ABSTRACT

1. Current situation:

Hepatitis B is a vaccine-preventable disease; however, chronic hepatitis B-associated mortality and morbidity contributes to a high public health burden in Vietnam. In some survey, the prevalence of HBV in Vietnam is 10-20% population especially in pregnant women (10-16%) and in children (2-6%). Thanks to the EPI, the HBV vaccine for children started in the year 1997, up to now, the prevalence of HBV among children under 10 years old decreased to 2%. Hope with EPI successful, HBV prevalence among children will obtain 1% in the year 2017. The HCV prevalence in Vietnam is 4-7% population chiefly among IDUs. HIV/Viral hepatitis co-infection is very common in Vietnam (about 40%)

2. Activities for viral Hepatitis control:

2.1 Goals: Reduce the transmission of, and morbidity and mortality caused by, hepatitis B, C and to minimize the personal and social impact of Vietnameses living with hepatitis B,C.

2.2 Objectives

- Reduce new hepatitis B, C infections
- Achieve and maintain high levels of hepatitis B vaccination
- Increase the proportion of people with chronic hepatitis B,C who have been diagnosed
- Increase access to appropriate management and care for people with chronic hepatitis B, C
- Reduce the burden of disease attributed to chronic hepatitis B, C
- Eliminate the negative impact of stigma, discrimination, and legal and human rights issues on people's health

2.3 Targets:

- Achieve HBV childhood vaccination coverage of 95 per cent
- Increase hepatitis B vaccination coverage of priority populations
- Increase to 60 per cent the proportion of all people living with chronic hepatitis B and 40% chronic HCV who are diagnosed
- Increase to 15 per cent the proportion of people living with chronic hepatitis B and C who are receiving suitable antiviral treatment.

3. Implementation and Evaluation:

- Formulation national strategic plan (2015-2010)
- Guideline in screening and management HBV/HCB and co-Infection with HIV
- Support from health insurance and agencies for treatment
- Evaluation the target annually

SESSION 1-3

PROGRAM

Epidemiology and Treatment of HBV infected patient in VietNam

PRESENTER

Dr. Tran Ngoc Anh
Hà Nội Medical University

EDUCATION

2002-	Royal North Shore University, Australia Specialized in Gastroenterogy
2000-2006.	Hà Nội Medical University PhD degree
1999.	Paris VI, France Specialized in Gastroenterogy
1996-1997.	Paris VI, France Specialized in Gastroenterogy
1992-1995.	Hà Nội Medical University Master in Medecine
1985-1991.	Hà Nội Medical University Medical School

ABSTRACT

Hepatitis B virus (HBV) infection is a serious global health problem, with 2 billion people infected worldwide, and 350 million suffering from chronic HBV infection. In Vietn Nam, chronic HBV infection is common and usually acquired perinatally or in childhood. Perinatal transmission is the main route of transmission. Safe and effective vaccines against HBV infection have been popular in Viet Nam. Antiviral treatment is the only way to reduce morbidity and mortality from chronic HBV infection. In Viet Nam, Peg IFN and Tenofovir, Entacavir have been the primary treatments to date. Peg IFN produces a durable response in a moderate proportion of patients but has undesirable side-effects and must be administered subcutaneously 1 time per week. Tenofovir, Entacavir monotherapy or in combination with nucleoside analogs are options for patients who have developed resistance to other therapies for chronic HBV, including lamivudine and adefovir. APRI, FIB4, FibroScan were simple, available and noninvasive biochemical marker to predict the presence or absence of liver fibrosis and cirrhosis with AUROC >0,7 in Viet Nam. Eight genotypes of HBV have been identified labeled A through H. All known HBV genotypes have been found in the Viet Nam, 63% to 18% distribution between HBV genotypes B and C. The relation between HBV genotypes and treatment response are needed before testing for HBV genotypes in clinical practice is recommended. There is a correlation between concentrations of HBsAg and HBV DNA in serum and it can be used as a marker for monitoring of HBV treatment in Viet Nam.

FOR REFERENCE

Prevalence of hepatitis C infection (HCV) in Viet Nam is low in the general population (2-3%) but concentrated among people who inject drugs. Up to 97% of people who inject drugs have been infected with hepatitis C virus. People who are chronically infected with hepatitis C have difficulty accessing treatment due to the high cost of the antiviral medication. HCV is classified into six major genotypes and more than 50 subtypes. HCV-1b, the most common genotype worldwide, is also the dominant genotype in Asia. HCV-2a and 2b are also common and HCV-6 is the most common (> 50%) in Vietnam. PegIFN α-2a or -2b in combination with RBV is the

current standard of care in Viet Nam. SVR rates are consistently higher in patients with HCV genotypes 2 and 3 than in those with genotypes 1 or 4. Vietnamese patients also appear to have a higher likelihood of achieving a SVR than Caucasians who receive the corresponding regimen. Rapid virological response (RVR) is the single best predictor of treatment response, such as lower body weight and higher doses of RBV, can help ensure the achievement of SVR in Vietnamese patients. Viet Nam is currently developing national guidelines for the treatment of hepatitis C. HCV-1,4,6 patients who have an RVR should be treated for 24 weeks if they have a low baseline level of virus (below 400,000–800,000 IU/ml), whereas those with a higher baseline HCV RNA level should be treated for 48 weeks, even if they have an EVR. Treatment should be stopped at Week 12 if the HCV RNA decrease is less than 2 $\log_{10}$ IU/ml, and at Week 24 if HCV RNA is still detectable (≥50 IU/ml). HCV-1 patients who have a delayed virological response can be treated for 72 weeks in the hope of minimizing the risk of relapse, provided that their HCV RNA is undetectable at week 24. In patients infected with HCV genotypes 2 and 3 who have an RVR and low baseline viral load (< 400,000–800,000 IU/ ml), shortening the treatment duration to 16 weeks can be considered at the expense of a slightly higher chance of post-treatment relapse. However, shortening the treatment duration should not be considered for HCV-2/3 patients who have advanced fibrosis, cirrhosis or cofactors affecting response (i.e. insulin resistance, metabolic syndrome, non-viral steatosis), even if they have low baseline viral and RVR, due to insufficient evidence for equivalent efficacy. Treatment should be stopped at Week 12 if the HCV RNA decrease is < 2 $\log_{10}$ IU/ml, and at Week 24 if HCV RNA is still detectable (≥50 IU/ml). HCV-2/3 patients who have either EVR or DVR or with negative cofactors affecting response could be treated for 48 or 72 weeks, respectively, provided that their HCV RNA is undetectable at Week 24.

SESSION 1-4

PROGRAM

Tenofovir and lamivudine in late pregnancy to prevent perinatal transmission of hepatitis B virus in highly viremic mothers in Vietnam

PRESENTER

Dr. Nguyen Van Bang
Hà Nội Medical University

EDUCATION

Graduated from Hanoi Medical University (HMU) in 1976, specialized as pediatrician in 1979.

WORK EXPERIENCE

- Working in Pediatric Department, HMU since 1979
- Working in Pediatric Intensive Care Unit of University Hospital, Caen, France from 1991 to 1996.
- Working in Pediatric Gastroenterology and studying on *Helicobacter pylori* infection and related pathology for PhD from 2001 to 2005 in France and continuing to study on the field since then.
- Associate Professor since 2009.

ABSTRACT

We evaluated effect and safety of lamivudine and tenofovir in late pregnancy for preventing perinatal transmission of hepatitis B virus (HBV) to infants born to highly viremic mothers. A total of 82 pregnant chronic HBsAg(+) women with high viremia (>10^7 copies/mL) at 32 weeks of gestation were randomly located in 2 groups (lamivudine 100mg or tenofovir 300mg daily for 8 weeks of prepartum to week 4 pospartum). Infants received recombinant HBV vaccine without HBIg and were followed until week 52. At birth, HBsAg was positive in 21/82 (25.6%) and HBV DNA detectable in 7/82 newborns (8.5%). However, the perinatal trasmission rate of hepatitis B virus at week 52 was only 1.2% (1/82 infants). We noted a sharp decrease of mean maternal viral load from 5.09 x 10^8 ± 3.19 x 10^8 copies/mL at week 32 of gestation to 1.13 x 10^6 ± 3.91 x 10^6 at labor ($p<0.001$) with 2 undetectable HBV DNA cases (2.3%). The viral load reduction was stronger in tenofovir-treated mothers than in lamivudine-treated ones ($p<0.028$), particularly in 4 $\log_{10}$ reduction ($p<0.001$). Both tenofovir and lamivudine in late pregnancy showed the same safety and strikingly reduced perinatal transmission of HBV to infants born to highly viremic mothers. No viral resistance to the drugs was noted. Drug adverse events were rare and transient allowing complete full course in all cases, and flare had been seen in no case.
Keywords. *Hepatitis B virus; mother-to-child perinatal transmission; highly viremic women; lamivudine, tenofovir; late pregnancy.*

SESSION 1-5

PROGRAM
Epidemiology and Treatment of HBV-infected Patients in Vietnam

PRESENTER
Dr. Nguyen Ngoc Phuc
Hà Nội Medical University

EDUCATION

WORK EXPERIENCE

ABSTRACT

According to WHO statsic, HCV has infected in an estimated 170 million people wordwide and the number of new infected cases is roughly 3- 4 million ones every year. The percentage of incidences with HCV is account for range of 4 – 6 % in some studies and focus on high risk gorups, including intravenous drug user (ICU) and dialysis patiens. Those are double major ways transmitted HCV in VietNam. Prevalence rates were singnificantly higher in ICU with55.6%, dialysic patiennts' rates are 26.6%, commercial sex workers are 8.7% , surgical patiens are 1.7% and recipients of mutiple blood transfusion are 6.0%. The lowset prevalence reported is the low risk group consists of blood donor, military reruit and percentage in VietNam is genotype 1 with 30.4% and genottype 6 with 54.4% the resat of is account for 15.2%. one reseach conducted in VietNam in 2012 were revealed the rate of patients with hepatocellular carcinoma (HCC) induced HCV is 3.7% and HCC is one of the crucial complications of HCV. According to the recommendations of the association liver as EASL and AASLD 2014, the treatment of hepatitis C virus currently used at the same time is 3 groups pegnterferon drug, ribavirin and DAA group. But in Vietnam, the application of all three drugs to treat the problem, because the cost of treatment is quite costly, indicated for the treatment is applied only to the age of the patient is not too high, patients without cirrhosis, no more reduction of blood cell lines, primary therapy is being applied peg-interferon + ribavirin treatment. Efficiency is achieved when treated with this regimen carved rather high, with 50-60% of patients achieved sustained viral response. Patients should be carefully assessed before treatment and during treatment should monitor the side effects of the drug are very tight, especially anemia side effects of ribavirin.

SESSION 2-1

PROGRAM

HBV AND HCV EPIDEMIOLOGY AND GENOTYPES SPREAD IN MONGOLIAN POPULATION

PRESENTER

Prof. Tsendsuren Oyunsuren
Institute of Biology, Mongolian Academy of Sciences, Ulaanbaatar, Mongolia

EDUCATION

1979-1983	Otvos Lorand University, Budapest, Hungary, PhD diploma in Genetics
1971-1976	Odessa University, Odessa, Ukraine, Bachelor of Science in Biology

WORK EXPERIENCE

1992-	Lecturer, Professor, School of Biology, National University of Mongolia and Ulaanbaatar University
1988-	Head, Laboratory of Molecular Biology, Institute of Biology, Mongolian Academy of Sciences, Ulaanbaatar, Mongolia

ABSTRACT

According to the Mongolian Health sector review, a total of 2 537 cases of viral hepatitis were registered at the national level in 2013, taking up 6.8% of all communicable diseases, and compared to the previous year its incidence decreased by 1.7%. Despite of it hepatitis infection still remains one of serious health problems being the main reason for HCC development. Unfortunately, Mongolia has a highest rate of HCC in world in last 5 years. In 2013 it was 101.6/100000 in male and 87.9/100000.
The aim of present study was to determine prevalence and genotypes HBV and HCV spread among the Mongolian population.

In total 13985 blood samples were collected from healthy individuals (1147), blood donors (3180) and liver patients (9658) and were by using serological and molecular biological methods (PCR, Sequencing).

In results, the overall prevalence of seropositivity for HBsAg was 32.0% and HBsAg positive rates were 10.4% in general population, 41,6% in liver patients, 5.7% in children under 10 years of age before the national vaccination program. In 1992 the mass vaccination has started for all newly born children. At present about 0.8% of children are non-responders for HBV vaccine. Genotype D is the most prevalent (98.4%), subgenotype D1 and D3 are spread, with predominant of subgenotype D1 (78.6%). The genotype A and genotype C/D hybrid cases were found.

The prevalence of anti-HCV in general population and in liver patients was 9.5% and 67.1%, respectively. HCV genotype 1b is predominant (98.9%) and the genotype 2a`was found.

In total HBV, HCV and HDV infections were found in 92% of HCC patients. HCV mono- and HBV, HDV double infection might be the main reason of HCC development. HCV and HBV/HDV infections were detected in 41.5% and 24.6% of HCC patients, respectively.

SESSION 2-2

PROGRAM

CHRONIC HEPATITIS B AND CHRONIC HEPATITIS C TREATMENT IN MONGOLIA

PRESENTER

Prof. Davaadorj Duger

Vice president for Clinical Affair, Mongolian National University of Medical Sciences

Ulaanbaatar, Mongolia

EDUCATION

2000-2004	Medical University of Lodz, Poland. Department of Hepatology and Infectious diseases. PhD fellowship
2001-2002	Medical University of Lodz, Poland. Postgraduate fellowship. Internal medicine
1992-1994	Medical University of Mongolia. Ulaanbaatar. Postgraduate fellowship. Internal medicine/Gastroenterology – Hepatology
1985-1992	Medical University of Mongolia. Ulaanbaatar. physician
1975-1985	Secondary and High School of Ulaanbaatar #6

WORK EXPERIENCE

- Vice president for clinical affair of Mongolian National University of Medical Sciences, 2014
- Vice president for clinical affair of Health Sciences University, 2013
- Senior lecturer-doctor. Health Sciences University, School of Medicine. Department of Gastroenterology and Hepatology 2005
- Consultant doctor of National Cancer Centre since 2009
- Consultant doctor of Songdo Hospital since 2009
- Chief hepatologist of Ministry of Health Mongolia since 2007

2005- 2007	Scientific secretary of Academic Council of School Medicine HSUM.
2000-2004	PhD, Medical University of Lodz, Poland. Department of Hepatology and Infectious diseases.
1999-2000	Research assistant. Medical University of Lodz, Poland. Department of Hepatology and Infectious diseases.

1994-1999	Lecturer-doctor. Medical University of Mongolia. Department of Gastroenterology and Hepatology
1992-1994	Assistant lecturer. Medical University of Mongolia. Department of Gastroenterology and Hepatology

ABSTRACT

By 2013 statistical data in Mongolia 1027.81 per 10,000 populations the digestive system diseases were registered. Since 1990, cancer remains the second leading cause of population mortality in the country. In 2013, cancer related mortality rate was 21.2% from total mortality and was 14.7 per 10,000 in males and 10.7 per 10,000 in females. The leading causes of cancer in males in Mongolia are liver, stomach, lung, esophagus, and prostate. The leading causes of cancer in females are liver, stomach, esophagus, cervix and breast. Unfortunately, 78.9% of HCC cases were diagnosed in late stages (III and IV) of the cancer in 2012. Liver diseases, especially chronic viral hepatitis B and C, its complications such as liver cirrhosis and HCC cause serious health problems in the country.

By the statistics data at least 1200-1300 cases of HCC and liver cirrhosis are being newly registered per year. Due to economical –political situation of last years, screening and follow up management of patients with liver pathology were lost. Since 2005 the Mongolian Health system has been regenerating and innovating in whole area of the country and these periods AASLD and EASL guidelines for chronic hepatitis B/C treatment were translated and introduced for medical services. In 2008 the First National Gastroenterology – Hepatology Guidelines was approved by the Mongolian Gastroenterology Society on the basic guidelines of AASLD /EASL and it was updated 2012. According to this guideline the viral markers (including HBsAg, HBeAg, HBsAb, HCV ab, HDV ab) , viral loads (HBV DNA, HCV RNA Cobas Taqman, Roche) abdominal USG with Doppler, liver biopsy, Fibroscan, CBC and LFT should be used for diagnosis of CHB, CHC as well as co-infection with HDV.

For treatment of CHB we use the first, second, third line therapy (including PEGASYS Roche, Baraclude, Telbivudine , Lamivudin, Tenofovir) since 2008. For treatment of CHC used the standard Interferon in 1996-2010 and since 2008, PEGASYS and Ribavirin are being used. For HBV/Delta treatment, we use PEGASYS.

For diagnosis and treatment of liver cirrhosis/ HCC additionally, the imaging diagnosis, endoscopy, cancers markers, punctual biopsy, interventional radiology, surgery even liver transplantation are being used since 2011.

Herewith, I would like to present the results of two studies such as ETR treatment for CHB and Side effect of Pegasys IFN Ribavirin treatment for CHC.

1. Entecavir monotherapy in nucleoside-naïve patients with CHB.

Patients prospectively enrolled from 2010 by UB Songdo hospital were evaluated for the cumulative rates of undetectable HBV DNA (HBV DNA determined by PCR assay) levels, alanine aminotransferase (ALT) normalization, hepatitis B e antigen (HBeAg) seroconversion and monitored for any side effect. Thirty-two patients with CHB infection, who received naïve-entecavir therapy for mean. The patients who had taken 0.5 mg/d of entecavir to control CHB were retrospectively studied. Result: Charts from 32 patients with HBsAg seen in the clinic since 2010, all of them 19 were men and 13 were women, average age was 40.5. There were two patients with co-infection HDV-Ab. Serum ALT level was for mean 137u/l. of 32 patients, 5 were HBe-positive, and 19 were HBe-negative. Unfortunately, in 8 patients were not determined. Before the antiviral treatment, serum HBVDNA levels were determined by the Real Time PCR assay; HBVDNA level in 14(43.75%) became less than 3 log copies/ml and 8 (25%) patients became more than 5 log copies/ml. The highest HBVDNA level was 8.0 log copies /ml and the lowest was 1925.50 copies/ml.

During the antiviral treatment, 6 patients had the liver transplantation surgery and 26 patients with compensated liver disease started to have an antiviral treatment. 23 patients with chronic hepatitis B infection, who took naive-entercavir therapy 0.5 mg per day were continued to have for 3 to 45 months. HBVDNA level in serum not detected 3.5 years /1 case/ and at least 4 months after /1case/ the treatment duration.

Conclusion: Fourteen patients of all with undetectable HBV DNA level in chronic hepatitis B infection, who received naïve-entecavir therapy for mean 19.0 months enrolled in this study. 4 patients after 8 month therapy became RT- PCR result negative for HBV DNA and 10 patients about 1 year later.

2. Side effects of antiviral treatment in patients with chronic disease.

We concluded that flu like symptoms occurred in 90% of patients and can be eliminated by taking the small dose of NSAIDs. Hematologic toxicities include anemia and leukopenia are prevalent in patients with HCV infection. These can be managed by using growth factors, or by reducing the dose. Thrombocytopenia is common in patients with HDV infection and it is one of the main causes of treatment discontinuation. Psychiatric problems including anxiety, chronic fatigue, irritability and depression are common in clinical adverse effects in mongolian patients under pegylated IFN based treatment. Since severe depression can be a cause of treatment discontinuation, early recognition and taking antidepressants are essential for completing treatment regimen. A case of IFN-induced thyroiditis is registered

among patients.

SESSION 3-1

PROGRAM

Functional Roles of Hepatitis Virus X protein (HBx)

PRESENTER

Prof. Seishi Murakami

Department of Sports and Health, Kanazawa Gakuin University

EDUCATION

1965-1969	Graduate course of Medical Science, Kanazawa University Doctor of Medical Science, Ph.D.
1964-1965	Internship at Medical School, Kanazawa University.
1959-1964	Kanazawa Univeristy Medical School MD

WORK EXPERIENCE

2013-	Chief in Coordinators of Hokuriku Life Science Cluster
2011-	Professor of Dept. Sports and Health, Kanazawa Gakuin University
2008-2013	Research Director of Hokuriku Innovation Cluster for Health Science.
2008-2009	Advisor to Kanazawa University
2006-2011	Associate Member of Science Council of Japan
2006-2008	March Special Advisor to the President of Kanazawa University, Collaborative Researcher of Cancer Research Institute, Kanazawa University.
2006	Emeritus Professor of Kanazawa University
2004-2006	Deputy President of Kanazawa University
2004-2006	Head of Center for Collaboration Research of Kanazawa Univeity (Dual duty)
2002-2004	Deputy President of Kanazawa University
1994-2006	Professor of Doctoral Course of Medical Science, Kanazawa University
1997-2006	Professor, Division Chief of Molecular Biology, Dept. of Molecular Oncology, Cancer Research Institute Kanazawa University
1994-1997	Professor and Chief, Dept. of Molecular Biology, Cancer Research Institute Kanazawa University

1980-1982	Visiting Associate Professor, Dept. of Biochemistry, School of Medicine University of Minnesota, U.S.A.
1978-1994	Associate Professor, Dept. of Biophysics, Cancer Research Institute, Kanazawa University
1969-1978	Research Associate, Dept. of Biophysics, Cancer Research Institute Kanazawa University

ABSTRACT

Mammalian hepadnaviruses, including HBV, are distinct from avian ones on their oncogenic property causing the incidence of hepatocellular carcinoma (HCC) among the world. HBx has been suspected as the culprit of hepatocarcinogenesis since X-ORF is not found in the avian genomes. On the way to explore molecular function of HBx in the tissue culture and the mice systems, HBx has been reported to modulate a variety of host cellular systems involving in tumor-promotion and tumorigenesis, and its direct or indirect host targets have been accumulated as reviews (1).

Clinical studies show the tight correlation between the extent of HBV replication and the HCC incidence implying a possible role of HBx on HBV replication. In this context, we reported that HBx is necessary for the efficient HBV transcription and replication using the transient HBV replicon system, and that the nuclear coactivator function of HBx might be responsible for the function (2). In the last several years with applying the advanced HBV infection systems, it has been clearly shown that the essential role of HBx on pgRNA transcription, thus resulting HBV replication, with cccDNA template (3). How the recruited HBx on HBV genome of mini-chromosome plays role(s) on pgRNA synthesis remains elusive although epigenetic regulation of chromatin structure would be the modulation mechanism (4) although the low content of cccDNA in the available HBV replication systems makes difficult for analysis of the molecular mechanism.

We will overview the molecular roles of HBx for the future contribution to the effective prevention and treatment of liver cancer.

References

1. Tang H et al (2006) Cancer Sci, 97(10): 977-83.
2. Tang H et al. (2005) J Virol, 79(9): 5548-56.
3. Lucifora J et al (2011) J Hepatol, 55: 996-1003.
4. Baloni L et al (2009) Proc Natl Acad Sci USA, 106: 19975-79.

SESSION 3-2

PROGRAM

Molecular Biology of Cancer Metastasis

PRESENTER

Prof. Katsuji Yoshioka
Division of Molecular Cell Signaling, Cancer Research Institute, Kanazawa University

EDUCATION

1987	Kyushu University Graduate School of Medicine, Japan, Ph.D.
1982	Kyushu University Graduate School of Pharmaceutical *Sciences, Japan, MSc.*
1980	Kyushu University, Faculty of Science, Japan, BSc.

WORK EXPERIENCE

2001-	Professor, Cancer Research Institute, Kanazawa University, Japan
1994-2001	Associate Professor, Cancer Research Institute, Kanazawa University, Japan
1992-1994	Research Fellow, University of California, San Diego, USA
1991-1992	Assistant Professor, Kyushu University, Faculty of Medicine, Japan
1987-1990	Assistant Professor, Kitasato University, School of Hygienic Sciences, Japan

ABSTRACT

Cancer metastasis is a critical determinant of cancer-related deaths. The study of cancer metastasis has grown exponentially, however, the molecular mechanisms underlying cancer metastasis are still poorly understood. We employed B16 melanoma cell line as a model system to study cancer metastasis, focusing on Sonic hedgehog (Shh) signaling pathways. B16 cells overexpressing the transcription factor Gli1, a major target of Shh signaling, showed increased metastatic activity. To gain insight into the molecular mechanisms, we performed microarray analysis and found that the expression of hypoxia-inducible genes was up-regulated, although the expression of hypoxia-inducible factors (HIFs) themselves remained unchanged in the cells overexpressing Gli1. Our findings suggest a novel mechanism by which Shh-Gli signaling regulates cancer metastasis by modulating the expression of HIF target genes. In this symposium, I will discuss this novel mechanism.

SESSION 3-3

PROGRAM

HIV infection in Asia

PRESENTER

Dr. Azumi Ishizaki

Viral Infection and International Health, Graduate school for Medical Science, Kanazawa University.

EDUCATION

2005-2009	PhD, Kanazawa University, Graduate School of Medical Science, Kanazawa, Japan
1994-1998	M. D., Kanazawa University, School of Medicine, Kanazawa, Japan
1992-1994	Premedical Course, Kanazawa University, School of Medicine, Kanazawa, Japan

WORK EXPERIENCE

2013-	Internist, Infectious Disease Specialist, Hanoi Family Medical Practice, Hanoi, Viet Nam
2007-2012	Infectious Disease Specialist, Medical Consultant, Houju Memorial Hospital, Ishikawa, Japan
2003-2005	Internist, Hanoi Family Medical Practice, Hanoi, Viet Nam
2002-2003	Department of Clinical Infectious Diseases Fellow, Toyama Medical and Pharmaceutical University, Toyama, Japan
2001-2002	AIDS Clinical Center Fellow, International Medical Center of Japan, Tokyo, Japan
2000-2001	Infectious Diseases Fellow, St. Luke's International hospital, Tokyo, Japan
1998-2000	Internal Medicine Residency, International Medical Center of Japan, Tokyo, Japan

ACADEMIC EXPERIENCE

2008-	Department of Viral Infection and International Health Assistant Professor, Kanazawa University, Graduate School of Medical Science, Kanazawa, Japan
2007-2008	Department of Parasitology Assistant Professor, Kanazawa University, Graduate School of Medical Science, Kanazawa,

Japan

ABSTRACT

HIV/AIDS is one of the major global public health issues. In 2013, there were an estimated 35 million people living with HIV in the world and 4.8 million in the Asian and the Pacific.

Combination antiretroviral drug therapy (ART) is the gold standard treatment for HIV/AIDS. ART has been scaling up especially in low- and middle-income countries over the last decade. As consequence, AIDS-related deaths have fallen by 27% since 2005, the new HIV infections have fallen by 6% since 2005, and especially the new HIV infections among children have declined by 15% since 2009 in the Asian and the Pacific. As ART coverage increases, the emergence of drug resistant HIV (DR) during the ART which leads treatment failure and the circulation of DR in the community become important concerns. How to detect the emergence of DR at proper timing and switch to secondary regimen is an urgent issue to be investigated.

In Asia, the outbreak of the HIV infection started from the injecting drug users (IDU) population, then spread to the female sex workers (FSW) and the general population. And now, the growing key population is a men who have sex with men (MSM). Some of them are IDU as well as selling sex to others. MSM is 19 times more likely to be living with HIV than the general population. The effective methods to prevent HIV transmission are different for each target populations. Harm reductions for IDU and all kind of supports for MSM are the important challenges in Asia and the Pacific.

Because the hepatitis viruses share the mode of transmission with HIV, co-infections of HIV with HBV and/or HCV are critical issues on care and management for people living with HIV especially in Asia.

SESSION 3-4

PROGRAM

HIV coinfection with hepatitis viruses in Asia

PRESENTER

Prof. Hiroshi Ichimura

Department of Viral Infection and International Health, Graduate School of Medical Sciences, Kanazawa University

EDUCATION

1991-1992	Visiting virologist, Cancer Research Institute, University of California, San Francisco, School of Medicine, San Francisco, USA.
1985-1987	Research Associate, Department of Biochemical Virology, Baylor College of Medicine, Houston, USA.
1980-1984	Doctor Course at Department of Virology, Tottori University, School of Medicine, Yonago, Japan. Doctor of Medical Science
1974-1980	Yamaguchi University School of Medicine, Ube, Japan.

WORK EXPERIENCE

2001-	Professor, Department of Viral Infection and International Health, Graduate School of Medical, Sciences, Kanazawa University, Kanazawa, Japan.
1999-2001	Professor, Department of International Environmental Health, School of Medicine, Kanazawa University, Kanazawa, Japan.
1994-1999	Associate Professor, Department of Microbiology, Kyoto Prefectural University of Medicine, Kyoto, Japan.
1994-1994	Assistant Professor, Department of Microbiology, Kyoto Prefectural University of Medicine, Kyoto, Japan.
1984-1994	Chief, Department of Virology, Institute of Clinical Research, Kure National Hospital, Hiroshima, Japan.

ABSTRACT

Persons at high risk for human immunodeficiency virus (HIV) infection are also likely to be at risk for other infectious pathogens, including hepatitis B virus (HBV) or hepatitis C virus (HCV). These are bloodborne pathogens transmitted through similar routes; for example, via injection drug use, sexual contact, or from mother to child during pregnancy or birth. HIV-positive persons who become infected with hepatitis B virus (HBV) are at increased risk for developing chronic HBV infection. In addition, persons who are co-infected with HIV and HBV can have serious medical complications, including an increased risk for liver-related morbidity and mortality. Coinfection with HIV and HCV is common (50%–90%) among HIV-infected injection drug users. HCV is one of the most important causes of chronic liver disease and HCV infection progresses more rapidly to liver damage in HIV-infected persons. Further, coinfection with viral hepatitis may complicate the delivery of antiretroviral therapy by increasing the risk of drug-related hepatoxicity and impacting the selection of specific agents (e.g., those dually active against HIV and HBV). Expert guidelines developed in the United States and Europe recommend screening of all HIV-infected persons for infection with HCV and HBV and appropriate management of those found to be chronically infected.

In this talk, I will introduce you the current situation of HIV co-infection with HBV/HCV in Asia, including some of our findings in the Philippine and Vietnam, and current approaches to management of HIV-infected persons coinfected with HBV or HCV in these countries.

SESSION 4-1

PROGRAM

Strategy for Follow-up Check-ups for Hepatitis Patients in Ishikawa, Japan

PRESENTER

Dr. Tetsuro Shimakami
Department of Gastroenterology, Kanazawa University Hospital, Japan

EDUCATION

1998-2004	Kanazawa University Graduate School of Medical Science
2001-2003	Graduate School Student in Molecular Biology, Cancer Research Institute, Kanazawa University
1998	Graduate School of Medicine, Kanazawa University

WORK EXPERIENCE

2013-	Assistant Professor, Kanazawa University Hospital, Department of Gastroenterology
2012-2013	Project Assistant Professor, Kanazawa University Hospital, Department of Gastroenterology
2011-2012	Medical staff in Kanazawa University Hospital, Department of Disease control and Homeostasis, Internal Medicine
2010-2011	Post doc fellow in The University of North Carolina at Chapel Hill, The Lineberger Comprehensive cancer Center (Stanley M Lemon's lab)
2008-2010	Post doc fellow in The University of Texas Medical Branch, Department of Microbiology and Immunology (Stanley M Lemon's lab)
1998-2008	MD, Department of Gastroenterology, Kanazawa University Hospital

ABSTRACT

In Japan, approximately 2% of the population is estimated to be infected with hepatitis C virus (HCV) or B virus (HBV). It is believed that, within this 2%, many do not know they are infected. It is vital to find, diagnose and correctly treat HBV/ HCV infected people because, if left untreated, these viruses can cause death from liver disease. Fortunately, effective anti-viral therapies have become available that can inhibit the virus, therefore, the Japanese Government is strongly suggesting that all people get hepatitis tests for HBV and HCV at least once in their life.

To encourage hepatitis testing, the Japanese national and local government provide free testing, at five year intervals, for people aged 40 – 70. To support identification, proper diagnosis and treatment for hepatitis virus infected people, the Ishikawa Prefectural Government started its own follow-up check-up program in 2002.

The 2002 program's main points were:

1. The local government did follow-up testing for Hepatitis- positive people.
2. The program initiated and Hepatitis information dissemination campaign for patients, doctors and health care workers via workshops and publications.
3. Standard protocols for liver imaging at detailed examinations were established.
4. To confirm accurate follow-up treatment, clinical conferences for doctors treating Hepatitis were introduced.

During years 2002 – 2006, among testing participants in Ishikawa Prefecture, 1333 people were found to be infected with HBV, and 1322 with HCV. In 2009, Kanazawa University Hospital, became a regional core institution and took over annual follow-up check-ups of hepatitis patients from local governments and created the Ishikawa Hepatitis Follow-up Program.

The 2009 program's main point is:

1. Both local government and KU do follow-up testing for Hepatitis- positive people.
2. Previously, only local governments were allowed to possess individuals' private information. Now, based on signed consent from citizens, local governments will share certain Hepatitis-related information with Ishikawa Hepatitis Follow-up Program- administered by Kanazawa University.

So far, 1100 out of 2900 hepatitis-infected patients have agreed to participate in this program. The Kanazawa University directly contacts consenting patients and follows-up to confirm they annually see specialized doctors in addition to primary doctors. Local governments continue to contact people who do not respond or accept direct contact with Kanazawa University.

In conclusion, the condition of all hepatitis-infected patients found by local governments can be checked annually by the local government or Kanazawa University. This kind of follow-up check-up system for hepatitis patients in Ishikawa has been distributed throughout Japan as a promising model

system.

SESSION 4-2

PROGRAM

TREATMENT OF HBV-INFECTED PATIENTS IN JAPAN

PRESENTER

Prof. Yasunari Nakamoto
Division of Gastroenterology, Faculty of Medical Sciences, University of Fukui

EDUCATION

1993	Ph.D. (Dr. of Medical Science), Kanazawa University, Kanazawa, Ishikawa, Japan (Thesis: Establishment of detecting system for surface antigen containing hypervariable regions of hepatitis C virus)
1989	M.D. Kanazawa University School of Medicine, Kanazawa, Ishikawa, Japan

WORK EXPERIENCE

2011-	Professor and Head, Second Department of Internal Medicine (Gastroenterology and Neurology), Faculty of Medical Sciences, University of Fukui, Japan
1996-2010	Assistant Professor, Department of Internal Medicine, Kanazawa University School of Medicine, Japan
1997	Research Advisor, Monbusho (the Japanese Government) Research Experience Fellowships for Young Foreign Researchers, Japan
1994-1996	Research Associate, working under Prof. Francis V. Chisari, M.D., The Scripps Research Institute, La Jolla, CA, U.S.A.
1993-1994	Research Associate, First Department of Internal Medicine, Kanazawa University School of Medicine, Japan
1991-1993	Graduate Research, Department of Biophysics, Cancer Research Institute, Kanazawa University, Japan
1989-1991	Resident in Internal Medicine, First Department of Internal Medicine, Kanazawa University School of Medicine, Japan

ABSTRACT

The following topics of hepatitis B virus (HBV) prevention and therapy will be principally discussed.

- Background of HBV Infection and Prevalence :

  > Hepatitis B: the virus and disease. Liang TJ. Hepatology. 2009 May;49(5 Suppl):S13-21.

  > Recommendations for identification and public health management of persons with chronic hepatitis B virus infection. Weinbaum CM, et al. Hepatology. 2009 May;49(5 Suppl):S35-44.

- Development of HBV Prevention Strategy in Japan :

  > Viral hepatitis and hepatocellular carcinoma prevention strategy in Japan. Oda T. Jpn J Cancer Res. 1999 Oct;90(10):1051-60.

- Treatments of Chronic Hepatitis B; Nucleoside Analogues vs. Interferons :

  > Benefits and risks of nucleoside analog therapy for hepatitis B. Dienstag JL. Hepatology. 2009 May;49(5 Suppl):S112-21.

  > Hepatitis B virus infection. Liaw YF, et al. Lancet. 2009 Feb 14;373(9663):582-92.

- Treatment Guidelines on Chronic hepatitis B :

  > Practical approach in hepatitis B e antigen-negative individuals to identify treatment candidates. Azmi AN, et al. World J Gastroenterol. 2014 Sep 14;20(34):12045-55.

  > Update on hepatitis B virus infection. You CR, et al. World J Gastroenterol. 2014 Oct 7;20(37):13293-13305.

  > Improving outcomes for patients with chronic hepatitis B. Gish RG. Hepatol Res. 2007 Jul;37(s1):S67-78.

- Prevention of HBV-Related Hepatocellular Carcinoma (HCC) :

  > Spontaneous seroclearance of hepatitis B seromarkers and subsequent risk of hepatocellular carcinoma. Liu J, et al. Gut. 2014 Oct;63(10):1648-57.

  > Prevention of hepatitis B virus-related hepatocellular carcinoma with antiviral therapy. Lai CL, et al. Hepatology. 2013 Jan;57(1):399-408.

  > Role of antiviral treatment for HCC prevention. Colombo M, et al. Best Pract Res Clin Gastroenterol. 2014 Oct;28(5):771-781.

  > Long-term entecavir treatment reduces hepatocellular carcinoma incidence in patients with hepatitis B virus infection. Hosaka T, et al. Hepatology. 2013 Jul;58(1):98-107.

> Hepatitis B: future curative strategies. Bertoletti A, et al. Curr Opin Infect Dis. 2014 Dec;27(6):528-34.

SESSION 4-3

PROGRAM

Reactivation of hepatitis B after immunosuppressive chemotherapy in Japan

PRESENTER

Dr. Naoki Oishi
Department of Gastroenterology, Kanazawa University Hospital, Japan

EDUCATION

2002-2004	Department of Molecular Biology, Cancer Research Institute of Kanazawa University (Prof. Seishi Murakami)
1999-2007	Kanazawa University Graduate School of Medicine.
1999	Graduate School of Medicine, Kanazawa University

WORK EXPERIENCE

2014-	Specially Appointed Associate Professor, Department of Stem Cell and Metabology
2012-2014	PhD, Gastroenterology, Kanazawa University Hospital
2010-2012	Research Fellow, Liver Carcinogenesis Section, Laboratory of Human Carcinogenesis, NCI, NIH, USA
2008-2010	Assistant Professor, Department of Emergency and Critical Care Medicine
1999-2008	MD, Department of Gastroenterology, Kanazawa University Hospital

ABSTRACT

Patients with current or past hepatitis B virus (HBV) infection are at risk of viral reactivation if they receive immune-modulating treatment or chemotherapy. This condition affects primarily hepatitis B surface antigen (HBsAg)-positive patients, but sometimes HBsAg-negative patients can be at risk, based only on evidence of past infection or occult infection with a low titer of detectable hepatitis B virus (HBV) DNA. The clinical outcomes vary with the different degrees of virologic and biochemical rebound, ranging from asymptomatic elevations in liver enzymes to hepatic failure and even death.

In Japan, 1-3% of patients are hepatitis B surface antigen-positive, and 20-25% of patients are hepatitis B surface antigen-negative with hepatitis B core antibody and/or hepatitis B surface antibody positively. In guidelines for hepatitis B virus reactivation, the prophylactic administration of an antiviral drug in hepatitis B surface antigen-positive patients is recommended, and periodic monitoring of hepatitis B virus DNA and the deferred pre-emptive administration of an antiviral drug after conversion to hepatitis B virus DNA positively are recommended in hepatitis B surface antigen-negative patients.

SESSION 4-4

PROGRAM

Treatment of HCV-infected patients in Japan and an Experimental Model of HCV Infection

PRESENTER

Prof. Masao Honda
Department of Advanced Medical Technology, Kanazawa University Graduate School of Health Medicine, Kanazawa, Japan

EDUCATION

1990	Department of Biophysics, Cancer Research Institute of Kanazawa University (Prof. Seishi Murakami)
1988-1992	Kanazawa University Graduate School of Medicine.
1988	Graduate School of Medicine, Kanazawa University

WORK EXPERIENCE

2007-	Professor, Department of Laboratory Medicine, Kanazawa University Graduate School of Health Medicine.
2001-2007	Associate Professor, Department of Infectious Disease and Disease Control, Kanazawa University Graduate School of Medicine.
1994-1997	Research Fellow of Division of Infectious Disease, Department of Medicine, University of North Carolina at Chapel Hill (Dr. Stanley M Lemon)
1994-2001	Assistant Professor of Department of Gastroenterology, School of Medicine, Kanazawa University
1992-1994	Resident of Department of Gastroenterology, School of Medicine, Kanazawa University

ABSTRACT

Of the 1.2 million people living with HCV in Japan, approximately 70% have genotype 1b. Further, a significant number of patients with HCV in Japan are over the age of 65, leading to more disease-related complications and a decreased likelihood of tolerating interferon-based therapies for HCV. Until 2011, in Japan, Peg-IFN and ribavirin (RBV) combination therapy for 48-weeks regimen was a standard therapy for the patients with chronic hepatitis C (CH-C) infected with high viral load and genotype 1b HCV. The rate of sustained virological response (SVR) was 50%. Multivariate analysis of various clinical factors associated with the treatment response revealed that IL28B genotype and stage of liver fibrosis were independent factors associated treatment response. We examined relationship between the expression of hepatic interferon stimulated genes (ISGs) and IL28B genotype and showed ISGs were up-regulated in liver of treatment resistant IL28B genotype and were down-regulated in liver of treatment sensitive IL28B genotype. Furthermore, we examined the mechanisms why efficacy of IFN-based therapy was hammered in patients with advanced liver fibrosis, using *in vitro* HCV replication system in which infectious JFH-1 and H77 derived clones were replicating. We revealed impaired mTORC1 nutrition signal and activated pro-fibrotic TGF-β signaling impaired IFN signaling substantially.

This year, the Japanese Ministry of Health, Labor and Welfare (MHLW) has approved Daclatasvir, a potent, pan-genotypic NS5A replication complex inhibitor, and Asunaprevir, a NS3/4A protease inhibitor. This dual regimen is Japan's first all-oral, IFN- and RBV-free treatment regimen for patients with genotype 1 CH-C, including those with compensated cirrhosis. Phase III study demonstrated that dual regimen achieved overall SVR24 among 84.7% of CH-C. Further, patients with compensated cirrhosis present at baseline had overall SVR24 rates of 90.9%. Thus combination of direct acting antiviral agents (DAAs) is effective and curable treatment regimen for CH-C including difficult to treat patients.