipah Virus: Should We Prepare For It?

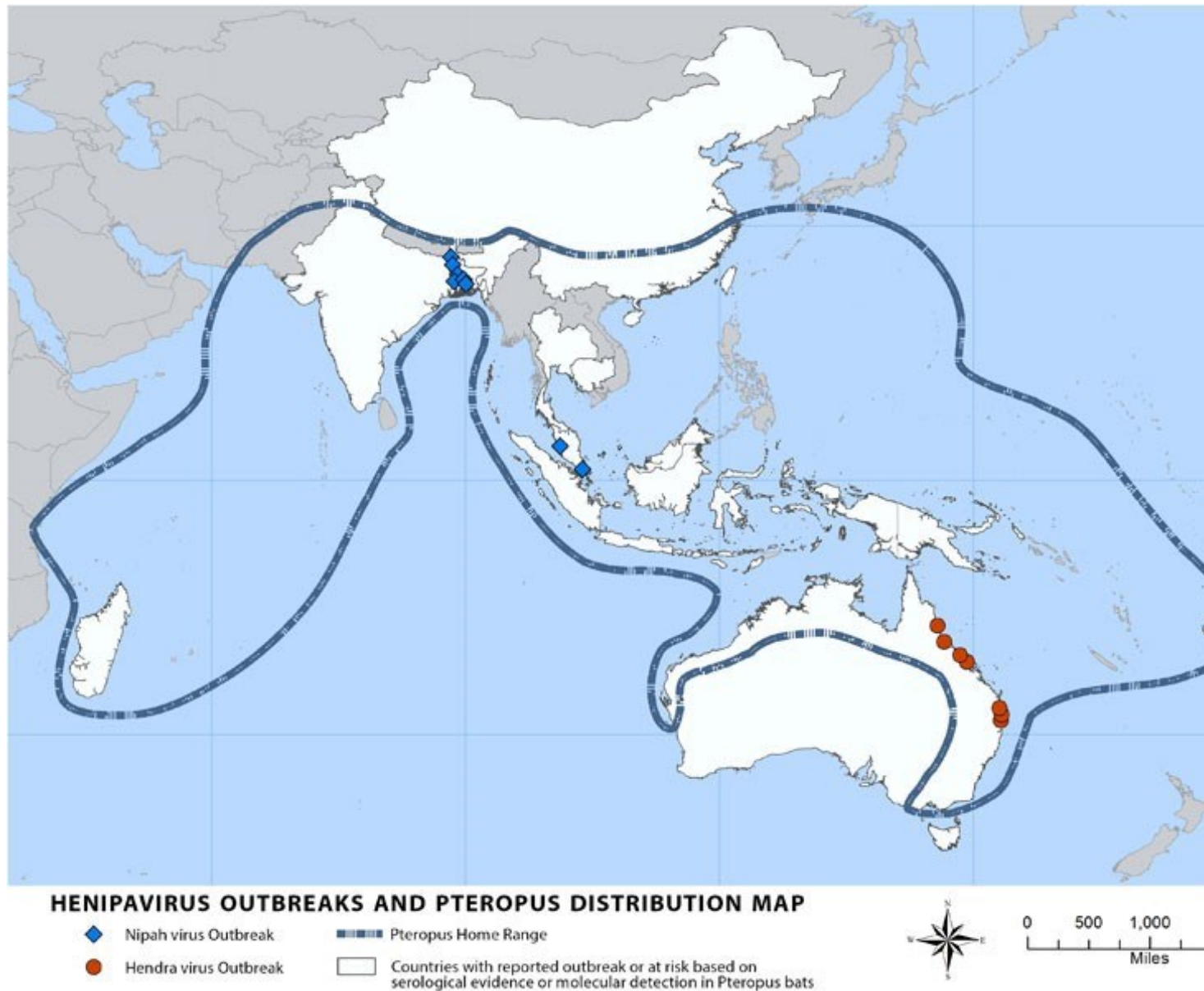
By: M.HELMI AZIZ



SCIENCE & RESEARCH

On 19 May 2018 three deaths from a family cluster and one death of healthcare worker due to Nipah virus (NiV) infection were reported in Kozhikode District, Kerala State, South India, India⁽¹⁾. From those four deaths, three were positive for NiV based on real-time polymerase chain reaction (RT-PCR) and IgM enzyme-linked immunosorbent assay (ELISA)⁽¹⁾. By 28 May 2018, fifteen people had been tested positive for NiV, and thirteen people from Malappuram and Kozhikode District died⁽¹⁾. This article will focus on NiV and how it might become a threat in Indonesia due to the natural host distribution and migration.

The name NiV came from the first isolate from a fatal human case in Kampung Sungai Nipah, a village in Negeri Sembilan^(2, 3). However, NiV first cases occurred in late September 1998 in villages near the city of Ipoh, Perak, West Malaysia, where pig farming was located^(2, 3). The NiV outbreak continued in this region until February 1999 and was followed by other outbreaks in Sikamat, Negeri Sembilan from December 1998 to January 1999 and in Bukit Pelandok in December 1998⁽²⁾. Humans who were infected with Nipah during these outbreaks had neurological disease, and Japanese B encephalitis (JE) was thought to be responsible^(2, 4). However, this suspected "JE" outbreak still created new

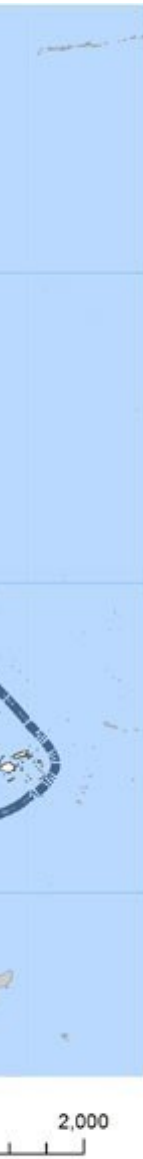


cases although the outbreak patients had previously been immunized against JE⁽²⁾. In addition, along with the human outbreak, reports of sick pigs with severe barking cough also emerged, which was very unusual for JE. These facts ruled out JE as the responsible agent for the outbreaks^(2, 4). The association between the ill pigs and humans was also supported by the non-existing new cases in Malay villages where Muslims, who are forbidden to have any contact with pigs and its products, predominantly live⁽²⁾.

In March 1999, virologists from University of Malaya were able to isolate the responsible virus that resembled the *Paramyxoviridae* virus, had cross-reactive

antibodies with Hendra virus, and was related to Hendra virus with 20% sequence difference^(2, 4). By that time, the outbreak had spread to Singapore due to imported live pigs from Malaysia, and it was found that the sequence isolates were identical with Malaysian NiV⁽²⁾. The outbreak in Malaysia ended after pig-culling operations, and the outbreak in Singapore ended after they banned the import of live pigs from Malaysia^(2, 4). Later, NiV outbreaks were reported from India and Bangladesh in 2001 and in the Philippines in 2014^(2, 4, 5).

So, why did India, Bangladesh, and the Philippines also have NiV outbreaks even though they did not import



live pigs from Malaysia? Soon, after the discovery of NiV, scientist found that the fruit bats/flying foxes (genus *Pteropus*, family *Pteropodidae*)⁽⁶⁾ were the natural reservoirs of NiV^(2, 5). If we look at the *Pteropus* distribution and migration map on the left, the three countries, including Indonesia, are within *Pteropus*'s home range⁽⁷⁾.

Unlike the outbreaks in Malaysia and Singapore, the outbreaks that occurred in India, Bangladesh, and the Philippines did not involve pigs as the intermediary host. The transmission of NiV in Bangladesh and India was due to the consumption of date palm tree sap that was contaminated with saliva, urine, and excreta of *Pteropus spp.*; the contact with sick domesticated animals; and the human-to-human transmission in house and hospital settings⁽²⁾. Meanwhile, in the Philippines, the NiCV transmission was presumably due to the direct exposure to infected horses and/or consumption of undercooked infected horse meat^(2, 8).

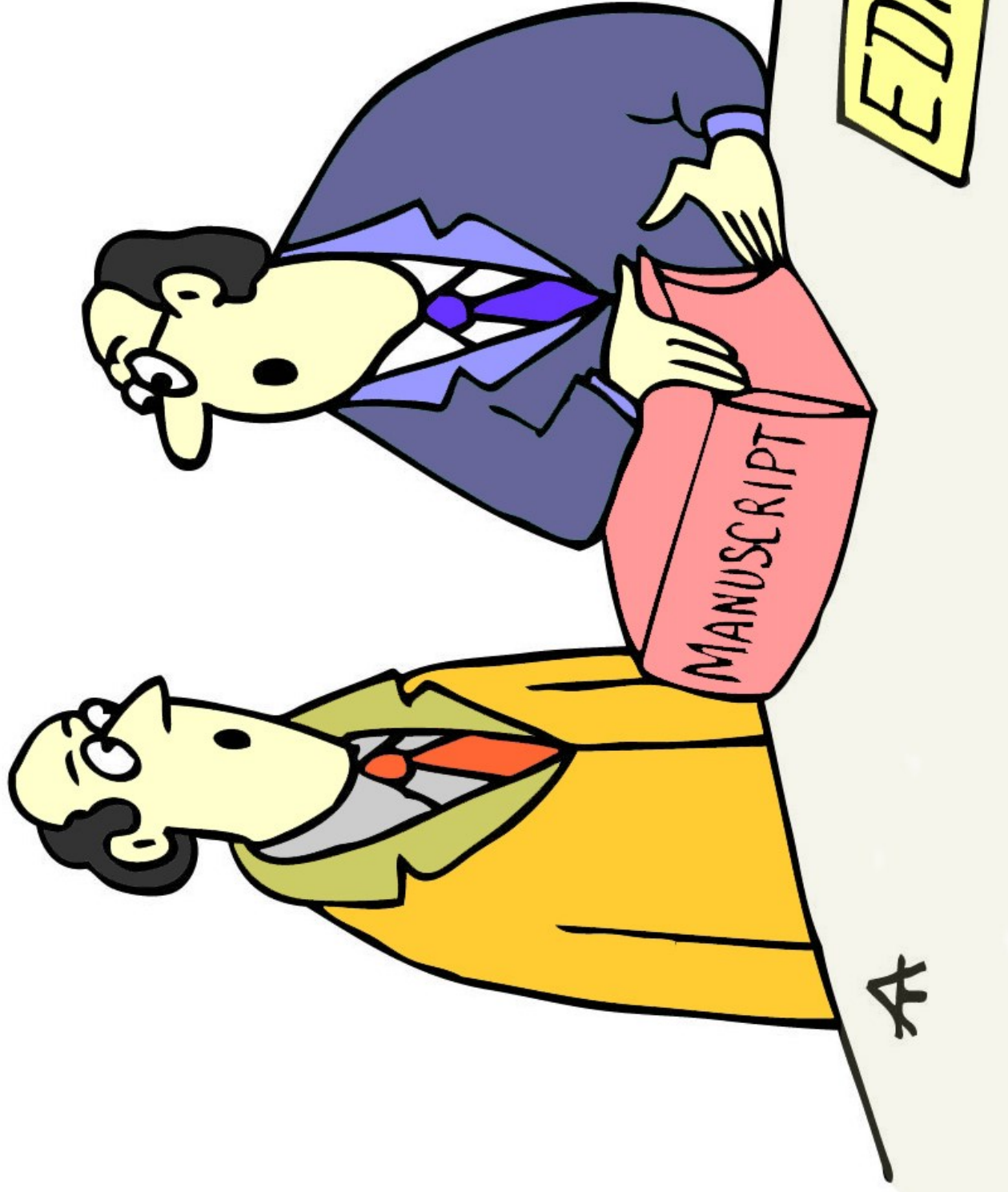
So, what are the symptoms when a person is infected with NiV? The incubation period of NiV ranges from four to sixty days with 90% of cases occurring in two weeks or less⁽²⁾. Similar to other viral infections, patients infected with NiV are presented with fever, headache, and dizziness. In addition, patients also show decrease consciousness that leads to severe encephalitis and brainstem dysfunction⁽²⁾. Neurological symptoms in NiV are diverse, multifocal, and have interesting features (relapse and late-onset encephalitis that could occur months or even years after the acute infection)⁽²⁾. These neurological symptoms commonly occurred in the outbreaks in Malaysia while in Bangladesh and India, the prominent symptoms were respiratory symptoms (occurred in half to two-thirds of cases)⁽²⁾. Later, it was found that there are two genetic lineages of NiV: NiV Malaysia (NiV-MY) and NiV Bangladesh (NiV-BD)⁽²⁾. Although those two strains are distinguishable, animal infection studies show that NiV-BD is more pathogenic than NiV-MY. Furthermore, NiV-BD infection in animals results in increased oral shedding and higher NiV replication in the respiratory tract, which supported why respiratory symptoms and human-to-human transmission were prominent in Bangladesh outbreak⁽²⁾.

We know what NiV is, what it does to humans, and how it is transmitted. The next question is, should Indonesia be aware of this virus? *Pteropus hypomelanus*, *Pteropus vampyrus*, *Eonycteris spelaea*, *Cynopterus*, *Scotophilus kuhlii*, and *Hipposideros larvatus* are bat species that are shown to have NiV and are circulating

in Indonesia⁽⁵⁾. A study conducted by Indonesian scientists in North Sumatra in 2013 showed that from 71 *Pteropus vampyrus* screened for NiV, 1.4% was positive for NiV infection by PCR and 13% of those bats had antibody against NiV⁽⁹⁾. Although a human case has never been documented in Indonesia, it should be noted that NiV is found in bats that circulate in Indonesia. Therefore, the potential for NiV outbreaks in Indonesia remains significant. Due to its high virulence, versatile transmission, no effective treatment, and significant mortality; it is necessary to develop NiV diagnostic capability and establish appropriate surveillance systems of NiV in Indonesia, so when NiV outbreaks occur, control measures can be quickly initiated.

References:

1. WHO. Nipah virus - India 2018 [updated 31 May 2018]. Available from: <http://www.who.int/csr/don/31-may-2018-nipah-virus-india/en/>.
2. Ang BSP, Lim TCC, Wang L. Nipah Virus Infection. *Journal of clinical microbiology*. 2018;56(6).
3. Hassan MZ, Sazzad HMS, Luby SP, Sturm-Ramirez K, Bhuiyan MU, Rahman MZ, Islam MM, Stroher U, Sultana S, Kafi MAH, Daszak P, Rahman M, Gurley ES. Nipah Virus Contamination of Hospital Surfaces during Outbreaks, Bangladesh, 2013-2014. *Emerging infectious diseases*. 2018;24(1):15-21.
4. Weatherman S, Feldmann H, de Wit E. Transmission of henipaviruses. *Current opinion in virology*. 2018;28:7-11.
5. WHOSEARO. Nipah Virus Infection. Regional Office for WHO South-East Asia.
6. Library TR. Malayan Flying Fox [updated November 06, 2017]. Available from: <http://www.robinsonlibrary.com/science/zoology/mammals/chiroptera/malayan.htm>.
7. CDC. Hendra Virus Disease (HeV): Centers for Disease Control and Prevention; 2014 [updated March 17, 2014; cited 2018]. Available from: <https://www.cdc.gov/vhf/hendra/outbreaks/distribution-map.html>.
8. Ching PK, de los Reyes VC, Sucaldito MN, Tayag E, Columba-Vingno AB, Malbas FF, Jr., Bolo GC, Jr., Sejvar JJ, Eagles D, Playford G, Dueger E, Kaku Y, Morikawa S, Kuroda M, Marsh GA, McCullough S, Foxwell AR. Outbreak of henipavirus infection, Philippines, 2014. *Emerging infectious diseases*. 2015;21(2):328-31.
9. Sendow I, Ratnawati A, Taylor T, Adjid RMA, Saepulloh M, Barr J, Wong F, Daniels P, Field H. Nipah Virus in the Fruit Bat *Pteropus vampyrus* in Sumatera, Indonesia. *PLOS ONE*. 2013;8(7):e69544.



"Can you redo this manuscript, John,
and make it less stupid?"

INA-RESPOND Newsletter

COVER LETTER: Yes. People Judge It by Its Cover

By: ALY DIANA

Most likely the editors of a journal (at least one) will read your entire paper before they decide to send it for peer-review process or reject it right away. Surprisingly, first impressions do matter. Good impressions can be a game changer in this situation. Moreover, creating deep, favourable impression will not do anybody any harm! So, let's spend some time to learn how to make a good cover letter that will give us great first impression.

These are some tips (and maybe tricks) about making a favourable cover letter in general. Rule number one: think of our reader! The editors of a journal, although they have to be great scientists, are not always experts in your field. Therefore, effective cover letter should be concise and clear, written in plain English, and have a strong selling point! Although not every editor will understand the details, every editor should appreciate our work's significance. Highlight the motivation for our study, frame our work in the context of current knowledge in the field, and briefly summarize the key scientific advances and conclusions reported in our manuscript.

Rule number two: think of our reader! When introducing our work to the editor, we can also take this opportunity to explain why the manuscript will be of interest to the journal's readers, something that is always at the forefront of an editor's mind. Summary statements should focus on the immediate importance and utility of our work to the community rather than emphasizing more distant objectives.

Cover letter is also the appropriate media to recommend potential reviewers (as long as not all of them are our families and best friends). We can also request to exclude certain individuals as referees (usually no more than 2 – 3 people; and should not be the entire fields or institutions). Most journals will respect our

request for excluding the referees, but only use the opportunity when necessary.

As cover letter is not shared with the referees, it should be used to provide confidential information such as conflicts of interest and to declare any related work that is in press or submitted elsewhere. If we think our work is truly ground-breaking and that another research group may be submitting similar results elsewhere, we can notify the editors and made a request for a fast-track review process. However, use this option with caution as it may make journal editors wary.

Last but not least, most journals require statements that indicate our manuscript's originality and obtained approval. For this purpose, we can use the following common statement: "*We confirm that this manuscript has not been published elsewhere and is not under consideration by another journal*"; and "*All authors have approved the manuscript and agree with its submission to [insert the name of the target journal]*".

Closing remarks: Please don't write another paper in the cover letter, general standard length for cover letters is around 2-2.5 pages (max). Please don't forget to check the instructions for authors from our target journal because the requirements of cover letter might slightly varied.

References:

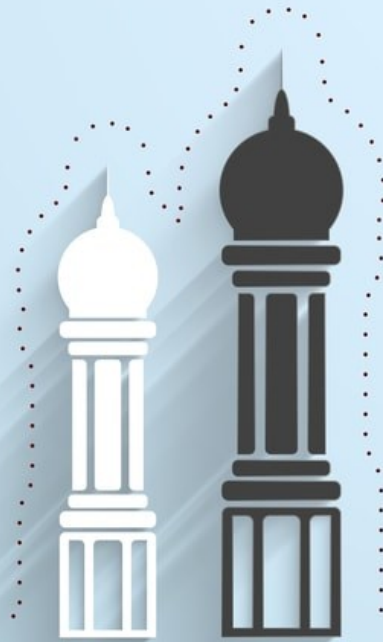
Doerr A. 2013. How to write a cover letter. <http://blogs.nature.com/methagora/2013/09/how-to-write-a-cover-letter.html>

Brief guide for submission to Nature. 2017. <https://www.nature.com/nature/for-authors/initial-submission>

Cover letters. 2018. <https://www.springer.com/gp/authors-editors/authorandreviewertutorials/submitting-to-a-journal-and-peer-review/cover-letters/10285574>



Eid-Al-Fitr



In Indonesia, which major population is Muslims, Eid al-Fitr is a very important day and it is joyously celebrated by its Muslims citizens. Eid al-Fitr celebrates the conclusion of the 29 or 30 days of dawn-to-sunset fasting during the holy month of Ramadan, a time for spiritual reflection where people spend time with loved ones and do charitable work.

Eid is traditionally celebrated for three days and is a national holiday in most countries with major Muslim population. Considering the massive commute done by Indonesians close to Eid al-Fitr, the Indonesian government implements joint holiday in addition to the Eid al-Fitr holiday. Eid al-Fitr begins on June 15 this year, and government institutions are closed for business from June 11 to 20. INA-RESPOND Secretariat follows government institutions and will resume its operations on June 21.

How is Eid al-Fitr celebrated in Indonesia?

Though the prayers and merriment are commonplace, Eid Al Fitr is commemorated differently across cultures. The greetings expressed, type of clothing worn, the gifts given to children, and the food enjoyed vary culture to culture.

Eid traditionally starts with prayers followed by a short

sermon. In some areas in Indonesia, the prayers take place outside, while others are hosted in mosques or large halls. After the prayers, Muslims wish the people around them a happy Eid. In Indonesia Eid is called *Lebaran*, so Indonesians say, "*Selamat Lebaran*" which means Happy Eid. In this special moment, many people wear traditional clothes, give gifts or money to children, and donate to charity. They also visit their families and friends (most people in Jakarta go back to their hometowns), and they sometimes visit graveyards to pray for their dead.

One famous dish that most Indonesians enjoy during *Lebaran* is *Ketupat Lebaran* (rice cake). Typically, the rice cake is served with sautéed vegetables (beans and chayote) braised in coconut milk, sweet meat stew or chicken braised in coconut milk, and spicy diced potatoes. Families or guests often bring sweets and cookies when visiting their relatives. They exchange greetings and also ask for forgiveness for their wrongdoings (by saying *Mohon Maaf Lahir Batin*). It is indeed a moment of joy!

On that note, INA-RESPOND Secretariat would like to wish you *Selamat Lebaran* and *Mohon Maaf Lahir Batin*. May you be showered with love, peace, warmth, and togetherness. Eid Mubarak! -dh

ketupat lebaran (rice cake)



chicken braised in coconut



spicy diced potatoes



sweet meat stew



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.

The INA-RESPOND newsletter welcomes all network members and stakeholders to contribute by submitting articles related to the network's studies and interests. Send your articles or subscribe to our latest newsletter by sending an email to INA.Secretariat@ina-respond.net

