ADC Letter
for Infectious Disease Control

Online ISSN 2424-0907
Print ISSN 2189-5171

Vol.3 No.2 2016.7.1

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TEIKYO

50th TEIKYO UNIVERSITY

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National Children's Hospital
New Building (Hanoi)

Philippine University

EDITORIAL

We are pleased to subscribe the ADC letter for infectious disease control: Volume 3 No. 2.
This issue has many varieties in the contents as below:

1. Introduction of Departments and Laboratories by ADC members
2. Progress reports of e-ASIA JRP with Vietnam and Philippines
3. Some reports associated with ADC members
4. Original article in Influenza
5. Events in ADC from January to June in 2016 and later
6. This journal will be linked to J-STAGE

If you have any questions and comments, send email to the Editorial.
Also, we will welcome to submit the original articles and reports to us.

No.1

ISO15189と微生物・細菌検査

帝京大学医学部臨床検査医学・帝京大学アジア国際感染症制御研究所（ADC） 古川泰司

2016年2月24日、我々の帝京大学医学部附属病院・中央検査部は、臨床検査室の国際規格であるISO15189認定を取得することができた（写真は、病院長室で行われた同授与式の時のもの）。概ね3年前より取得へ向けて準備してきた活動が報われ、また、非常に幸運なことに同時期に保険診療上の施設加算として、国際標準検査管理加算が制定された。このことにより、認定継続への経済的バックボーンも確保することができ、今後とも、特定機能病院の検査室として、質の高い検査を継続的に遂行していく所存である。

同規格は、検体検査全体を対象とするもので、微生物・細菌検査に特化したものではないが、当然これらの検査に対しても、非常にハードルの高い要求事項があげられている。この認定を得るために必須の事項を簡単に説明すると、検査室で行われているすべての業務・プロセスに対して、品質マネジメントシステム（quality management system, QMS）を構築し、確実に実践していくということである。具体的な業務としては、個々の検査業務そのもの、およびその遂行に必要な物品・試薬などについて、行ったことの文書化・記録化を確実に行い、トレーサビリティを確保すること、そして、それを元に内部および外部の要員（personnel）によって定期的な監査を行い、継続的に検査プロセスの改善・向上を図ると言うことになろう。言葉で言えば、簡単なようであるが、実働している状況では、膨大な労力と結果としての文書が発生している。しかし、確かにこの運用を行う事で、検査全体のプロセスは我々検査部内部の者にも、また、直接のユーザーである診療科のスタッフにも、見えやすいものになっていると考えている。また、何らかのトラブル・問題点が発生したとき、その実態を正確に把握でき、対処方法もより適切なやり方を考えることができるようになっていると思う。医療の現場では、“文書化、見える化”を実際に行うのは大変なことだと改めて認識を新たにしているが、また、これまで十分に行われてこなかったからこそ、その効果に関しても手ごたえを感じている。

特に医療の分野では、検査業務は診療のみならず、研究・学術活動の根幹部分あるいはインフラであると言えよう。これまでその結果に対する第三者評価は十分行われてこなかったと言わざるを得ないが、これからは微生物・細菌検査を含む認定された範囲の検査結果については相当の安心感を持って結果を判断して頂いて良いと思われる。今後とも、ADC研と密な関係性を維持しながら、病院検査室として有用な検査を遂行するとともに、学術活動にも貢献していきたいと考えている。

Taiji Furukawa
Department of Laboratory Medicine, Teikyo University School of Medicine

Our laboratory (central laboratory of Teikyo University Hospital) obtained the accreditation of ISO15189, an international standard of Hospital laboratory faculty, on 2016/2/24. The requirement to obtain this accreditation was very hard, and we had spent for about 3 years to arrange preliminary matters for this accreditation. Fortunately, Japanese health insurance system decided to support this international standard from this year (additional reimbursement to international standard tests), and we now had financial backbone to maintain this accreditation. Thus, we can continue to perform various laboratory tests including bacteriology and virology tests with very high standard of accuracy.

The subjects of this accreditation are not specific to bacteriology and virology tests, but all in-vitro diagnostic tests are included. The requests to each test are very detailed and strict, and we believe that the accuracy of bacteriology and virology tests have been enhanced. The entire activity to obtain the accreditation is occasionally called “developing quality management system, QMS”. We have to assure tractability to all result from our laboratory, and have to make records or documents of through process of all tests in our laboratory.

The subjects of this records/documents making process include not only the test process itself, but quality assessments of vendors and suppliers of items needed to complete tests are also included. We also perform periodical audit by personnels both in and out of our laboratory based on the records/documents provided through the process. These activities are expected to contribute improving the entire test processes, and the test users can expect accurate test results constantly.

Laboratory tests, we consider, are the fundamentals or infrastructures of medicine. We believe that the tests with assured accuracy supported by QMS would give essential contribution to both patient care and research.

No.2

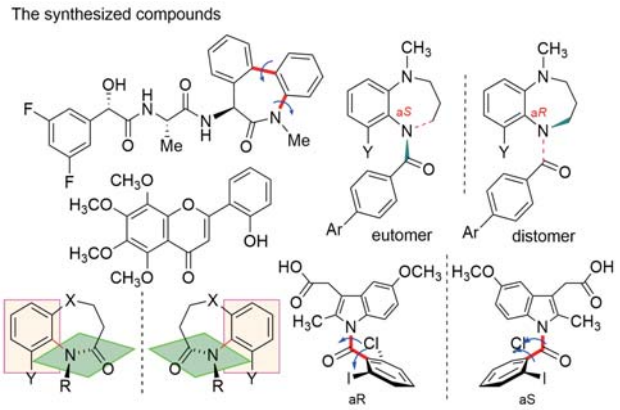
The Laboratory of Organic Chemistry

帝京大学薬学部医薬化学講座有機化学研究室
帝京大学アジア国際感染症制御研究所 （ADC） **高橋秀依**

私達の研究室は、医薬品の化学構造式に隠れたアトロプ異性を見出すことを主な研究テーマとしています。アトロプ異性（軸不斉）は、ビアリール化合物に代表されるように、立体障害によって単結合の回転が妨げられて生じます。あまり知られていませんが、医薬品の化学構造を構成するアミド結合には、アトロプ異性が存在する可能性があります。もちろん、結合軸の回転が起こるとアトロプ異性は消えてしまいますが、ある程度の立体障害をもつ構造の場合は、回転障壁が高くなり、安定な化合物としてアトロプ異性体を単離することができることがわかってきました。私達は、医薬品候補化合物を創出することをめざし、生物活性が期待されるアトロプ異性体をそれぞれ合成し、その活性を調べています。アトロプ異性を有する生物活性化合物が新薬の開発に役立つことを祈っています。

Hideyo Takahashi
Laboratory of Organic Chemistry
Faculty of Pharma Science, Teikyo University

The main theme of our research group is the elucidation of the atropisomerism in the bioactive compounds facilitating new drug designs and syntheses. Atropisomerism is a kind of chirality that arises from differential substitution around a bond that renders the rotational conformers. Atropisomerism is most commonly recognized in the context of biaryl structures, however, it can also arise in an amide motif, which is one of the most important structures found in drugs. The racemization of atropisomers can occur spontaneously through bond rotation. As such, atropisomers can exist as isolable enantiomers when there is a large degree of hindrance to rotation. We have synthesized atropisomerically stable analogues of drugs to observe differential biological activity. We believe that our studies on atoprisomeric bioactive compounds will lead to providing molecules useful for the development of new drugs.



新任の挨拶

アジア国際感染症制御研究所特任教授　山本友子

本年4月より、アジア国際感染症制御研究所（ADC研究所）の特任教授を務めております山本友子です。私は1972年千葉大学薬学部を卒業後、修士課程に進学し研究をスタートさせました。その後は、北海道大学大学院医学研究科（博士課程大学院生）、千葉大学薬学部（助手）、米国ユタ大学医学部（visiting assistant professor）、千葉大学医学部（非常勤講師）、杏林大学医学部（講師・助教授） を経て、2000年に千葉大学薬学部教授に就任し、微生物薬品化学研究室を主宰しました。この約40年間、主に細菌学領域で研究を続けてきました。2015年3月に定年となりましたが、同年4月からは千葉大学真菌医学研究センターの特任教授として、感染宿主応答ネットワークプロジェクトを推進しております。本年4月からはADC研究所との併任ということになります。私が関わってきた研究は、細菌学の基礎から感染症学に至るまで多岐にわたっていますが、現在は「(1) サルモネラ属細菌の感染と宿主応答　(2) 薬剤耐性菌の耐性機構　(3) 難治性慢性感染症治療薬となるAnti-persister compounds」の3つに絞り、国内外の多くの共同研究者の協力を得て研究を続けております。

21世紀を迎えた今日でもなお、人類は、結核、エイズ、マラリアをはじめとする多くの感染症の脅威に曝されています。さらに薬剤耐性病原体の出現と蔓延等、数多くの新しい問題にも直面しています。1992年にアメリカ大統領府は、感染症への警告を「Emerging and Re-emerging Infectious Diseases」のキーワードをもって公表し、感染症は地球規模の問題であり、その解決には「Global Alert, Global Response」が重要であることを一貫して訴えてきています。さらにG-サイエンス学術会議での共同声明テーマ「病原微生物の薬剤耐性問題：人類への脅威（2013）、感染症と抗菌薬耐性：その脅威と対策（2015）」が示すように、感染症克服は21世紀に持ち越された最大の医学的課題の一つと言っても過言ではないでしょう。このような中で「世界的視野に立った感染症制御に関わる研究・教育活動」を推進するADC研究所の果たす役割は大きいものと言えます。私は、これまでの細菌感染症と薬剤耐性菌の研究経験を基に「Global Antibiotic Resistance」の克服に貢献していきたいと考えております。

Inauguration Address

Tomoko Yamamoto
Asia International Institute of Infectious Disease Control, Teikyo University

I have joined the research team in Asian International Institute of Infectious Disease Control (ADC Institute) as research professor in April 2016. I am a graduate of Chiba University Faculty of Pharmaceutical Sciences, in 1972. I was awarded a Ph.D. in Pharmaceutical Science, Kyushu University in 1981 and another Ph.D. in Medicine, Tokyo University in 1991. I served as assistant professor in Chiba University Faculty of Pharmaceutical Sciences, visiting assistant professor in University of Utah College of Medicine, associate professor in Kyorin University School of Medicine, and full professor in Chiba University Graduate School of Pharmaceutical Sciences. I retired in March 2015 and joined Chiba University Medical Mycology Research Center (MMRC) as research professor. At present, I serve as research professor in both ADC Institute and MMRC. For many years, my research has been in various fields; bacterial infections, antibiotic resistance, molecular chaperone and AAA^+ protease. My current research topics include: (i) molecular mechanism of *Salmonella* infection and host response, (ii) mechanism of bacterial resistance to antibiotics, and (iii) anti-persister compounds as a new class of antibiotics to treat chronic infections.

Even in the 21st century, human beings are threatened by large infectious diseases such as Tuberculosis, AIDS and Malaria. In addition, we have been challenged by the increase of drug resistance in infectious agents. In 1992, the Executive Office of the President of USA warned us of a treat of infectious diseases with a key word "Emerging and Re-emerging Infectious Diseases" and has been taking a strong stand for that the comprehensive strategy with "Global Alert and Global Response" is needed to combat the threats. In 2013, G8 ministers released a joint statement "Drug Resistance in Infectious Agents: A Global Threat to Humanity". In 2015, G7-Science Academies Statement "Antimicrobial Resistance: Threats and Necessary Action" was also released. These emphasize that the infectious diseases continue to pose a serious international threats and tackling the threats is major health security challenge of the 21st century. In the current situation, the ADC Institute that globally conducts the research and education on the control of infectious diseases plays an important role on combating the global threat to humanity and I will address the problem "Global Antimicrobial Resistance of Pathogenic Bacteria" throughout my research career.

Report-1

結核終息戦略達成のための研究

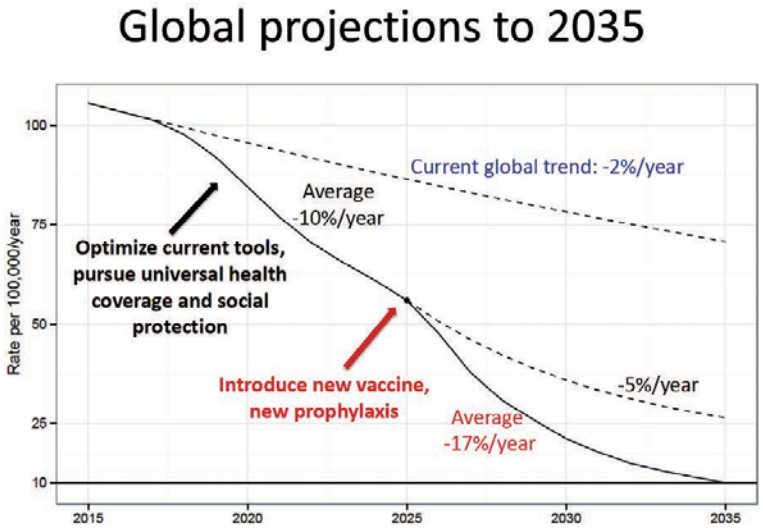
公益財団法人結核予防会結核研究所　加藤誠也

世界保健機関（WHO）は2014年5月に結核終息戦略を発表した。この戦略の2035年までの目標は極めて野心的である。すなわち、1）2015年に比較して結核死を95%減少させること、2）2015年に比較して結核罹患率を90%減少させること、3）結核に起因する壊滅的な費用負担を強いられる家庭をなくすこと。これらの目標達成のために次の三本柱が設定された。1）患者中心の結核医療と予防、2）骨太の政策と支援システム、3）研究と革新の強化。結核の世界戦略の中に研究の役割が位置づけられたのは初めてであるが、その背景は以下のとおりである。

現状の世界の結核罹患率は図に示したように、年率2%程度低下しているが、これでは新しい目標の達成には小さすぎる。そのために、新戦略は2025年までは、現存する技術の最適化、universal health coverageと社会保障を進めることによって、年率10%の罹患率減少達成を目標としている。これは20世紀における先進国の経験に基づいている。日本は1950年代後半から1980年までの20年以上にわたって、約10%の罹患率減少を達成した。これは結核対策の歴史の中でも輝かしい記録である。この罹患率低下に貢献した要因は、結核予防法に基づくしっかりとした政策、社会経済状況全般の改善等がある。しかし、その要因のどのような要素が結核負担の低減に有効であったかは明確になっていない。それらを明らかにすることは、先進国の経験をそれぞれの高まん延国の状況に応じて活用するために貢献するであろう。私たちは、世界の結核対策に貢献するために、自らの歴史を振り返り研究する必要がある。

2025年以降の10年間は、新しいワクチンと新しい発病予防法の導入によって、年率17%の罹患率減少が期待されている。BCGは特に小児における活動性結核の予防に役立っているが、新しいワクチンは既に感染している人たちの活動結核発病を防ぐことも期待されている。なぜなら、WHOの推計によると世界人口の三分の一すなわち約20億人が既に結核に感染しており、目標達成のためには、既に感染している人たちの予防は必須である。

また、高リスク集団に広く使用できるより効果的で安全な発病予防法の開発も必須である。今のところ、新しいワクチンも発病予防法も有望なものは聞いていない。基礎科学の革新的な発見が画期的な製品開発に道を開くかもしれない。有望なワクチンや発病予防法のみならず、周辺の技術開発も求められる。例えば、予防的介入法の開発には、予防効率のデータを得るために2年以上の経過観察を必要とするため、長い期間がかかる。従って、活動性の病気への進展を評価できるよいバイオマーカーが開発されると、予防的介入法の効率を証明する時間の短縮の一助となる。このように世界の結核関係者は研究と革新の強化によって結核終息戦略の目標達成の道を切り開くため協働する必要がある。



Seiya Kato MD. PhD
Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association

World Health Organization (WHO) addressed the End TB Strategy in May 2014. The targets of the strategy by 2035 are very ambitious: 1) 95% reduction in deaths due to TB (compared with 2015), 2) 90% reduction in TB incidence rate (compared with 2015), 3) No affected families face catastrophic costs due to TB. In order to attain these targets, three pillars were set up: 1) Integrated, patient-centered TB care and prevention, 2) Bold policies and supportive systems, 3) Intensified research and innovation. This is the first time that role of research is listed up in global TB strategy. The background is as follows;

As is shown in the figure on the right, currently global trend of incidence shows only 2% decline, which is too small to attain the new target. So the strategy aims for attain 10% reduction of incidence up to by 2025 by optimizing current tools, pursuing universal health coverage and social protection.

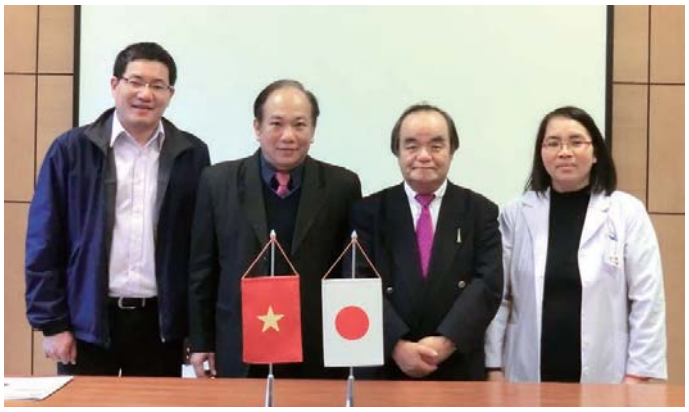
This is based on experiences in developed countries during the 20th century. Japan achieved approximately 10% decline over a period of more than 20 years, from late 1950's to 1980, which is an outstanding record in the history of TB control. The factors contributing to the decline in Japan were implementation of robust policies based on TB control law, overall improvement of socio-economic condition etc. However it is not clear what components of the factors really worked to reduce the TB burden. Clarifying them will contribute to utilizing the experiences of developed countries in the context of respective high burden countries. We have to review and study our history to contribute to the global TB control.

In the following 10 years from 2025, we are expected to attain 17% reduction in incidence annually by introducing new vaccine and new prophylaxis. BCG works to prevent active TB especially in children. The new vaccine is expected to prevent active disease from already existing infected population as well. It is because one third of global population, i.e. 2 billion people, have already been infected with TB according to the WHO estimate and. control of the infected population is necessary to attain the target. It is also crucial to develop more effective and safe prophylaxis, which can be widely used for high risk group. So far, we have not heard of promising candidates for new vaccine or prophylaxis. Innovative discovery in basic science may lead to development of revolutionary product. Not only candidate vaccine or prophylaxis but also adjacent technology is required. For example, it takes a long period of time to develop preventive intervention as it needs more than 2 years of observation to obtain data on the preventive efficacy. So developing good biomarker that can estimate active disease progression will help to shorten time to prove the efficacy of the preventive intervention. Likewise, Global TB community has to work together to find the way for attaining the target of the END TB Strategy by intensifying research and innovation.

公益財団法人結核予防会　結核研究所
The Research Institute of Tuberculosis

Report-2

National Pediatrics Hospital, Hanoi, Vietnam



2015 年度のプロジェクト成果打ち合わせ（インフルエンザチーム）

Discussion about Project Progress Report of 2015 FY (Flu Team)

2016.2.25-3.2

2015 年度のプロジェクト成果打ち合わせを行った（インフルエンザチーム）
Discussion about Project Progress Report of 2015 FY (Flu Team)
From Left: Drs. Phuc, Hai, Suzuki, Thuy

2016 年度のプロジェクト計画打ち合わせ（インフルエンザチーム）

Discussion about Project Plan for 2016 FY (Flu Team) with Drs. Hai, Dien, Thuy Phuc and Other Members 2016.5.2-6

関連事項 Implicated Topics

ハノイ医科大学との単位互換協定の内諾

Agreement for Academic Exchange and Cooperation between Hanoi Medical University, Vietnam and Teikyo University, Japan

国立小児病院：新病棟内新ラボ設置計画助言

Advice to Set Up New Laboratories in NCH

Report-3

Research Institute of Tropical Medicine (RITM), Philippines

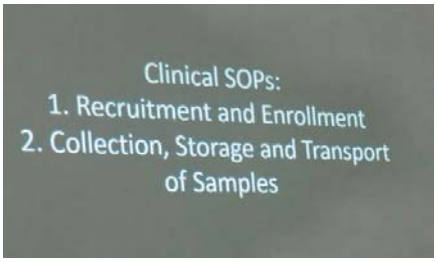
RITM にて 2015FY のまとめと 2016FY の準備

2016.2.29

2015 年度のプロジェクト成果と 2016 年度の計画について打ち合わせを行った
（インフルエンザチーム）

Discussion about Project Progress Report of 2015 FY and Plan of 2016 FY (Flu Team)

Drs. M. Jiz, E. Segubre-Mercado, J. Jesus, V. Dulalia, L. Nillos K. Suzuki, M. Lucero, S. Gachalian at RITM



フィリピン大学（医科大学、科学大学）との単位互換協定の内諾

Agreement for Academic Exchange and Cooperation between Philippines University (Medical University and Science University), Philippines and Teikyo University, Japan

2016.3.1

Agreement for Academic Exchange and Cooperation between Philippines Medical University, Philippines and Teikyo University, Japan

Drs. S. Gachalian, A. Majia (Dean), K. Suzuki, M. Lucero at Philippines Medical University

Drs. Bascos, Suzuki, Balmaceda (Dean) at Philippines Science University

Lecture at Genetic Institute

At office of Society of Pediatrics, Philippines

Report-4 e-ASIA Project Annual Meeting

RITM, Philippines 2016.6.23

RITM Members

1. Marilla G. Lucero
2. Salvacion R. Gatchalian
3. Joanne Dejesus
4. Edelwisa Segubre-Mercado
5. Maril Jiz
6. Vernoni E. Dulalia
7. Leilani T. Nillos
8. Diana May Ocampo
9. Catherine Tupas
10. Jobel San Pedro
11. Camille Culong

ADC, Teikyo University
Kazuo Suzuki

National Children's Hospital, Hanoi, Vietnam 2016.6.24

STEERING COMMITTEE RECORD

2015年度ADC運営委員会記録

1. 病院長あいさつ　帝京大学附属病院長　藤森　新
   ADC研究所ができて3年目を迎える。その間にシンポジウムの開催やADC Letterの発行や留学生を受入れて、活発に活動している。かつて当病院ではAcinetobacterの感染でアウトブレイクがあったが、今は感染症のパイオニアになった。
2. 平成27年度事業報告
   1）研究所の現状報告：1年間のイベント一覧の説明
   2）さくらサイエンスプラン：附属病院との連携、結核研究所との連携
   3）国際シンポジウム：大阪大学木村英作教授によるアフリカの医療事情の講演
   4）バイオセーフティ講習会：日本語で1回、英語で1回
   5）ADC Letter：Vol.2発行。日英併記。アジアの国からの論文投稿がしやすいようにする。国会図書館、ISSN、J-STAGEに登録した。
3. 平成27年度事業報告の承認：出席15名、委任状16名（運営委員数35名）
4. 平成28年度事業計画
   1）27年度に続き、e-ASIAの継続。最終年の全体会議をマニラで行う。
   2）28年度さくらサイエンスプランに応募した。ベトナムから2名の参加希望がある。
   3）帝京大学アジア研修プログラムとして、医学部5年生7人がベトナムで研修をする。
   4）帝京大学創立50周年記念国際シンポジウムにはADC研からもguest speakerを招聘する。
5. 平成28年度事業計画案が承認された。出席15名、委任状16名（運営委員数35名）

European Vasculitis Society-Annual Meeting 2016

2016.6.17

Leiden University Medical Centre, The Netherlands

Prof. Kazuo Suzuki presented.

AGENDA

09:00	**EUVAS Annual General Meeting**	
09:15	**EUVAS Plenary Meeting – Petal updates**	
	Genetics	Augusto Vaglio
	Registries	Mark Little
	Database	Kerstin Westman
	Clinical Trials	Alan Salama / David Jayne
	Serumbank (ANCA testing)	Marten Segelmark
	Serumbank (biomarkers)	Marten Segelmark
	Histopathology	Ingeborg Bajema/Emma v. Daalen
12:00	**Lunch - Naturalis Museum** (next door to LUMC)	
13:00	**Topics**	
	EULAR/ERA-EDTA/EUVAS guidelines	David Jayne
	European Reference Networks	Mark Little
	An AAV patient reported outcome	Alfred Mahr
	Hydroxychloroquine in AAV	Alina Casian
	IDES in anti-GBM	Marten Segelmark
	Clinical trials (industry)	David Jayne
	Clinical trials (EUVAS)	David Jayne
	Invitation to Tokyo 2017	Kazuo Suzuki
	Anti-moesin in vasculitis in dermatology	Kazuo Suzuki
	Future meetings	
16:00	**Close**	

SPECIAL REPORT

低線量放射線の影響：福島から何を学ぶ

宇野賀津子
公益財団法人　ルイ・パストゥール医学研究センター

The Real Effects of Low-dose Radiation: Lessons from Fukushima accident

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Louis Pasteur Center for Medical Research

Abstract

The March 2011 nuclear incident in Fukushima, led to severe concerns about radiation contamination. To alleviate the fears among residents my colleagues and I started to provide scientific information about the real effects of how low-dose radiation affects humans. I explained that most effects of low dose radiation result from not only direct radiation exposure but also the effects from broken water derived radicals, such as oxygen radicals that are regularly produced by respiration. Although radiation contamination was not ignored, there are other critical lifestyle factors that may increase the risk of cancer in Fukushima residents including obesity, stress, lack of exercise and poor diet. I said that a comprehensive risk evaluation is required! Additionally, we must pay attention that high mortality, due to initial evacuation suggests that evacuation of the elderly was not the best life-saving strategy for the nuclear disaster. Careful consideration of the relative risks of radiation exposure and the risks and benefits of evacuation is essential.

Low dose radiation, Crisis communication, Oxygen radical, Repair system, Anti-oxidant foods

抄録

2011年3月11日の地震、津波に端を発した福島第一原発事故は、福島に多大の放射能汚染をもたらした。その放射能汚染の健康影響に対する評価は研究者間でも大きく異なり、住民は混乱した。このことは、原発事故がある程度落ち着いた2011年夏以降も、県外避難者が増え続けたことからも明らかである。ここでは低線量放射線の健康影響をめぐる混乱と、その対処法、特に高齢者や病人の原子力災害時における避難のあり方について考察する。

1. はじめに

3.11以降、放射線はたとえ少量でも生体影響があるので、極力浴びないほうが良いとの考えを元に、低線量放射線の影響が語られた。特に原爆反対運動の先頭に立った物理系学者は、少しでも影響があると低線量放射線の影響を語った。一方、医学・生物系では医療の場で使われている放射線・生体が日常的に浴びている放射線量と比較して、この程度は大丈夫との意見が多かった。特に生物・医学系では、2000年以降に研究が進んだ遺伝子が傷ついた時になされる、生体の修復機構に関する認識があったことも大きい。筆者は、人の免疫機能の研究者として、がんの再発を防ぐライフスタイルの研究などにも取り組んできた経験から、恐怖で免疫機能が低下する方が、わずかに高い放射線量の影響よりも、がんリスクをあげると考えた。この考えは、今にいたるまで基本的には変わっていない。

2. クライシスコミュニケーション

a. フェーズの定義：クライシスのフェーズを分けて考えることは大事である。

1. 平時の緊急対応（リスクコミュニケーション）
2. 緊急時（クライシスコミュニケーション）
3. 復興期（ポストクライシスコミュニケーション）

それぞれの時期に応じたコミュニケーションの方策がある。特に今回の福島事故に関してのクライシスコミュニケーションは必ずしも成功したとは言えないと考える。特に、1ヶ月後に飯館村避難となったのは、政府への信頼を失墜させたと、私自身は考えている。これがもっと早い段階で、米軍やスピーディの結果を反映させて決めることが出来ていたならば結果は違っていただろうと思っている。

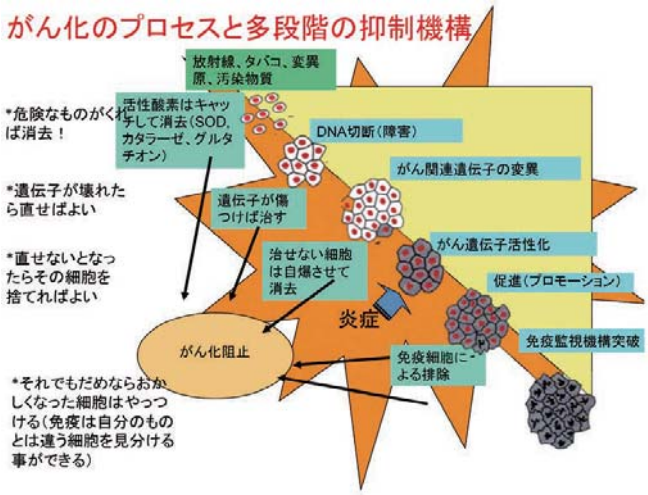
b. 過大に語るのが正義か

もともと放射線の被ばく線量と影響の間には、しきい値がなく直線的な関係が成り立つという考え方のLNT仮説は国際放射線防護委員会（ICRP）でも、「この仮説は放射線管理の目的のためにのみ用いるべきであり、すでに起こ

ったわずかな線量の被曝についてのリスクを評価するために用いるのは適切ではない」としていた。放射線防護の立場からは、安全側に判断しようという趣旨の産物である。ところがこれが事故後ひとりあるきしてしまった。さらに放射線健康影響の専門家でもない研究者（と称するひと）が、子供への影響は数十倍といったものだから、特に母親層に多大の不安を与えた。

私自身は長年のがん患者の免疫機能の測定経験から、事故直後から、現時点では福島事故で放出された放射線の影響より、放射線に対する過剰な恐怖による免疫機能低下の方が、がんリスクを上昇させると考えていた。研究者の一部には、少しでもリスクが有るなら言うのが正義だとの意見もあったが、多くの人の反応を見たとき、クライシス時には現実からかけ離れたオーバーな表現は、返って別のリスクを上昇させると考えた。

その後放射線発がんについて調べる中で、低線量放射線の影響のかなりの部分が体内の水分子にあたって出来た活性酸素によること、傷ついた遺伝子の大部分は修復されていること、その結果、低線量放射線の場合、多くの傷は治してしまうこと、直しきれないと判断するとアポトーシスに至ることも多い事を確認した。さらには免疫機構による変異細胞の排除を含め、何段階ものがんを抑制する監視機構を持っていることをきちっと説明すべきだと考えた。事故後出た本の中には、放射線で遺伝子が傷つくと、それが蓄積してがんになる等と説明する物理学者がいたりして、これを信じている人が多数いた。そこで、リスクコミュニケーションの立場からは、がん化を抑制する生体の持っているシステムを強化することを提案すべきだと考えた。特に、ポストクライシス期においては、1日でも早く回復に向かえるように、前向きな提案が必要と考えた。



実際に広島長崎の被爆者研究などからも、食生活の有り様はその後のがんリスクに影響することが明らかにされていたので、機能性野菜や果物胚芽成分の摂取、動物性脂肪・蛋白質、塩分制限を推奨したアメリカのデザイナー・フーズ計画を「低線量放射線の影響を克服する食事として有用」ということで紹介した。これは、私自身がんの再発を予防する食事ということで、それまでに調べてきた経緯もあった。2012年からは、食品の放射能汚染も心配したよりも軽微であったことから、以降はがん・成人病を予防する食事として紹介している。さらには、福島には有数の農業県である。実際、食品の汚染検査でも、福島の食品の汚染は、線量から予想されるレベルと比較すると、意外と軽微であった。これは福島の土が粘土質であったことも幸いしているが、福島の農業関係者の努力の賜でもある。ポストクライシスに於いては前向きな提案が必要と考え、同じ農業県でもあり、日本一の長寿県である長野県の取り組み、「予防に重点をおいた地域の自主的な健康作り運動」を学ぼうと提案した。放射線量を量って大丈夫な野菜はしっかり食べよう！と提案、イソジンうがい液を使った食品の抗酸化能を時間する実験と組み合わせてお話する中で、一定の理解をえることができたと考える[1)]。

3. 原子力事故時の避難弱者対策

福島では岩手、宮城の被災3県のなかで、避難関連死が圧倒的に高く、今では地震・津波関連死を上回っている。実際避難命令がでると、多くの老人ホームでは、入居者を手配されたバスに乗せ、避難先に移動した。寝たきりの方も、バスに乗せたという。そして移動途中、移動先で多くの方が亡くなった。特に避難先を2カ所以上移動したケースでは、結果は悲惨であった[2)]。私は日本赤十字社の「原子力災害における赤十字活動ガイドライン」作成の委員の一人として、避難弱者対策については特に密に議論した[3)]。その結果、原子力災害時においては、爆発などの直接の被害がなく、鉄筋コンクリートの建物内で線量が低い場合には、慌てて逃げないで避難先や避難体制が整ってから避難する方が、被害は最小限に抑えられることを確認した。いずれにしても、地域の線量判断や、交通事情など総合的なリスク判断が必要と考えられる。特に、医療者におかれては線量計で線量を確認しつつ、患者およびそれを支えるスタッフの総合的なリスクを考えた、その時々の対策・判断が求められる。

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Severe acute respiratory distress syndrome induced by influenza compared with other viral infections and effects of intravenous immunoglobulin infusion therapy in Vietnamese children

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Received June 1, 2016; **Revised** June 24, 2016;
Accepted June 27, 2016

Abstract

Acute respiratory distress syndrome (ARDS) associated with A(H5N1) avian influenza virus infection develops severe ARDS, and also other types of influenza among children. It is an urgent mission to elucidate the mechanism of influenza-associated ARDS and to develop a therapeutic strategy. For this purpose, we have been co-operating the prospective study for severe ARDS with National Hospital of Pediatrics–Hanoi (NHP-Hanoi) from October 2007. During 2007/10 to 2013/03, 102 patients were diagnosed as severe ARDS matched in the criteria of prospective study. Among them, influenza viruses were detected from tracheal lavage fluid and/or nasopharyngeal aspirate (NPA/TLF) samples with PCR in 8 cases; A(H5N1), A(H1N1)pdm09, A(H3N2). These 8 cases and 9 cases of severe ARDS with A(H5N1) infection before 2007/10 were considered as influenza group together. During 2007/10 to 2013/03, other viruses were detected in 22 severe ARDS cases (not-influenza group): CMV, HRV, ADV, RSV and Measles. When the clinical data were analyzed in 17 influenza group and 22 not-influenza group respectively, significant differences were observed in pH and $PaCO_2$ in arterial blood gas analysis (ABGA) and also AST/ALT values, white blood cells and platelets counts in the serum. Survival probability analysis showed the significant differences between the groups (p=0.0023 by log-lank test, p=0.0013 by Wilcoxon test) resulting longer survival days in not-influenza group. In addition, intravenous immunoglobulin infusion (IVIG) treatment showed difference in survival profile of patients especially in influenza-associated ARDS, suggesting that the IVIG therapy may be effective against severe ARDS with pneumonia. Our results will provide the crucial clinical information.

Keywords: acute respiratory distress syndrome (ARDS); children; Influenza viral infection; IVIG therapy; survival probability

Abbreviations used

ADV: adenovirus, ARDS: acute respiratory distress syndrome, AST: aspartate amino transferase, ALT: alanine transaminase, CMV: cytomegalovirus, CRP: C-reactive protein, HRV: human rhinovirus, IVIG: intravenous immunoglobulin infusion, LDH: lactate dehydrogenase, MOH: ministry of health, PICU: pediatric intensive care unit, PLT: platelet, PT: prothrombin time, RBC: red blood cell, RSV: respiratory syncytial virus, TLF/NPA: tracheal lavage fluid and/or nasopharyngeal aspirate samples, WBC: white blood cell

Introduction

The pediatric acute respiratory distress syndrome (ARDS) remains one of the most important severe diseases in pediatric intensive care, which still has high mortality rate in nowadays. ARDS is a prime example of a disease that affects both children and adults, although ARDS occurs with less frequency in children than in adults[1)] and the risk factors and pathophysiology of ARDS are similar in both adults and children[2)]. The most common trigger of ARDS is infectious disease, most commonly in the lower respiratory tract, that is pneumonia[3,4)]. However, the severity of ARDS is sometimes different according to the kinds of infections. Avian influenza A(H5N1) viral pneumonia is one of the typical infectious diseases which induces severe ARDS with low survivability[5)]. The primary influenza viral pneumonia, which occurs in avian A(H5N1) influenza, often leads the patients to severe ARDS. On the other hands, the main complication of seasonal influenza virus infection is upper airway infection, which sometimes occurs together with, or is followed by, bacterial pneumonia and ARDS. In Vietnam, there might be some ARDS trigger of viral infections, which rarely exist in the other area, such as avian influenza

A(H5N1) pneumonia. Thus the surveillance prospective and retrospective study has been planed and held with pediatric intensive care unit (PICU) in National Hospital of Pediatrics, Hanoi (NHP-Hanoi, Vietnam).

We here showed the difference of the mortality between severe ARDS induced by influenza and other viral infection, and the efficacy of high dose γ globulin infusion (IVIG) treatment for the severe ARDS as anti-inflammatory therapy.

Materials and Methods

Data source and study design

Prospective study: After permission of Ethical Committee in NHP-Hanoi (ref. no. NHP-RICH-07-001, 2007/9/30) and MOH-Vietnam (Ministry of Health, Vietnam), the study had started in pediatric intensive care unit (PICU) of NHP-Hanoi from 1st October 2007 until the end of March 2013. Written informed consent was obtained from the parents of each patient, according to the study protocol. The entry criteria of the patients in the prospective study are as follows; 1. The patients who admitted the PICU-NHP with ARDS under intra-pulmonary reason (pneumonia), and needed mechanical ventilation. 2. The patients aged over one month. 3. The P/F ratio (PaO_2/FIO_2 ratio) ≤ 100 mmHg in arterial blood gas analysis during the stay in the PICU. ARDS was diagnosed according to American European Consensus Conference (AECC) criteria (1994). The AECC ALI and ARDS criteria are used most commonly to diagnose ALI and ARDS in adults and children, utilizing four clinical parameters: a) acute onset; b) severe arterial hypoxemia resistant to oxygen therapy alone (PaO_2/FIO_2 ratio ≤200 mmHg (≤26.6 kPa) for ARDS and PaO_2/FIO_2 ratio ≤300 mmHg (≤40 kPa) for ALI); c) diffuse pulmonary inflammation (bilateral infiltrates on chest radiograph); and d) no evidence of left atrial hypertension[6]. Because our study had been conducted since 2007 and the study protocol had made in 2006, we do not use the Berlin Definition as ARDS definition in our study[7]. However, we use 'severe ARDS' as 'ARDS with P/F ratio under 100 (the Berlin Definition)' in this manuscript. Serum, and TLF/NPA samples were collected on admission to PICU-NHP from each patient. Arterial blood gas analysis, cell blood counts and several kinds of chemical serum parameters were examined on admission of PICU. All patients were tracheal intubated and mechanical respiratory support was performed basically with the National Institutes of Health ARDS Clinical Trials Network (ARDS Net) ventilator management protocol for adults (http://www.ardsnet.org/) as a PaO_2 target of 55 to 80 mmHg (7.3 to 10.7 kPa) (SpO_2 target 88%-95%) according to the AECC strategy (1998)[8].

This study was designed as observational study (not interventional study), thus treatments for the patents were decided as same as possible among the patients with Vietnam side clinicians. Therefore, primary endpoint of the study was the time of discharge from PICU in alive without artificial respiratory support or in dead. We followed all patients up to the Hospital discharge, and confirmed that all survived patients had discharged from hospital healthy without respiratory failure.

Retrospective study for avian A (H5N1) influenza: Before 2007, we have ten avian A(H5N1) influenza cases in NHP-Hanoi, which we reported before (*J Infect Dis* 2009)[5]. We had been able to collect the same data and samples (TLF/NPA) of the prospective study of those ten cases and confirmed nine cases among ten matched in the criteria of above prospective study as severe ARDS. Thus we had 9 cases of avian influenza A(H5N1) infection induced severe ARDS.

Viral genome detection

Influenza type A and B were detected by rapid influenza detection Kit (Mizuho Medie, Tokyo, Japan) from TLF/NPA samples of each patient. Then influenza viral genomes of the type A including A(H5N1), A(H1N1)pdm09, A(H3N2) and type B were examined by RT-PCR method with viral detection primers in each patients. Additionally, in case that a clinician decided to detect other viral genomes, it was able to examine following viral genomes by PCR or RT-PCR method with viral detection primers; HRV, ADV, RSV, Measles, and CMV. All examinations above had been performed by NHP biological laboratory.

Treatment design

In this study, the antibiotics were used for bacterial infection according to the sensitivity analysis after the pathogen of pneumonia was decided by PCR. When CMV, or influenza viral genome was identified, gancicrovir, or ocertamivir was administrated, respectively. The prophylactic use of antibiotics was also performed according to the standard formula.

The AECC-1998 and the ARDS Network study had not recommended the steroid administration for ARDS/ALI patients both in the acute phase nor the chronic phase of ARDS in adults[9,10]. Also World Health Organization (WHO) treatment strategy in the Avian Influenza A(H5N1)infection[11] had neither recommended steroid use. Based on these recommendations, steroid was not selected in this study. Instead, a intravenous immunoglobulin therapy for sever ARDS, two grams/kg IVIG therapy against the ARDS was performed. The following infusion protocol of immunoglobulin is employed as 1 gram/kg/day for 1 hour in two days, one or two days after admission to PICU-NHP. Because ethically randomized control study is difficult, this study was planned as observational study. Thus the IVIG therapy in this study was planned to do for all patients within criteria. Finally the patient's parents had decided either perform the IVIG therapy or not, mainly according to their financial support, not depends on the clinician's decision.

Statistics

Statistical methods

Fisher's exact test was employed for bivariate analysis of categorical data. The nonparametric Mann-Whitney test was used for two-group comparisons of continuous data. Survival curves and rates were calculated by the Kaplan-Meier method. The log rank (Mantel-Cox) test was used for the comparison of two survival curves. All statistical analyses were done with SPSS software (version 14.0).

Role of the funding source

S.K. reviewed the clinical data, which were provided by L.T.N., director of NHP, who had full access to the data, in an anonymous format suitable for the purposes of the study. T.T.B.P., L.T.N., K.S., H.N., and S.K. made the final decision for this publication.

Results

One hundred-two of 106 patients enrolled in the prospective study were diagnosed as severe ARDS matched in the criteria and 4 cases were dropped out from the study because the P/F ratio of these 4 cases did not become ≤ 100 during the stay in PICU-NHP. And 9 cases were enrolled from retrospective study, as mentioned before. The mortality rate of 102 severe ARDS cases (P/F ≤ 100) at PICU of NHP-Hanoi is 47%.

Viral genome detection

In 30 patients among 102 cases in the prospective study, the following viruses were detected from TLF/NPA samples; 8 cases were Influenza viruses: avian influenza A(H5N1) [3 cases], A(H1N1)pdm09 [4 cases], A(H3N2) [1 case] and 22 cases were other viruses: CMV [5 cases], HRV [12 cases], ADV [6 cases], RSV [4 cases], and Measles [1 case]. In some patients double or triple kinds of viral genomes were detected, among them Rhinovirus was most frequently existed. Thus totally 17 cases were enrolled as Influenza-ARDS group (I-group) and 22 cases as not Influenza-ARDS (NI-group) group.

Patient's background and laboratorial examinations

In the patients' background data, differences were observed in gender, age and body weight between I-group and NI-group (I-group: M:F=12:5, age 5.80 ± 3.71 years, weight 16.38 ± 7.41 kg; NI-group: M:F=4:18, age 1.30 ± 3.00 years, weight 4.51 ± 2.03 kg) (table 1). In the Respiratory parameters, significant differences were observed in pH and $PaCO_2$ values of arterial blood gas analysis (ABGA) between the groups. Also blood examination test showed significantly higher AST/ALT values in the serum, and lower white blood cells and platelets counts in the I-group (table 2).

Comparison between I- and NI-group

Survival probability analysis showed the significant differences between the groups (p=0.0023 by log-lank test, p=0.0013 by Wilcoxon test) (figure 1) resulting longer survival days in NI-group (I-group: 13, NI-group: 31 days). Test of equality of survival distributions (Kaplan-Meier method) for the different levels of cause category showed significant difference between groups; Log-lank test: Peto-Peto p = 0.0005, Cochran-Mantel-Haenszel p = 0.0001; Wilcoxon test: Gehan-Breslow p = 0.0003, Peto-Prentice p = 0.0003. Mortality rate was also much higher in I-group than NI-group (I-group: 88%, NI-group 64%).

IVIG therapy in Influenza group

IVIG therapy was performed in 4 patients among 17 patients in I-group, and rest of 13 cases immunoglobulin were not administered during the stay in PICU-NHP with patient's parental decision. No differences were observed in gender, age or body weight between IVIG therapy and no IVIG groups (IVIG (+): M:F=3:1, age 5.35 ± 3.70 years, weight 15.88 ± 7.53 kg; IVIG (−): M:F=9:4, age 5.35 ± 3.70 years, weight 18.00 ± 7.83 kg). Respiratory parameters and blood examination showed also no differences between groups. Significant difference was observed only in survival probability between groups with

Table 1. Difference in background data between I-group and NI-group

	I-group n=17		NI-group n=22		P value
	M or + or D	F or - or A	M or + or D	F or - or A	
Gender	12	5	4	18	0.0012
Age (year)	5.80±3.71		0.39±0.49		0
Weight (kg)	16.38±7.41		4.51±2.30		0
P/F ≤ 100 on admission	13	4	19	3	0.4247
Prognosis	15 (88%)	2	14 (64%)	8	0.0811
MODS	8	9	14	8	0.3005
BT onset	38.85±0.77		37.28±0.86		0
Days onset	12.71±5.29		26.00±12.48		0.0006

Table 2. Difference in arterial gas analysis and blood examination data between I-group and NI-group

	I-group n=17	NI-group n=22	P value
pH	7.43±0.11	7.29±0.10	0.0004
PaO_2	61.96±49.39	52.12±16.35	0.8762
$PaCO_2$	34.87±12.94	58.02±17.03	0.0001
FiO_2	0.86±0.25	0.89±0.21	0.9853
P/F	96.45±137.36	64.58±32.36	0.9543
P/F lowest	39.18±18.80	44.27±21.89	0.5515
AST	1943.75±3510.36	188.24±248.58	0.0015
ALT	741.29±1406.39	139.84±400.27	0.0174
LDH	1615.09±854.76	1170.92±1003.37	0.1427
WBC	4526±3746	14575±7382	0
RBC	3730±1103	3822±1018	0.5946
PLT	141.69±61.30	350.05±109.23	0
CRP	6.39±10.26	4.13±6.52	0.4992
PT	76.50±33.81	79.54±21.78	0.8262

Kaplan-Meier method (Log-lank test: Peto-Peto p=0.0360, Cochran-Mantel-Haenszel p=0.0104; Wilcoxon test: Gehan-Breslow p=0.0409, Peto-Prentice p=0.0467) between IVIG (+) and IVIG (-) groups (figure 2) resulting in the longer survival time (days) (IVIG (+): 20.5 vs. IVIG (-): 11.0 days).

Discussion

In our study, totally 102 cases were diagnosed as severe ARDS matched in the criteria and 9 cases were enrolled from retrospective study, as mentioned before[5]. In 30 patients among 102 cases in the prospective study, 8 cases were influenza viruses and 22 cases were other viruses. We analyzed totally 39 cases of viral infection related severe ARDS cases. Among them, 17 cases were enrolled as Influenza-ARDS group (I-group) and 22 cases as not Influenza-ARDS (NI-group) group. The survival probability analysis showed more than twice longer survival days in NI-group, which indicated that influenza virus infection might be one of the factors of severity in pediatric ARDS (Figure 1).

In the patients' background data, differences were observed in gender, age and body weight between I-group and NI-group. The A/H5N1 cases that induced severe ARDS in NHP-Hanoi were elder compared to the other severe ARDS patients[5]. This might be the reason that both age and weight were higher in I-group. Blood examination test showed significantly higher AST/ALT values in the serum, and lower white blood cells and platelets counts in I-group (table 2). These results also reflect the influence of the number of A/H5N1 cases in I-group, because the elevation of serum aminotransferases, leukopenia and thrombocytopenia are relatively common features in H5N1 patients[5,12].

In the Respiratory parameters, $PaCO_2$ values of arterial blood gas analysis (ABGA) was higher in NI-group on admission, consequently pH values showed acidosis in NI-group. The lower $PaCO_2$ values indicated that the ventilation capacity was higher in I-group than in NI-group, however oxygenation capacity failed similarly in both groups (PaO_2 had no significant difference). This fact might come from the differences of mechanism developing ARDS. In influenza induced ARDS, it is pointed out that the influenza viruses infected into epithelial cells and destroy the alveolar directly[13]. Because the diffusion capacity of carbon dioxide through the alveolar epithelium is twenty times higher than that of oxygenation capacity[14], once alveolar membrane destroyed by influenza viral infection to alveolar epithelial cells, oxygenation failure occurs first then carbon dioxide retention gradually develops depend on the areas of destroyed alveolar membrane. Thus influenza induced ARDS patients might be less severe in respiratory parameters on PICU admission, then respiratory failure rapidly progressed to die. Survival probability analysis showed the significant differences between the groups (p=0.0023 by log-lank test, p=0.0013 by Wilcoxon test) (figure 1) resulting longer survival days in not-influenza group (I-group: 13, NI-group: 31 days).

Among viral infected pneumonia, influenza virus might be more severe pathogen for ARDS (Table 1). Severity of the Avian influenza A(H5N1) was discussed as followings; 1) NS1 gene of H5N1 influenza virus is suspected to play an important role on the severity of the diseases[15]. The RNA binding domain of influenza A virus NS1 protein affects secretion of tumor necrosis factor α, interleukin-6, and interferon in primary murine tracheal epithelial cells[16]. 2) NS1 and H_2O_2-MPO stimulate chemokine production associated with inflammatory responses. In NS1-transfected cells concentrations of IL-8 and MCP-1 increased associated with MPO concentration[17].

In Vietnam, several viral infections occurred severe ARDS and the mortality rate of ARDS associated with viral infection was high. The mortality rate of 102 cases of severe ARDS cases in this study was 47%, however in the viruses detected cases (I- plus NI -group) it significantly increased to 70%. To our knowledge, the mortality rate by age has not been discussed precisely for pediatric patients with ARDS. The mortality rate among pediatric patients of acute lung injury with a P/F ratio below 100 was reported to be ~35%[18]. The mortality rate of virus not detected cases of NHP-Hanoi in this study is 36.7%, which showed that PICU of NHP-Hanoi made appropriate therapy against the severe ARDS. In the avian influenza A(H5N1) infected pediatric ARDS cases, high mortality rate and the difference of survival curve between not-H5N1 cases has been reported previously[5]. In adults, several studies suggested that the viral infection in patients with pneumonia were frequently requiring ICU admission and might cause severe forms of pneumonia[19,20]. From the Berlin definition, which is the latest definition and statistical study in ARDS, the mortality rate of mild, moderate and severe ARDS are significantly different as 27, 32 and 45%[7]. The definition of severe ARDS is P/F ratio ≤ 100, that is very similar to our study criteria. Thus the overall mortality of 47% in this study thought to be appropriate, although the Berlin definition is not for pediatric patients. And the mortality rate of 70% in viral infected ARDS cases in our study is obviously too high compared to severe ARDS in the Berlin Definition.

The treatment protocol against the inflammation of the lung was controversial. One study for the ARDS with sepsis showed the effectiveness for low-dose methylprednisolone (MP) infusion[21], the available evidence does not support the use of MP in treating early or late ALI/ARDS[8]. The AECC-1998 and the ARDS Network study and the WHO treatment strategy had not recommended the steroid administration for ARDS/ALI patients[9,10] and also in the Avian Influenza A(H5N1) infection[11], respectively. Thus we decided not to use steroid infusion for the patients in this study, instead to choose the administration of immunoglobulin. In our study, significant differences was observed in survival probability between IVIG (+) and IVIG (−) groups (figure 2) resulting in the longer survival time (days) (IVIG (+): 20.5 vs. IVIG (−): 11.0 days). Although our study was not randomized control study of IVIG therapy, still the biases of clinicians were minimum. Our result showed a possibility that the IVIG therapy will be effective against severe ARDS with pneumonia.

Concerning about intravenous immunoglobulin therapy, the 2g/kg IVIG therapy has been established to be a standard anti-inflammatory therapy against the Kawasaki disease[22]. And this IVIG therapy might be one of the strongest therapies against inflammatory diseases and reduces vascular oxidative stress in patients with Kawasaki disease[22]. Thus theoretically, the IVIG therapy could be effective to the severe ARDS.

The limitation of this study is that this study is not etiological study. We had done PCR study of TLF/NPA samples in every

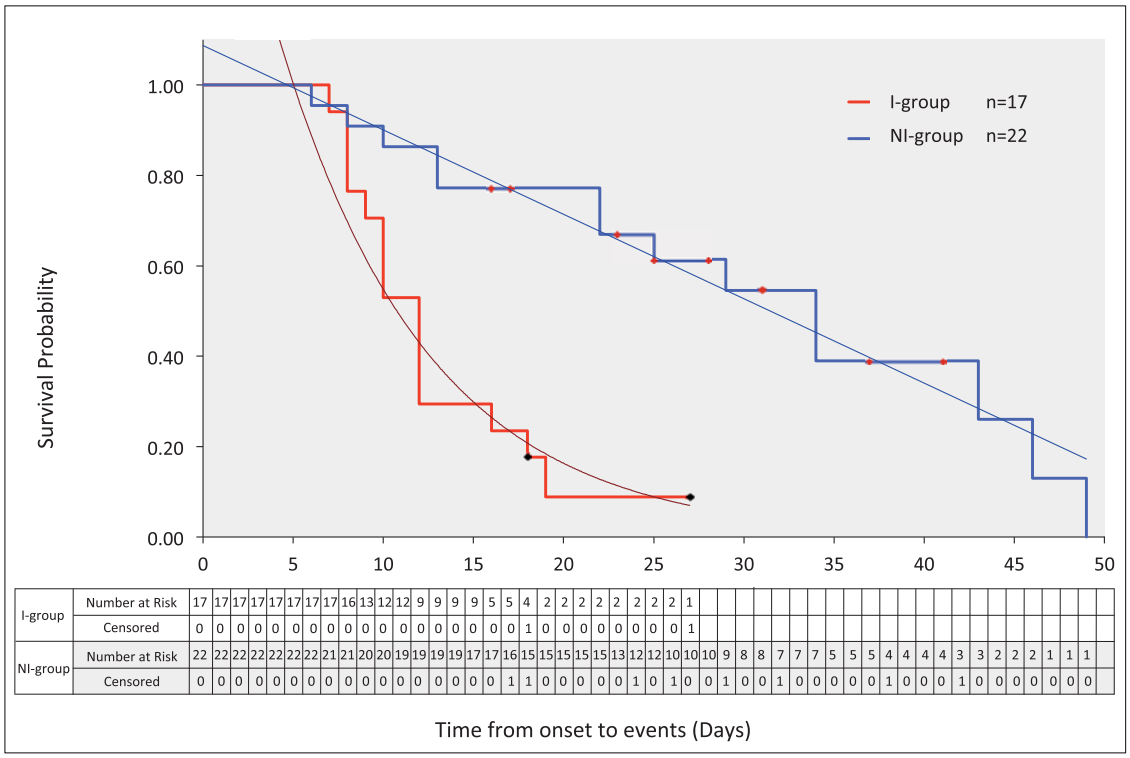

Figure 1. Survival probability curve-of patients infected with influenza virus and non-influenza virus.
Survival time (days) of each group; I-group: n=17/13.00 days, NI-group: n=22/31.143 days. Survival profile was performed with Kaplan-Meier method.

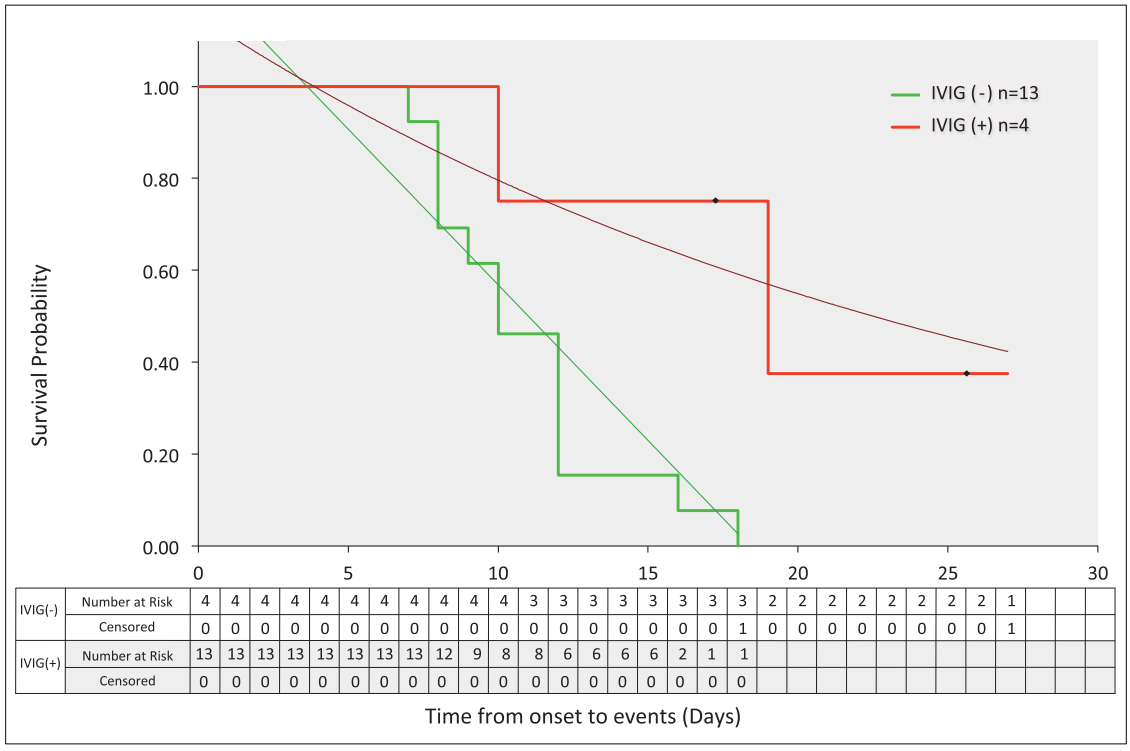

Figure 2. Survival probability curve of patients treatment with IVIG or without IVIG.
Survival time of each group; IVIG(+), n=4, 20.5 days, IVIG(-), n=13 11.0 days.

samples on A(H5N1) influenza virus, but other viral genomes were checked only clinician's decision, thus there might be a possibility that more patients would have the viral infection.

In Vietnam, several viral infections occurred severe ARDS and the mortality rate of ARDS associated with viral infection was very high. Among them in the influenza-associated ARDS, mortality rate was much higher than the others (Influenza: 88%, not Influenza 64%). These results reinforce the importance of further research on the etiology of viral infection induced severe ARDS, especially H5N1 influenza. Our study will pro-

vide the crucial clinical information for development of the strategies of future therapeutic options. There might be a possibility that the IVIG therapy will be effective against sever ARDS with pneumonia.

Acknowledgement

This study was supported by the Health and Labour Sciences Research Grants on Emerging and Re-emerging Infectious Diseases (H22 Shinko-Ippan-014) from the Ministry of Health, Labour and Welfare, Japan and for Scientific Research by the e-ASIA Joint Research Program from Japan Agency for Medical Research and Development, AMED, Japan.

Disclosure

The authors have no financial conflict of interest.

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50th ANNIVERSARY SYMPOSIUM

ADC International Symposium on “Infectious diseases and Host-defense”

Auditorium of Teikyo University
September 16th, Friday, 2016

Organizer:
Prof. Kazuo Suzuki, Director of Asia International Infectious Disease Control (ADC), Teikyo University

Opening Remarks 13:00-13:05

Session I　Infectious Diseases 13:05-15:10

Prof. Takeshi Kurata, NIID, & International University of Health and Welfare, Japan
Chair: Visiting Prof. Shoji Kawachi, ADC and Tomakomai City Hospital, Japan
Associate Prof. Tran Minh Dien, Vice Director of the National Children’s Hospital, Vietnam
Chair: Dr. Thuy Phung, Laboratory Chief, the National Children’s Hospital, Vietnam
Prof. Kiyoshi Kita, Nagasaki University, School of Tropical Medicine and Global Health, Nagasaki, Japan
Chair: Prof. Tomoko Yamamoto, ADC, Tokyo, Japan
Dr. Seiya Kato, Vice Director, Research Institute of Tuberculosis, Tokyo, Japan
Chair: Visiting Prof. Kiyoko Akagawa, Kitasato Institute, Tokyo, Japan

Session II　Host Defense and Vaccination 15:45-17:45

Dr. Stavros Selemidis, Department of Pharmacology, Monash University, Clayton, Australia
Chair: Prof. Yasuo Ono, Teikyo University, Tokyo, Japan
Prof. Pratima Ray, Department of Biotechnology, Faculty of Science, Jamia Hamdard University, India
Chair Prof. Koichi Makimura, Teikyo University, Tokyo, Japan
Prof. Hiroshi Ushijima, Department of Microbiology, Nippon University School of Medicine, Japan
Chair Prof. Masakazu Mimaki, Teikyo University, Tokyo, Japan

Closing Remarks 17:45-18:00

INTERNATIONAL MEETING AND SYMPOSIUM

開催したイベント　（2016.1.1～2016.6.30）

日程	イベント名	演者など
2016年6月24日（金）	e-ASIA Project Meeting	Annual Meeting　Hanoi, Vietnam
2016年6月23日（木）	e-ASIA Project Meeting	Annual Meeting　Manila, Philippines
2016年6月17日（金）	EUVAS Meeting 2016	David Jayne, Ingeborg Bajema, EUVAS members Leiden, The Netherlands
2016年5月10日（火）	危機管理と防災	Kazuo Suzuki　　臨床大講堂
2016年5月2日（月）～5月6日（金）	e-ASIA Project Meeting	Discussion of Project Progress Report of 2016 FY（Flu Team) Hanoi, Vietnam
2016年4月6日（水）13:15～14:45	講義「世界にはばたく医療人」の開始	Kazuo Suzuki, Tomoko Yamamoto, et al　　大学棟306講義室
2016年3月1日（火）	e-ASIA Project Meeting	Agreement for Academic Exchange and Cooperation between Philippines University (Medical University and Science University), Philippines and Teikyo University, Japan Manila, Philippines
2016年2月25日（木）～3月3日（木）	e-ASIA Project Meeting	Discussion of Project Progress Report of 2015 FY（Flu Team) Hanoi, Vietnam
2016年1月14日（木）15:30～18:00	第12回国際シンポジウム「福島原発事故後の危機管理と病院の対応」	1. 宇野賀津子（ルイ・パストゥール医学研究センター・基礎研究部室長） 2. 及川友好（南相馬市立総合病院　副院長） 3. 森田知宏（相馬中央病院 内科） 大学棟104講義室

今後のイベント情報　（2016.7.1～2016.12.31）

日程	イベント名	演者など
2016年11月	バイオセーフティ講習会	ADC　　セミナー室
2016年10月17日（月）～10月18日（火）	e-ASIA Project Meeting	Annual Meeting　　Manila, Philippines
2016年9月21日（水）	危機管理と防災	防災訓練　　臨床大講堂
2016年9月16日（金）13:00～18:00	50th Anniversary Symposium	ADC　　臨床大講堂
2016年8月26日（金）16:00～18:00	医学部5年生ベトナム実習報告会	本部棟2F会議室3および4
2016年8月14日（日）～8月21日（日）	TASP Training for 7 Students (5-year)	NCH-NHP and Hanoi Medical University　　Hanoi, Vietnam
2016年7月5日（火）	内閣官房、厚労省の訪問	ADC Members　　ADC Lab