シンポジウム　１日目

Symposium Day 1

October 4 9:00 ー 18:20

長崎ブリックホール・３階国際会議場

International Ball Room at 3rd floor, Nagasaki Brick Hall

●シンポジウム

S1-01　Forty years of malaria vaccine development: advances and challenges!

Howard Engers
Armauer Hansen Research Institute

Malaria remains among the top ten unmet medical needs with respect to infectious diseases worldwide. Globally, the overwhelming majority of individuals at risk of dying from infection with Plasmodium falciparum malaria are children under five living in Africa. It is estimated that over 1, 000 African children die each day from malaria! Over the past four decades, considerable progress has been made in basic and clinical research related to the development of a malaria vaccine. This research was driven by the early observations that experimental infection of animals or humans with irradiated sporozoites resulted in high levels of protection against challenge with malaria-infected mosquitoes. Subsequently, many new and promising immunological approaches were attempted, ranging from use of synthetic peptides to recombinant proteins to DNA vaccines to whole parasite vaccines. Several novel adjuvants have been tested for the first time in humans paired with candidate malaria antigens. Unfortunately, candidate vaccines tested in clinical trials to date have not provided the desired levels of sustainable protection against natural infection in African children. Indeed, the actual mechanism(s) of immunity required for development of protection in naturally immune individuals remain to be elucidated. Conducting clinical research and malaria vaccine trials in vulnerable populations of healthy volunteers such as infants, children and pregnant women presents considerable ethical as well as scientific and logistical challenges for the scientists, sponsors and stakeholders in question. It will take more basic research, improved global collaboration and a better defined overall strategy in order to produce an effective, affordable malaria vaccine.

S1-02　Traditional Herbal Medicine for the Control of Tropical Diseases

Kesara Na-Bangchang[1)], Juntra Karbwang[2)]
[1)]Chulabhorn International College of Medicine, Thammasat University, Thailand, [2)]Department of Clinical Product Development, Institute of Tropical Medicine (NEKKEN), Nagasaki University

Throughout history, traditional herbal medicine has afforded a rich repository of remedies with diverse chemical structures and bioactivities against several health disorders. A common issue of herbal medicine is the limitation of information on their pharmacological activities and their active constituents. Traditionally, the use of herbal medicine has been based on empirical treatment and passed on from generation to generation with information available only in local journals. This prevents several herbal medicines from being developed to their full potential. The presentation will focus on research and development of Atractylodes lancea (Thunb) DC. (AL: family Compositae) as a potential chemotherapeutic for cholangiocarcinoma (CCA), the bile duct cancer commonly found in Southeast Asia. The dried rhizome of AL is a medicinal plant used in Chinese ("Cang Zhu"), Japan ("So-jutsu") and Thai ("Khod-Kha-Mao") traditional medicine for its various pharmacological properties including anticancer, anti-inflammation and antimicrobial activities, activities on central nervous, cardiovascular, and gastrointestinal systems. The major constituents in the essential oils from AL rhizome are β-eudesmol, hinesol and atractylon. Preliminary investigation has demonstrated its promising anti-CCA activity both in vitro and animal (Opisthorchis

viverrini/dimethylnitrosamine-induced CCA in hamsters and CCA–xenografted nude mice) models with high selectivity index comparing with the standard drug, 5-fluorouracil. It also showed virtually no toxicity with only minimal CNS effects on locomotor activity at the maximum dose of 5, 000 mg/kg body weight. Studies are underway to identify active constituent(s) which contribute to anti-CCA activity as well as its pharmacokinetic and pharmacodynamic properties.

S1-03 Treatment of parasitic skin diseases with dimeticones – a new family of compounds with a purely physical mode of action

Feldmeier Hermann
Institute of Microbiology and Hygiene, Campus Benjamin Franklin, Charité University Medicine, Berlin, Germany

Epidermal parasitic skin diseases (EPSD) are common in the tropics and sub-tropics. They are caused by mites, lice and other blood-sucking insects. In resource-poor countries they are associated with considerable morbidity. Hitherto, EPSD are treated with insecticides with a neurotoxic mode of action. The efficacy of this treatment is variable, and the development and spread of resistant mites and lice is alarming.

A new concept for treating EPSD is presented which is based on the topical application of dimeticones, silicone oils of low viscosity which rapidly kill insects and mites by a physical mode of action. They creep into the respiratory system and block oxygen supply. The physical mode of action makes the development of resistant parasite strains very unlikely. Due to their safety and efficacy, dimeticones are promising candidates for population-based intervention programmes targeted against EPSD in resource-poor settings.

S2-01 “MDA - Lymphatic Filariasis”

Kazuyo Ichimori
Lymphatic Filariasis Elimination, Department of Control of Neglected Tropical Diseases, World Health Organization

Lymphatic filariasis is one of the neglected tropical diseases. It is estimated that 120 million people are currently infected and that 1.403 billion live in areas where filariasis is endemic. Lymphatic filariasis is a leading cause of chronic disability worldwide, including of 15 million people who have lymphoedema (elephantiasis) and 25 million men who have hydrocoele.

The Global Programme to Eliminate Lymphatic Filariasis (GPELF) has been one of the most rapidly expanding global health programmes in the history of public health. The programme was launched in 2000 in response to resolution WHA50.29, with the goal to eliminate lymphatic filariasis as a public-health problem by 2020. The GPELF has two strategic aims: (i) interruption of transmission, using combinations of two medicines delivered to entire populations at risk, a strategy known as mass drug administration (MDA); and (ii) morbidity management and disability prevention (MMDP), by providing access to basic care to every affected person in endemic areas. The World Health Organization has developed a policy framework and guidelines for Member States to accelerate their efforts towards elimination of lymphatic filariasis by 2020.

Of the 73 endemic countries, 56 have started implementing MDA, of which 12 countries have moved to the post-MDA surveillance phase. During 2000-2012, more than 4.2 billion doses of medicine were delivered to a cumulative targeted population of 979 million people. The achievements made in MDA will be summarized.

S2-02　集団治療による住血吸虫症病害対策の試み　ー最良の方法の模索と撲滅への道すじ
Morbidity control of schistosomiasis by mass drug administration: How can we do it best and what will it take to move on to elimination?

Daniel G. Colley
University of Georgia, USA

The World Health Organization (WHO) has, for some time, encouraged countries endemic for schistosomiasis to control morbidity from this disease through mass drug administration (MDA) of the well-tolerated drug, praziquantel (PZQ). With the London Declaration in January 2012 and the promise by Merck Serono to eventually donate 250 million PZQ tablets per year, most endemic countries in sub-Saharan Africa have now developed national plans to do MDA for schistosomiasis morbidity control. More recently, based on two World Health Assembly (WHA) resolutions (WHA 54.19 & WHA 65.21) on schistosomiasis, countries are further encouraged to eliminate schistosomiasis, where feasible. The fight against schistosomiasis is therefore in a critical period of tremendous opportunities and equal challenges. How do we do the most effective job of MDA? What tools do we need to do this job better? How will we know when to move from morbidity control to elimination? What combinations of interventions, beyond MDA, are needed to eliminate transmission? The Schistosomiasis Consortium for Operational Research and Evaluation (SCORE) has its Secretariat at the University of Georgia and with programs in more than 24 institutions in 17 countries it is trying to answer these very practical questions through multiple large field-based studies and the evaluation or development of better diagnostics for schistosomiasis. This presentation will summarize the current status of morbidity control and elimination programs and the operational research by SCORE that we hope will provide much-needed answers for national program managers so they can most effectively pursue these critical public health programs.

S2-03　中国におけるアルテミシニン開発, ACTによるマラリア撲滅研究
The research experience of Artemisinin and ACTS in China, the study of how to elimination malaria by ACTS

Jianping Song, Changsheng Deng
Guangzhou University of Chinese Medicine

Malaria is the one of major diseases which threatens people' s life in Africa. Out of humanitarianism, Chinese scientists has contributed to research of Artemisinin and ACTS more than 30 years, China provides long-term antimalaria assistance to Africa and gain great achievements. In Moheli, the island of Comoros, the antimalaria group used a new strategy which universal medication and proactive intervention. They established not only an effective antimalaria system and reporting system but also a local antimalaria team. Furthermore, they enhanced publicity and put mass protection and treatment into effect. Finally, they achieved significant result. In order to

apply those successful experience to other countries in Africa, this paper summed up those experience and inspirations.

S3-01　感染症研究国際ネットワーク推進プログラムについて
About J-GRID (the Japan Initiative for Global Research Network on Infectious Diseases)

Yoshiyuki Nagai
Center of Research Network for Infectious Diseases, RIKEN, Tokyo, Japan

Since infectious diseases heed no national borders, international research collaboration across borders must be enhanced. The Ministry of Education, Culture, Sports, Science and Technology (MEXT) of Japan launched the J-GRID program in 2005, which consists of the two elements; (1) construction of collaboration centers in Asian and African countries on a reciprocal basis between a Japanese university/institution and a counterpart in the host country and (2) connecting those collaboration centers into a network and setting up its headquarters, CRNID. J-GRID initiated with 5 collaboration centers in 3 Asian countries has expanded to include 13 centers in 8 countries (6 in Asia and 2 in Africa). The aims of J-GRID include conducting high quality research on infectious diseases of regional and global importance, and advancing technologies and developing human resources in the field. In this way, J-GRID is expected to contribute to the public health of the host countries, our own country and the world. After the completion of the first start-up phase (2005-2009), J-GRID has stepped up its activity for the second phase (2010-2014). While the first phase was just like an incubation period, the second phase should be the exponential growth phase, maximizing its research activities. Indeed, J-GRID is now generating remarkable research outcomes with an increasing number of publications. The mid-term evaluation made by the MEXT in FY2012 commended J-GRID as an ideal model led by Japan, a world leader of science and technology, and highly recommended that the program be continued for years to come after 2014.

S3-02　途上国の地方におけるフィールドリサーチの課題：フィリピンにおける小児肺炎に関する研究の経験から
Challenges to conduct a field research in rural setting of developing countries: Our experience on pediatric pneumonia study in the Philippines

Hitoshi Oshitani
Department of Virology, Tohoku University Graduate School of Medicine, Sendai, Japan

Acute respiratory infection is still a major cause of deaths in infants and young children in developing countries. We have been conducting a research project on pediatric pneumonia in the Philippines. We have been conducting a hospital based etiology study in a referral hospital in Leyte Island. We identified several important findings thorough this hospital based study including an importance of viral etiologies in hospitalized cases with a diagnosis of severe pneumonia. However, a hospital based study has some critical limitations. First, many cases even with severe pneumonia may not be hospitalized. Second, it is difficult to identify risk factors for developing severe illness by analyzing the data only from severe cases. Third, it is impossible to establish more effective and feasible interventions without knowing a real situation in the communities. Therefore we have initiated a community based

study in a remote island of the Philippines. In this study, we follow up all under 5 children with following objectives; 1) to identify a real incidence of severe pneumonia; 2) to reveal etiologies of severe pneumonia; 3) to analyze risk factors for developing severe illness; 4) to establish more effective and feasible interventions. There are a number of difficulties and challenges to conduct a community based field research in resource limited settings, including managing many project staff, obtaining approvals from different levels, maintaining high quality data, solving many logistic issues and so on. Despite all these difficulties and challenges, such field researches are needed to establish more effective and feasible interventions.

S3-03　ベトナムの住民コホートを利用した小児感染症の研究
Population based cohort study for Pediatric Infectious Diseases Research in Vietnam

Laymyint Yoshida
Department of Pediatric Infectious Diseases, Institute of Tropical Medicine, Nagasaki University, Nagasaki,

A population based cohort study on Pediatric Infectious Diseases was established at Khanh Hoa Province, central Vietnam in 2006, to determine the etiology and risk factors for severe pediatric infectious diseases (SPID) such as acute respiratory infection (ARI), diarrhea and dengue which are the major causes of under 5 mortality. A population census survey was conducted to collect demographic, social-behavioral data and disease burden on SPID. The study site covered a population of 353, 525 residing in 75, 826 households with 24, 781 children less than 5 years. Hospital databases from two hospitals covering the region were obtained. Linking the census survey and hospital databases, we were able to investigate on a variety of SPID such as environmental tobacco smoking exposure and increased risked of pediatric pneumonia hospitalization, population density, water supply and risk of dengue fever and animal livestock and risk of hospitalized diarrhea. To determine incidence, viral etiology and risk factors for pediatric ARI/pneumonia, we setup a population based prospective hospitalized Pediatric ARI surveillance at Khanh Hoa General Hospital, Nha-Trang in February 2007. The study has revealed RSV, rhinovirus and influenza A as major viral pathogens, role of multiple viral infection and its interaction with bacteria in the development of pneumonia. In addition, we are also conducting a birth cohort study to investigate the incidence of congenital infection and its impact on physical-neurological development, and role of host genetic polymorphism on SPID hospitalization in Vietnam. Population mobility, high cost of regular census update and low mortality are the challenges.

S3-04　西アフリカ・ガンビア共和国におけるB型肝炎の制圧：ワクチンと核酸アナログ製剤によ る2つ のPopulation-based interventions to reduce the public health burden related with hepatitis B virus infection in The Gambia, West Africa

Yusuke Shimakawa[1, 2)]
[1)]Faculty of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine,
[2)]PROLIFICA Project, MRC Unit

Hepatitis B virus (HBV) infection is highly endemic and hepatocellular carcinoma (HCC) has been the

commonest type of malignancy in The Gambia. In 1986, a nation-wide trial of the HBV vaccine was initiated to evaluate the effectiveness of infant HBV vaccinations in preventing HCC in adulthood. As instantaneous universal vaccination was impossible for logistic/financial reasons, the vaccine was introduced into the Expanded Programme of Immunisation (EPI) of The Gambia in a phased manner, called the "stepped-wedge" design. There were 17 EPI teams, and each covered a defined area of the country. Initially only one EPI team administered the HBV vaccine to all newborns in the catchment area, while newborns registered in other areas during this period constituted the unvaccinated control group. Three months later, the second EPI team provided the HBV vaccine and by 1990 countrywide coverage was achieved. To assess the outcome, a national cancer registry was founded and all HCC patients in this birth cohort will be linked with the vaccine trial database. Although the universal vaccination has been successful in reducing the prevalence of chronic HBV infection in young Gambians, the incidence of HCC will not decline over the next three decades as people infected prior to the immunisation programme will continue to develop the diseases. To reduce the HCC incidence through community-based screening of HBV infection and provision of antiviral therapy, the PROLIFICA (Prevention of Liver Fibrosis and Cancer in Africa) Project started in 2011. Study hypothesis as well as design will be further discussed.

S3-05　アフリカのへき地病院における臨床研究：タンザニアでの経験から
Challenges to Clinical Research in a Rural African Hospital; a perspective from Tanzania

Nadjm Behzad
National Hospital of Tropical Diseases, Oxford University Clinical Research Unit, Hanoi, Vietnam

The severe febrile illness study was established in 2005 through EU funding. The aim of the project was to define the aetiology of febrile disease in children admitted to a hospital in Tanzania.Challenges arose in many areas:Study design: An initial plan to recruit only the severely ill was revised to enroll all febrile admissions leading to a more comprehensive dataset but much increased costs. Operationally a decision was made to set up a paediatric acute admissions unit (PAAU) in the hospital to facilitate recruitment and to provide appropriate initial care in line with perceived ethical obligations. This had knock on effects relating to the responsibilities that were taken on but also some unexpected positive outcomes.Study personnel: Recruitment of an overseas coordinator was hampered by lack of funds, whilst local research staff were sometimes called upon to make up deficiencies in the hospital staffing. Lack of staff made it impossible to recruit patients around the clock, seven days a week creating the challenge of ensuring representative sampling. Quality control: Studies based on clinical examination create unique quality control challenges; how to ensure that clinical staff are examining in a systematic and reproducible way. We designed a sub-study to both explore this and improve quality.Summary: Setting up clinical research projects is severely resource poor settings creates many challenges including those of an operational, technical and ethical nature. Whilst there are no 'right answers' an awareness of these problems can help overcome them.

シンポジウム　２日目

Symposium Day 2

October 5 9:00 ー 17:10

長崎ブリックホール・３階国際会議場

International Ball Room at 3rd floor, Nagasaki Brick Hall

●シンポジウム

S4-01　Dengue vaccine development: current status and future challenges

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[1)]BIKEN Endowed Department of Dengue Vaccine Development, [2)]Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand, [3)]Research Institute for Microbial Diseases, Osaka University, Osaka, Japan

Dengue fever (DF) and its more severe form, dengue hemorrhagic fever (DHF), are major global concerns. An estimated 50-100 million DF and 250, 000-500, 000 DHF cases occur every year, with approximately 2.5 billion people at risk of infection throughout tropical and subtropical areas of the world. Even in the temperate region, imported cases are a problem. DF and DHF are thus the most important mosquito-borne viral diseases in the world. Unfortunately, no licensed vaccines or antivirals are available. The causative agents are four serotypes of dengue virus, members of the genus Flavivirus in the family of Flaviviridae. Infection with any of these serotypes can cause DF and DHF.The dengue vaccine development started since the first isolation of DENV in 1943. Because one of the possible mechanisms to cause DHF upon infection with one serotype is the presence of non-neutralizing cross-reactive antibodies against other serotypes, combination of vaccines against each of four serotypes (tetravalent vaccine) is desired for developing an effective and safe dengue vaccine. To date, several vaccine strategies have been used for dengue tetravalent vaccine development. However, a recent report of the world's first clinical trial to evaluate the protective efficacy of a dengue tetravalent vaccine candidate described low protection against dengue virus type 2 infection. Therefore, dengue vaccine development still remains a big challenge.

S4-02　デング熱媒介蚊のコントロール：将来への展望
Dengue vector control: new insights leading to novel tools?

Constantianus Koenraadt
ワーニンゲン大学, 昆虫学教室

In the absence of a vaccine or an effective drug, control of dengue focuses on attacking the mosquito vector in its aquatic or terrestrial life stages. The investigation into the ecology of the mosquito and its requirements for reproduction, have led to the development of a series of classical tools such as source reduction, the use of natural enemies for population reduction and insecticides. Despite local successes, dengue has not been eliminated and is on its return in some areas. Therefore, alternative approaches, consisting of the use of Wolbachia and the release of transgenic mosquitoes, are developed and advocated. In parallel, more fundamental research has emerged recently about the role of the environment in mosquito and virus development as well as about the mating behaviour of the mosquito. An important question remains whether these new insights will actually lead to novel and practical tools for dengue vector control.

S5-01 Analyses of entry mechanisms of novel emerging viruses using pseudotype VSV system

Hideki Tani
Department of Virology No1, National Institute of Infectious Diseases

Emerging infectious diseases include newly identified diseases caused by previously unknown organisms or diseases found in new and expanding geographic areas. Viruses capable of causing clinical disease associated with fever and bleeding are referred to as viral hemorrhagic fevers (VHFs). Arenaviruses and Bunyaviruses, both belonging to families classified as VHFs are considered major etiologies of hemorrhagic fevers caused by emerging viruses; having significant clinical and public health impact. Because these viruses are categorized as Biosafety Level (BSL) 3 and 4 pathogens, restricting their use, biological studies including therapeutic drug and vaccine development have been impeded. Due to these restrictions and the difficulties in handling such live viruses, pseudotype viruses bearing envelope proteins of VHF viruses have been developed using vesicular stomatitis virus (VSV) as a surrogate system. Here, we report the successful developments of two pseudotype VSV systems; bearing the envelope proteins of Lujo virus and severe fever with thrombocytopenia syndrome (SFTS) virus, both recently identified viruses of the family *Arenaviridae* and *Bunyaviridae*, respectively. My presentation will summarize the characterization of the envelope proteins of Lujo virus including its cellular receptor use and cell entry mechanisms. In addition, I will also present a brief introduction of SFTS reported in Japan and the diagnostic studies in progress using these newly pseudotype VSV system.

S5-02 NおよびG蛋白質への弱毒化変異の導入による安全な新規狂犬病生ワクチン株の作出
Generation of a novel live rabies vaccine strain with a high level of safety by introducing attenuating mutations in the nucleoprotein and glycoprotein

Naoto Ito
Gifu University　応用生物科学部　人獣共通感染症学研究室

Rabies is a viral zoonotic disease characterized by severe neurological symptoms and a high mortality rate (almost 100%). The current live rabies vaccine strain is attenuated by only one mutation (Arg-to-Glu) at position 333 in the glycoprotein (G333). This fact generates a potential risk of the emergence of a pathogenic revertant by a back mutation at this position during viral propagation in the body. To circumvent this risk, it is desirable to generate a live vaccine strain stably attenuated by multiple mutations. However, little is known about attenuating mutations other than that at G333. In this study, we found that amino acid substitutions at positions 273 and 394 in the nucleoprotein (N273/394) (Phe-to-Leu and Tyr-to-His, respectively) attenuated the pathogenicity of the oral live vaccine strain ERA, which has a virulent-type Arg at G333. Then we generated ERA-N273/394-G333 strain attenuated by the combination of the above mutations at G333 and N273/394, and we checked its safety and immunogenicity. ERA-N273/394-G333 strain did not cause any symptoms in adult mice after intracerebral inoculation, indicating a low level of residual pathogenicity of this strain. Also, we found that the risk of the emergence of a pathogenic revertant of ERA-N273/394-G333 strain was lower than that of the ERA-G333 strain, which has a single attenuating mutation at G333. Furthermore, intramuscular inoculation of this strain induced protective immunity in adult mice against lethal rabies infection. These results indicate that ERA-N273/394-G333 strain is a promising candidate for a live rabies vaccine strain with a high level of safety.

S5-03　南アフリカ共和国におけるリフトバレー熱ウイルスの疫学及び病原性
Epidemiology and pathogenesis of Rift Valley fever virus in South Africa

Petrus Jansen Van Vuren, Antoinette A.Grobbelaar, Shalekof Sharon, Archer Brett, Janusz T. Paweska
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Rift Valley fever (RVF) is a mosquito borne viral zoonosis endemic to Africa and the Arabian Peninsula causing high mortality and abortion rates in young and pregnant domesticated ungulates respectively. Humans develop disease ranging from a mild flu-like illness to more severe complications including hemorrhagic manifestations, encephalitis or death. During outbreaks in South Africa between 2008 and 2011, 302 human cases were laboratory confirmed including 25 deaths, with the major risk factor being direct contact with animal tissues, blood or other bodily fluids. The pathogenesis of RVFV infection on a molecular level is not completely understood. We present here some efforts to better understand the pathogenesis of RVFV during the recent South African outbreak by investigating the possible role of host immune response, virus replication and virus diversity. Analysis of serum cytokines indicates a dysregulation of inflammatory responses in RVFV infected individuals. Above or below normal serum levels of certain cytokines respectively clearly indicates a fatal outcome from RVFV infection. There was no significant difference between viremia levels in serum from fatal and non-fatal cases and also not between the genomes of viruses isolated from fatal or non-fatal cases. These results, combined with our previous results in a mouse model, seem to indicate that variation in disease progression between fatal and non-fatal cases is more likely a result of modulation of individual host-driven responses including inflammation, apoptosis, T- and B-cell immunity. Some of the cytokines identified in this study could be used as markers for fatal outcome in RVF patients.

S6-01　肺炎球菌ワクチンによるグローバルな肺炎球菌感染症の制御

大石　和徳
国立感染症研究所　感染症疫学研究所

世界で160万人の肺炎球菌による死亡数のうち, 5歳未満の小児の死はその約半数を占めている。小児死亡の直接死因は肺炎, 敗血症, 髄膜炎であり, 主に途上国で発生している。2000年に米国で７価肺炎球菌結合型ワクチン(PCV7)が小児に対する定期接種として導入され, 5歳未満の小児における侵襲性感染症の罹患率は激減した。その後, WHOは5歳以下の肺炎死亡が多いすべての国に PCVの使用を推奨し, 2009年にはさらに途上国で重要な血清型１, 5, 7Fを含むPCV10が, さらに2010年には血清型3, 6Aや19Aを含むPCV13が導入されている。一方, GAVIの支援により, とりわけ低～中所得の国々におけるPCVの定期接種ワクチンとしての導入が進んでいる。米国ではPCVの定期接種化により10万人あたり6人の死亡を減らすのに対し, アフリカのガンビアでは10万人あたり700人の死亡を減らすことが期待される。また, 総年収US$1, 000以下のGAVI支援該当72ヶ国を対象とした乳幼児に対するPCV接種した場合, その生後3-29ケ月の小児の死亡379万人の7%にあたる約26万人の死亡を予防できるとされている。これらの予測から, アジア, アフリカの途上国の乳幼児に対するPCVの定期接種化が期待されている。わが国では2010年11月にPCV7は2009年10月にわが国で承認され, 2010年11月に「子宮頸がん等ワクチン接種促進事業」が始まり, 5歳未満の小児に対するPCV7接種の公費助成が開始された。2013年4月の予防接種法の改正に伴い, PCV7が定期接種ワクチンとなり, 2013年11月にはPCV13への切り替えが予定されている。また, 現在, 高齢者に対する23価肺炎球菌莢膜ポリサッカライドワクチンの定期接種化に関する議論が進行中である。

S6-02　新型インフルエンザパンデミックの出現を見据えたワクチン開発に何を望むか

小林　治
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スペインかぜ以降, 香港カゼ, A(H1N1)pdm09などの例をみると, 新規インフルエンザ株のパンデミック後にそのまま季節性株となる事が少なくない。このような新規インフルエンザのパンデミック終息後の季節性への移行は, ワクチン開発にとって大きな意味をもつ。季節性インフルエンザワクチンは生体に十分な抗体産生を誘導しかつ毎年接種しても長期的な安全性が確保されしかも安価である事が望まれるが, 一方の新型インフルエンザに対するワクチンは, 十分なプライミング効果を有しかつ高い安全性をもつワクチンを迅速に生産しなくてはならないという性質が要求される。現在, ワクチン開発を巡っては, 様々なテクノロジーが導入されている。従来の発育鶏卵を用いた方法は鶏卵の準備段階から半年以上の時間を有し, 汚染リスクを伴い, 鶏卵アレルギーなど特定集団への安全性が懸念されるなどの問題があった。これに対してMDCKやVeroなどのインフルエンザに感受性が高い細胞培養系を用いるとワクチンの大量生産に好適とされている。A(H5N1)についてはBaxter社, Solvay社, Novaltis社が治験段階であり, 日本ではデンカ生研, 阪大微研などが研究段階である。また, 共通抗原を用いるユニバーサルワクチンではインフルエンザウイルスのM2やHA/NP/M1の保存性が高い部位をリニア連結する方法が試みられているが, 実際の効果についての検証は十分とは言えない。また, マイクロニードルによる皮内, 経鼻といった投与経路の変更によってより高い免疫効果が期待されるという報告も相次いでいる。本講演では新型インフルエンザパンデミックの出現を見据え, ワクチン開発にあたって何を期待するのかについて, 臨床家の視点から述べたい。

S6-03　HIV予防のグローバル戦略とワクチン開発への期待

田沼　順子
独立行政法人国立国際医療研究センターエイズ治療・研究開発センター

抗レトロウイルス療法(antiretroviral therapy: ART)で予後が改善されたとはいえ, 世界では毎年250万人の新規HIV感染者が発生し, HIVが人類にとって脅威であることに変わりはない。しかしHIV-1発見からの30年間, 多くの研究者により絶え間ない努力が続けられてきたが, 未だ実用化に至ったHIV予防ワクチンは存在しない。HIVが宿主の免疫応答そのものを利用して増殖することや, 様々な防御免疫へのエスケープ変異を獲得すしやすいことがワクチン開発の大きな壁となっている。他にも, 多くの地域特有の流行株, 動物モデルの限界, 資源の限られた国でも使用可能な安価なワクチンが求められること, 大規模な臨床試験が必要なこと等, 様々な課題が挙げられる。

一方で2011年にHIV診断後すぐにARTを開始することで男女間感染を約95％阻止できたとする臨床試験HPTN052の結果が発表された。その画期的成果に対する世界の反応は早く, 現在すでに感染者に対する早期治療(Treatment as Prevention)は世界のHIV予防戦略の中心となっている。また, 最近暴露前予防(Preexposure Prophylaxis: PrEP)の有効性も明らかとなってきた。これらARTを効果的に使う手法は, 実用化が進まない予防ワクチンにかわって, 有望な感染拡大阻止策として重要視されている。

しかし, 予防ワクチン開発への期待が途切れた訳では決してない。これまでに臨床的に有効性が証明された唯一の予防ワクチンであるRV144は, タイでの臨床試験で31.2％の感染阻止効果があったという。RV144の効果はまだ実用化に十分とはいえないが, この研究で今後の開発に寄与する様々な知見が得られている。日本発のものを含めワクチン候補はまだ多数あることから, 今後の臨床研究の成果に大いに注目したい。

S7-01　福島原発事故と県民健康管理調査

山下　俊一
長崎大学　原爆後障害医療研究所

東京電力（株）福島第一原発事故では, 複合災害の上に情報災害の様相までも呈しましたが, 医学系学術専門団体の多くが, 迅速かつ的確な被ばく医療情報を社会に発信しています。その結果, 風評被害に惑わされる事無く, 福島県においては, 妊産婦の健康が守られた事は感謝の念に耐えません。また内部被ばくも最小限に抑えられています。その反面, 避難などに伴う震災関連死の報告は痛恨の極みです。事故から2年半が経過しましたが, 事故直後の放射性降下物, とりわけ放射性ヨウ素の甲状腺内部被ばくの影響, それに引き続き放射性セシウムによる環境・食の汚染と健康影響への問題をどのように論理的に理解し, 県民の健康を長期に渡り見守るのかが, 多くの困難の中で問われています。すでに, 国際社会では原発事故への対応が多角的に議論され, その準備や対応策がガイドラインとしても認識されてきましたが, 日本では原発安全神話の中で放射線教育が全く不十分であり, 医療関係者も放射線防護と健康リスクの考え方に習熟していませんでした。その反省も踏まえて, 福島県内では放射線リスクコミュニュケーションと地域医療の改善に向けた努力が幅広く展開されています。平成23年5月から福島県においては, 全県民の健康見守り, すなわち健康管理調査事業が, 県と医大を中心とし国の復興支援の中でいち早く立ち上がりました。全県民を対象とした基本調査（初期4ヶ月間の外部被ばく線量推計）と, 避難住民を中心とする詳細調査をその骨子として実施されています。甲状腺など身体的影響への不安のみならず精神・社会心理的影響が大きいものがあります。特に, チェルノブイリの経験から, 乳幼児期～思春期にかけた放射性ヨウ素内部被ばくによる甲状腺発がんリスクが懸念されています。これらの解決策には, 長期にわたる放射能環境汚染に対する防護の課題と, 実際の健康リスク問題の理解を推進する包括的な取組みが必要です。

S7-02　感染症の危機管理

郡山　一明
Emergency Life-Saving Technique Academy of KYUSHU

医療機関おける感染症対応の目的は, 感染症に罹患した個人を治癒することにある。一方, 経済を含めた社会活動維持の観点から見た場合, 感染症対応の目的は, 感染症に罹患していない集団を如何に護るか, すなわち感染症流行の発生阻止と拡大防止にある。両者は個人と集団, 罹患後と罹患前という対極の関係なのだ。近代社会は公衆衛生の向上とワクチン接種によって感染症発生阻止と拡大防止を図ってきた。逆に言えば, ワクチンが存在しない新興感染症に対して近代社会は未だ無防備である。そればかりか, 近代社会の特徴である「都市化」と「人間の移動」は感染症拡大に対して構造的脆弱性を提供している。事実, この数年でもSARS, 新型インフルエンザは世界にとって大きな脅威となった。これからは, 感染症の社会影響を最小限に抑え込む「感染症の危機管理」の概念・方法論を構築するとともに, 関係する人々に普及していくことが極めて重要である。The control of infections in medical institutions is the act of curing individuals with infections. On the contrary, “risk management of infections, ” aimed at maintaining social activities, lies in the protection of the population of individuals without infections. They are the opposite of each other in terms of individuals versus the population, and pre-infection versus post-infection. In the future, it will be very important to establish the concept and methodology of “risk management of infections” to minimize the social impact of infections, as well as to disseminate them to the individuals concerned.

セミナー　１日目

Seminar Day 1

October 4 17:10 ー 18:20

長崎ブリックホール・３階国際会議場

International Ball Room at 3rd floor, Nagasaki Brick Hall

●セミナー

Sem-1　発熱, 発疹, 意識障害を呈した80歳女性

佐藤　昭裕[1)], 水野　泰孝[1)], 池田　秀樹[3)], 中村　造[1)], 松本　哲哉[2)], 神田　哲郎[3)]
[1)]東京医科大学病院　感染制御部, [2)]東京医科大学　微生物学講座, [3)]長崎県五島中央病院　内科

【症例】80歳女性
【主訴】発熱　腰痛
【現病歴】来院5日前から腰痛が出現し, 起床困難となり自宅で臥床していた。来院前日に近医を受診し採血を施行された。受診時38℃の発熱があり, NSAIDs処方され帰宅となった。来院当日, 近医で施行された採血で肝機能障害が指摘され, 発熱も持続していたため当院へ紹介受診となった。
【既往歴】高血圧症(内服加療中)
【入院時現症】意識JCS2-20, 体温39.6℃ , 血圧144/89mmHg, 脈拍85/分, SpO2 93% R.A.。頭頸部:　眼瞼結膜貧血なし, 眼球結膜黄染なし, 咽頭軽度発赤あり, 頚部リンパ節触知せず, 項部硬直なし　胸部:　心音純　雑音なし, 呼吸音清　腹部: 腸蠕動音正常, 腹部膨隆なし, 圧痛なし　背部: CVA叩打痛なし 皮膚所見:　四肢・体幹に発疹が多発
【検査所見】WBC 10610 / μl, RBC 388 $\times 10^4$ / μl, Hb 11.5/dl, Plt 10.0 $\times 10^4$/ μl, BUN 25.6mg/dl, Cr 0.75mg/dl, T-Bil 0.46mg/dl, AST 136IU/L, ALT 88IU/L, LDH　484IU/L, CK 210IU/L, Na 135.8mEq/L, K 3.21mEq/L, Cl 99.3mEq/L, CRP 15.08mg/dl.

Sem-2　発熱, 意識障害, DICを呈した海外渡航歴のない58歳, 男性

泉川　公一[1, 2)], 栗原　慎太郎[1, 2)], 高園　貴弘[1)], 森永　芳智[3)], 中村　茂樹[1)], 今村　圭文[1)], 塚本　美鈴[1, 2)], 柳原　克紀[3)], 森田　公一[4)], 河野　茂[1)]
[1)]長崎大学大学院医歯薬学総合研究科 感染免疫学講座（第二内科）,
[2)]長崎大学病院　感染制御教育センター , [3)]長崎大学病院　検査部,
[4)]長崎大学熱帯医学研究所　ウイルス学分野

症例は58歳, 男性, 海外渡航歴なし。2005年11月30日から39℃を超える高熱, 全身倦怠感により近医受診。感冒様の咳嗽や咽頭痛などは認めず, インフルエンザ抗原も陰性であったが, オセルタミビルによる治療が開始された。同日夕になり, 全身倦怠感が増強するため近医を再受診し同院入院となった。血液検査上, 肝機能障害, 血小板減少, 白血球減少を認め, 腎機能障害は認めなかった。その後, 経時的に肝機能異常は増悪し, 2系統の血球減少に加えてFDP増加, PT延長とDIC兆候を認め加療された。12月2日早朝より, 幻覚, 不穏出現し, 全身倦怠感が強くなり, 意識障害の進行を認めたため, 12月3日当院紹介入院となった。当院入院時現症　体温39.9℃ , 血圧100/60, 心拍96/分, JCS (I-3-R), 貧血なし, 黄疸なし。呼吸器, 心所見正常。腹部に肝, 脾触れず, 軟。浮腫なし。神経学的所見明らかな所見なし。リンパ節腫大なし。当院入院時検査所見　WBC 1120/ μl, RBC 575万/ μl, Hb 18.1g/dl, PLT 24000/ μl, AST 1016 U/l, ALT 443 U/l, LDH 2384 U/l, CK 766 IU/l, CRP 0.36mg/dl

Sem-3　発熱, 咽頭痛, 咳で発症し低酸素血症を来したミャンマー人の5歳女児

鵜沼　直穂子[1, 10)], 中村（内山）　ふくみ[2, 10)], 関　雅文[3, 10)], 明田　幸宏[4, 10)], 本村　和嗣[5, 10)],
大西　健児[6, 10)], Ekisariyaphorn Ratthakhet[7)], Ruenweerayut Ronnatrai[8)], 大石　和徳[9, 10)]
[1)]自治医科大学　附属病院　感染症科, [2)]奈良県立医科大学・病原体／感染防御医学講座,
[3)]大阪大学医学部附属病院・感染制御部, [4)]大阪大学微生物病研究所・臨床感染症学研究グループ,
[5)]大阪大学微生物病研究所・日本・タイ感染症共同研究センター , [6)]都立墨東病院感染症科,
[7)]Dept. Pediatrics, MaeSot General Hospital, Tak, Thailand, [8)]Dept. Intern Med, MaeSot General Hospital, Tak, Thailand, [9)]国立感染症研究所感染症疫学センター ,
[10)]第5回タイ・ミャンマー国境現地で学ぶ熱帯感染症医師研修メンバー

【症例】 ミャンマー人の5歳女児
【主訴】 発熱, 咽頭痛, 咳, 呼吸苦
【既往歴】 特記事項なし
【現病歴】 MaeSot General Hospital入院の4日前より発熱, 咽頭痛, 咳があり, 入院前日より呼吸苦が出現した。入院当日に呼吸苦が激しくなり前医を受診した。SpO_2 64%（室内気）と低酸素血症が認められたため, 挿管され緊急に転送された。
【入院時身体所見】 意識レベル：清明　血圧123/63mmHg　脈拍114回/分　呼吸回数30回/分　SpO_2 100%（挿管／酸素投与下）体温37.5℃℃体重13kg　頭頸部：両側性の扁桃腫大と白苔付着
【入院時血液検査】 WBC 30, 300/μL (Neu 91.7%)　Hb 10.4 g/dl Hct 31.8%　Plat 427 K/μL Na 132 mEq/L K 3.3 mEq/L Cl 104 mEq/L BUN 11.1 mg/dL Cre 0.6 mg/dL TP 6.8g/L Alb 3.8g/dL T.Bil 0.45 mg/dL AST 20 U/L ALT 16U/L
血液塗抹標本（ギムザ染色）：マラリア原虫認めず
【CXR】 右上葉に浸潤影あり

学会受賞講演　１日目

Awardee’s Lectures Day 1

October 4 14:10 ー 15:00

長崎ブリックホール・３階国際会議場

International Ball Room at 3rd floor, Nagasaki Brick Hall

●学会賞受賞講演（日本熱帯医学会賞）

PL-01　東アジアにおける日本脳炎ウイルスの分子疫学解析

森田　公一（長崎大学熱帯医学研究所・ウイルス学分野）

熱帯医学領域では現在も蚊によって媒介されるウイルス性疾患は重要であるが、温帯に位置する国々に住む人々にとっても、これらのウイルスの移動や変異の状況を把握しておくことは疾病対策上重要な課題である。

日本脳炎ウイルスは熱帯アジアにその起源をもつと考えられる蚊媒介性ウイルスであり、現在でも東南アジアを中心に依然として多くの患者が発生している。世界保健機関はアジア地域で年間2万人～3万人の患者が発生していると見積もっている。我が国においても1960年代にワクチンが普及する前には年間数千名の患者発生が報告されていた。しかし現在では患者発生数は年間10名を切っており、このため一般の国民には感染リスクが無くなったと誤解している人々も多い。しかしながら、自然界においては毎夏（特に九州や関西、四国では）、ウイルスが確認されており感染リスクは依然として存在している。

従来、日本では冬に蚊がいなくなるため、ウイルスがどのように冬を越しているのかは長い間なぞであり、日本脳炎ウイルスは日本本土の何らかの動物、昆虫の体内で越冬するという「越冬説」と、毎年初夏に南方から鳥や蚊によってウイルスが日本に持ち込まれるとする「飛来説」が二者択一的に議論されてきた。

この問題を解決するため、長崎大学熱帯医学研究所のウイルス学分野では先代の五十嵐章名誉教授の時代から東南アジアと日本で日本脳炎ウイルス採取し、その時代で利用可能な分析手法を用いて解析を実施してきた。現在もJ-GRID(文部科学省の感染症研究国際ネットワーク推進プログラム)によりこのフィールド調査は継続されている。

そして最近、アジアと日本で分離された日本脳炎ウイルス600株以上のE蛋白遺伝子全塩基配列を用いた分子疫学解析から、日本脳炎ウイルスは熱帯アジアで日常的に遺伝子変異を起こしていること、そして東南アジアから中国を経由して、朝鮮半島や日本へ頻繁に飛来していることを明らかにした。しかし一方では、少数ではあるが一部のウイルス群は日本国内で冬を越し翌年の初夏にふたたび出現していることも明らかになった。先にふれた古い科学論争の結論としては「引き分け」ということだったが、公衆衛生学的には飛来説が証明された事は特に重要である。つまり、アジアや中国で脳炎患者を発症させているグループのウイルスが頻繁に日本に持ち込まれている事実が明らかにされたのである。

この研究成果の示す教訓は日本脳炎ウイルスにとどまらない。熱帯地域は微生物を含めて生物の宝庫であり、未知のウイルスが現在も頻繁に発見されている。加えて既知の微生物も絶えず変異を起こしている。熱帯地域でのフィールド研究を通して我々はその実情を知ることが可能であり、熱帯地域の人々のためにも、また世界の他の地域で生活する人々の安全と健康のためにも、熱帯医学フィールド研究を継続してゆくことが重要である。

●学会賞受賞講演（研究奨励賞）

PL-02　フィールドからラボ、ラボからフィールドへ～ラオス・サバナケットにおける人獣共通寄生蠕虫感染症～

サトウ　恵（新潟大学大学院保健学研究科）

2004年以降現在まで年に数回ラオスにおいて蠕虫感染症のフィールド調査を行っている。現地で蔓延している蠕虫は主に食物由来性の寄生虫で、淡水魚を生食することで感染するタイ肝吸虫、異形吸虫類、棘口吸虫、汚染された野菜や水から感染する鉤虫、そして牛・豚肉から感染するテニア類などが見られ、地域によっては住民のほぼ100％が感染している。我々は現地においてKato-Katz法による検便、投薬治療･健康教育などを行い、必要に応じて濾便により成虫を集めている。現地で採取した便の一部を使用し分子生物学的解析により、顕微鏡検査のみでは把握出来ない蠕虫種の鑑別を行っている。それまでの調査では顕微鏡検査で診断が下されていたため、異形吸虫類の虫卵もタイ肝吸虫卵と報告され、タイ肝吸虫の感染率は真の感染率より多く報告され、またタイ肝吸虫の感染傾向なども正確なものではなかったと思われる。鉤虫に関しては種によってメインの感染経路や宿主が異なるが、種の鑑別を行わなければ適切な健康教育・対策を行えない。寄生虫学研究、感染症対策を行う上でフィールド、ラボでの両方の調査はそれぞれに大事であるが、また双方向性に結果を還元していくフィードバックも必要であり、そこから次の研究のシードも得られる。また寄生虫感染症はヒトと寄生虫のみの関係でなく、環境要因の影響も大きく受ける。タイ肝吸虫は２つの中間宿主（淡水貝･魚）を必要とし、生息地である水田、側溝の状態、また生育地の天候、降水量などに影響を受けるため、今後、温暖化やメコン川上流でのダム建設よる感染症への影響も考えていく必要がある。そのためには多方向から感染症を考える必要があり、多彩な分野の協同での研究が必要である。今後とも現地の人々、共同研究者などのコミュニケーションを重視し調査・研究を行い、現地の人に還元していきたい。

●学会賞受賞講演（相川正道賞）

PL-03　Towards elimination of malaria in the Philippines

Pilarita Tongol-Rivera
Department of Parasitology, College of Public Health, University of the Philippines Manila

Malaria control program of the Philippines is succeeding, on the evidence of impressive decline of malaria cases and deaths over a considerable period, the exclusion of malaria in the top ten leading causes of morbidity and mortality.

The anti-malaria strategies that have been implemented include early diagnosis and prompt treatment, strengthening vector control, surveillance and epidemic management, ensuring the quality of these services, intensifying health promotion, building local capacity in management and sustainability of the malaria program, and stratification of malarious areas.

Recipients of local capability building such as barangay (village) microscopists and availability of logistics-supplies, reagents and antimalarial medicines, through external support (GFATM, AusAID, RBM, APMEN and ACT Malaria) ensure early diagnosis and proper treatment. However, the increasing local support for logistics has been noted. The role of the barangay microscopists as extension of the health centers' malaria diagnostic services in Palawan and the other project sites has been noteworthy.

The goal for the next 5 years is to accelerate the transition from malaria control to elimination by 2020-2025. This is planned to be achieved by ensuring universal access to reliable diagnosis, highly effective treatment and preventive measures, capacitating the local governments to own, manage and sustain the malaria program.