ICMS 2008

International Crisis Management Symposium on CBRN and Emerging Infectious Diseases

September 13th - 16th, 2008

Chiba Institute of Science (Choshi, Japan)

Program / Abstract Book

View from this Institute "Mt. Fuji"

Byoubugaura, Choshi

Organizing Committee of CIS Symposium 2008

c/o Chiba Institute of Science, 15-8 Shiomi-cho, Choshi, Chiba 288-0025, Japan
E-mail: sympo@cis.ac.jp
Homepage: http://www.cis.ac.jp/~sympo/

View from this Institute: National Park "Byoubugaura"

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Introduction from the Symposium Vice President

The first trial to provide a scientific meeting on crisis management was performed on 2005 at this Institute. It was the International Symposium on NBC Terrorism Defense from June 17 to 19, 2005. The participants to this Symposium came together from various fields and countries and talked about the ways how to prevent terrorisms by nuclear, bio, and chemical materials as well as those by explosives. Before the 2005 Symposium, a number of meetings have been organized about the terrorisms. However, most of those meetings were of political or commercial purposes. In such meetings, people cannot expect to accumulate needed knowledge against terrorisms free from the policy of a certain country. Thus, at that time we realize the need of scientific approaches for preventing disasters by terrorisms. Indeed, the 2005 Symposium was the first scientific one against terrorisms.

After that Symposium, we have planned the second one. Later we change somewhat our mind and the topics of the second symposium are considered to be of the disasters with which people in the world are seriously damaged. Those include influenza pandemic, food safety, medical malpractice, hospital infection, environment pollution, fires and explosions, radioactive contamination, bio and chemical material accidents. On behalf of the Organizing Committee of the Symposium, I hope that all the participants enjoy this Symposium and utilize the obtained knowledge to enhance the safety of our society. Please effectively use this opportunity and get useful knowledge against serious disasters.

Because of the language barrier, some presentations would not be easy to understand. This abstract book is prepared to overcome such difficulty. This abstract book would be useful to further understand the presentations.

Toshisuke HIRANO

Symposium Vice President of the Organizing Committee
President, Chiba Institute of Science, Choshi, Chiba, Japan

Introduction from the Congress Chairman

Chiba Institute of Science was the first college in Japan to open a school of Crisis Management, which was established in 2004. The next year was the 10th anniversary of the Tokyo subway sarin terrorist attack, and Chiba Institute of Science held its first CBRN (NBC) conference to commemorate it.

Now CIS is proud to present a second symposium, expanding the original topic of CBRN (NBC) to also include emerging infectious diseases, which are another grave threat to public health. We are glad to welcome attendees from many different countries around the world and every corner of Japan who are in many different areas of crisis management, and we believe that everyone will benefit from our presenters' shared expertise.

The first chemical terrorism incident directed at citizens took place in Japan in 1994 by the same extreme religious group, Aum Shinrikyo, who would later release poison gas on the Tokyo subway.

Another case of chemical weapon use against civilians was during the Iran-Iraq War in 1980-1988. Although these were considered acts of war and directed mainly at soldiers, citizens in villages near the war zone were often affected and took terrible casualties. Iraq used a massive amount of chemical weapons in its offensives throughout the war, including mustard gas, tabun, and sarin.

Although both of these uses of chemical weapons were important, they are often overshadowed by other world events and many people have forgotten about them or never knew about them at all. Therefore, for my opening speech, I would like to present about both these events briefly.

Anthony T. TU

Congress Chairman of the Organizing Committee
Professor Emeritus, Department of Biochemistry and Molecular Biology, Colorado State University, Fort Collins, CO, USA
Visiting Professor, Department of Crisis Management, Chiba Institute of Science, Choshi, Chiba, Japan

Organizing Committee of CIS Symposium 2008

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[Symposium Vice President]

Toshisuke HIRANO (President, Chiba Institute of Science)

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Tsuyoshi MIURA (Assistant Professor, CIS)
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***CIS: Chiba Institute of Science**

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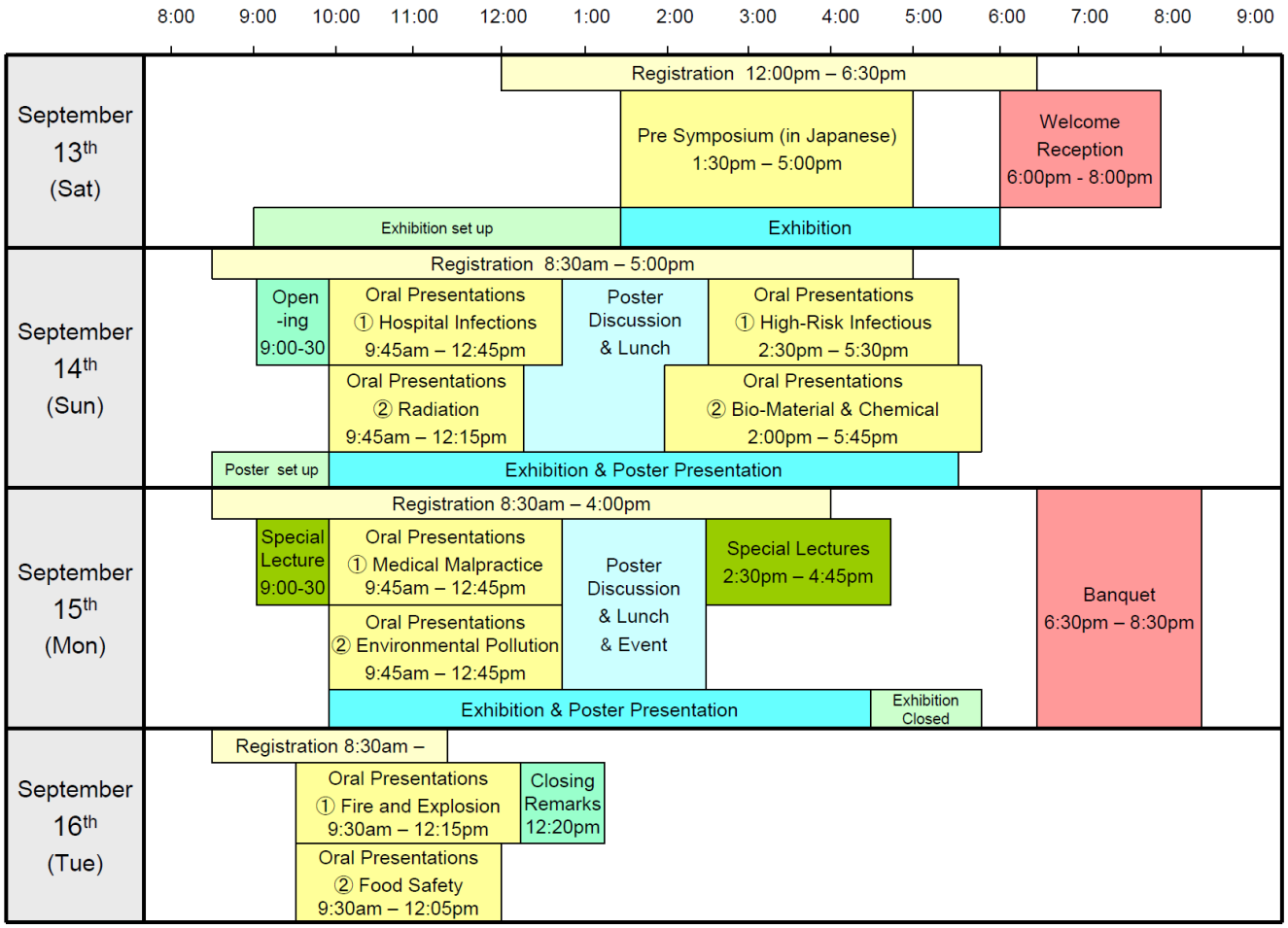
Symposium Meeting Calendar

Schedule at a Glance



Saturday, September 13th

12:00 pm – 6:30 pm	Registration	Reception Desk
1:30 pm – 5:00 pm	Pre Symposium (in Japanese)	Site 1
1:30 pm – 6:00 pm	Exhibits Open	Welfare Building
6:00 pm – 8:00 pm	Welcome Reception	Café Marina

Sunday, September 14th

8:30 am – 5:00 pm	Registration	Reception Desk
9:00 am – 9:30 am	Opening Ceremony	Site 1
9:45 am – 5:30 pm	Poster Area Open for Viewing	Welfare Building
9:45 am – 5:30 pm	Exhibits Open	Welfare Building
9:45 am – 12:45 pm	Session “Hospital Infections”	Site 1
9:45 am – 12:15 pm	Session “Radiation Emerging Disasters”	Site 2
12:15 pm – 2:30 pm	Lunch Time	Welfare Building

12:45 pm – 1:45 pm	Poster Session 1	Welfare Building
1:15 pm – 2:15 pm	Poster Session 2	Welfare Building
2:00 pm – 5:45 pm	Session “Bio-Material & Chemical Emerging Disasters”	Site 2
2:30 pm – 5:30 pm	Session “High-Risk Infectious Diseases”	Site 1

Monday, September 15th

8:30 am – 4:00 pm	Registration	Reception Desk
9:00 am – 9:30 am	Special Lecture	Site 1
9:45 am – 4:30 pm	Poster Area Open for Viewing	Welfare Building
9:45 am – 4:30 pm	Exhibits Open	Welfare Building
9:45 am – 12:45 pm	Session “Medical Malpractice”	Site 1
9:45 am – 12:45 pm	Session “Environmental Pollution”	Site 2
12:45 pm – 2:30 pm	Lunch Time and Event	Welfare Building
2:30 pm – 4:45 pm	Special Lectures	Site 1
6:30 pm – 8:30 pm	Banquet	Inubosaki Keisei Hotel

Tuesday, September 16th

8:30 am – 11:00 am	Registration	Reception Desk
9:30 am – 12:15 pm	Session “Fire and Explosion”	Site 1
9:30 am – 12:05 pm	Session “Food Safety”	Site 2
12:20 pm – 12:40 pm	Closing Ceremony	Site 1

General Information

Registration and Information

Registration will be held in the Symposium Reception Desk, Chiba Institute of Science beginning Saturday, September 13th, during the following hours:

Saturday, September 13th	12:00 pm – 6:30 pm
Sunday, September 14th	8:30 am – 5:00 pm
Monday, September 15th	8:30 am – 4:00 pm
Tuesday, September 16th	8:30 am – 11:00 am

On-Site Fees

Regular Participants	JPY 20,000 *
Student	JPY 5,000 *
Company	JPY 100,000 * (Max 10 people)
Banquet Ticket	JPY 5,000

* Does not include banquet ticket.

Scientific Sessions

All scientific sessions will be held in Chiba Institute of Science. The presentations will begin on Sunday morning, September 14th at 9:45 AM and will end on Tuesday, September 16th at 12:15 PM.

Poster Sessions

A number of scientific posters will be presented in two poster sessions to be held in Welfare Building at Chiba Institute of Science.

Setup	Saturday,	September 13th	1:30 pm – 6:00 pm
	Sunday,	September 14th	8:30 am – 9:45 am
Available for Viewing	Sunday,	September 14th	1:30 pm
	~ Monday,	September 15th	4:00 pm
Remove	Monday,	September 15h	4:00 pm – 5:30 pm
Disucussion			
Session 1	Sunday,	September 14th	12:45 pm – 1:45 pm
Session 2	Sunday,	September 14th	1:15 pm – 2:15 pm

Program / Abstract Book

Each Symposium registrant (early and regular registration) will receive one copy of the Program / Abstract Book. Additional copies may be purchased at the Reception Desk for 1000JPY per Book, while supplies last.

Name Badges

Symposium registrants are required to wear their Symposium name badge at the time. The name badge is required for admission to all scientific sessions, exhibits and social functions.

Meal Functions

The Saturday evening Welcome Reception, lunch, and coffee breaks are included in all registration fees. In order to attend the banquet (Monday evening), tickets must be purchased by 10:00 AM Sunday, September 14th.

Welcome Reception

All participants and accompanying guests are invited to the Symposium Welcome Reception on Saturday evening, September 13th. The Reception will be held in the Café Marina at Chiba Institute of Science, and will include beer, alcohols, soft drinks, foods, and desserts.

Banquet

The Symposium Banquet will be held on Monday evening, September 15th at the Inubosaki Keisei Hotel. To join the Symposium Banquet, there are shuttle bus from Symposium site to the Hotel. In order to attend the banquet (Monday evening), tickets must be purchased by 10:00 AM Sunday, September 14th.

Transportation

There are two ways to visit Choshi: 1) Access from Tokyo Station; 2) Access from Narita (Tokyo International Airport). Details are described in the Symposium website. Please contact us for questions on transportation (E-mail: sympo@cis.ac.jp).

Emergency Medical Services

In case of medical emergency, please contact the Symposium Reception Desk or the staff of the Organizing Committee.

Important Telephone

Symposium Secretariats

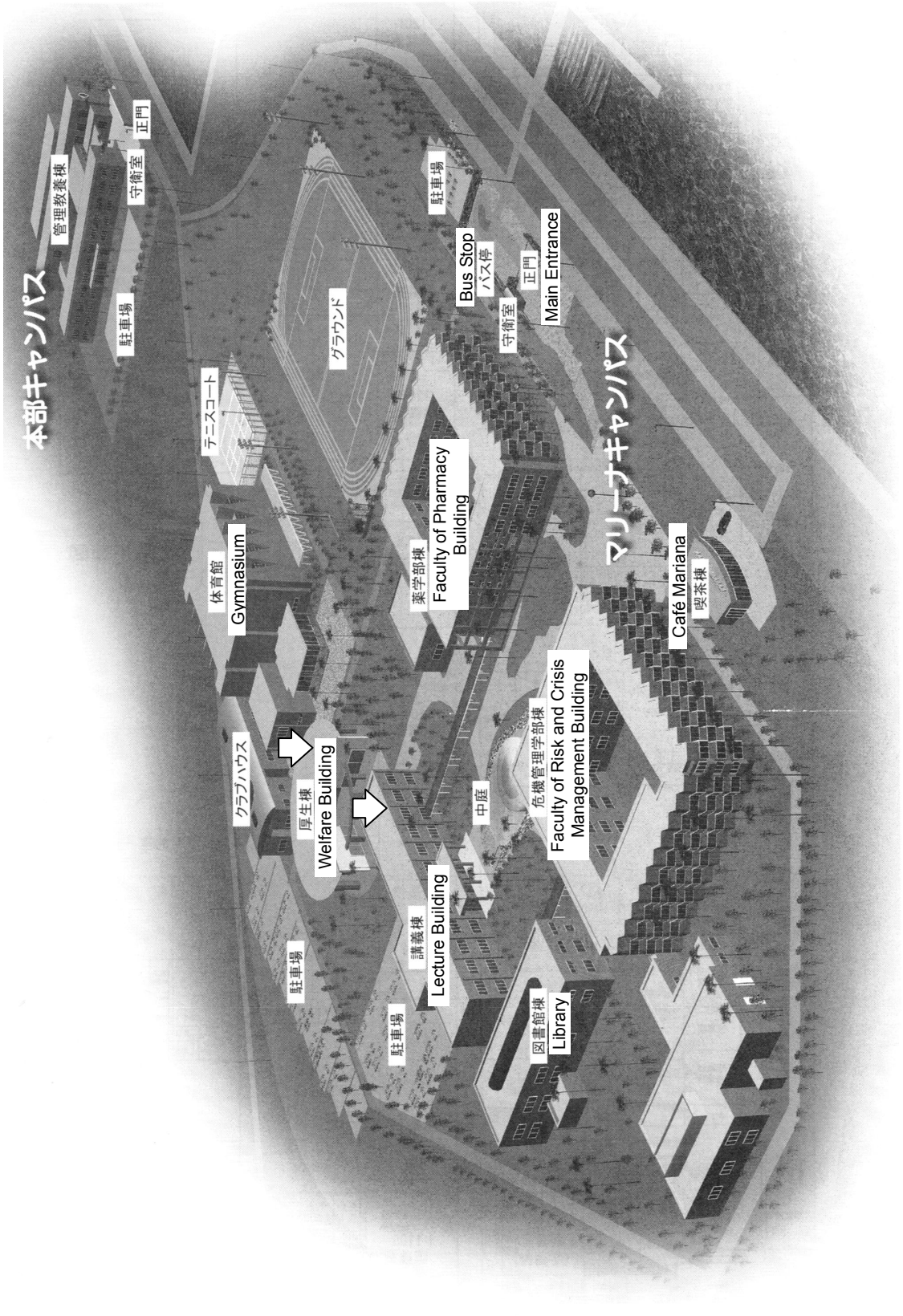
Masahiro MORI	0479-30-4676	mmori@cis.ac.jp
Hiroyasu OHTAKA	0479-30-4706	hohtaka@cis.ac.jp

Symposium Office

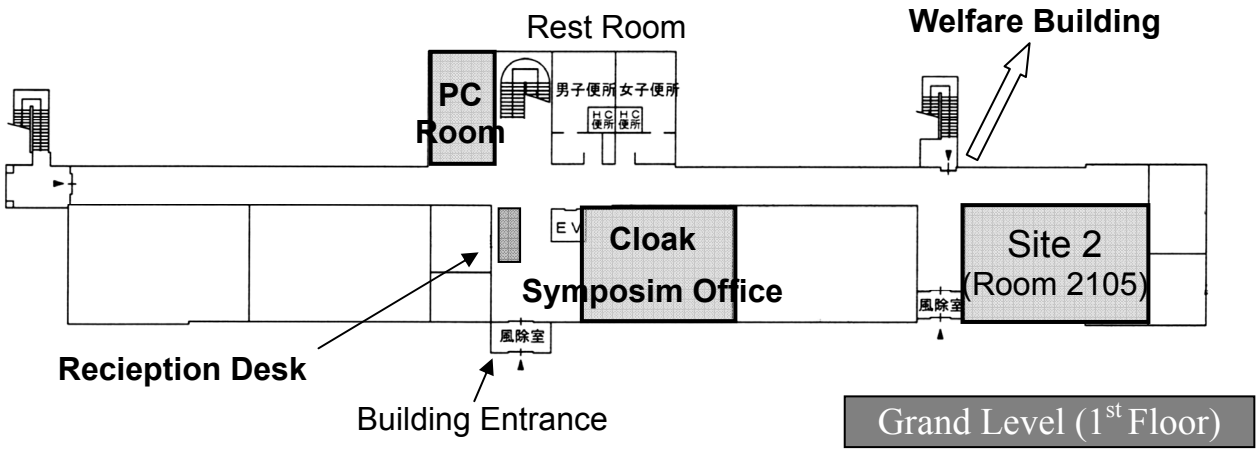
Chiba Institute of Science, Symposium Office / Symposium Reception Desk
Phone: 0479-30-4706
E-mail: sympo@cis.ac.jp

Floor Plan

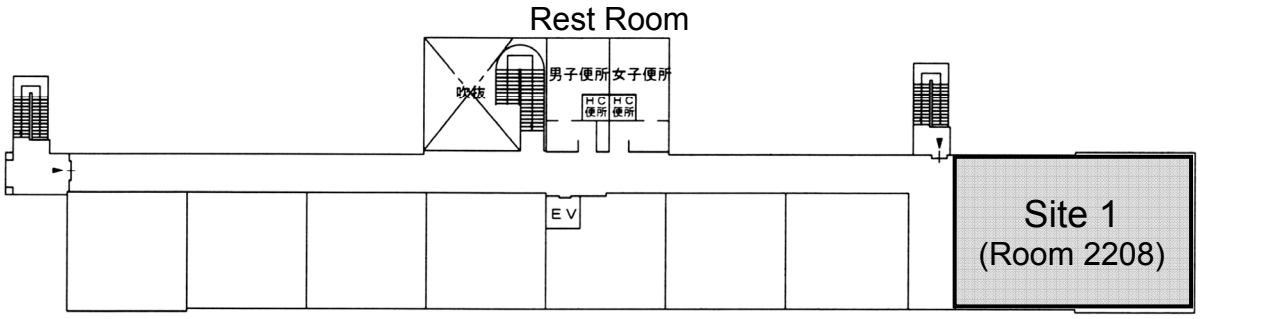
Chiba Institute of Science Campus Map



Lecture Building

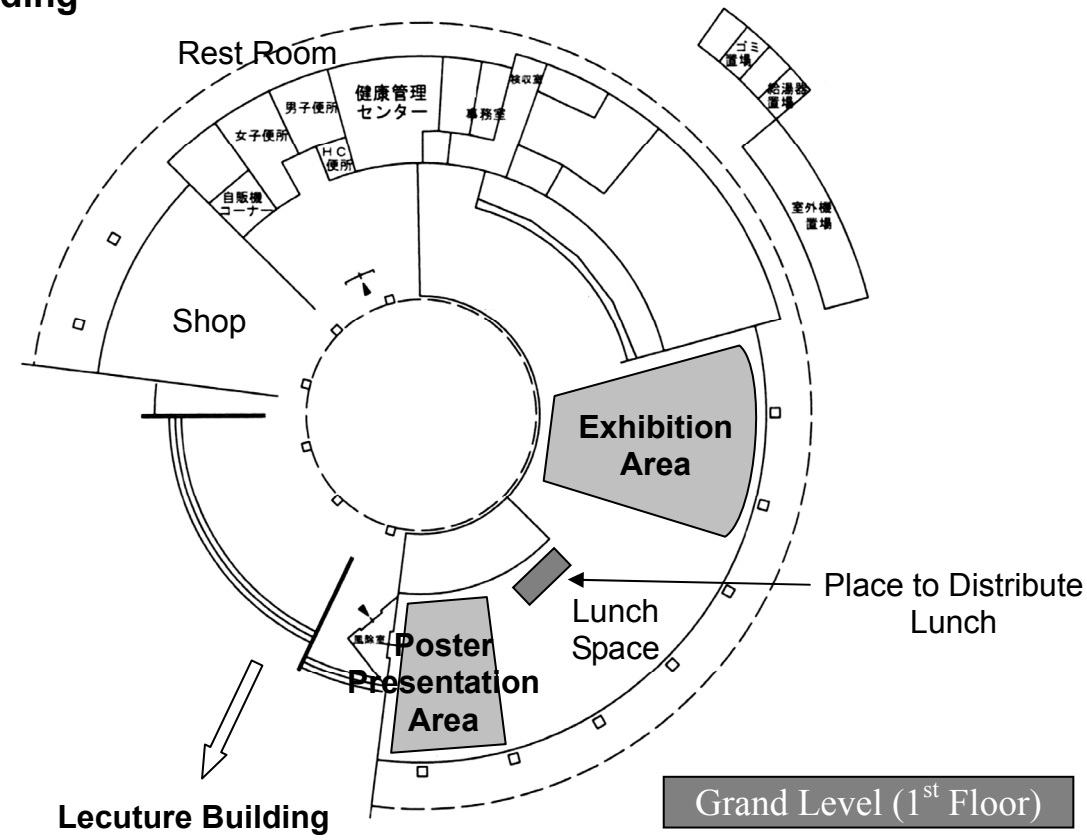


Grand Level (1st Floor)



2nd Floor

Welfare Building

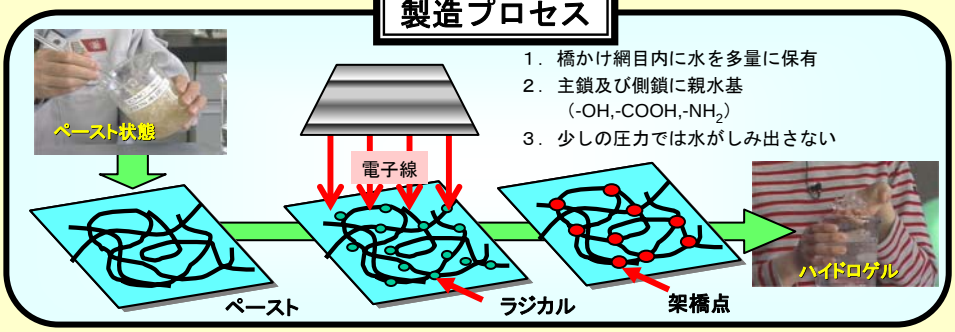


Grand Level (1st Floor)

日本原子力研究開発機構

JAEA：Japan Atomic Energy Agency

製造プロセス



創傷被覆材

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販売：大鵬薬品（株）

ハイドロゲルの特長

従来の処置法（ガーゼ＋軟膏等）と比較して
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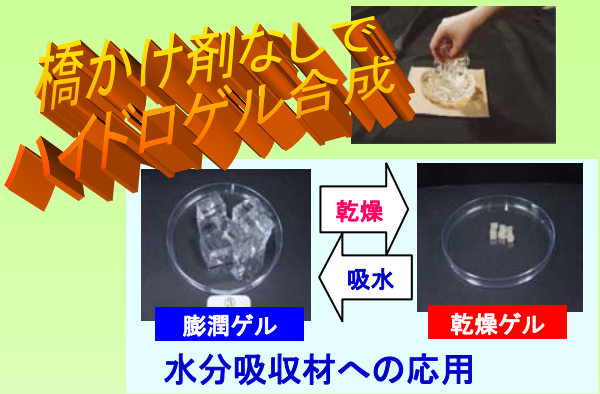
- **創面に固着せず**、創傷処置時の**苦痛が少ない**

ハイドロゲル（PVA）の応用



水分吸収材への応用

靴ずれ防止材

ジェルプロテクター
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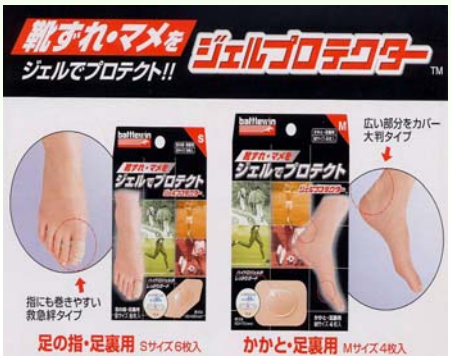
ハイヒールや運動靴などの
痛い靴ずれやマメに効果



問い合わせ先　：　産学連携推進部
Tel: 029-284-3415　Fax: 029-282-3679
E-mail:　sangaku.techno@jaea.go.jp

Symposium Sponsors

The Organizing Committee of CIS Symposium 2008 gratefully acknowledges the following organizations and companies *for their sponsorship of the International Crisis Management Symposium on CBRN and Emerging Infectious Diseases.*

Chiba Institute of Science（学校法人 加計学園 千葉科学大学）
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Chemical Society of Japan（日本化学会）

Choshi City（銚子市）

Crisis & Risk Management Society of Japan（日本危機管理学会）

Fire and Disaster Management Agency（総務省消防庁）

Institute of Social Safety Science（地域安全学会）

Japanese Association of Medical Technology Education（日本臨床検査学教育協議会）

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Scientific Program

Saturday, September 13th

13:30-17:00 **Pre Symposium** **(Site 1)**

18:00-20:00 **Welcome Reception** **(Café Marina)**

Sunday, September 14th

9:00-9:30 **Opening Ceremony** **(Site 1)**

9:45-12:45 **Session 1: Hospital Infections** **(Site 1)**

Chairpersons: **Kunihiro MIMURA (Japan)**
Noboru FUJITANI (Japan)

9:45-9:50 **Opening**

9:50-10:15 **[L01]** **Hayato MIYACHI (Tokai University School of Medicine, Japan)**
New aspects in health-care associated infections and their control: An important role of organizations for activity and adherence to guidelines

10:15-10:40 **[L02]** **Masashi EMOTO (Gunma University Faculty of Medicine, Japan)**
Basic Knowledge of Host Defense Mechanism

10:40-10:50 **Coffee Break**

10:50-11:15 **[L03]** **Yaoko TAKANO (Keio University Hospital, Japan)**
The Contribution to Prevention of Hospital-Acquired Infections from a Viewpoint of Nurse's

11:15-11:40 **[L04]** **Takeshi NAKAZAWA (Juntendo University Bureaus Hospital, Japan)**
The Contribution to Prevention of Hospital-Acquired Infections from Medical Technologist's

11:40-12:05 **[L05]** **Yukimitsu SATO (Tokyo-Kita Social Insurance Hospital, Japan)**

The Present Status and Prospects of Nosocomial Infection Prevention in Patient Safety - from a Viewpoint of Crisis Management-

12:05-12:15 **Coffee Break**

12:15-12:45 **Session Discussion**

9:45-12:15 Session 2: Radiation Emerging Disasters (Site 2)

Chairpersons: **Anthony T. TU (USA)**
Takamitsu KATO (Japan)

9:45-9:55 **Opening**

9:55-10:30 **[L06]** **Takeshi YASUDA (National Institute of Radiological Sciences, Japan)**

The Biological Effects of Radiation Exposure and the Examples of Radiation Accidents

10:30-11:00 **[L07]** **Yoshitaka MATSUMOTO (National Institute of Radiological Sciences, Japan)**

The Radiation Exposure and the Possible Biological Effects in the Clinical Therapy and the Medical Diagnosis

11:00-11:15 **Coffee Break**

10:30-11:00 **[L08]** **Takamitsu KATO (National Institute of Radiological Sciences, Japan)**

The Massive Radiation Exposure and its Risk Management

11:45-12:15 **[L09]** **Yoshikura HARAGUCHI (National Disaster Medical Center, Japan)**

Earthquake and the Problems of the Damage to the Nuclear Plant -Focusing on the Medical System Experienced from the Chuetuoki Earthquake, 2007-

12:15-14:30 Poster Presentation and Lunch (Welfare Building)

12:45-13:45 **Poster Session 1**

13:15-14:15 **Poster Session 2**

14:30-17:30 **Session 3: High-Risk Infection Disease** **(Site 1)**

Chairpersons: **Toshiyuki MASUZAWA (Japan)**
Toshiyuki SHIBAHARA (Japan)

14:30-15:00 **[L10]** **Nobuhiko OKABE (Infectious Disease Surveillance Centr., Japan)**
Influenza Pandemic

15:00-15:30 **[L11]** **Koichi OTSUKI (Kyoto Sangyo University, Japan)**
Avian influenza as an important zoonosis

15:30-15:45 **Coffee Break**

15:45-16:15 **[L12]** **Hitoshi OSHITANI (Tohoku University Graduate School of Medicine, Japan)**
Influenza Pandemic Preparedness from Global Perspective

16:15-16:45 **[L13]** **Mikio DOI (Ibaraki prefectural central hospital, Japan)**
Key Points of Planning for Pandemic Influenza in Ibaraki Prefecture: Lessons from the Experience of Avian Influenza A/H5N2 Infection in Poultry in 2005

16:45-17:15 **[L14]** **Taisuke HORIMOTO (University of Tokyo, Japan)**
Molecular mechanisms of avian influenza virus infection in humans and designing vaccines for pandemic influenza

17:15-17:30 **Session Discussion**

14:00-17:45 **Session 4: Bio-Material and Chemical Emerging Disasters** **(Site 2)**

Chairpersons: **Anthony T. TU (USA)**

14:00-14:15 **[L15]** **Shahriar KHATERI (Janbazan Medical & Engineering Center, Iran)**
Update on Long-Term Effects of Exposure to CW Agent -Health Status of Iranian Survivors of Iraq's Chemical Warfare-

14:15-14:55 **[L16]** **David TRUDIL (New Horizons Diagnostic Corp, USA)**
The Changing Scene of Bio Detection and Response from Anthrax to Avian Flu

14:55-15:35 **[L17]** **David R. FRANZ (Midwest Research Institute, USA)**
Biological Terrorism: Perceived Threats and Response in the United States

15:35-15:55 **[L18]** **Kamil KUCA (University of Defence, Czech Republic)**
Development of the Oxime Hi-6 - Antidote Number One in Case of Nerve Agent Poisonings

15:55-16:10 **Coffee Break**

16:10-16:30 **[L19]** **Hideyuki YANAGIBASHI (Ministry of Defense, Japan)**
Research on Analytical Algorithm of Chemical Agent Gas Using RGB Value of Reaction Surfaces as an Index

16:30-17:10 **[L20]** **Chang YU-TAI (Taipei Medical University, Taiwan)**
Experience of SARS in Heping Hospital of Taiwan

17:10-17:30 **[L21]** **Moon-Young YOON (Hanyang University, Korea)**
Novel Application to the Diagnostic Nanobiosensor for Anthrax

17:30-17:45 **Session Discussion**

Monday, September 15th

9:00-9:30 **Special Lecture** **(Site 1)**

9:00-9:30 **[S01]** **Akira SAKAI (Chiba Institute of Science, Japan)**
Reinforcement of the Measures Against Forged or Altered Passports and Documents at Narita International Airport

9:45-12:45 **Session 5: Medical Malpractice** **(Site 1)**

Chairpersons: **Wataru SAITOU (Japan)**
Masafumi FUJIMOTO (Japan)
Mitsushi TAKEDA (Japan)

9:45-9:55 **Introductory Remarks**

9:55-10:15 **[L22]** **Eikichi KOU (Chiba Pharmaceutical Association, Japan)**
The Crisis-Management and the Approach of Insurance Pharmacy of Preparation Accident Prevention on Medical Treatment Safety Management Committee of the Chiba Pharmaceutical Association

10:15-10:35 **[L23]** **Yoko WADA (Toho University Medical Center, Ohashi Hospital, Japan)**

Introduction of Medical Treatment Safety Committee in TOHO University Medical Center, OHASHI Hospital and Crisis-Management in Nursing Department

10:35-10:55 **[L24]** **Hideyuki SHIMIZU (Teikyo University Chiba General Hospital, Japan)**

Prevention of Medical Malpractice from the View Points of Hospital Pharmacist

10:55-11:05 **[L23]** **Tetsuto KANZAKI (Chiba Institute of Science, Japan)**

Prevention of Medical Malpractice from the View Points of Medical Doctor

11:05-11:20 **Coffee Break**

11:20-11:40 **[L25]** **Tadatsugu TANINO (Industrial Technology Laboratories, Shionogi & Co., Ltd., Japan)**

Designing of Formulation and Manufacturing Processes for Prevention of Medical Malpractice and Quality of Product

11:40-12:00 **[L26]** **Shinji HIRAMOTO (Industrial Technology Laboratories, Shionogi & Co., Ltd., Japan)**

Medication Errors Caused by Pharmaceuticals and an Approach by the Pharmaceutical Industry to Prevent Them. - From the View Point of Packaging, Labeling, and Containers -

12:00-12:45 **Session Discussion**

9:45-12:45 Session 6: Environmental Pollution (Site 2)

Chairpersons: **Noboru FUJITANI (Japan)**

9:45-9:55 **Introductory Remarks**

9:55-10:30 **[L27]** **Akio KOIZUMI (Kyoto University Graduate School of Medicine, Japan)**

Risk and Crisis Management for Environmental Pollutants

10:30-11:05 **[L28]** **Iwao UCHIYAMA (Kyoto University, Japan)**

Crisis Management and Communication for Environmental Pollutants

11:05-11:20 **Coffee Break**

11:20-11:55 **[L29]** **Yoshinori INOUE (Nippon Filcon Co., Ltd., Japan)**
Development of a Novel Chelate Resin and its Application to Determination of Trace Elements in Water Samples

11:55-12:30 **[L30]** **Yoko ENDO (Tokyo Rosai Hospital, Japan)**
Risk Management in Occupational Health

12:30-12:45 **Closing Remarks**

12:45-14:30 **Poster Presentation, Lunch, and Event** **(Welfare Building)**

14:30-16:45 **Special Lectures** **(Site 1)**

Chairpersons: **Toshiyuki SHIBAHARA (Japan)**
Akira SAKAI (Japan)

14:30-15:30 **[S02]** **Hiroshi KIDA (Hokkaido University, Japan)**
Ecology of Influenza Viruses in Nature, Birds, and Mammals Including Humans

15:30-15:45 **Coffee Break**

15:45-16:45 **[S03]** **Tetsuro MIYASHITA (Oriental Land Co., Ltd., Japan)**
Crisis Management Theme Park

18:30-20:30 **Banquet** **(Inubosaki Keisei Hotel)**

Tuesday, September 16th

9:30-12:15 **Session 7: Fire and Explosion** **(Site 1)**

Chairpersons: **Toshisuke HIRANO (Japan)**
Lijing GAO (Japan)

9:30-9:40 **Introductory Remarks**

9:40-10:05 **[L32]** **S. M. LO (City University of Hong Kong, China)**
An Application of Computer Simulations for People Evacuation Management in a Complex Setting

10:05-10:30 **[L33]** **Timothy J. Murphy (University of Findlay, USA)**
Development of an Emergency Management Academic Program: A Case Study

10:30-10:55 **[L34]** **Nobuhiko SHIRAISHI (Nuclear and Industrial Safety Agency, Ministry of Economy, Trade and Industry, Japan)**
Current Situation of Accidents Involving Hazardous Materials in Japan and Measures taken by Organization Concerned

10:55-11:10 **Coffee Break**

11:10-11:35 **[L35]** **Takashi TSURUDA (National Research Institute of Fire and Disaster, Japan)**
Fire Investigation for Emergency Management

11:35-12:00 **[L36]** **Kazuhiro YAMAMOTO (Nagoya University, Japan)**
Evacuation Simulation in Fire by Real-Coded Cellular Automata

12:00-12:15 **Closing Remarks**

9:30-12:05 Session 8: Food Safety (Site 2)

Chairpersons: **Noboru FUJITANI (Japan)**
Masakiyo HOSOKAWA (Japan)

9:30-9:40 **Introductory Remarks**

9:40-10:20 **[L37]** **Fujio KAYAMA (Jichi Medical University, Japan)**
Exposure Assessment and Health Effect Evaluations of cadmium in Japan

10:20-11:00 **[L38]** **Ginji ENDO (Osaka City University Medical School, Japan)**
Risk Assessment on Arsenic in Seafood

11:00-11:15 **Coffee Break**

11:15-11:55 **[L39]** **Hiroyuki SUMI (Kurashiki University of Science and the Arts, Japan)**
The Functionality of Natto and its activity for Promoting Fibrinolysis

11:55-12:05 **Closing Remarks**

12:20-12:40 Closing Ceremony (Site 1)

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マグネット	4000G	12000G
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代理店

Poster Presentations

Sunday, September 14th

12:45-13:45 **Poster Seeeion 1** **(Welfare Building)**

[P01] **ABUBAKIROVA M.I.**
Toxicology of Colubridae (Rear-Fanged Snakes) Venom from Uzbekistan

[P02] **Kazutoshi HASEGAWA, Susumu OHNO and Masaaki SEKIYA**
The Development of the Quantified Check List for Safety Manegement in the Poisonous and/or Deleterious Substances-handling Manufacturing Industries

[P03] **Eri KAWASHIMA, Hideyuki YANAGIBASHI, and Shiroh HISAJIMA**
Automatic Identification of Color Change Reaction by Chemical Agent Using RGB Value

[P04] **Naohiro MURONOI, Hideyuki HAYASHI, and Shiroh HISAJIMA**
Detection of Microorganisms by TOF-MS

[P05] **Tadashi OKADA, Kentaroh HAYAKAWA, and Shiroh HISAJIMA**
High-Speed Sorting of Microorganism by Photomicrograph

[P06] **Makoto UCHIDA, and Shiroh HISAJIMA**
Discrimination of Biological Agents (Analysis by High-speed Amplification of DNA)

[P07] **Vladimir CHUPIS, Alexander KARPOV, Mikhail KURGUZKIN, Andrei LESCHEV, and Alexei LIPANOV**
Environmental Monitoring and Ecological Analysis Controlling the Running of the Facilities for Chemical Weapons Storing and Destruction

[P08] **Miroslav POHANKA, Daniel JUN, and Kamil KUCA**
Pesticides and Nerve Agents Assay Based On Electrochemical Biosensor

[P09] **Yumi UNE, Kotoe SOEDA, Asuka SANBE, Satoru SUZUKI, Takeshi NIWA, Hidemasa IZUMIYA, Haruo WATANABE, and Yukio KATOU**
Salmonellosis due to Salmonella Enterica Serotype Typhimurium DT40 in Sparrows (Passer montanus) in Japan

[P10] **Jiri KASSA, Jana KARASOVA, Jiri BAJGAR, Kamil KUCA, and Kamil MUSILEK**
A Comparison of Neuroprotective Efficacy of Newly Developed Oximes (K203, K206) and Commonly Used Oximes (Obidoxime, HI-6) in Tabun-Poisoned Rats

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[P11] **Kamil KUCA, Kamil MUSILEK, Daniel JUN, and Miroslav POHANKA**
Structure-Activity Relationship as a Tool for the Development of New Promising Oximes

[P12] **Kamil MUSILEK, Ondrej HOLAS, Veronika OPLETALOVA, Daniel JUN, and Kamil KUCA**
Novel Reactivators of Acetylcholinesterase against Paraoxon Intoxication

[P13] **Miroslav POHANKA, Daniel JUN, and Kamil KUCA**
Aflatoxin Assay Using an Acetylcholinesterase Based Biosensors

13:15-14:15 **Poster Seeeion 2** **(Welfare Building)**

[P14] **Koji MORITA, Noboru WATANABE, and Mitsuhiro OKAZAKI**
Molecular Genetical Analysis of Nosocomial Infections Caused by blaCTX-M-3-harboring Strains of Enterobacteriaceae

[P15] **Yoshikura HARAGUCHI, Hosei NISHI, Yozo TOMOYASU, Tohru ISHIHARA, Masami HOSHINO, Shinji HOSOTSUBO, Kaori HIRAGO, and Nathane L ROHDEN**
Medical Measurement against Flue Pandemic-including the social measurement

[P16] **Tsuyoshi HAYASHI, Yuko UCHIDA, Chiaki WATANABE, Nobuhiro TAKEMAE, Masaji MASE, Shigeo YAMAGUCHI, and Takehiko SAITO**
Characterization of Highly Pathogenic Avian Influenza Viruses Isolated During 2006-2007 in Myanmar

[P17] **Kazuya I.P.J. HIDARI, Yoshimasa TANAKA, Yo-Hei MINAMIJIMA, Makoto OGATA, Takeomi MURATA, Yoshinobu MIWA, Taiichi USUI, and Takashi SUZUKI**
Characterization and Application of Glycopolymers Carrying Sialyl Lactosamine Repeats for Inhibition against Influenza Virus Infection

[P18] **Kai INOUE, Soichi MARUYAMA, Hidenori KABEYA, Yumi UNE, and Yasuhiro YOSHIKAWA**
Small Exotic Animals as Potential Reservoirs of Zoonotic Bartonella Species

[P19] **Keita KAWATANI, Toshiyuki MASUZAWA, Marija MILUTINOVIĆ, Takashi FUKUI, and Yoshihiro OKAMOTO**
Detection of the Borrelia Burgdorferi Sensu Lato and Anaplasma Phagocytophilum in Host-seeking Adult Lxodes Ricinus Ticks Collected in Serbia

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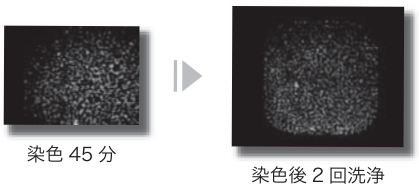
- 傾斜する分注吸引ヘッド＆プレステージ
- 96/384 ウェルプレート対応
- タッチパネルで簡単操作

【セット内容】

本体、分注ヘッド、吸引ヘッド、自動補給付き試薬槽
オーバーフロー洗浄層

HEK293 細胞を用いた評価

細胞：HEK293（10,000 個　24 時間培養）
蛍光色素：Fluo4-AM（5μM　45 分染色）



染色 45 分　　染色後 2 回洗浄

細胞を 45 分間染色し、2 回洗浄した場合において
細胞の剥離は見られなかった。

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デコンシェルター

シャワーノズルは360℃回転　－　短時間、少水量で効果的な除染が可能です

1列　少人数対応タイプ

モデル：SD1-TTB02-GZ

標準カラー　：外装　－　黄色、　内装　－　白
総重量：約32kgs
展開時寸法(巾x奥行x高)　内寸：約1820 x 1520 x 2260mm
収納時寸法(巾x奥行x高)　外寸：約　800 x　800 x　800 mm
シャワーノズル数：7ヶ（ノズル水量：2.75ℓ/分）
ハンドシャワー：1ヶ
標準装備：収納用バッグ・アンカーキット・補修キット含む

2列　タイプ

写真のモデルはSD2-TZB02-GZ　と　傷病者用コンベヤー(オプション)

モデル：SD2-TZB04-GZ

標準カラー　：外装 ①サイド － 黄色、②天井 - 黄色 ・ 内装 - 白
総重量：約42kgs
展開時寸法(巾x奥行x高)　内寸：約2430 x 3050 x 2260mm
収納時寸法(巾x奥行x高)　外寸：約 980 x　980 x　980mm
シャワーノズル数：10ヶ（ノズル水量：2.75ℓ/分）
ハンドシャワー：2ヶ
標準装備：収納用バッグ・アンカーキット・補修キット含む

モデル：SD2-TZB08-GZ

標準カラー　：外装 ①サイド － 黄色、②天井 - 黄色 ・ 内装 - 白
総重量：約80kgs
展開時寸法(巾x奥行x高)　内寸：約2430 x 6100 x 2260mm
収納時寸法(巾x奥行x高)　外寸：約1220 x 1220 x 1220mm
シャワーノズル数：20ヶ（ノズル水量：2.75ℓ/分）
ハンドシャワー：4ヶ
標準装備：収納用バッグ・アンカーキット・補修キット含む

3列　タイプ

写真モデルはSD3-UZA08-GZ　と　傷病者用コンベヤー

＊　4列タイプもご提案可能です

モデル：SD3-UZA08-GZ

特徴：傷病者専用ラインを設けたモデル

中央のラインを歩行のできない傷病者専用とし
介護者2名が対応できるようスペースを広く確保しています。

標準カラー　：外装 ①サイド － 黄色、②天井 － 黄色 ・ 内装 - 白
総重量：約97kgs
展開時寸法(巾x奥行x高)内寸：約3350 x 6100 x 2430mm
収納時寸法(巾x奥行x高)外寸：約1380 x 1380 x 1380mm
シャワーノズル数：合計20ヶ（ノズル水量：2.75ℓ/分）
ハンドシャワー：合計4ヶ
標準装備：収納用バッグ・アンカーキット・補修キット含む

マスデコンシステム

連結が容易なことから
2列･3列タイプを連結して一度に多数の除染が可能になります。

各モデルは　シャワー機能を使用しなければ
救護用テントとして、又調整本部や司令室等多目的用途に対応できます。

給湯 － 除染 － 排水溜の一環した設備を提案いたします。

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フレーム式　新世代多目的シェルター

スタート

30秒

35秒

40秒

60秒

除染システム・救護用テントのご案内

スピーディ

エアーの注入不要
フレームは連結が不要なカムロック構造　（カムロックは特許取得）
一体型の考えから生まれた合理的な構造　－　緊急時に迅速な組み立てが可能

タフ

軽量、コンパクト
シートは外も内もPVCコーティング　－　耐薬品性に優れている、UV加工済
従来のエアー式に比べ耐久性が大幅にアップ

2008.4

Abstracts

Reinforcement of the Measures against Forged or Altered Passports and Documents at Narita International Airport

Akira SAKAI

Chiba Institute of Science, Chiba, Japan (Former director of Narita Immigration Bureau)

Current Circumstances

There seems to be no end to foreign nationals who enter Japan with the use of forged or altered passports, and therefore the seriousness of forged or altered documents should not be disregarded because they are, in particular, frequently used as a means for international organized crime groups to secretly commit serious crimes such as human trafficking and terrorist actions.

In recent years, forged documents used in the immigration procedures have become increasingly more elaborate and sophisticated. These documents are produced in various ways such as changing the holder's photograph or entering false information on the holder's identity. Some foreign nationals also obtain passports by dishonest means such as changing their own identity, or pretending to be others such as by changing their own faces through surgery to match the photograph indicated on the passports.

Most foreign nationals who intend to enter Japan with the use of such forged passports seem to aim at working illegally, and some of them may have been exploited by terrorists or international organized crime groups. From the point of view of assuring public security, it is urgently necessary in immigration control to establish a solid and strong system to detect such forgery or alteration of document at the national borders without fail and prevent crimes from being committed in Japan.

Establishment of Document Examination System

In order to reinforce the system for examining forged documents, it is of utmost importance to not only introduce high performance devices but also to improve the ability to examine documents of each personnel member of the Immigration Bureau. With the aim of improving such ability, the Narita Immigration has provided training on general knowledge and skills of document examination for all personnel.

[S02]

Ecology of Influenza Viruses in Nature, Birds, and Mammals Including Humans

Hiroshi KIDA [1,2,3)]

[1)] Department of Disease Control, Graduate School of Veterinary Medicine,
[2)] The Research Center for Zoonosis Control,
[3)] OIE World Reference Laboratory of Highly Pathogenic Avian Influenza,
Hokkaido University, Sapporo 060-0818, Japan

Recent outbreaks of highly pathogenic avian influenza have spread worldwide. The causal H5N1 virus has jumped the species barrier and caused severe disease with high mortality in limited number of humans who are specifically susceptible to infection with this avian influenza virus strain. A concern is that the H5N1 virus alone is assumed to cause next pandemic in humans. Since each of the subtypes of *influenza A virus* perpetuates among migratory ducks and their nesting lake water in nature and any subtype of avian viruses can contribute genes in the generation of reassortants in pig, none of the 16 HA and 9 NA subtypes can be ruled out as potential candidates for future pandemic strains. Another concern is that the virus returned to feral water birds may perpetuate in their nesting lake water. It is, therefore, important to have information on all influenza A subtype viruses circulating in feral ducks, domestic poultry, and especially in pigs around the world.

We have, thus, carried out global surveillance study of avian influenza and influenza virus isolates of 61 combinations of HA and NA subtypes have been isolated from fecal samples of ducks. So far, 78 other combinations have been generated by the genetic reassortment procedure in chicken embryos. Thus, 234 non-pathogenic avian influenza virus strains of 139 combinations of HA and NA subtypes have been stocked for vaccine strain candidates and diagnostic use. Their pathogenicity, antigenicity, genetic information and yield in chicken embryo have been analyzed and registered in the database opened at web site (http://virusdb.czc.hokudai.ac.Jp/vdbportal/view/index.jsp).

Finally, I would like to stress that avian influenza must be completely controlled in avian species by the “stamping-out policy” and that drastic improvement of measures, especially of vaccine for the control of seasonal influenza in humans is of crucial importance in order to assure the effective preparedness for the emergence of pandemic influenza virus strain.

自然界、鳥とヒトを含む哺乳動物におけるインフルエンザウイルスの生態

喜田 宏 [1,2,3)]

1） 動物疾病制御学講座，北海道大学大学院獣医学研究科，札幌，日本
2） 人獣共通感染症リサーチセンター，北海道大学，札幌，日本
3） OIE World Reference Laboratory of HP Avian Influenza，札幌，日本

H5N1 亜型の高病原性鳥インフルエンザウイルスに感染した家禽と野生水禽の被害が、アジア、中東、ヨーロッパおよびアフリカの 62 カ国に拡がった。その内 14 カ国では、計 380 余名のヒトがこのH5N1 ウイルスに感染し、6 割が死亡している。この H5N1 ウイルスがヒトの新型ウイルスとして世界流行を起こす可能性が高いとのWHOの警告に応じた各国は人体用H5N1ウイルスワクチンと抗ウイルス薬の備蓄を始めた。果たして、これで新型ウイルス対策は十分であろうか。20 世紀に新型ウイルスは3回出現した。一方、高病原性鳥インフルエンザは、野鳥を家禽化した古代から発生していたに違いないが、その原因ウイルスがヒトに伝播して、インフルエンザの大流行を起こしたことを示す記録は見あたらない。過去の新型ウイルス出現のメカニズムを検証し、これから出現する新型ウイルスに備える対策を確立しておく必要がある。

家禽、家畜とヒトのインフルエンザ A ウイルスの遺伝子はすべて水禽、特にカモの腸内ウイルスに由来する。自然宿主であるカモは、夏にシベリア、カナダやアラスカの北営巣湖沼でウイルスに水系経口感染し、大腸の上皮細胞で増殖したウイルスを糞便と共に排泄する。8月中旬、カモは南方に渡り始める。その後、湖沼水中のウイルスは凍結保存される。

ブタの呼吸器上皮細胞には、ヒトのウイルスばかりでなく、鳥のウイルスに対するレセプターもあるので、ヒトのウイルスと鳥のウイルスがブタに同時感染すると、両ウイルスの遺伝子再集合体が生ずる。その中で、鳥のウイルスの HA 遺伝子を持ち、ヒトに伝播したものが新型ウイルスである。1968 年の新型ウイルス A/Hong Kong/68 (H3N2)株は、カモがシベリアの営巣湖沼から家禽(アヒル)に持ち込んだH3 ウイルスと、ヒトに流行していた H2N2 ウイルスがブタに共感染して生じた遺伝子再集合体である。H2N2ウイルスも1957年に同様の経路で出現したものと推定される。1918年のH1N1新型ウイルスは、北米系統の鳥インフルエンザウイルスを起源とする。その伝播経路も、カモ→家禽→ブタ→ヒトであろう。すなわち、これまでの新型ウイルスはカモのウイルスが家禽と家畜を介してヒトのインフルエンザウイルスと遺伝子を交換したものである。

H1-H15 何れの HA 亜型の鳥由来インフルエンザウイルスもブタの呼吸器に感染し、増殖する。したがって、何れの亜型の HA 遺伝子をもつ再集合体もブタの呼吸器で産生され、新型ウイルスとして出現する可能性がある。過去の新型ウイルスの HA と NA 遺伝子は、現在もカモのウイルスに保存されている。従って、インフルエンザウイルスの自然宿主である渡りガモ、家禽、家畜(特にブタ)とヒトのインフルエンザのグローバルサーベイランスを不断に展開し、それぞれの宿主で優勢に分布するウイルスの亜型を明らかにするとともに、ウイルスの生態、宿主域、哺乳動物に対する病原性、生物性状およびヒトの免疫状態を精査した上で、H5N1 を含め、何れが新型ウイルスとして登場する可能性が高いかを評価、予測する必要がある。

疫学調査で分離されるウイルスの中から、抗原性、生物性状と遺伝子の解析成績に基づいて全ての亜型のウイルス株を選出、保存しておけば、新型ウイルスの出現に際して、ワクチンと診断のために的確な株を直ちに提供できる。私達は、自然界のカモから分離したすべての亜型の非病原性インフルエンザAウイルス株および遺伝子ライブラリーを構築し、ウェブサイトに公開した(http://virusdb.czc.hokudai.ac.Jp/vdbportal/view/index.jsp) 。既に、国内外の26試験研究機関にこのライブラリーからウイルス株、遺伝子または標準抗血清を供給した。これらは、サーベイランス、診断、ワクチンの試製などに活用されている。

[S03]

Crisis Management Theme Park

Tetsuro MIYASHITA

Security Department, Oriental land Co., Ltd, Japan

As one of the largest establishments attracting large number of guests in Japan, Tokyo Disney Resort welcomes approximately 25,000,000 guests per year from all over the world and all over the country. Because it is the only entertainment facility established under the name of Disney in Japan, it faces risks unique to the Disney brand. Today, I'm going to give you some examples of these risks and measures against them.

First, I cover the risks that accompany an establishment attracting large number of guests. In the land two kilometers square located at the edge of Urayasu City, approximately 70,000 people stay in the two Parks, and, if employees are included, up to 100,000 people stay in the Resort at one time in one day. So the measures we have to implement against risks are unique to an establishment that indicate a high concentration of people. Some of the recurrent risks are natural disasters. If epicentral earthquake occurs, it can cause extensive damage to the Resort. It is a matter of great urgency to develop plans in partnership with political offices for rescue activities, for people who have difficulty in returning home, and for evacuation life. For the risks of infectious diseases, pandemic can cause widespread damage as Tokyo Disney Resort serves as a source of infection, and if people keep away from the Resort, it experiences an economic shock. In addition, places where many people gather are accompanied by incidents and accidents and there is great risk of criminal offenses.
Next, the Disney brand receives worldwide attention as one of the largest entertainment companies of the world and as a symbol of an American company. So particular measures have to be implemented against risks. We benchmark antiterrorism measures against the Disney facilities located in the United States to implement appropriate measures.
Also, in conjunction with the measures for respective crisis management issues, I give an overview of information risk, such as how we are affected by the information disseminated primarily on the Internet in recent years and by the media coverage at the time of the risk, as one of the important factors in our risk control.

テーマパークの危機管理

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株式会社 オリエンタルランド 運営本部 セキュリティー部

テーマパークや遊園地は、多くの利用者が集中して滞在する集客施設であることから、感染症などのリスクが高く、予防・対処に対する手順の整備が必須である。また、米国産のテーマパークは、ハリウ

ッド映画がテーマに設定されていたり、映画会社が経営母体であることから、日本における米国文化の象徴として見られることが多く、米国内の企業同様のリスクが存在する。今回の講演では、自然災害、感染症、テロ等万が一発生した場合影響の大きいリスクについて説明する。

[L01]

New Aspects in Health-Care Associated Infections and Their Control: An Important Role of Organizations for Activity and Adherence to Guidelines

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Recently, there appeared new aspects in health-care associated infections (HAIs) such as emergence of new pathogens (e.g., SARS-CoV associated with the severe acute respiratory syndrome [SARS], Avian influenza in humans), evolution of known pathogens (e.g., *C. difficile,* noroviruses, community associated MRSA [CA-MRSA]), and continued increase in the incidence of HAIs caused by multidrug-resistant organisms (MDROs) in all healthcare settings. In responding to them, new isolation protocol based on accumulated evidence was issued, emphasizing importance of organizational characteristics with administrative involvement (Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings 2007: CDC). However, there are no universally successful approaches in the era of HAIs with the new aspects, particularly in the large tertiary referral hospital. In this presentation, a role of organizations for activity and adherence to guidelines are reported, on the basis of a study on stepwise implementation of strategies for control of methicillin-resistant staphylococcus aureus (MRSA), and a lesson from experience of a suspected case with SARS.

【Organizations for activity on the control of health-care associated infections】

The trend of MRSA rates and their relationship with stepwise implementation of preventive strategies in Tokai University Hospital during a 76-month period was retrospectively analyzed with a quasi-experimental design. Implementation of strategies including a feedback process with case- and epidemic-reporting, an infection control team and office, and a preventive guideline for MRSA did not result in reduction in monthly MRSA rates in the hospital. When infection control link nurses were organized and their activities became full-scale, there appeared significant reduction in arithmetic mean of the monthly rates of MRSA from 6.3 to 5.0%. Thereafter the MRSA rates remained low for 2 years. To the contrary, MRSA rates in high-risk areas remained high. The sustained reduction of MRSA rates in the hospital can be related to introduction of the infection control link nurse system on the basis of continuous enforcement of basic and multidisciplinary approaches such as hand-hygiene adherence.

【A lesson from SARS for preparedness for Avian influenza in humans】

There is similarity between Avian influenza and SARS in that both are an infectious and fatal disease, and highly contagious to medical staffs through a transmission route of aerosol or droplets. In the beginning of the endemic, it is essential to assure early detection and isolation of imported cases. The experience of SARS may provide implication for the risk management for Avian influenza. At the epidemic of SARS in 2003, a 27-years old Japanese female presented a high fever and acute

respiratory distress with pulmonary infiltrates after traveling South East Asia, and thus was suspected to have SARS. A successful approach was adherence of healthcare personnel to a timely revised preventive guideline including control programs for surveillance and triage.

【Summary】

Successful approaches in the control of MRSA and experience of SARS would be useful also in that of other MDRDs and Avian influenza, respectively, with the same transmission routes. In the control of HAIs with the new aspects, control programs successful in high-risk areas would be critical.

医療関連感染の新たな展開とコントロール：日常的組織活動とガイドライン遵守の意義

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近年の病院感染の傾向は、新たな病原体、既知病原体の進化、多剤耐性微生物の出現と、医療提供の場での拡がり（医療関連感染）を呈している。これら病院感染の新たな様相に対して、一律に有効な方策は確立されていない。病院感染の新展開に対して、MRSA の制御、SARS の経験を通して有効な方策を検討した。日常的組織活動としてリンクナース設置、迅速かつ柔軟な管理プログラム（ガイドライン）作成と職員浸透が重要と考えられる。

[L02]

Basic Knowledge of Host Defense Mechanism

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院内感染を考えるにおいて必要な感染防御機構の基礎知識

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我々が生活する環境には無数とも言える微生物が存在しているが，通常これらの微生物に対して感染を起こすことはない。これは，環境中に存在する微生物の多くがヒトに対して病原性を有さないことに起因しているが，同じ病原性を有する微生物が生体内に侵入した場合，発症するヒトもいれば発症しないヒトもいる。これは，個人個人に備わった免疫力の違いによるところが大きく，抵抗力の強いヒトは発症しないが，抵抗力の弱いヒトは病原性がそれ程強くない微生物が侵入した場合でも発症する（日和見感染）。このことは，微生物側の病原因子（あるいは量）だけでなく，宿主側の防御因子（あるいは免疫応答の強弱）も発症するか否かを決定する重要な因子であることを意味する。言い換えれば，院内感染を理解する上において，生体内における防御反応を理解することは極めて重要であり，宿主の感染防御機構を理解せずして，院内感染を語ることができないと言っても過言ではない。古来より，人類はある感染症に罹ると同じ感染症に2度と罹患しないということを経験的に習得していること（2度なし現象）から，今日の生体防御学は微生物学研究を礎として築かれたことは言うまでもない。本シンポジウムでは，病原微生物に対する防御反応に関わる細胞や免疫応答を概説することにより，生体が病原微生物からの攻撃に対して，如何に巧妙かつ確実に生体内から排除するのかについて述べ、院内感染の予防を考える上において、生体内の感染防御機構を理解することが如何に大切であるかを、聴衆の皆さんと共に考えてみたい。

The Contribution to Prevention of Hospital-Acquired Infections from a Viewpoint of Nurse's

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院内感染とその予防 ー看護師の立場からー

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施設内の感染対策にかかわる看護師の資格には感染症看護専門看護師と感染管理認定看護師の二種類がある。いずれも施設内で患者個人や職員を含む集団に対して感染を防止するための活動を行っている。ICT（インフェクションコントロールチーム）の一員として、あるいは院内感染対策専任者（特定機能病院に配置が義務づけられている）として、施設内の感染防止にかかわるシステム作り、感染症サーベイランス、発生時対応、現場の相談に応じている。

病棟や外来の看護師の感染対策上の役割も重要である。臨床現場には重篤な基礎疾患や治療により免疫力が低下した患者や侵襲的な処置を実施されている患者が多く存在している。これらの患者が安全に医療を受けるために、科学的根拠に基づいた感染対策を実践し、かつ異常の早期発見に努めることが重要である。特に血管内留置カテーテル、尿道留置カテーテル、人工呼吸器に関連した感染症は施設内で発生する感染症の多くをしめることから、管理方法のみならず感染症サーベイランスにより発生状況を把握して管理方法改善につなげる。

教育によって科学的根拠を理解しても継続して実践することが難しいことは、誰もが実感することである。特に手指衛生については、どの施設においても十分に実践していると言えない現状がある。カテーテル管理などの医療器具管理についても、感染経路を理解し、実践方法を理解して適切に実施できるようになってはじめて感染防止を考慮したカテーテル管理の実践になる。また決められたことを実践するだけでなく、患者の状態を把握しながらアセスメントして実践することが看護師の重要な役割である。

医療従事者が感染対策を継続するためには、定期的に教育啓発が実施される必要があるが基礎的知識を繰返し指導されてもあまり効果がない。実践状況や実例などをとおして具体的な教育啓発が効果的である。

発表では、具体的な看護師の役割や活動内容について説明する。

[L04]

The Contribution to Prevention of Hospital-Acquired Infections from Medical Technologist's

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検査技師の立場から 院内感染予防への取組み

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院内感染予防の中心は、標準予防策の実践にある。標準予防策は、医療施設において広く認知されながらも、スタッフ全員が日常的に正しく実践するのは難しく、感染対策チームの間では、如何に向上させ、維持していくかが最大の課題となっている。チーム医療では各部門に特化した職員の集まりの中で、相互に連携をとって機能的に活動しなければならない。一般的に検査技師が行う感染対策としては、アウトブレイクを未然に防ぐ目的で日常検査のデーターを使用したサーベイランスが中心となっている。しかしチーム医療として現状の感染対策業務に役立てるためには、標準予防策の徹底に役立つ検査方法やデーターの提供方法にシフトする必要がある。標準予防策の動機付けをするために当院では、①徹底した病棟監査と指導、②手洗い実施率の評価、③擦式アルコール製剤の使用量評価、④病棟別の微生物の伝播状況評価、⑤標準予防策やハンドケアなどの講習会の開催、⑥病院内外にアピールするポスター掲示、⑦抜打ちの手指や環境培養、⑧研修医制度を利用した感染対策研修などを実施している。検査技師が中心となり実施する内容としては、④や⑦などの項目がある。しかし実際には実施するタイミングや内容が問題となるため、これら全般の感染対策業務と連携させたアプローチが必要である。当院では、平成17年9月より病院全体の事業として、標準予防策徹底に取組んでいる。検査技師として感染対策室に入り、標準予防策の徹底に対する取組み内容と成果について紹介する。

The Present Status and Prospects of Nosocomial Infection Prevention in Patient Safety - from a Viewpoint of Crisis Management -

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医療安全における院内感染予防の現状と展望
―危機管理の視点から―

佐藤 幸光

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1999年1月に発生した大学病院での医療事故以来、産・官・学が連携しながら、各医療施設では、医療安全体制の整備と医療事故防止に取り組んで現在に至っています。 しかしながら、現在もなお依然として、医療事故が軽減されたとは言い難い現状にあります。「医療安全の質」・「医療技術の質」・「医療サービスの質」などの3つの質に裏付けされた「医療の質」が問われてきている中で、ヒューマン・エラーに起因した結果生じた事例や医療機器類の誤動作や不整備及びシステムエラーによる事例など、さまざまな状況下でのアクシデントや医療事故に至る までの事例発生に枚挙にいとまがありません。

近年、医療安全をより良く推進していく上で、院内における感染予防対策の体制作りと、とくに、感染が発生した後の危機管理体制の構築が非常に重要であると考えます。国内外においても、今夏ごろから新型インフルエンザの猛威が予想されている中で、これに対する緊急的な予防措置を講じるための体制作りが叫ばれています。各医療施設においてもしかり、院内感染の発生を未然に防止するとともに、ひとたび発生した感染症が病院内外に拡大しないような施策を講じていくことが大切な要件となります。そのためには、施設管理者（病院長）などが、積極的に各部署の感染制御に関わり、院内の感染対策委員会及び感染対策チーム（ICT）などが中心となって、院内職員に対して組織横断的な対応と教育・啓発活動を実施していく必要があります。 ここでの日々の活動を通じて、感染対策に精通した専門家の視点を背景に、院内における医療安全管理室や医療安全管理委員会などと密接な連携のもとに「医療安全」を進めていくことが理想的な形態であるとともに、院内外のステークホルダーに対する情報開示及び連携を図りながら危機管理的な対応が急務であると考えます。

今回の発表に際しては、①院内感染対策の現況と今後への展望、②院内感染対策用のマニュアルの整備上のポイント、③有効な感染防止対策としての標準予防策を的確に実施する方法、④リスクコミュニケーションを介在した効率的な危機管理体制のあり方等について言及します。

[L06]

The Biological Effects of Radiation Exposure and the Examples of Radiation Accidents

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Our life is well associated with radiation and radioactive materials. For example in the medical field, we use radiation as a tool for diagnostic usage in Chest x-ray and CT test, radiotherapy, and sterilization of medial equipments by high dose radiation. Radiation is also used for non-destructive inspection, processing of tire and plastic materials in industrial fields, germination prevention of potato and improvement of breed in agriculture. Japan is one of the countries which highly rely on nuclear power plant using radioactive uranium isotope for electrical source. Although radiation and radioactive materials are essential for our life, there is a risk for huge disaster with improper operation and usage. There were several nuclear associated accidents in Japan, for example, a uranium processing facility in Tokai village Ibaraki prefecture in 1999 and two thefts of radioactive iridium192 for non-destructive inspection in Chiba 1971 and 2008. I will introduce not only Japanese accidents but also global accidents such as Chernobyl and Goiania. I will also talk about radiation effects for human bodies after radiation accidents from radiation biology aspects. At last, I will introduce relief place activity in refuge and methods for radiation de-contamination processes in case of nuclear disaster.

放射線の生体影響と放射線事故例

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放射線や放射性物質は、我々の日常生活の様々なところで利用されている。例えば医療では、レントゲンやCTなどによる検査、ガンの放射線治療、医療用器具の滅菌などに放射線が利用されている。また、工業では非破壊検査やタイヤ・プラスチックの加工などに、農業ではジャガイモの発芽防止や品種改良などに放射線が利用されている。原子力発電には放射性同位体のウランが使われているが、日本は発電源としての原子力への依存度が世界的にみても高い国である。このように、放射線や放射性物質の利用は我々の生活に必要であるが、誤った操作や利用などにより大きな事故につながる危険性がある。日本では、1999年に、茨城県東海村のJCOウラン加工施設で大きな放射線事故が起きた。また、1971 年に千葉県市原市で非破壊検査用の放射性線源であるイリジウム 192 による被ばく事故が起きた。さらに、今年になって同じ市原市で、非破壊検査用のイリジウム線源が盗ま

れるという事件が起きている。これら日本で起きた放射線事故に加えて、チェルノブイリやゴイアニアなど、これまで世界中で放射線の事故が起きており、これらの事故について紹介する。また、放射線事故によって人体にどのような影響が及ぼされるのかについて、放射線の生物学的影響の視点から解説する。最後に、原子力発電所等の災害が起きた場合に、避難所での救護所活動や放射能汚染の除染方法について紹介する。

[L07]

The Radiation Exposure and the Possible Biological Effects in the Clinical Therapy and the Medical Diagnosis

Yoshitaka MATSUMOTO

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Recently radiation has been contributing to our society from several aspects. Especially radiation generators and radioisotope is essential tools in medial diagnostic and therapy. For example, in the diagnostic fields, CT test, angiography, nuclear medicine tests such as SPECT and PET are used, and in radiotherapy, high energy X-ray treatment, brachytherapy, charged particle therapy can treat tumors in hospitals.

After Roentgen discovered X-ray in 1895, we have been used radiation freely, but now we use radiation with regulation and professional usage in medicine to prevent side effect of radiation. We all know annual chest X-ray test and CT scan in medicine, and radiation is widely accepted in society. However, not many people know the actual radiation doses in diagnose and treatment and side effects of them.

There are no limits for radiation exposure in medicine because positive effect should exceed the bad side. But in 2004, one report in Lancet mentioned tumor 3.4% of incidence in Japan is associated with medical radiation exposure.

This report reminds us to think about medical radiation exposure again.

In the session, I will talk about the radiation exposure and risk from medical diagnosis and treatment, and with such a lower dose, what kinds of biological effect will occur in cells or individual. My session will be focused on safety usage of radiation in medicine.

放射線治療及び診療時の放射線被ばくの実態とその影響

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近年様々な場面における放射線の社会寄与が増え続けています。特に医療の現場においては，様々な疾患の診療や治療と放射線発生装置や放射性同位元素を使用とは，非常に密接な関係にあると言えます。例を挙げれば，診断領域としてCT 検査，血管造影検査，放射性同位元素を用いた核医学検査（SPECT や PET）などがあり，治療領域としてはがんを主な対象とした高エネルギーX 線治療，小線源治療，粒子線治療などがあります。医療放射線の歴史を見れば，1895 年にレントゲン

により発見されたX線は当初誰でも自由に使用することができましたが，X線障害が問題となったことで人体に対するX線照射は医療という枠組みの中で行われることとなりました。胸のX線撮影やCT検査などが一般的に用いられ，医療における放射線利用は日本においても周知のものとなってきております。しかし，実際に検査や治療で「どれくらいの放射線が照射されているのか」，「照射された放射線の量が生物学的にどういった意味を持つのか」などは，まだまだ一般的に知られていないのが現状です。そもそも医療における放射線被ばくは「益が害を上回る」という大前提を元にしており，線量を制限することで必要な検査や治療が行えないような事態を生じないため線量限度が設けられておりません。しかし，2004年医学専門誌Lancet誌で「日本人のがんの3.2%は診断X線による」との報告がなされ，この値の妥当性には議論があるものの医療における放射線被ばくを再度考えるきっかけとなっています。会場では，「医療の現場で行なわれる検査や治療によって患者がどれくらいの放射線を浴びる可能性があるのか」を提示し，それに平行して「そのような線量でどのような生物学的な影響が細胞または個体レベルで起こりうるのか」を示すことで，現在の医療における放射線利用の安全性について総括的にお話しできればと考えています。この講演が，一般の方の放射線に対する認識と関心をわずかにでも高めるきっかけとなればと幸いと考えております。

[L08]

The Massive Radiatoin Exposure and its Risk Management

Takamitsu KATO

Research Center of Charged Particle Therapy, National Institute of Radiological Sciences, Japan

First of all, I should define a high dose irradiation as massive external radiation exposure in this risk management symposium talk. They are very rare occasions but we know several accidents in nuclear facilities, exposure from atomic and nuclear weapons, and possible suffering from a radioactive dirty bomb by terrorist activities. I would like to talk about some diffusion models for the emitted radioactive materials in dirty bomb situation. And I will explain about a chromosome aberration analysis assay as an established biomarker for estimating dose of radiation exposure for human body. Several new techniques will be also explained in this session.

Nuclear weapons in Hiroshima and Nagasaki in 1945 results in relatively high exposed A-bomb survivors (Hibakusya). Ones who were irradiated with more than 6Sv had small possibility for survival but if absorbed dose was less than 4Sv, they can survive for a long time as other unirradiated control cohorts. Their health was monitored and accumulated for more than 50 years in the Radiation Effect Research Foundation.

The famous nuclear accident in Chernobyl emitted about 10t amount of radioactive materials. In this accident, radioactive Iodine was fall out onto the ground and absorbed in glass. Cow ate those radioactive glasses. Kids drunk milk from those cow. And end up with absorbing Iodine. High risk of thyroid cancers was reported in Chernobyl accidents.

Although no terrorists actually use the dirty bomb so far, it is easy to imagine those spread nuclear materials would lead people in massive panic and heavy damages in society and economics if it happens in anywhere. I will also present several models of dispersion of radioactive materials in different conditions.

Although a high dose exposure accident is life threatening situation, it is very difficult to determine the actual radiation exposed doses because absorbed doses is depending on not only distance from radioactive materials but also condition around ones such as shielding. One of the best and classic methods is a chromosome aberration analysis from peripheral lymphocytes. I will explain the limitation of chromosome aberration analysis and recent developing methods for quick analysis.

大規模な放射線被ばくとその危機管理

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大線量放射線に対する危機管理は、外部からの大線量被爆を想定すべきであろう。そのような事例は極めてまれではあるが、放射能を取り扱う施設において起こる事故。水素爆弾、原子爆弾により放出される放射線による被曝、テロリストの活動により起こりうるダーティボム（汚い爆弾）による被害の可能性をここでは扱う。さらに、飛散した放射能の拡散モデル。放射線による被曝量を測定するバイオマーカーとしての染色体損傷。またこれに変わる最新のバイオマーカーの開発について解説する。

日本は、広島・長崎に原子爆弾が投下され、多くの人が比較的高線量の被爆をした。6Sv（シーベルト）以上の被爆者では、長期生存の可能性は極めて少ないが、4Sv 以下の被爆の場合、長期生存の可能性は高く、その後のがん発症などの健康状況を放射線影響研究所のデータをもとに発表する。

また原子力施設事故として有名なチェルノブイリ発電所での事故では10トンの放射性物質が放出され、これによりヨーロッパ広域が汚染され、今でも事故現場から半径30キロメートルは立ち入り禁止である。放出された放射能では、特にヨウ素が人体に影響を与えた。地上に降り注いだ放射性ヨウ素は植物に吸収され、これを家畜が餌として食べ、人間が汚染された牛乳を飲んだことで子供に甲状腺ガンが多発したことが報告されている。

現在まで、ダーティボムを使用したテロリストは存在しないが、仮に東京都心で何者かが放射能を爆破とともに撒き散らした場合、放射性物質の半減期にもよるが、広域が立ち入り禁止となり、人々がパニックになることは容易に想像できる。また放射性物質の拡散を条件ごとに検討したものを発表する。

最後に、これら大線量放射線の被曝は生命の危機となりうるが、実際にどの程度の被爆をしたのかは、距離だけではなく、周りの環境に大きく左右され、被爆量を調べるのには、専門的な手法が必要となる。そのうちのひとつであり、現在最も良く使われている染色体損傷の解析とその解析方法、そしてその限界について述べる。また、アメリカ政府の後押しで、より簡便な被爆量解析を行う方法の探索がアメリカでは活発に行われているが、それについて述べる。

[L09]

Earthquake and the Problems of the Damage to the Nuclear Plant - Focusing on the Medical System Experienced from the Chuetsuoki Earthquake, 2007

Yoshikura HARAGUCHI, Hosei NISHI, Yozo TOMOYASU, Tohru ISHIHARA, and Hiroshi SUZUKI

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The Chuetsuoki earthquake, July 2007 hit the Kashiwazaki-Kariwa nuclear plant as well as the Kashiwazaki city and its surroundings.

Our medical support started from the early phase in the disaster area, which are reported, mainly focusing on the nuclear /radiological problems.

Materials and Methods: Data were obtained just after the earthquake (the next day), 10 days' later and 8 months' later. The damage of the plant and the results from the survey meter were studied.

Results: Basically no prominent leakage of the radioactive substance existed, although mechanical damage of the building in the plant was relatively serious and minimal leakage of radioactive substances into the air/sea might have existed as shown in the figure. No serious health problems or trauma patients was found.

Discussion and Conclusions: In this earthquake, fortunately the nuclear plant was not deeply destroyed without serous radioactive substance leakage. However, several problems are pointed out:

(1) The largest degree of earthquake should be included in the assumption,
(2) The role of off-site center is expected, even if it is thought that the radiation disaster is unlikely,
(3) Medical preparedness should be planned considering the large number of patient involved

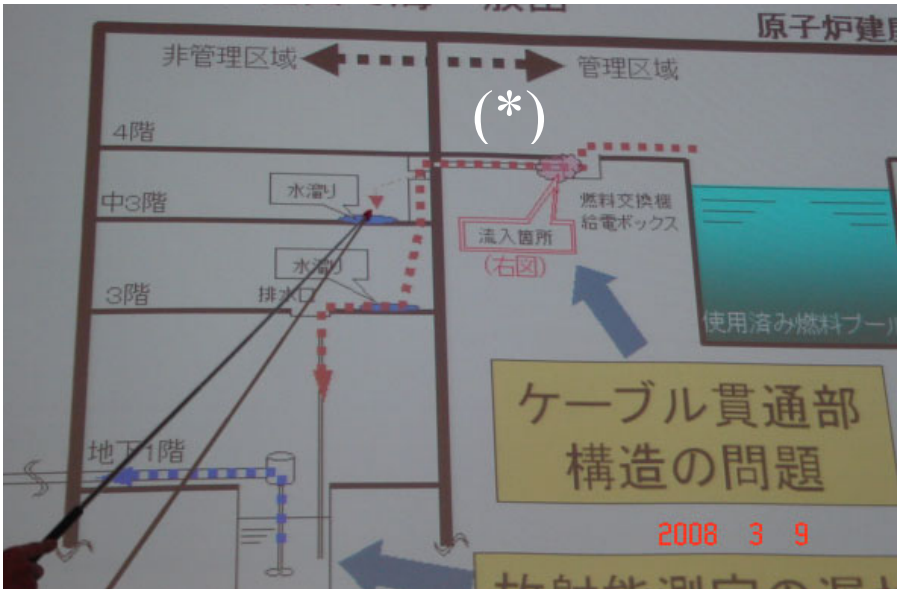

Figure: Minimal leakage of water contaminated with radioactive substance occurred from the asterisk(*) through the pointed route toward the basement level.

地震と原子力災害—中越沖地震における経験を中心に

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平成 19 年 7 月に発生した中越沖地震では、地域住民に対する被害も多かったが、特に柏崎刈羽原子力発電所への影響が問題視された。

早期より現地での災害医療にあたった経験から、原子力発電所における災害時の医療面からの問題点を中心に検討した。

検討対象：被災地、および柏崎刈羽原子力発電所および周囲地域。検討日時は、被災翌日および 10 日後および約 8 ヶ月後。検討方法は、周囲の放射線レベル等の測定結果と、発電所における被災状況・医療体制状況。

検討結果：原発内外を含めて、基本的には、人体に影響を与えるような明らかな放射線漏出等の被害は認められなかった。しかし、想定値以上の震度によりハード面での被害はかなり高度と思われた。原発施設内の人的被害も問題とはならなかった。

考察・まとめ：原子力発電所としては、地震に抵抗性があると考えられた。しかし、課題としては、想定上の地震に遭遇したときの準備は必ずしも十分ではなかったことに加えて、off-site center としての役割が期待されること、多数被ばく患者発生時には対応困難なことがあげられた。

[L10]

Influenza Pandemic

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An influenza pandemic occurs when a new influenza virus capable of causing severe disease transmits easily among humans. Since there is no immunity to a newly emerging virus or virus endemic in the past in the human population, it can cause a pandemic – an epidemic on a global scale. With the continuing spread of the avian influenza A(H5N1) virus in poultry and wild birds in Asia, Europe and further African countries. The number of human infections among epidemic bird infections is increasing up to around 300 cases and fatality rate is around 60%. There is a growing risk of an influenza pandemic in humans.

While it is impossible to predict with accuracy when a pandemic might occur or its exact impact, the potential for widespread human infection – accompanied by severe illness and death – cannot be dismissed. An avian influenza pandemic also would cause catastrophic social and economic disruption. In fact, a pandemic is more than a health crisis; it is a challenge that must be met by all sectors of society.

Preparation can mitigate the direct health, social and economic impacts of a pandemic. WHO recommends that each country and area have in place a pandemic preparedness plan.

In Japan, the guidelines for the next influenza pandemic (phases 4-6) were prepared on March 26, 2007. The guidelines are included quarantine measures, public health response, medical response, public response and others. The national and prefecture governments each started to stockpile of influenza antiviral agents for total 25 million doses for therapeutic use. A total of 20 million doses of A/H5N1 pre-pandemic vaccine were stockpiled in 2008, and large scale field trial for safety and efficacy are planed. Infection Control Law has been amended that H5N1 infection and pandemic virus infection can be handled under the law. However, more concrete plan for pandemic phase such as medical plan including priority for vaccination or treatment, social distancing, work plan among pandemic phase in every sectors etc should be discussed seriously and be prepared.

In this symposium, pandemic and pandemic plan for influenza will be discussed in the point of view for health crisis management.

Avian Influenza as an Important Zoonosis

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Avian influenza is one of the most important zoonoses. Highly pathogenic avian influenza (HPAI) virus subtype H5N1 continue to circulate and cause disease not only in free-living birds but also in domestic ones throughout Asia, Europe and Africa.

Free-living water fowls are considered the reservoir of all influenza A viruses. They are known to carry various subtypes of viruses including H5 and H7, but usually in the low pathogenic form. Considerable circumstantial evidence suggests that migratory birds can introduce low pathogenic H5 and H7 viruses to poultry flocks, which then mutate to the highly pathogenic form. Actually an avirulent H5N3 isolate from whistling swan became highly pathogenic after 24 consecutive passages through air sacs, followed by five passages in chick brain (Ito et al. 2001). This achievement proves clearly that highly pathogenic avian influenza viruses could arise from avirulent strains maintained in wild waterfowl. Origin of the present H5N1 influenza viruses is also thought to be an avirulent one harboured in some water fowl.

Avian influenza virus H5N1 subtype has been shown to transmit to humans and led to the fatal sporadic outbreak and has become threat to the public health.

人獣共通感染病としての鳥インフルエンザ

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鳥インフルエンザは重要な人獣共通感染病である。現在，強毒の H5N1 亜型ウイルスはアジア全域、ヨーロッパなどのユーラシア大陸ばかりでなくアフリカ大陸にも広く分布して家きん類及び野鳥にも感染している。高病原性鳥インフルエンザは広範囲に発生し続けている。

野生の水鳥がすべての A 型インフルエンザウイルスの本来の宿主であると考えられている。これらの水鳥は弱毒の H5 あるいは H7 亜型ウイルスを持ち運んでいる事が知られている。これらの弱毒の H5 あるいは H7 ウイルスが鶏群に感染が起きた場合、鶏から鶏へ感染が続いた時に変異が起きて、強毒のウイルスに変わる事と考えられている。実際に演者らがコハクチョウから分離した H5N3 ウイルスは、24代気嚢接種による継代を重ね，更に5代脳内接種を重ねる事により典型的な強毒ウイルスに変異した。H5N1 ウイルスが人に感染して死亡する事例が増えており、公衆衛生上懸念される。

[L12]

Influenza Pandemic Preparedness from Global Perspective

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Avian influenza, caused by influenza A (H5N1) virus, continues to cause outbreaks among poultry and wild birds worldwide. It has spread from Asia to other regions including Europe, the Middle-East, and Africa. The number of cases of human H5N1 infection also continues to rise. These historically unprecedented outbreaks have raised serious global concerns about the imminent arrival of an influenza pandemic.

Better preparedness for an influenza pandemic is a key for mitigating its impact. Many countries have started developing and implementing national influenza pandemic preparedness plans. However, every country is facing to difficult issues and challenges encountered in preparing for a pandemic. And the level of preparedness is varies between countries. Pharmaceutical interventions such as antivirals and vaccines are a key intervention during a pandemic. But it is expected that there would be a severe shortage of antivirals and vaccines. Non-pharmaceutical interventions such as school closures, home isolation, home quarantine and border control measures may also be able to slow down the spread of the virus. In most of situations, it is necessary to implement pharmaceutical and non-pharmaceutical interventions at same time to mitigate the impact. Recent studies using an epidemiological model have shown that these interventions may reduce the impact significantly. But advance planning is essential to implement these interventions in a large scale.

An influenza pandemic is a global issue and it requires a global collaboration to respond to a pandemic threat. World Health Organization (WHO) is coordinating such global effort.

Key Points of Planning for Pandemic Influenza in Ibaraki Prefecture: Lessons from the Experience of Avian Influenza A/H5N2 Infection in Poultry in 2005

Mikio DOI

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Ibaraki prefecture is located in the northeast of Tokyo, Japan, and has a population of 3 million. Its population density is much lower than that in Tokyo metropolitan area. The chicken population in chicken farms in this prefecture is 11 million, one of the largest populations in Japan. In June 2005, the anti-H5N2 avian influenza antibody was isolated from a farm in this prefecture for the first time in Japan. By February 2006, the virus was isolated or an anti-H5 antibody was identified from chickens in 40 chicken farms in Ibaraki prefecture and 5.7 million chickens were culled, though this H5N2 influenza virus did not result in death of the infected chickens. For these eight months the total number of people, 46 thousand, who were engaged in killing poultry and about 3.5 thousand people were needed for health check of 36 thousand of culling-workers. There found no influenza-like symptoms among people who were engaged in killing poultry under infection preventive condition, but serological test revealed at least twenty employees in the chicken farms were suspected infection probably due to exposure to the virus or contaminated environment.

Through H5N2 outbreak in poultry the Ibaraki prefecture had learned much about the crisis management, such as the control of man power and logistics, mitigation measures for the damages of community as well as economy, and decision making without reliable evidence and prediction for future, namely in the try- and- error type of manner.

In compliance with WHO Global Influenza Preparedness Plan (May 2005) and Pandemic Influenza Preparedness Action Plan of the Japanese Government (November 2005), we have improved action plans and strategies against influenza pandemics. The key points we have learned from H5N2 infection in Ibaraki are as follows; 1) cross-sectional cooperation among departments of prefectural government in order to make decision in time and place, 2) education for stakeholders and citizens to empower them to participate in public decision-making work, and 3) reinforcement of public health center as a frontline for crisis management to coordinate healthcare surge capacity, prioritization and delivery of health services, and policy decision among municipalities. Based on these key points and the estimation model of pandemic influenza impact, mitigation plans and strategy of Ibaraki prefecture will be presented.

[L14]

Molecular Mechanisms of Avian Influenza Virus Infection in Humans and Designing Vaccines for Pandemic Influenza

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Recent outbreaks of highly pathogenic avian influenza A virus infections (H5 and H7 subtypes) in poultry and in humans (through direct contact with infected birds) have had major economic repercussions and have raised concerns that a new influenza pandemic will occur in the near future. Eradication of pathogenic avian viruses appears to be the most effective way to prevent influenza pandemics, although this strategy has not proven successful thus far. Effective vaccines against H5N1 virus are, therefore, urgently needed. Reverse genetics-based inactivated vaccines have been prepared according to WHO recommendations, licensed, and stockpiled in several countries including Japan, following their assessment in clinical trials. However, the effectiveness of these vaccines in a pandemic is not guaranteed. We must, therefore, continue to develop alternative pandemic vaccine strategies. Here, we discuss the molecular features of H5N1 virus infection in humans, and review the current strategies for the development of H5N1 influenza vaccines, as well as some future directions for vaccine development.

鳥インフルエンザウイルスのヒトへの感染機構とパンデミックに対するワクチン開発

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H5N1 亜型の高病原性鳥インフルエンザがアジアのみならずヨーロッパ、アフリカへと拡大した。これまでにヒトへの感染が 400 例近く報告され、240 名以上が死亡している。次第に明らかになってきた高病原性鳥ウイルスのヒトへの感染分子機構は、わずかな変異でこの鳥ウイルスが世界的大流行（パンデミック）を引き起こす可能性を示している。インフルエンザの制圧には抗ウイルス薬とワクチンが用いられる。しかし、H5N1 のタミフル耐性ウイルスもわずかではあるが分離されており、さらに、昨今の H1N1 耐性ウイルスの侵淫を考えると、人類が今最も切望しているのは、効果的な H5N1 ワクチンの開発であろう。WHO が推奨する組換えウイルスを基盤とする不活化ワクチンの備蓄も進行中であるが、その実際の効果は不透明である。本講演では、鳥インフルエンザウイルスのヒトへの感染機構、および H5N1 ワクチンの現状と今後の展望についてまとめてみたい。

[L15]

Update on Long-Term Effects of Exposure to CW Agent -Health Status of Iranian Survivors of Iraq's Chemical Warfare-

Shahriar KHATERI

CW Victims Research Unit, Janbazan Medical & Engineering Center, Iran

[L16]

The Changing Scene of Bio Detection and Response from Anthrax to Avian Flu

David TRUDIL

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The Anthrax events of 2001/2002 caused the USA and others to re-assess there response to bio events. Prior to the few, high profile anthrax letters and many hoax events the US was ill-prepared to respond to such scenarios. In the years afterward there was debate between the USG and first responders and how to respond to a bio event. This also included collection and detection.

The evolving discord has led to a review of methods as well as antibodies and regents. Additionally, lessons where learned in the issues of performing effective evaluations of these systems, including anthrax spore methods. Determination of an effective response strategy was also discussed. The view gradually changed from one of “culture” and PCR, to a layered multiple technology approach. This concept satisfied the concerns of both first responders in the field as well as scientists in the lab.

Eventually bio threats, however, have morphed into not just those included on a limited biowarfare threat list, to ones that could be either man made or naturally occurring. Ones that could effect humans, the environment or plants and animals. This broader definition now includes the new emerging pathogens such as avian flu and antibiotic resistant strains as well as foot and mouth disease. There is even more interest in global coordination with this expanded biothreat. Some countries may improve communication, infrastructure and response due to the old line threats of anthrax and ricin while even more feel the need to prepare for and respond to the threat from “mother nature”.

Examples of the lessons learned as well as potential strategies and technologies will be presented. These includes the anthrax “problems” and new technology opportunities to address the emerging diseases. The utilization of less sensitive, rapid field methods vs lab methods will be of particular focus. Additionally, more use of what has been perceived as “old” approaches have been re-visited to offer hope for developed and developing countries alike.

Biological Terrorism: Perceived Threats and Response in the United States

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Biological security and our perception of what it means has become suddenly more complex in the first decade of the 21st century. During the cold war, the enormous Soviet offensive biological weapons program, though poorly understood, was the focus of concern and preparation. In the early 90s it was still state-sponsored biological warfare, this time in Iraq. The 'anthrax letters' in the shadow of the World Trade Center attacks in America drove new funding for biodefense preparation, containment laboratories and countermeasures research. Shortly thereafter, concern about biodefense proliferation and the biotech revolution brought us the 'dual-use dilemma'. At the same time, the world continues to shrink and microbes circulate within and among our human, animal and plant populations ever more efficiently. Biodefense spending, boosted after the events of 2001 continues today, even as much countermeasures thought and resources have been refocused on pandemic flu. The capability to manipulate biology, for good or ill, is spreading rapidly around a globe. In many parts of the developed world, business biotech is flourishing. In the developing world, where public health capacity-building is needed, concern about communicable disease dwarfs any concern about bioterrorism or dual-use abuse of biology. At the same time our risk perception is now influenced more by asymmetric warfare than by superpowers. While the potential for intentional harm with biology is enormous and the risk of an incident or outbreak is probably small, the real threat is extremely difficult to know. As the players have changed from state sponsors to sub-national groups or even individuals, the agents, methods and targets of concern have also changed. We can no longer rely on preemptive hard power and traditional public health programs to protect our populations and our food chains. On the positive side, engagement with allies in preparation and response for bioterrorism can help protect all our citizens. While preparation for response after an attack is necessary, we may have underestimated the value of working together for prevention. International collaboration on disease surveillance, development of medical countermeasures and response planning will directly support early warning, situational awareness and the leveraging of tools, tactics and experience of others. Working together on hard medical problems provides a better understanding of legitimate capabilities, potentially intent, and may even undermine the popular support for terrorism by increasing human security; this is prevention. Dr. Franz will summarize the history of the threat and the perceived threat of intentional misuse of biology and the value of broad international engagement in the science and health sectors as a means of reducing the likelihood of intentional catastrophic biological events. Like technical medical or physical countermeasures for response, international engagement alone will not protect the citizens of our countries; however, we must consider this option as part of our tool kit as we move into an ever smaller and more biotechnologically adept world.

[L18]

Development of the Oxime Hi-6 – Antidote Number One in Case of Nerve Agent Poisonings

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Oxime HI-6 (1-(2-(hydroxyiminomethyl)pyridinium)-3-(4-carbamoylpyridinium)-2-oxapropane) belongs to the most promising acetylcholinestrase reactivators – antidotes used against nerve agents (sarin, cyclosarin, tabun, VX, etc.). According to the present knowledge, its reactivation potency is the highest compared to other commercial oximes (pralidoxime, obidoxime, trimedoxime, MMB4).[1,2] Thanks to its promising reactivation potency, the development of this compound and its further large-scale production were done at our department within last four years. In this presentation, we would like to summarize our results to show what we have done in this topic. We will describe preparation of twelve different HI-6 salts (sulfate, chloride, acetate, bromide, phosphate, mesylate, tartrate, iodide, malonate, salicylate, maleinate, tosylate), their quick TLC and HPLC analysis and solubility testing. Furthermore, chloride (Cl) and dimethanesulfonate (DMS) salts of the HI-6 were tested in vitro and in vivo to compare their reactivation differences.

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2. Kuca K, Jun D, Bajgar J. Currently used cholinesterase reactivators against nerve agent intoxication: comparison of their effectivity in vitro. Drug & Chemical Toxicology. 2007; 30: 31-40

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Research on Analytical Algorithm of Chemical Agent Gas Using RGB Value of Reaction Surfaces as an Index

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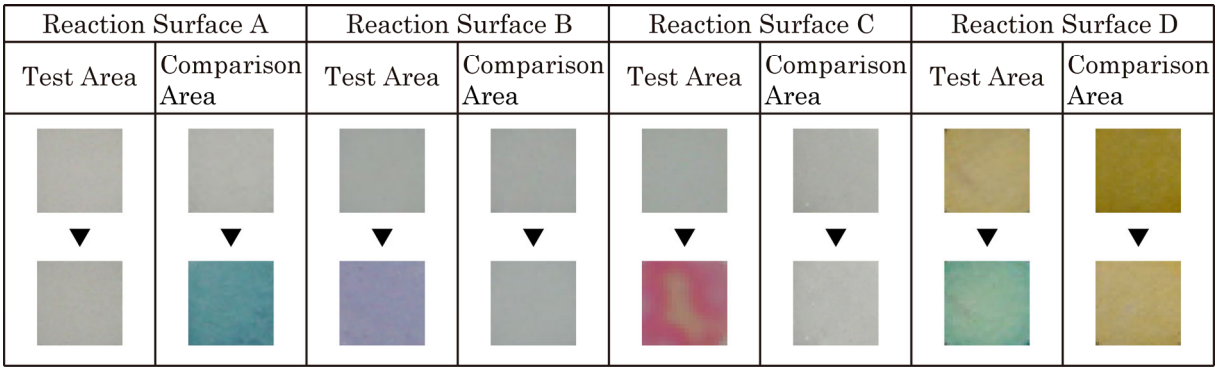
In recent years, threat of the terrorism using chemical agent is on the rise on a global scale and each country proceeds research. We also have been studying a portable automatic detector for gaseous chemical agent. For the detector, we focused on the U.S. Army's M256A1, the detection principle of which is based on color changes of reaction surfaces. It has four reaction surfaces for four types of chemical agent. For automatic detector, analytical algorithm that distinguish the color changes is indispensable. In this study, an algorithm to judge the existence of chemical agent is considered.

Figure 1 shows typical color changes of four types of reaction surface. "Test Area" means the surface exposure to agent, "Comparison Area" means no exposure to agent. And the changes of RGB values of "Reaction Surface A" are shown in Figure 2. It is possible to judge whether is "Test Area" or "Comparison Area" using "R value". For other three reaction surfaces, it was concluded that it is also possible to judge the existence of chemical agent using one parameter of RGB value as an index.

Figure 1 Typical color changes of each reaction surface



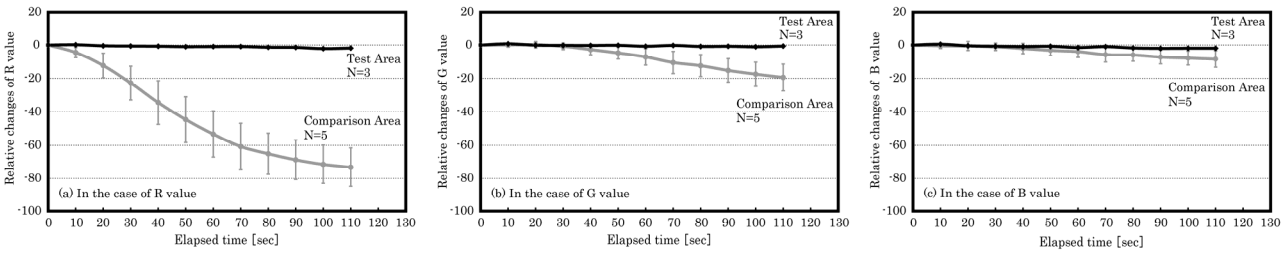


Figure 2 The changes of RGB values of "Reaction Surface A"

[L20]

Experience of SARS in Heping Hospital of Taiwan

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Novel Application to the Diagnostic Nanobiosensor for Anthrax

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Bacillus anthracis is a spore-forming bacterium causing the disease anthrax in humans and is a potential bioterrorism agent requiring extensive medical treatments within a few hours of initial inhalation. Therefore, the rapid detection and continuous monitoring of the spores in the environment prior to infection is highly important for human health and safety. Recently, a field of molecular diagnostics has been explosively expanded with a support of nanomaterials coupled with numerous biomolecules. Due to the high specificity and affinity, antibodies have been commonly adapted in clinical diagnostics where systematic fluids from sources, such as human blood, are screened for the indication of disease. However, antibodies, which are proteins that are functionally dependent on their characteristic three dimensional structure formed by various weak interactions, can be disrupted by chemical and physical processing for a tailored nanodevice. Also, its large molecular size makes it difficult to recognize small molecules efficiently and to access several regions on a target simultaneously.

Herein, we propose a novel approach based on the small diagnostic peptides with polyvalency using *B*. anthracis as a model system. We designed polyvalent functional probe containing diverse small peptides and signal probes on a flexible polymer backbone. We have screened the diverse peptides by M13 phage display techniques, which were engineered to increase specificity, affinity, and ability for the biosensor application. These small peptides having a dozen of amino acids show to interact with multiple regions of a target with little steric hindrance and this polyvalency can be expected to increase specificity and affinity of the peptide and to amplify sensitivity by multiple signal generating molecules on the polymer backbone. Polyvalency of complex polymers can provide a novel window of molecular probes for continuous, field-ready, and easy to use diagnostics, which coupled with currently available sensing techniques, such as electronic transducers, microcantilevers, quantum dot, and SERS.

Key words: High-throughput Assay, Inhibitor, Biosensor, Polyvalent functional peptide, Functional detection polymer, Sensitive diagnostics

[L22]

The Crisis-Management and the Approach of Insurance Pharmacy of Preparation Accident Prevention on Medical Treatment Safety Management Committee of the Chiba Pharmaceutical Association

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千葉県薬剤師会医療安全管理委員会の危機管理と保険薬局の調剤事故防止への取り組みについて

黄 栄吉

千葉県薬剤師会医療安全管理委員会委員長

千葉県薬剤師会（以下県薬と称す）は、2003年度に調剤過誤防止プロジェクト委員会を発足させ、その後、2007年度に常設委員会として医療安全管理委員会（以下委員会と称す）に組織改変が行われた。この間の5年間の主な活動について報告する。

はじめに活動の大きな柱としては、伝達講習会による会員への医療安全に対する意識向上を図ることであった。各支部の医療安全担当者に対して、医療安全の為の危機管理等について、県薬委員会主催の伝達講習会を開催し、その後各支部の会員に伝達講習会の内容を周知させることを継続している。主な伝達講習会は年1回のペースで、これ迄計4回開催し、必要に応じ県薬の医療安全委員が支部に出向き、支部での伝達講習会開催支援を行い、会員の知識向上、情報の共有化を図ってきた。伝達講習会の内容は、当初日本薬剤師会からの資料を活用していたが、後半は、委員会独自で「調剤事故防止マニュアル」、「医薬品の安全使用の為の業務手順書」を作成し伝達講習内容とした。

また、柏市での調剤事故を教訓として、一人薬剤師等の保険薬局において、調剤過誤を防ぎ、かつ調剤過誤を早期に発見できる「調剤事故防止ツール」を開発した。その内容の概略を紹介しながら、その普及に向けての取り組みと、今後の委員会の活動予定を報告する。

Introduction of Medical Treatment Safety Committee in TOHO University Medical Center, OHASHI Hospital and Crisis-Management in Nursing Department

Yoko WADA

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東邦大学医療センター大橋病院における医療安全委員会と看護部における危機管理

和田葉子

東邦大学医療センター大橋病院副看護部長

東邦大学医療センター大橋病院の医療安全委員会の紹介と、リスク回避に向けての取り組み、看護部における薬に関するインシデント事例を紹介し、日々行っていることの中から、医療安全についての活動を報告する。

病院のオーダリングシステムを利用して独自開発した「インシデント・アクシデント速報告書」の活用や、報告書の集計、分析を行い、システムや危険因子の変更・改善したことなど研修会を通して周知徹底するようにしている。研修医や新人看護師を対象とした研修でも安全を重視した研修を行っている。

看護部においては平成 19 年度の報告書の38％が薬に関するインシデント報告である。持参薬を退院時渡し忘れてしまうことがあり、病棟薬剤師が不在になる土日に起こりやすく、薬剤師・看護師合同の検討会を持ち、改善した。また誤認防止の観点から、薬品の外見上の色彩による現場の混乱についても報告する。

[L24]

Prevention of Medical Malpractice from the View Points of Hospital Pharmacist

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医療過誤防止とその対策―病院薬剤師の視点から―

清水 秀行

帝京大学ちば総合医療センター薬剤部部長

2007 年の医療法改正は、医療の安全を担保するための改正であると言われています。医療現場では毎日のようにヒヤリハットが報告されており、医薬品に関わる事例も多く含まれます。今回の改正で、病院の管理者に医薬品安全管理責任者の設置が義務付けられました。医薬品安全管理責任者の有資格者は薬剤師に限定されているわけではありませんが、薬剤師が勤務している施設では薬剤師がこの職に当たるのが最も適切であると言えます。病院における医薬品安全管理責任者の役割から医薬品に関わる医療過誤防止の方向性を考えます。一方、薬剤部業務に関する医療過誤の防止対策として注視したいのが、調剤における処方監査と病棟における薬剤管理指導業務です。どちらもキーワードは薬学的管理です。今回は処方監査の重要性について事例を通して認識いただきたいと思います。また、薬剤管理指導業務では近年、持参薬の薬剤師による管理やお薬手帳を活用した入院・外来のシームレスな薬歴管理が求められています。また、本年度の診療報酬改定では、「救命救急入院等を算定している患者に対して行う場合」が新たに認められました。これらの業務について、当院での取り組みを紹介させていただきます。

Prevention of Medical Malpractice from the View Points of Medical Doctor

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35% of medical malpractice concerning about pharmaceuticals are order errors of medical doctors by the report, January to March on 2008, of Japan Council for Quality Health Care (JCQHC). To decrease these errors, it is essential to know what kinds of medication errors happen and to research how to prevent them. Here, I'll present real cases of medication errors to suggest preventive methods of medical malpractice.

医療過誤防止とその対策 ～医師の立場から～

神崎　哲人

千葉科学大学 薬学部 教授

[L26]

Designing of Formulation and Manufacturing Processes for Prevention of Medical Malpractice and Quality of Product

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"False recognition" and "improper use of medicine" of medical products may occur irrespective of the scale of medical institutions. To prevent these, respective medical institution has proactively introduced not only education programs for staff but also software and/or hardware system for handling medical supplies. Moreover, pharmaceutical companies have devoted steady efforts in improvement of image discrimination of products by formulation designing in the development stage and also in prevention of contamination in medical products, which might cause health damage of patients, by production controls in the commercial manufacturing stage.

In this presentation, some case studies of the above-mentioned formulation designing and production controls performed in pharmaceutical companies are reported.

医療過誤防止と医薬品品質確保のための製剤設計・製造設計

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医薬品等における「誤認」「誤薬」は，医療機関の規模に関係なく発生する可能性があるため，各医療機関は職員の啓発・教育のみならず，それぞれ独自の事故防止システムを積極的に導入している．一方，我々医薬品メーカー側においても，医薬品の「誤認」「誤薬」を可能な限り回避できるような製剤設計に努めるとともに，一方では，健康被害の原因ともなりうる製造工程における医薬品の汚染を防止するために，製造システムの設計とさらなる改良にたゆまぬ努力を傾注している．今回は，医薬品メーカーにおけるこれらの製剤設計，製造設計の事例を簡単に紹介する．

一般的に，製剤からの薬物の溶出性とか含量均一性など，医薬品が本来その機能として具備すべき品質に対しては，GMPにもとづいた厳重な管理システムが構築されており，これらの機能性に問題のある製品が出荷されることは考えにくい状況にある．しかしながら，医薬品の汚染とりわけ異物混入に関しては，数百万錠に1錠の発生であっても問題化することがあり，それはもはや統計的品質管理のおよぶ領域ではなくなっている．このため異物に関してはより厳格な対応が必要となる．今回は医療過誤とあわせて，この部分にも焦点をあててみたい．

Medication Errors Caused by Pharmaceuticals and an Approach by the Pharmaceutical Industry to Prevent Them -From the View Point of Packaging, Labeling, and Containers-

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It was not until 1999 that medication errors began to attract social interest. At that time, a wrong patient was operated on in a certain university hospital and the report “To Err is Human: Everybody Makes a Mistake” was issued to the public by The National Academies Institute of Medicine: IOM in the US. Thereafter in Japan, various notifications to prevent medication errors were issued by the Ministry of Health, Labour, and Welfare and measures have been increasingly being taken based on them.

In this presentation, the speaker will show the audience some examples of improvement in pharmaceutical packaging which have been so far considered and actually implemented by the pharmaceutical companies, mainly by the speaker’s company, under these circumstances to prevent medication errors.

医薬品の医療過誤と製薬業界における防止対策の取り組み －包装表示・容器の視点から－

平本慎次

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我が国で医療過誤に対する社会的関心が寄せられるようになったのは，1999 年の某大学病院における手術患者の取り違え事故が起こったことに加え，当時，米国において「To Err is Human：人は誰でも過ちを犯す」の報告が全米科学アカデミー医療研究所（The National Academies Institute of Medicine：IOM）から公表されたことによると思われる．その後，我が国においても，医療過誤を防止するため厚生労働省から各種関係通知が発出され，これにもとづいた対策強化が進められている．本講演では，こうした状況のなかで，製薬企業がこれまで検討に取り組み，医薬品包装における医療過誤防止対策として既に実施済みの改善策の一例について，弊社の事例を中心に紹介する．

[L28]

Risk and Crisis Management for Environmental Pollutants

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Industrial chemicals are also one of the most important products by modern technology. More than 100,000 chemicals are in the market and about 3,000 chemicals are estimated to be newly introduced into the market annually. There have been several incidents, in which human exposures to chemicals have occurred insidiously. Some of such incidences unveiled unexpectedly high levels of polybrominated diphenyl ethers in human breast milk in the early 1990s and of perfluorooctanate in 2000s in human serum in Japan.

Monitoring unexpected exposures systemically is an essential activity of risk management for environmental pollutants. Human specimen bank is essential to reconstruct long-term-trends of exposures and computer simulation is useful to estimate the source of exposures.

In recent years due to the rapid spreading industrialization, large amounts of various environmental pollutant are transferred across the borders. For example, it is known that the yellow sand storm from China is known to convey various environmental chemicals to neighboring countries. However, it remains unknown to what degrees the cross-border-transfers of environmental pollutants from one country to other countries may have impact on population-exposure levels in other countries.

We have established a human specimen bank (The Human Specimen bank, Kyoto University). This bank has collected human specimens from 1970s to present in Japan, Korea and China as archives. We are also producing a computer simulation model, which enables us to describe transfer of the environmental pollutants globally.

In addition to the infrastructure, special emphasis should be paid for the development of the education program for effective management of emergencies such as oil spills, chemical terrorisms and chemical hazardous incidences. Those program should be targeted to workers such police, fire and ambulance and volunteers. The subjects taught should cover basic chemistry, impact on the body, impact on the environment, response of services, integrated response, appropriate legislation, exercises in management. A case-based short-term (bout 2weeks) program may be effective for training.

Crisis Management and Communication for Environmental Pollutants

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It is 1990's that risk management about the chemical substance began in our country. Therefore, environmental problems by soil pollution by the lead or dioxins, or the asbestos pollution surface in all parts of Japan. I would like to talk about the case studies about crisis management and health risk communication for these problems.

Case 1: Although a guideline for preventing the scattering of asbestos was released on 1996, but there have been some examples, when the guideline was not observed. Due to lack of effective control measures when extended re-construction of a nursery school in Tokyo was performed in July, 1999, infants and children were exposed to asbestos. At the beginning, since information about the health effects of asbestos exposure was insufficient, their guardians got confused and angry against administrators. About 40 days after the occurrence of the incident, communication among guardians, the administration, and two specialists began. A committee was formed to oversee work to assess health effects, etc. The health risk assessment indicated that, as a result of asbestos exposure, most babies and children in the nursery school had incurred an increased lifetime cancer risk exceeding the prescribed threshold of 1:100,000. Therefore, it was decided that a committee should follow up all the exposed children over their entire lifetimes

Case 2: Dioxins and related compounds and the lead which were largely beyond a standard from the soil of a large-scale housing complex built, where there was a chemical factory before, were detected. More than 3,000 families include children have lived over 30 years there. The administration office set up expert Committee and discussed measures immediately. In addition, crisis communication meeting were performed among the residents and committee members repeatedly and explained possibility of health effects and measures for soil pollutants. Finally blood levels of dioxins and the lead in children and their mothers were measured. Fortunately, these levels were within normal limit. A risk management committee including certain residents is active even now.

Dealing with the aftermath of these problems was a new experience for local government. All meetings of the committee were open to the public. These procedures were new departures in Japan.

[L30]

Development of a Novel Chelate Resin and Its Application to Determination of Trace Elements in Water Samples

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Analyses of metal elements in environmental and biological samples are important to understand contamination level of harmful elements but also significant to recognize of impact to ecosystem and human health. ICP-AES and ICP-MS, which can accomplish simultaneous multi-element analysis, are widely used to analyze these samples. In these methods, however, separation techniques will be often required to decrease interferences of matrix elements such as alkali and alkaline earth elements which are generally contained at large amounts in these samples. In proposed various separation techniques, solid-phase extraction with chelate resin is useful for analyses of various samples, especially water samples. The chelate resins introducing iminodiacetate group (IDA resin) are commercially available from various manufacturers, so the IDA resins are conveniently utilized for the extraction of elements. However, the IDA resins have lack of abilities to extract the target elements quickly and to remove the high amount matrix elements effectively. We have developed a novel chelate resin having long chain chelating group that is carboxymethylated polyethylenimine (CM-PEI resin, Fig. 1). The developed resin has unique adsorption properties for the elements (Fig. 2). Alkali and alkaline earth elements are scarcely trapped on this resin at pH below 7 due to ion exclusion effect having the CM-PEI resin. In contrast, many harmful elements such as copper, cadmium, and lead can be extracted quantitatively and rapidly over the wide pH range. Furthermore, this resin can also extract some oxo-acids such as molybdate and tungstate effectively under the acidic conditions. In this lecture, the characteristics of the developed chelate resin for separation of elements and its application to analysis of trace elements in environmental and biological samples will be presented.

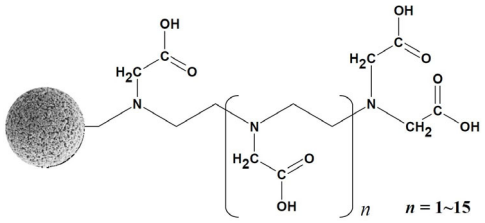

Fig.1 Chemical structure of CM-PEI resin

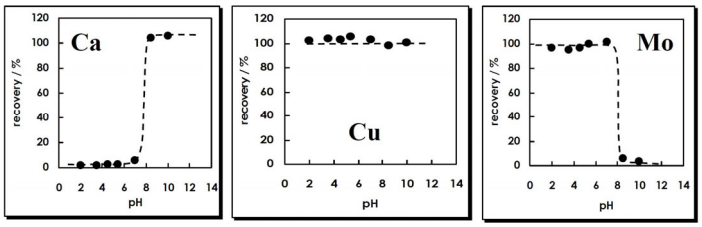

Fig. 2 Extraction behaviors of elements on CM-PEI resin

Risk Management in Occupational Health

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In risk management of chemical substances related to occupational health in the private sector, Occupational Exposure Limits (OELs) are used for hazard identification and risk assessment. OELs are recommended by the Japan Society for Occupational Health (JSOH) for about 200 chemicals as reference values for prevention of adverse health effects on workers due to occupational exposure to chemical substances. The Occupational Exposure Limit-Mean (OEL-M) for mean concentration of a chemical substance is defined as the reference value for the mean exposure concentration at or below which adverse health effects due to a substance do not appear in most workers working for 8 hours a day, 40 hours per week under a moderate workload. The Occupational Exposure Limit-Ceiling (OEL-C) of occupational exposure to a chemical substance is defined as the reference value for maximal exposure concentration of a substance during the working day at or below which adverse health effects do not appear in most workers. The principal reason why OEL-C is recommended for some substances is that their toxicities often cause immediate adverse effects such as skin irritation or CNS suppression. The Occupational Exposure Limit Based on Biological Monitoring (OEL-B) is defined as the reference value for data obtained by biological monitoring at or below which adverse health effects do not appear in most workers exposed to a chemical. Special care is required in the handling of carcinogens and sensitizers. Occupational carcinogens are primarily classified based on epidemiological findings in addition to the results of the animal experiments. Occupational sensitizers, which induce allergic reactions in humans, are listed and recommendations are made for them regarding maximum exposure to the airway and skin. For assessment of risk, the results of measurement of chemical concentrations in a work environment are compared with the targeted OEL or hazard level, to maintain a safer and more comfortable work environment.

[L32]

An Application of Computer Simulations for People Evacuation Management in a Complex Setting

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Natural and man-made hazard does not necessarily result in disaster in an area. It hinges upon: (1) the risk and the strength of the hazard; (2) the population density; (3) the integrity of structures; and (4) the efficiency of hazard management implemented in the areas. From this perspective, Asia Pacific Region is one of the highly risky regions in view of the tremendously growth in the urbanization process. The super high density of population and the super high rise structures in this region pose an immense risk of disastrous consequence just even triggered by a trivial natural or man-made hazard. Recognizing this, a variety of organizations at all levels of government and in the public and private sectors have increased consideration of emergency management.

We understand that absolute prevention of disasters and restricting their spread may be impossible. Evacuation of people from the hazardous region(s) is per se a way to reduce the ill effects of disasters and evacuation planning is prima facie one of the critical components in emergency management. This article briefly outlines the framework of emergency management and discusses the use of computer simulations for evaluating different people's evacuation strategies for an urban area.

Development of an Emergency Management Academic Program: A Case Study

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University academic programs in the area of emergency planning and emergency response have grown at an alarming rate in the past five to seven years in the United States. Curriculums for these academic programs are based upon the need for a solid foundation of required knowledge, skills and abilities needed for the discipline. This needed knowledge can be based upon one or more of the following: 1) governmental rules and regulations, 2) employee/employer needs assessment, 3) discipline specific best management practices, 4) trade association guidelines or standard operating procedures, 5) and academic research. This presentation focuses on development of emergency management curriculum at The University of Findlay based upon governmental requirements and best management practices.

[L34]

Current Situation of Accidents Involving Hazardous Materials in Japan and Measures Taken by Organization Concerned

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Fire and Disaster Management Agency has maintained statistics on accidents (fire, explosion and leakage) at facilities where hazardous materials such as petroleum and other chemicals which have potential fire hazard, are used or stored. The FDMA analyses the data in order to take safety measures by amendment of regulations and issuing directives to local fire authorities. The statistics are announced annually to the public from the FDMA. However, the number of accidents involving hazardous materials has been increasing since 1994 and hit a record in 2007. While the number of fires and explosions has increased slightly, leak accidents increased drastically to 1.5 times as many as was in 1998. The FDMA considers that prevention and mitigation of such accidents is extremely important subject from the view point of both fire safety and environment protection, and has taken actions and done researches in corporation with various organizations concerned. In this paper, current situation of accidents involving hazardous materials with some recent examples and measures taken by the FDMA, local fire authorities, research institutes and industries concerned to reduce accidents are shown.

Fire Investigation for Emergency Management

Takashi TSURUDA

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National Research Institute of Fire and Disaster conducts root cause investigation of a fire accident by the request of local fire authority or on its own initiative. The NRIFD investigative staff includes chemical and mechanical engineers, and fire investigators with experience in local fire authorities. After a NRIFD team reaches a fire incident site, investigators work with the local fire authority and other regulatory agencies. A draft of findings is submitted to the Institute for consideration. The final report is submitted to the local fire authority. The lessons from NRIFD investigations are also submitted as articles for journals and/or presentations for symposia. As NRIFD arranged its investigative members are able to depart for the scene of a fire accident with a minimum of delay, members initiates the investigation with initial information. Fire sites may expose members to certain hazards from such things as explosive, flammable, toxic, or radioactive materials, sharp or heavy objects, high pressure or high temperature equipment, and disease. The NRIFD investigative members will cooperate with the local incident commander to determine hazards at the fire site and safety resources available to the investigative members. In this paper, examples of hazards determinations during investigations including silo explosions, hydrogen-oxygen detonation in a nuclear power plant, steam line rupture in a nuclear power plant, transformer fire in a nuclear power after earth quake, and titanium-water /oxygen /perfluorinated hydrocarbon fire in a pilot hydrogen station of 40 MPa operation pressure are shown.

[L36]

Evacuation Simulation in Fire by Real-Coded Cellular Automata

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Fire is one of the most serious disasters. The damage in fire is mainly caused by high heat fluxes from the flame, accidental explosions, and toxic species in smoke generated by combustion reaction, which causes fatalities, destruction of houses and buildings, and air pollution. In order to mitigate these losses, it is important to design the room size and exit location in the building for the fire evacuation to set the evacuation route and provide effective instruments including fire extinguishers and alarms. Additionally, an appropriate management for safety such as dairy training for fire evacuation is needed. In planning individual actions for safety and evaluating the effectiveness of facilities and instruments, it is plausible to understand the phenomena in fire and validate the fire evacuation plan in advance. However, it is difficult to conduct experiments inside the building in fire, because the costs are expectedly huge, and the people are exposed to danger. Therefore, the simulation of fire evacuation is needed. For this purpose, we need to describe the evacuee's behaviors in fire. Since its dynamics is caused by collective crowd behavior, we have difficulties to handle directly each motion by solving coupled differential equations. In this study, we present simulation of fire evacuation by real-coded Cellular Automata (RCA), which is our new approach for pedestrian dynamics. Here, we consider the evacuation from a relatively large room with one or two exits. To describe the flame spread in fire, a percolation model is applied, where the flame position is determined stochastically. In the simulation, we focus on several parameters including the number of people in room, the distance of evacuation route from the flame, and the location of the exit.

Exposure Assessment and Health Effect Evaluations of cadmium in Japan

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A half of total dietary cadmium intake comes from rice. Since 2001, we have been investigated in relationship between dietary cadmium exposure and health effects such as renal tubular and bone mineral density among 1310 farm housewives in 5 districts in Japan, who have been consumed their rice harvested in their paddy. The estimates of total dietary Cd exposure revealed that 0.5 - 2.5% of the participants in district A were exposed to a higher Cd dose than the current Provisional Tolerable Weekly Intake (PTWI), i.e. 4.5 - 20.3% in district B, 6.9 - 22.2% in district C, 24.0 -52.5% in district D, and 35.6 - 66.8% in district E. Creatinin-adjusted urinary Cd (U-Cd) increased age-dependently, and correlated with the degree of Cd contamination in the districts. Renal biomarkers showed statistically significant increases in an age-dependent manner in all the districts, but were correlated with neither U-Cd nor B-Cd, nor R-Cd. Multiple regression analysis depicted no significant increase in the prevalence of renal biomarkers in each district after adjustment for age. In regards of bone mineral density (BMD), we collected blood and urine samples and medical and nutritional information, and measured forearm BMD. Analysis of the data for subjects grouped by U-Cd level and age-related menstrual status suggested that cadmium accelerate the increase of urinary calcium excretion around the time of menopause and the subsequent decrease in BMD after menopause. However, multivariate analyses showed no significant contribution of cadmium to BMD or urinary calcium excretion, indicating that the results mentioned above were confounded by other factors. These results indicate that environmental exposure to cadmium at levels insufficient to induce renal dysfunction does not increase the risk of osteoporosis. In conclusion, this study results showed that renal tubular dysfunction and bone mineral loss remains the same among female farmers exposed to life-long dietary Cd close to or above the current PTWI.

[L38]

Risk Assessment on Arsenic in Seafood

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There is sufficient evidence in humans that arsenic causes cancers of the urinary bladder, lung and skin. There is sufficient evidence in experimental animals for the carcinogenicity of dimethylarsinic acid (DMA), which is one of the metabolites of inorganic arsenic. In 2004, the UK Food Standards Agency advised not to eat Hijiki (Hizikia fusiforme) seaweed because of the high levels of arsenic that it contains.

The toxicity and carcinogenicity of arsenic depend on its species. Speciation analysis of urinary arsenic is required to clarify the health risks of arsenic intake. Individuals living in Japan consume much seafood that contains high levels of organoarsenics. Speciation analysis of urinary arsenic was performed for 210 Japanese male subjects without occupational exposure using high performance liquid chromatography with inductively coupled plasma mass spectrometry (HPLC-ICP-MS). The median values of DMA and arsenobetaine (AsBe) were 42.6 and 61.3 μgAs/l, respectively. These findings indicate that DMA and AsBe levels in Japan are much higher than those found in Italian and American studies. It appears that the high levels of DMA and AsBe observed in Japan may be due in part to seafood intake.

Hijiki is a traditional food and used as part of a balanced diet in Japan for centuries. To clarify the risks of Hijiki ingestion, a 42-year-old male volunteer ingested 825 μg of inorganic arsenic compounds contained in eight servings of commercial Hijiki food, after refraining from eating seafood for 3 months. The maximum concentrations of arsenate (AsV), arsenite (AsIII), monomethylarsonic acid (MMA) and DMA were found at 4, 6.5, 13 and 17.5 h after ingestion, respectively. AsBe concentration was very low, and almost constant throughout the observation period. A total of 28% of ingested arsenic was excreted in urine. The total amounts of AsV, AsIII, MMA and DMA excreted in urine over 50 h were 11.2, 31.8, 40.9 and 104.0 μgAs, respectively. After eating one serving of Hijiki, arsenic intake and urinary excretion were at levels similar to those in individuals affected by arsenic poisoning. Long-term ingestion of Hijiki might elevate the risk of carcinogenicity.

The Functionality of Natto and Its Activity for Promoting Fibrinolysis

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Since ancient times, proteins that are foreign to a living organism have been ingested, aiming for their activation in vivo. One such example is the oral administration of streptokinase, which is generated from Streptococci and whose research work has mainly been conducted outside of Japan. It is indeed true that the effects of ingesting streptokinase through the mouth in the form of buccal tablets are rather strong, including inducing nosebleed. Dasen, an oral enzyme that is made by Takeda Pharmaceutical Co., Ltd., and is well-known in Japan, is quite effective for reasons that are not totally clear. There are numerous similar proteases, such as kimotab and lysozyme, and for such formulations produced by microorganisms, the effects and the risks are inseparable.

A related substance is a foodstuff from Japan called natto, which is the result of a modification of beans through pure culture (monobacteria), a rarity in the food industry. The strong nattokinase generated in the process is a protein with single polypeptide chains of pI8.6 and a molecular weight of 28,000. When nattokinase enters the human body, it contributes to smoother blood circulation, helping to prevent myocardial infarction and cerebral infarction —a dream way to maintain good health. There are also other approaches using several different types of microorganism including Temphe molts. It all comes down to the questions of what is produced by these genes Rhizopus and whether it is risky or effective.

Bacillus subtilis natto is the only known microorganism capable of producing vitamin K2, which has drawn widespread attention for the important role it plays in preventing osteoporosis, and also has inhibitory activity against platelet aggregation. Bacillus subtilis natto produces dipicolinic acid that acts against Helicobacter pylori, and contains many polyamines, which help prevent the inflammation of blood vessels.

We compile data from various test results concerning natto, and raise some issues.

食の安全と危機管理:納豆の機能性および線溶亢進作用について

須見洋行

倉敷芸術科学大学生命科学部生命科学科，倉敷，日本

生体において異物であるタンパクを摂り，利用していこうというのは数多くあった。Streptococci から生じるストレプトキナーゼの経口投与はその一例である。バッカルの形でそれを口から飲めば強すぎて鼻血が出るというのは言い過ぎではなく，事実である。また，我が国で有名な武田製薬のダーゼンもなぜかよく効く経口酵素剤である。その他，キモタブ，リゾチームなどそうしたプロテアーゼは挙げるときりがないが，これら微生物が生む製剤は危険さと効能とが表裏一体の関係にある。

我が国の納豆は食品業界では珍しく純粋培養（単一菌）による豆の修飾といえる。そして，それが作り出す強力なナットウキナーゼは分子量 28,000，pI8.6 の単一ポリペプチド鎖構造のタンパクである。これが身体に入ると，血液が「さらさら」となり，心筋梗塞や脳梗塞を防いでくれる，まさに夢のような話なのである。その他，テンペ菌などの複数の菌を用いた話もある。やはりこれら菌による生産と目的とするものの効能のどちらが表に出てくるかの問題である。

納豆菌は世界でも骨粗鬆症に重要なビタミン K2 を唯一生産できる微生物でもある。また，血小板凝集抑制能を持つ。ピロリ菌にとって厳しいジピコリン酸を生産する他，血管の炎症を予防してくれるポリアミンなどを含む。こうした納豆に係る様々な成績をまとめ，問題提起したい。

Toxicology of Colubridae (Rear-Fanged Snakes) Venom from Uzbekistan

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There are about 3000 snake species on the earth. Of these, 400 species are venomous and dangerous for humans. The family Colubridae is the largest family in the suborder Serpentes, which comprises more than 60% of all snake species. In the snake fauna of Uzbekistan , there are more than 10 snake species of the family Colubridae. Of these, the venoms of some snake species are toxic for humans and animals.

Despite a high number of the snakes Colubridae in comparison with other snakes, the biochemical composition and the mechanism of the effect of neurotoxins on biological membranes remain relatively poorly studied.

The goal of our work is to develop the methods of extraction and purification of biologically active compounds, neurotoxins, from the venoms of Colubridae snakes and to study the mechanism of the effect of purified components with the aim of their application in medicine and pharmaceutical industry.

Six snake species, namely, Coluber ravergieri, Natrix tessellata, Psammophis lineolatum Brandt, Coluber tyria (Linneus), Coluber rodorochachis and Elaphes dione Pallas (the family Colubridae) are widespread in Uzbekistan . However, these snakes have not been studied zootoxicologically, as yet.

For the first time, the toxicological properties of the venom of Colubridae snakes were studied in tested preparations (for mice, toxicity of the venom (LD50) using the venom of Psammophis Lineolatum brandt -7,21 mg/kg, Coluber ravergieri - 9,67 mg/kg, Coluber tyria (Linneus) - 9,65 mg/kg, Coluber rodorochachis - 10,64 mg/kg, Elaphe dione Pallas - 9,84 mg/kg and Natrix tessellata- 20,23 mg/kg. The venoms showed the phospholipase and protease activities.

The venoms and fractions of Colubridae snakes were for the first time shown to form single ion channels on bilayer lipid membranes with predominating cation selectivity.

The venoms and fractions of Colubridae snakes uncouple oxidative phosphorylation of isolated mitochondria. The venom of Coluber ravergieri in experiments on frog neuro-muscular synapses acts similarly to cobra neurotoxins, blocking holinergic receptors of postsynaptic membranes

The venoms and preparations made from snake venoms are in wide use in medicine as anesthetics and anti-inflammatory drugs against various kinds of pains. In this respect, the study of neurotoxins of the Colubridae snakes open new avenues for the use of natural biomaterials for the prevention of cardio-vascular diseases, which show a tendency of a wide distribution in various states of the world.

[P02]

The Development of the Quantified Check List for Safety Manegement in the Poisonous and/or Deleterious Substances-handling Manufacturing Industries

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T ABSTRACT: The authors have developed the quantitative risk assessment method of the check list, giving added weight to their check statements individually. In order to build the system of the quantified check list, firstly, the investigation reports of the whole accidents related to the poisonous and deleterious substances in Japan were collected from the manufacturing industries for the limited period of recent five years. Secondary, from the points of view of the organization factors and the technical factors, the accident causes were investigated and analyzed into the detailed factors. According to the statistical analysis for the cause factors, the importance of the cause factors was quantitatively calculated. Thirdly, approximately twenty check statements were extracted from each accident as the safety measures to avoid the causes in principle. The more important a check statement was, the more times the statement was repeatedly extracted. The number of times the statement was extracted was obtained. These deducted check statements were classified into and distributed to the organization factors and the technical factors. Consequently fourthly, based on both the importance of factors and the extracted times, every statement was expressed in numerical value. And, about four hundreds check statements in total were deduced. And finally, the importance on the statements weighed simplistically into four magnitudes.

Keywords: risk, assessment, check list, poison, management, accident, process

Automatic Identification of Color Change Reaction by Chemical Agent Using RGB Value

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When persons are exposed to chemical agents, they are given damage immediately. Therefore, it is necessary to detect chemical agents on the contaminated area immediately, and a portable chemical agent detector which we can operate easily on the contaminated area is very useful. There is a chemical agent detector whose principle is based on color change reaction between a chemical agent and reagents. The detector has some features like low false detection rate and high detection sensitivity. However, the operation of the detector is complicated due to injection of reagents etc. If the color change is quantified optically, it is possible to develop an automatic chemical agent detector with high reliability.

We conducted the color change test to study the feasibility of automatic detection with simulants solution. We used dimethyl sulfate (DMS) as the simulants of sulfur mustard and triethyl phosphate (TEP) as the simulants of nerve agent. In the experiments, we added simulants solution of constant concentrations (DMS: 0.04-2μg/ml, TEP: 10-100mg/ml) to the detection paper for color reaction and gave color to the paper. Then, we took an image of the color change by CCD camera and analyzed RGB value of the image. And we found the simple algorithm of automatic detection for chemical agents by optical analysis.

There are a correlation between the concentrations of simulants solution and the color density for the sulfur mustard detection paper. The correlation between the concentrations and (R+G+2B)/4 values is shown in Figure 1. We propose the algorithm to determine the concentration level by (R+G+2B)/4 values.

For the nerve agents detection paper, we can determine the existence of nerve agents only from R value. We will conduct the color change test with chemical agents and make an advanced algorithm for automatic detection at the next step.

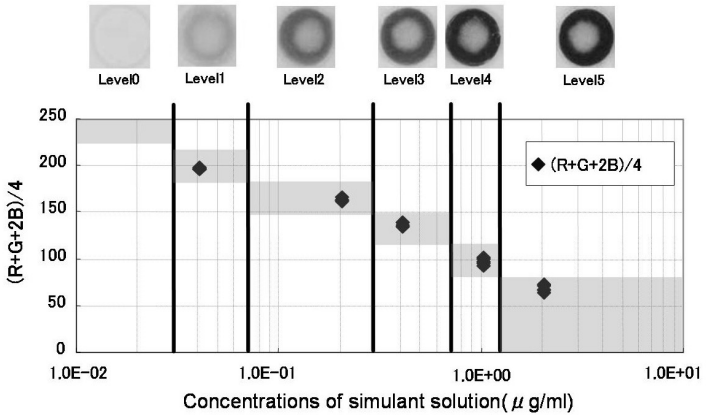

Figure1 Determination of concentration levels on the detector paper for sulfur mustard by RGB values

[P04]

Detection of Microorganisms by TOF-MS

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The effectiveness of the microorganism detection technology which used the mass spectrometry was examined. The following two kinds of methods were tested, and both detection performances of the microorganism were verified. In this report, we present the results.

①We aimed at the sensitivity improvement for the mass analysis method to detect and identify the microorganism. We tried the method to use the concentrated plate when analyzing the mass of surface protein of the microorganism directly.

In comparison with the normal plate, this method increased the sensitivity about ten times. This test was examined about E.Coli and spores of bacillus subtilis.

②We aimed to simplify the spectrum to facilitate its analysis. Processing the microorganism with the acid before mass analysis, the protein in the microorganism is extracted.

In this method, the spectrum was simplified, so that the peaks can be clarified.

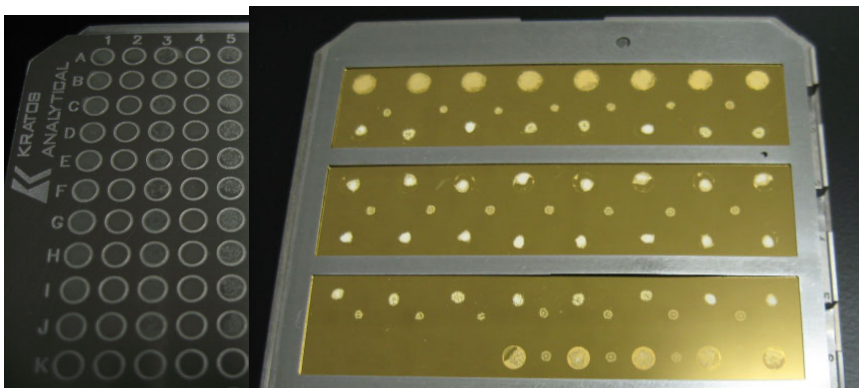

Figure 1　Typical views of the plates prepared for measurements
（Left: Normal plate　　Right: Concentrated plate）

High-Speed Sorting of Microorganism by Photomicrograph

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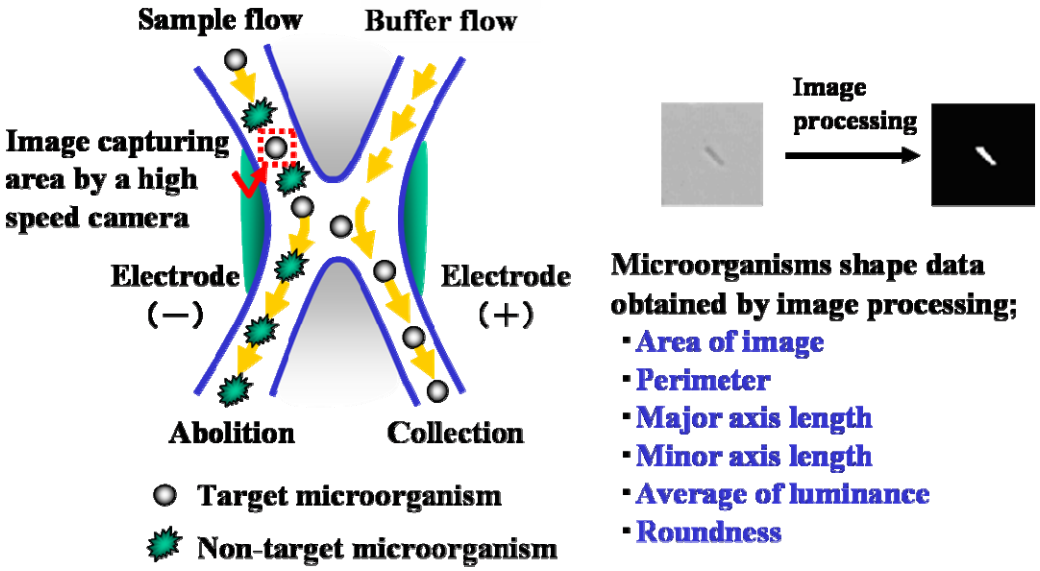
Recently, biological agent's threat becomes an important problem from the viewpoint of the National security. The particles such as dusts and harmless microorganisms exist in the atmosphere. These become "obstructive noise" for the biological agent's identification, and they decrease the accuracy of biological agent's identification and increase the identification time. Therefore, to identify rapidly the biological agent in high accuracy, it is important to separate the biological agent from atmospheric dusts and harmless microorganisms which are contained in samples collected from atmosphere.

We manufactured an on-chip cell sorter which separates target particle from view of the shape. This device obtains microscopic image of the particle which flows flow-channel of microchip with high speed camera, and judge target particle by shape and feature of particle which are calculated from the microscopic image. In that case, the target particles are separated from other particles by the impressed voltage. We confirm separation *Bacillus subtilis* from mixture of *E. coli*, the yeast, and *Bacillus subtilis*. Though the maximum separation rate of this device is 200 cells /second, we will improve this rate to one digit or more in the near future. Moreover, we investigate atmospheric microorganisms, and obtained microscopic image of 24 kinds of atmospheric microorganisms, and make the database concerning those shape and feature. Attention is necessary for the microorganism not included in this database for biological agent detection.

In the future, we plan further investigation, making a reliable database about atmospheric microorganism.



Mechanism of an on-chip cell sorter

[P06]

Discrimination of Biological Agents (Analysis by High-speed Amplification of DNA)

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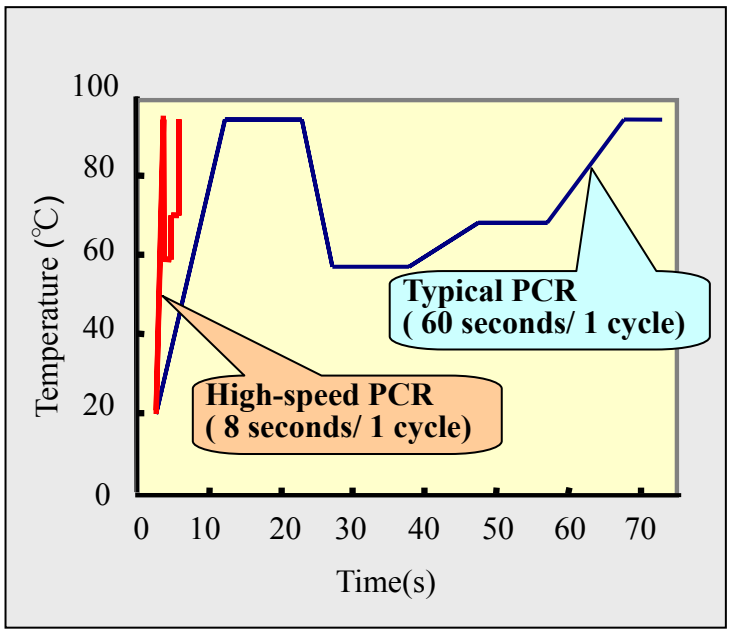
We pay attention to DNA of the microorganism to detect the biological agent, and are developing the system which accurately detects it within 15 minutes using High-speed PCR(Polymerase Chain Reaction).

In case that air sample is collected by biological detection system, the number of biological agent which is included in the collecting sample is very small amount. So it is necessary to increase the number of DNA for identifying the microorganism. There are DNA chip etc. as the method for identifying the microorganism by analysis of the DNA. It is necessary to increase the number of DNA before we identify the microorganism by the DNA chip etc. On the other hand, even if a little amount of DNA is included in the sample, the microorganism can be identified by PCR.

It takes 30 minutes to amplify DNA by typical PCR, but by High-speed PCR it is possible to amplify DNA within 5 minutes. As a result, even if the small amount of DNA of an atmospheric microorganism are included in the sample, it was possible to amplify the target DNA peculiarly and identify the microorganism. We show that it is possible to detect the biological agent rapidly by amplifying DNA of the biological agent using high speed PCR.



Temperature Cycles of High-speed PCR and typical PCR

Environmental Monitoring and Ecological Analysis Controlling the Running of the Facilities for Chemical Weapons Storing and Destruction

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3) Ministry of Natural Resources of Udmurt Republic, Izhevsk, Russia
4) Regional Center for Ecological Monitoring, Izhevsk, Russia

The experience gained through the activity for environmental safety surrounding the facilities for chemical weapons storing and destruction located in Udmurt Republic of Russian Federation has been reported. Based on the sampling of background and current level of hazardous chemical components the systematic approach for the evaluation of environmental safety has been performed.

Safety is the crucial factor of the Program of chemical weapons destruction in Russia. Thus, the spending for safety amounts from sixty up to seventy per cent of the overall operational cost of the factory. Following such a policy, the comprehensive system for State ecological control and monitoring of the facilities for chemical weapons destruction has been established according to the Russian Federal law assigning the process of chemical disarmament.

As for the specific factory (#1203, located in Kambarka, Udmurt Republic), the activity for ecological control and monitoring is carried out by the Ministry of Natural Resources of Udmurt Republic (Izhevsk) collaborated with the Research Institute of Industrial Ecology (Saratov). Actual work for environmental analysis has been started several months before the launching of facility. Background level in natural conditions surrounding factory's protected area has been previously analyzed. With the facility putting into operation (March 1, 2006), regulating State control of the emission source is performed.

By the two years period of the implementation of State ecological control and monitoring of the factory #1203, the following basic operations have been outlined:

- The result of analysis of facility's emission source reported quarterly for the specific poisonous pollutants, which are here products of lewisite decomposition (arsenic compounds). As shown the requirement of Maximum Permissible Concentration has been satisfied.
- The sampling of ambient air in the factory's protected area is carried out biannually. Along with poisonous substances and its decomposition products, the level of general pollutants is analyzed. Unlike the proper concentration of poisonous gases, unsupervised daily observations have shown critical atmospheric air pollution by general industrial compounds from December till April due to seasonal activity of civil establishments (heating installations mainly).
- The water resources quality is controlled by sampling of wastewater in spots located 500 meters from the spillway both upstream and downstream along Kama river.

- The quality of underground water resources is controlled by the comparison of sampling the well located within the factory territory and the model one located in similar surroundings but far enough to vouch for the lack of facility running effect.

As a result of described activity, a substantial amount of information has been collected on the quantitative characteristics of spatial and timing dynamic distribution of poisonous and hazardous chemical components and general industrial pollutants. Such a database is used for the implementation of the systematic approach for the evaluation of environmental and human safety surrounding the operation of the facility for chemical weapon destruction. Generally, this direction of investigation is performed in the form of expert system using the GIS (Geographic Informational System) technology with corresponding linking with attributive field parameters for natural resources inventory data and ambient conditions.

Pesticides and Nerve Agents Assay Based On Electrochemical Biosensor

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Electrochemical biosensors based on recognition capability of enzyme acetylcholinesterase were found suitable for organophosphates pesticides and nerve agent detection. Capability of developed method was tested using selected insecticies (methamidophos, paraoxon methyl, paraoxon ethyl) and nerve agents (sarin, cyclosarin, soman, tabun, VX). Screen printed sensors with platinum working and auxiliary, and Ag/AgCl reference electrode were used throughout experiments. Concept of assay was established on following of acetylcholinesterase inhibition by analyte. Acetylcholinesterase digested acetylthiocholine and created thiocholine as cholinesterase reaction product was oxidized on working electrode. Mentioned assay was able to detect as low as 10 nA organophosphate within a quarter hour.

[P09]

Salmonellosis due to *Salmonella Enterica* Serotype Typhimurium DT40 in Sparrows (*Passer montanus*) in Japan.

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This paper reports the first known outbreak of *Salmonella enterica* serotype Typhimurium DT40 infection in Eurasian tree sparrows in Japan.

[History] From December 2005, dead sparrows were observed frequently in a wide area of Hokkaido. The number reached 1,517 by July 28, 2006 (Hokkaido Government Office publication). Several organizations conducted investigations into these specimens, but the cause of death was not elucidated.

[Materials and Methods] We carried out pathological and microbiological examination on 15 sparrows collected in the area where the mass deaths occurred, to elucidate the cause. All samples were examined according to regular pathological methods, and the crop, liver, spleen and intestine were offered for general bacterial and *Salmonella* examination. Isolated *Salmonella* strains were subjected to serotype and phage typing. We also performed drug sensitivity tests and genetic screening by PFGE examination and RAPD analysis. To further assess *Salmonella* derived from the sparrows, we inoculated it into paddybirds, using *Salmonella* derived from a food poisoning patient as control.

[Results] Ingluviitis, splenomegaly and hepatomegaly with white nodules were constantly observed. Bacterial and necrotizing ingluviitis was especially characteristic. Histological findings showed colonization by gram-negative, rod shaped bacteria, and necrotizing lesions were observed in many visceral organs. *Salmonella* were isolated from many organs in all sparrows and were identified as serotype Typhimurium. The isolated bacteria did not show citric acid resolution, and catalase testing revealed only a very weak reaction. The isolates showed an indistinguishable band pattern on pulse-field gel electrophoresis and random amplified polymorphic deoxyribonucleic acid testing, and the same antibiotic resistance profile, and were phage typed as phage type 40(DT40). The control birds did not die, but the birds that were inoculated with DT40 from the dead sparrows suffered disease onset or died.

[Discussion] In Europe, North America and New Zealand, mass death of wild birds such as finches and especially sparrows due to *S. enterica* serotype Typhimurium has been reported and this infectious disease is attracting attention as a cause of sharp decline in populations of these birds. The pathological findings concerning the dead birds in these countries correspond with those of the present case. We considered the situation in Europe and America where there was a mass outbreak in the winter season, and our results indicated that Salmonella Typhimurium was also the cause of the mass death of

sparrows reported throughout Hokkaido. In New Zealand, an increase in human infection by *S. enterica* serotype Typhimurium was seen at the same time as the epizootic causing high mortality in sparrows occurred, suggesting that sparrows were the source of infection in humans. Therefore caution must be taken to guard against *S. enterica* serotype Typhimurium infection in public health, animal health and for conservation of species in wild birds. Phage type DT40, which we detected in the present study, had not previously been isolated from humans and animals in Japan, despite its importance as a cause of mass death of sparrows in Norway, North America and the U.K. We confirmed the high pathogenicity of DT40 based on an infection experiment. The route or mechanism by which this agent entered Japan is not known.

[P10]

A Comparison of Neuroprotective Efficacy of Newly Developed Oximes (K203, K206) and Commonly Used Oximes (Obidoxime, HI-6) in Tabun-Poisoned Rats

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The neuroprotective effects of newly developed oximes (K203, K206) and commonly used oximes (obidoxime, HI-6) in combination with atropine in rats poisoned with organophosphorus nerve agent tabun at a sublethal dose (180 μg/kg i.m.; 80% LD_{50}) were studied. The tabun-induced neurotoxicity was monitored using a Functional observational battery and an automatic measurement of motor activity. The neurotoxicity of tabun was monitored at 24 hours and 7 days following tabun challenge. The results indicate that only K203 and obidoxime in combination with atropine allow all tabun-poisoned rats to survive within 7 days following tabun challenge while two non-treated tabun-poisoned rats and one tabun-poisoned rat treated with K206 or HI-6 in combination with atropine died within 7 days. Only one of newly developed oximes (K203) combined with atropine seems to be effective for a decrease in tabun-induced neurotoxicity within 24 hours after tabun sublethal poisoning although it is not able to eliminate tabun-induced neurotoxicity completely. On the other hand, the neuroprotective efficacy of commonly used oximes (obidoxime and HI-6) as well as one of newly synthesized oxime (K206) is significantly lower in comparison with K203 according to the number of eliminated tabun-induced neurotoxic signs at 24 hours after tabun challenge. Due to its neuroprotective effects, K203 appears to be suitable oxime for the antidotal treatment of acute tabun poisonings.

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Structure-Activity Relationship as a Tool for the Development of New Promising Oximes

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Acetylcholinesterase (AChE; EC 3.1.1.7) reactivators are important group of drugs used in the case of intoxications with highly toxic organophosphorus compounds such as pesticides (paraoxon, chlorpyrifos etc.) and nerve agents (sarin, tabun etc.). After the sarin terroristic attack in Tokyo subway, their development employed many scientists from both - military and civilian sectors. Due to the rapid synthesis and evaluation of the biological activity of many new chemically different structures of new potential antidotes in our laboratories, we would like to discuss relationship between structure of AChE reactivators and their biological activity. Because of wide range of organophosphorus nerve agents and pesticides, we would like to focus only on reactivators of cyclosarin-inhibited AChE. Presented results are based on our in vitro studies with more than one hundred structurally different AChE reactivators, which were conducted during last five years. In this presentation, the main structural requirements influencing reactivation potency of currently available compounds are discussed.

[P12]

Novel Reactivators of Acetylcholinesterase against Paraoxon Intoxication

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The reactivators of acetylcholinesterase (AChE, EC 3.1.1.7) are very important components in the treatment of intoxications caused by organophosphate inhibitors such as nerve agents and pesticides [1]. These inhibitors covalently bind to active site of mentioned enzyme and irreversibly inhibit its activity. The reactivator breaks the inhibitor-enzyme covalent bond and restores its activity. Unfortunately, there is no reactivator applicable for every type of inhibitor; it means that every structural change in the molecule of inhibitor needs a specific structure of the reactivator [2].

Several series of AChE reactivators have been prepared in the Czech Republic since 2003. Their design was primarily focused on nerve agents; however, they were also excellent reactivators of paraoxon-inhibited AChE [3]. The SAR study of reactivators for paraoxon was developed and will be presented.

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Aflatoxin Assay Using an Acetylcholinesterase Based Biosensors

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The presented study approach acetylcholinesterase (AChE) as a biorecognition element useful for construction of low cost; however, low detection limit analytical devices for aflatoxin (AF) assay. AChE activity can be easily followed by measuring one of the enzyme reaction products: thiocholine that could be either chronoamperometrically oxidized or led to react with Ellman´s reagent resulting in strong shift of absorbance at 412 nm. Microplate photometric assay and amperometric biosensors were chosen as convenient transducers. We have approved feasibility of AChE for analytical application during the first phase of experiments. In the further round, we tested analytical properties of photometric microplates and amperometric biosensors during measuring protocols. Finally, we can proclaimed that obtained limit of detection was under 10 ppb for the both of described methods when solution of AFB1 was assayed. Another way of AChE based biosensor performance was investigation of complexes stability when biosensor was placed into reaction cell. Dissociation of complex AFB – AChE had dissociation rate constant k_{dis} = 0.0047±0.0005 s^{-1}. The half time ($t_{1/2}$) of complex dissociation was 146 s.

[P14]

Molecular Genetical Analysis of Nosocomial Infections Caused by *bla*CTX-M-3-harboring Strains of *Enterobacteriaceae*

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β-lactam resistance profiles of 3,975 nosocomial isolates of *Enterobacteriacea*e, i.e., *Citrobacter freundii* (n=163), *C.koseri* (n=125), *Enterobacter aerogenes* (n=233), *E.cloacae* (n=423), *Escherichia coli* (n=1,100), *Klebsiella oxytoca* (n=288), *K.pneumoniae* (n=789), *Morganella morganii* (n=104), *Proteus mirabilis* (n=66), *Providencia rettgeri* (n=34), *P.stuartii* (n=58), and *Serratia marcescens* (n=496), from inpatients were investigated. Three hundred and twenty isolates (8.2%) showed resistance to third generation cephalosporins (3GC). Of the 226 monobactam-resistant isolates in above 3GC-resistant strains, 35, i.e., *C.freundii* (n=3), *C.koseri* (n=2), *E.aerogenes* (n=2), *E.cloacae* (n=12), *E. coli* (n=2), *K.oxytoca* (n=2), *K.pneumoniae* (n=10), and *S.marcescens* (n=2), expressed a typical ESBL-cefotaximase profile (cefotaxime MIC>ceftazidime MIC) with clavulanic acid synergy. Molecular methods identified 35 ESBL-producing strains harboring a plasmid–mediated CTX-M-3 type ESBL gene *(bla*CTX-M3).

CTX-M-3 型βラクタマーゼ遺伝子保有腸内細菌による院内感染の分子遺伝学的解析

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入院患者から分離された腸内細菌科の細菌 3,975 株、即ち、*Citrobacter freundii* (163 株), *C.koseri* (125 株), *Enterobacter aerogenes* (233 株), *E.cloacae* (423 株), *Escherichia coli* (1,100 株), *Klebsiella oxytoca* (288 株), *K.pneumoniae* 789 株), *Morganella morganii* (104 株), *Proteus mirabilis* (66 株), *Providencia rettgeri* (3 株 4), *P.stuartii* (58 株), *Serratia marcescens* (496 株)のβラクタム薬耐性傾向を調べた。320 株(8.2%)が第 3 世代のセファロスポリン（3GC）に耐性であった。3GC 耐性でモノバクタムに耐性を示す 226 株の内 35 株、即ち、*C.freundii* (3 株), *C.koseri* (2 株), *E.aerogenes* (2 株), *E.cloacae* (12 株), *E. coli* (2 株), *K.oxytoca* (2 株), *K.pneumoniae* (10 株), *S.marcescens* (2 株)がクラブラン酸に阻害される典型的な cefotaximase タイプの ESBL (cefotaxime の MIC>ceftazidime の MIC)を産生することが確認された。これらの株が保有するラクタマーゼ遺伝子について分子遺伝学的解析を行った結果、35 株全てがプラスミド性に CTX-M-3 型 ESBL 遺伝子(*bla*CTX-M3)を保有することが明らかになった。

Medical Measurement against Flue Pandemic-including the social measurement

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Different consideration is necessary against the so-called NBC(Nuclear, Biological and Chemical) Hazard compared with measures against natural disaster.

Nowadays, outbreak by new type (new strain) influenza is feared, in which the casualty number is suspected to increase with parabolic curve.

Measures for maintaining social activity is also thought to be important as well as effective medical system. Our trial is presented.

RESULTS: Measures should be prepared from macroscopic viewpoint in addition to microscopic methods.

Macroscopically, the following points are characteristic: The hardware/mechanical damage is minimal. However, the negative effects for people's activity or workforces are prominent. The area involved will become worldwide. Repeated or recurrent attack will be caused. Therefore, inhibition of social activity will last for long-term, as well as the severe influence in mental/psychological aspects in the public. Early recognition and information system are essential.

Microscopically, it is essential to prepare the necessary sanitary goods as well as to educate hygiene and the preventive medicine for public widely, in order to inhibit/minimize the outbreak.

DISCUSSION and CONCLUSIONS: For measuring outbreak, (1) medical/emergency system, including hospital, police, rescue/fire department, self-defense forces, (2) governmental supporting system should be prepared. Moreover, if it is considered to minimize the long-term influence of outbreak, coordination between (3) the lifeline maintaining organization/company, (4) other enterprises, schools, and systems of local residents' association system should be added. Manuals or guidelines against the outbreak, and drill should be repeated from various different viewpoints.

鳥インフルエンザ・新型インフルエンザに対する医療対応―社会的視点を踏まえて

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NBC(Nuclear, Biological and Chemical Hazard)災害では、地震・風水害等の自然災害における医療とは異なった対応が必要である。

特に、大規模感染症、中でも発生が危惧される新型インフルエンザでは、被害が経時的に放物線状に増大する可能性がある。災害医療対応を考える上でも社会的な視点がより重要と考えられる。我々の取り組みの現状を提示し、問題点、これからのあり方を検討した。

検討結果：自然災害と比較した違いとして、新型インフルエンザによる大規模感染症発生時の大きな特徴としては、巨視的・微視的観点から指摘できる。

被害の形としては、前者として、ハード面での直接被害は極僅かであるが、その規模が世界的なこと、被害の波が繰り返す可能性があること、大規模社会活動休止期間が長期にわたることによる社会の疲弊が想定されること、広範囲の多数の住民に精神／心理学的影響が大きいこと、後者としては、個々の感染を通して速やかな拡大が想定されることから、緊急医療に加え、予防・衛生的な対応が普及するする必要があることがあげられる。

考察・まとめ：新型インフルエンザによる大規模感染症発生時は、(1)医療施設・警察／消防／自衛隊等の医療対応にあたる機関、(2)地方自治体・政府等の公的施設・機関対応、に加え、長期対応を想定した(3)ライフライン関係の機関・企業の準備態勢、(4)その他の企業・学校・地域住民体制等の全ての組織を含んだ協力体制が整備される必要がある。そのための多面的な視点からのマニュアル・ガイドライン作成、訓練の施行が必要である。

Characterization of Highly Pathogenic Avian Influenza Viruses Isolated During 2006-2007 in Myanmar

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In Myanmar, its first highly pathogenic avian influenza (HPAI) outbreak occurred in March 2006, followed by two outbreaks in 2007. Here, we analyzed HPAI viruses of H5N1 subtype isolated in 1st and 2nd outbreaks in Myanmar. Firstly, we performed phylogenetic analysis of the hemagglutinin (HA) gene of four HPAI isolates (A/chicken/Pyigyitagon/204/2006 from 1st outbreak in March 2006, A/chicken/Hmawbi/517/2007, A/guinea fowl/North Okkalarpa/834/2007, and A/quail/Mingalardone/866/2007 from 2nd outbreak in March 2007). It showed that the isolate from 1st outbreak belongs to clade 7 of the classification system created by WHO/OIE/FAO H5N1 Evolution Working Group, whereas all isolates examined from 2nd outbreak belong to clade 2.3.4 (Fujian-like strain). This result showed that genetic origins of HPAI viruses differ between two outbreaks, suggesting that at least two introductions of the HPAI viruses have occurred in Myanmar. Thus, result here suggested the importance of the monitor of cross-border movements of poultry or poultry-related materials to minimize the expansion of HPAI virus exposures. In addition, we examined the pathogenicity of A/chicken/Hmawbi/517/2007 for chickens and domestic ducks. All chickens died by 48 hours after intranasal inoculation of the virus (mortality; 100%), whereas only two ducks died by day 6 and 8 after inoculation (mortality; 25%). Moreover, HA inhibition assay of post-infection serum from surviving ducks revealed that all of the surviving ducks seroconverted by day 14 after inoculation. These results showed that A/chicken/Hmawbi/517/2007 causes lethal infection for not only chickens, but also domestic ducks, suggesting that the control measures on domestic ducks are important in Myanmar to eradicate the HPAI virus from the country.

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[P17]

Characterization and Application of Glycopolymers Carrying Sialyl Lactosamine Repeats for Inhibition against Influenza Virus Infection

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Influenza viruses infect cells through binding of virus hemagglutinins to sialic acid-containing carbohydrates as receptors on the host cell surface. Influenza viruses isolated in humans and other animals seem to have originated in wild birds. Sialic acid-containing carbohydrate molecules expressed on the host cell surface are essential determinants for both cross-species transmission and epidemics in a specific host. Influenza viruses recognize sialic acid linkages in the receptors, such as sialyl lactosamine (sialyl LacNAc) structures, sialylα2-3/6Galα1-3GlcNAcβ1-R and sialylα2-3/6Galβ1-4GlcNAcβ1-R.

To control cross-species transmission of influenza viruses, it is necessary to elucidate the mechanisms of the interaction between influenza viruses and sialo-glycoconjugate receptors expressed on different hosts. Inhibitors containing receptor carbohydrate determinants that prevent virus entry may be useful tools to address such issues. We synthesized and characterized sialyl glycopolymers carrying lactosamine repeats as influenza virus inhibitors. We also applied such glycopolymers carrying multivalent sialyl LacNAc oligosaccharides for further investigation of the molecular mechanisms underlying the interaction of influenza viruses with different species through specific carbohydrate structures.

Small Exotic Animals as Potential Reservoirs of Zoonotic *Bartonella* Species

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[Objectives] Last decade, it has been reported that zoonotic *Bartonella* species were isolated from various small mammals in a number of countries. With globalization, many wild and captured animals have been traded as pets throughout the world. Therefore, we investigated the prevalence of *Bartonella* species among imported small animals whether these animals may serve as the reservoirs of the organisms or not in Japan.

[Materials and Methods] The prevalence of *Bartonellae* was bacteriologically investigated in 546 mammals (6 families including 23 genera, and 28 species) imported as pets from Asia (China, Thailand, and Indonesia), North America (U.S.A), Europe (Netherland and Czech), and the Middle and Near East (Egypt and Pakistan) to Japan. A phylogenetic analysis was performed by DNA sequences of citrate synthase gene (*gltA*) of the isolates.

[Results] Of the 546 mammals examined, 367 animals were wild and captured and 179 animals were bred and maintained in breeding facilities. In total, 137 (37.3%) wild animals were infected with *Bartonellae*, while only 5 (2.8%) domesticated animals harbored the organisms. A total of 407 isolates obtained was classified into 53 sequencing types (STs) based on *gltA*, and classified into 11 groups, including 4 related groups with the type strain of *B. washoensis*, *B. grahamii*, *B. elizabethae*, and *B. clarridgeiae* by phylogenetic analysis. The sequence homologies between the isolates and each related type strain of *Bartonella* species showed 94.6% to 97.4% for *B. washoensis*, 98.4 to 98.7% for *B. grahamii*, 95.5% to 100% for *B. elizabethae*, and 96.2% for *B. clarridgeiae*, respectively. The other 7 groups were distantly related to any existing *Bartonella* species. *B. washoensis*-, *B. grahamii*-, and *B. clarridgeiae*-like bacteria were obtained from only family *Sciuridae*, while *B. elizabethae*-like bacteria were isolated from different three families such as *Sciuridae*, *Muridae*, and *Dipodidae*. Of the 142 *Bartonella* positive animals, 25 animals were found to be co-infected with different STs of *Bartonella* species.

[Conclusions] We revealed that imported pet animals carried several *Bartonella* species with a high rate including probably 7 novel species and may serve potential new reservoirs of zoonotic *Bartonella* species in Japan.

[P19]

Detection of the Borrelia Burgdorferi Sensu Lato and Anaplasma Phagocytophilum in Host-seeking Adult Lxodes Ricinus Ticks Collected in Serbia

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Lyme borreliosis and human granulocytic anaplasmosis (HGA) are tick-borne infections. To evaluate prevalence rate of these pathogens, a total of 287 unfed adult Ixodes ricinus ticks were collected from vegetation in 2001, 2003, and 2004 at 18 localities throughout Serbia. Using PCR technique, we detected species-specific sequences, rrf-rrl rDNA intergenic spacer for Borrelia burgdorferi sensu lato and p44/msp2 paralogs for Anaplasma phagocytophilum, respectively, in total DNA extracted from the ticks. These prevalence rates were that for B. burgdorferi sensu lato (42.5%) and A. phagocytophilum (13.9%). The presence of five B. burgdorferi sensu lato genospecies, namely, B. burgdorferi sensu stricto, B. afzelii, B. garinii, B. lusitaniae, and B. valaisiana was identified by restriction fragment length polymorphism (RFLP) analysis. The most frequent B. burgdorferi sensu lato genospecies was B. lusitaniae, followed by B. burgdorferi sensu stricto. Coinfection by B. burgdorferi sensu stricto and B. lusitaniae was the frequently observed among ticks infected with B. burgdorferi sensu lato genospecies. Coinfection by B. burgdorferi sensu lato and A. phagocytophilum appeared in 24 ticks. Sequencing of p44/msp2 paralogs of Serbian A. phagocytophilum showed that they were unique and distinct from those of A. phagocytophilum in other countries. These findings indicate a public health threat in Serbia of tick-borne diseases caused by the B. burgdorferi sensu lato and A. phagocytophilum.

Characterization of Rickettsial DNA (Spotted Fever Group) From Ticks Collected In Kagoshima Prefecture, Japan

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In 2007, 251 ticks were collected by flagging method in Kagoshima prefecture, Japan. These ticks were dissected and the DNA was extracted from salivary glands of the individual ticks. PCR was performed using *gltA* primers specific for spotted fever rickettsiae in each of tick specimens. Of 251 ticks, 16 were PCR-positive (6.3%): 7 of 21 *Haemaphysalis hystricis* (positive rate 33%), 2 of 140 *H. formosensis* (1.4%), one of 9 *H. flava* (11%), and 6 of 12 *Amblyomma testudianruim* (50%). None of *H. longicornis* were positive (0/69 ticks). Sequence and phylogenetic analyses based on *gltA* revealed that (i) rickettsial DNAs from *H. hystricis* were closely related, but not identical, to *Rickettsia montanensis* (similarity 99%), (ii) DNA from *H. formosensis* was far from any other rickettsia species (similarities 93 to 96%), and (iii) DNAs from *A. testudinarium* were identical to that of *R. tamurae*. The rickettsial *rompA* and 16S rDNA amplified from *H. hystricis* were further analyzed. The results showed that the amplified DNA sequences from *H. hystricis* were located distantly from any other rickettsia species sequences (similarities 87 to 91 %) in the phylogram of *rompA*, and were closely related to *R. rickettsii* (similarity 99%), *R. massilliae* (99%), and followed by *R. japonica* (98%) in the tree of 16S rDNA.
In Kagoshima prefecture, it is one of endemic areas for Japanese spotted fever. However, in this study, *R. japonica* which is causative agent of Japanese spotted fever was not detected. Taken together, this study suggests that rickttsiae from *H. hystricis* and *H. formosensis* seems to be new spotted fever group rickettsiae in Japan and may be a new causative agent of Japanese spotted fever.

[P21]

Leptospirosis in Squirrels Imported from United States to Japan

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Leptospirosis is a worldwide zoonosis caused by infection with Leptospira interrogans sensu lato species. Leptospira is mostly transmitted to humans through contaminated water or soil and by direct contact with a variety of infected animals. To date, a variety of wild animals have been imported from foreign countries to Japan.

In this study, 2 men working at an animal trading company were infected with Leptospira spp. Leptospira isolates from 1 patient and 5 of 10 squirrels at the company were genetically (flagellin gene and DNA gyrase B subunit gene sequences) (Fig 1) and serologically identical and were identified as Leptospira kirschneri.

These findings show that exotic pets represent a substantial hazard. The outbreak demonstrated how new infectious diseases could be emerging because of importation from overseas. If, during shipping and housing of the animals, the infection were to have expanded among southern flying squirrels, the infection rates and risk for humans would have increased. The leptospirosis cases reported here warn against importing exotic animals.

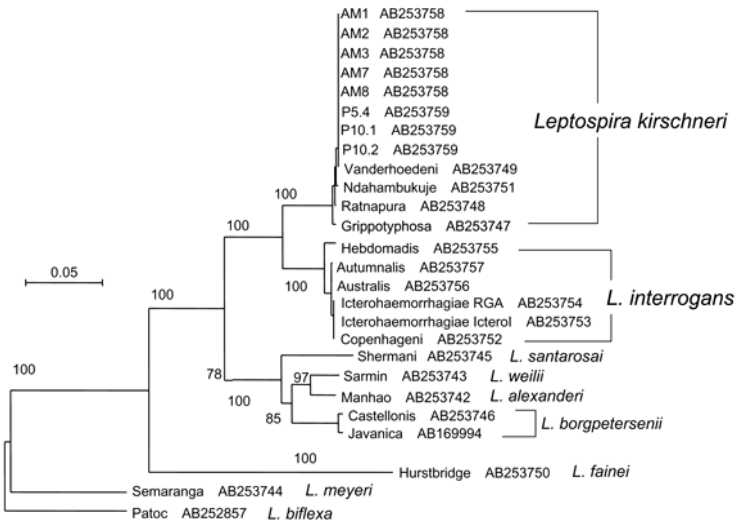

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Figure 1. Phylogenetic tree based on the *Leptospira* DNA gyrase B subunit gene (*gyrB*) sequence. The sequences obtained have been deposited in DDBJ/GenBank/EMBL with accession numbers indicated.

Mutation mechanism of the highly pathogenic avian influenza virus into humans

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The highly pathogenic avian H5N1 influenza A viruses have spread to numerous countries in Asia, Europe and Africa, infecting not only large numbers of chickens and related poultry, but also an increasing number of humans, with lethal effects. In this context, infection and transmission mechanism of the virus into the avian, and other animals including humans must be elucidated in order to construct the safety for poultry food. We confirmed that 1) Chicken and Quail intestine express human type influenza virus receptors *(N*-linked Neu5Ac2-6Gal-sequences). Therefore, chickens and quails in the market have molecular character as an intermediate host for H5N1 transmission to humans, and could generate new influenza viruses with pandemic potential. 2) Amino acid substitution in H5N1 avian virus Hemagglutinin, Ser227Asn; Glu75Lys, Leu123Pro, Asn193Lys; Leu129Val, Ala134Val; Gln192Arg, Asn182Lys are responsible to bind human type receptor (Neu5Ac2-6Gal-sugar chains). We have characterized several native highly pathogenic H5N1 strains which bind to human receptor with pandemic potential. 3) Global surveillance of the mutation of receptor binding specificity of highly pathogenic avian influenza viruses (H5N1, H9N2 and H7N7) is necessary.

[P23]

A Study on the Preventive Law for Influenza (H5N1) In Japan

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Establishment of effective control measures against influenza (H5N1) pandemic is of urgent need all over the world. Damage and influence by infectious disease are different among nations and law functions as a control system only for domestic risks in each nation. Therefore, we need a global standard to decrease risks of pandemic diseases. In Japan, risks of influenza (H5N1) is estimated to be "class 2" in the preventive law, so-called '*Kansensho-Ho*', in accordance with the WHO's regulation. Influenza (H5N1) pandemic is estimated to affect at least 4 million citizens (30% of the population) in Tokyo. However, we are facing the absolute lack of the preparedness. For example, there are 34,000 medical doctors, including all fields, but only 12 hospitals (92 beds) are authorized for quarantine of patients in the class 2 category. Thus, from practical views of public health, the quarantine and prevention systems of Japan appears apparently insufficient. In terms of well-coordinated preparedness for pandemic in Japan, a variety of risks should be properly recognized and classified. We present ideas to decrease risks of the pandemic, including improvement of the corresponding laws.

Detection of *Leptospira* Antigen by ELISA and Immunochromatographic Assay

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[Introduction] Laboratory test of leptospiral infection is based on either isolation of the pathogen from the specimen or the detection of specific serum antibodies. The pathogen isolation is laborious and expensive and may not be successful. And the antibody detection is not effective during the early period of infection, but once the antibody is produced, its presence continues for a long time. The aim of our study is to develop an assay method for detecting the *Leptospira* antigen in urine for early diagnosis of leptospiral infection. This time, we report the preliminary study on the *Leptospira* antigen detection by the anti *Leptospira* antibody-based ELISA and immunochromatographic assay (ICA).
[Materials and Methods] The whole organism sonicates of *Leptospira* spp. and urine samples collected from the mice that were inoculated whole organism of *L. interrogans* serovar Autumnalis were prepared. ELISA was carried out by conventional method using HRP-labeled antibody and 3, 3', 5, 5' -tetramethylbenzidine as a substrate. ICA device was constructed by manual procedure. ELISA and ICA were used for detecting *Leptospira* antigen, using anti-*L. biflexa* antibody. Real-time PCR amplification of the flagellin gene (*flaB)* was performed to determine the cell number in urine sample.

[Results and Discussion] The minimal concentration of *Leptospira* antigen in PBS which could be detected by ELISA and ICA was 40 ng/mL and 1,000 ng/mL, respectively. 25 of 50 (50%) urine samples could be determined the cell number in a range from 10^3 to 10^7 cells per mL by real-time PCR. However ELISA was positive for 46 of 50 (92%) urine samples, and there observed discrepancy between results of real-time PCR and ELISA. It was suggested that some soluble antigens came out in the urine collected from infected mice, and then ELISA was more sensitive than real-time PCR as a result. ICA was positive for 19 of 50 (38%), and its sensitivity was low. It was indicated that ICA, without washing process, was susceptible to the effect of interference components in urine.

[Conclusion] Both ELISA and ICA are able to detect *Leptospira* antigen in urine. But further improvement is needed to establish a rapid and simple assay method for the testing of leptospiral infection.

[P25]

Treatment of Implants in the Oral Surgery Which Prevents Medical Malpractice

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Recently, treatment of an inn plant in the oral surgery is popularized remarkably, and generally popularized. A Wide is in the adaptation disease worldwide due to the material and the progress of the technique. However, the report of the medical malpractice along with this is on the increase, too. Report a method in consideration of the operating plan that safety was pursued to this.

医療過誤を防ぐ口腔外科におけるインプラント治療

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Ⅰ目的: 近年, 口腔外科におけるインプラント治療は目覚しく普及し, 一般的に普及している. 世界的にも適応症は材料とテクニックの進歩によって広がっている. しかしながら, これに伴う医療過誤の報告も増加している. これに対して, より安全性を追求した手術プランを考慮した方法を報告する.
Ⅱ概要: インプラントの手術において、その埋入位置、方向、角度や深さは重要な因子となる. 我々は, 迅速かつ効果的により高精度なインプラントの埋入を行うために, 誤差補正機能を有する 3D - CT ナビゲーションシステムを用いたオリジナルサージカルガイド(Kis-System)を作製した.
Ⅲ結果: ガイドシステムを使用したインプラント手術は良好であり, 開発後 10 年を経過するが医療過誤に発展するような問題もなく経過している.
Ⅳ考察と結論:インプラント関連メーカーから様々なサージカルガイドが販売されている. 中には大きな誤差によって手術中にトラブルが生じる報告も耳にする. 我々の CT データの誤差補正機能を用いたオリジナルサージカルガイド(Kis-System)はインプラント手術を安全に行えた.

Measures to Prevent Medical Malpractice Related to Radiopharmaceuticals

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Radiopharmaceuticals are defined as “radiation emitting drugs” in the ministerial ordinance Regulations for Manufacturing and Handling of Radiopharmaceuticals of the Ministry of Welfare (current Ministry of Health, Labour and Welfare). They are offered in radiation shielding containers to prevent exposure to radiation. Differently from ordinary pharmaceuticals, it is difficult to directly read the labels on the vials and syringes. Therefore, we offer the following measures to prevent mix-ups while preventing exposure to radiation in hospital settings.

The representative forms of supply of radiopharmaceuticals are vials, syringes, and freeze-dried products that are prepared in hospital.

Vial products are becoming less common in order to prevent exposure to radiation during the transfer to disposal syringes in the hospital. When transferring radiopharmaceuticals into disposal syringes, we use peel-off labels taken from the product's lead container and attach the labels to the surface of dedicated tungsten containers to accommodate and shield the disposal syringes containing the drug. In addition, we offer dedicated product name stickers for the disposal syringe rods.

Syringe products are most commonly used as pre-filled syringes. Compared to vial products, syringe products are effective in preventing exposure to radiation because the preparation does not involve the transfer of drug solutions. The drugs can be easily administered simply by attaching a syringe rod ans a needle to the tip of the syringe. Products of this type are often taken out of the lead container beforehand for well-timed administration. Therefore, in order to prevent mix-ups of the syringes (with tungsten shielding) after taken out of the containers, the product name and radiant quantity are shown on the plastic parts that fix the tungsten shield and the syringe. We also provide dedicated product name stickers to attach to the syringe rods.

Finally, freeze-dried products for in-hospital preparation are prepared (radiolabeling) in hospital settings using separately supplied ^{99}Mo-^{99}mTc generators. The preparation is done basically by mixing. If the products are heated or mixed in a fixed order, we provide dedicated heaters or marketing equipment to ensure correct preparation. Also, we provide dedicated product name stickers to be attached to the rod of the disposal syringes to which prepared drug solution is transferred.

[P27]

Statistical Consideration of Incident Report Case in Dental Medic

Nagayasu MATSUMOTO

Matsumoto Dental Clinic, Tokyo, Japan

I considered dangerous frequent occurrence time and other things in dental medical treatment from the result of the analysis based on incident reports of about 200 people

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歯科医療従事者におけるインシデントレポート事例の統計的考察

松元 長泰

まつもと歯科クリニック，東京，日本

約 200 名のインシデントレポートをもとに分析した結果を踏まえて、歯科医療において危険な多発時間などを考察した。

It Fries Medical Care Cooperation and A Second Opinion About The Oral And Maxillofacial Surgery

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In the oral and maxillofacial surgery treatment importance of the medical care cooperation and the second opinion is pointed out from the difference of the treatment with the primary care organization (the dental office)

大本組

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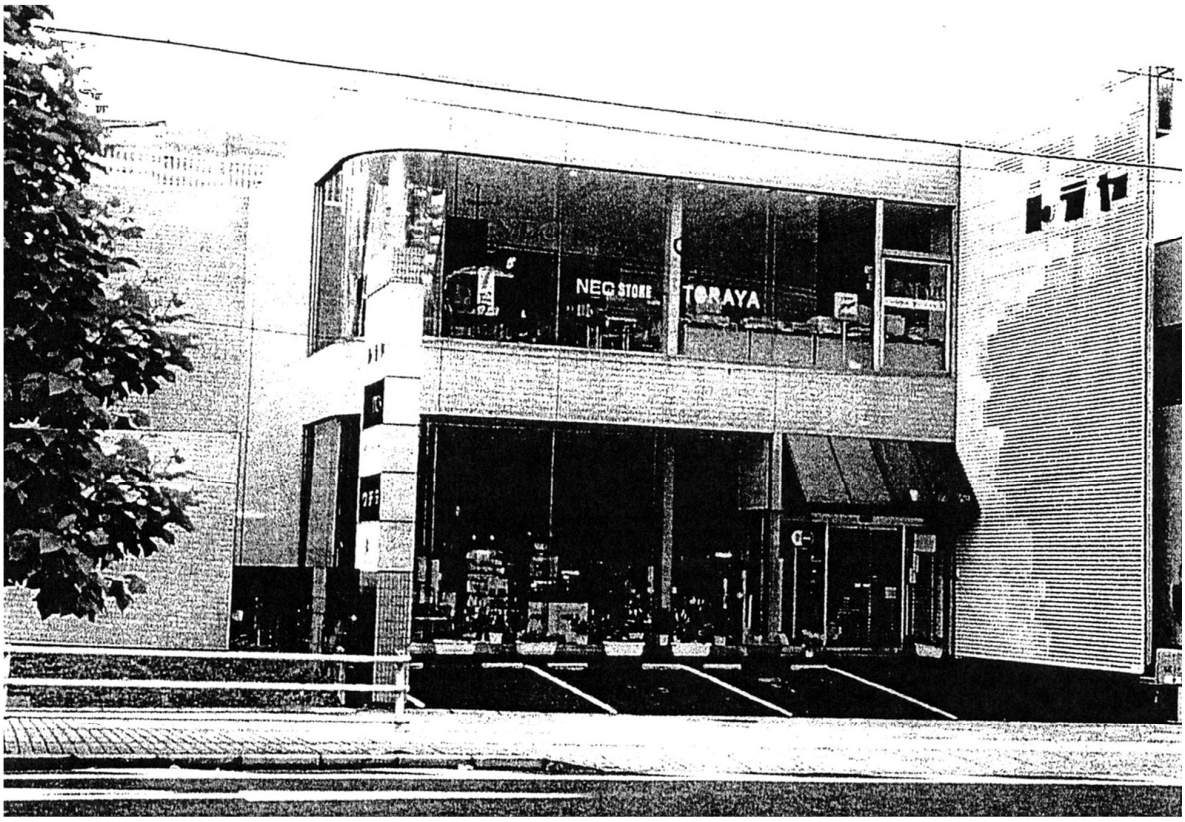

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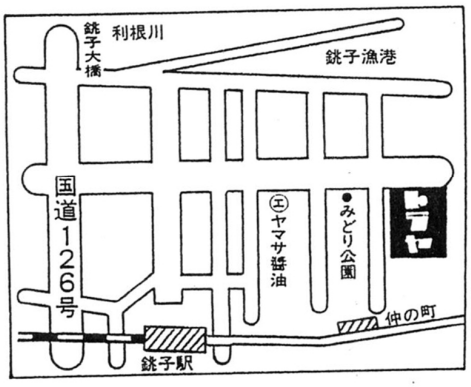

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Proceedings

Risk management for radiation

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Abstract

Radiation gives us great useful tools for the cancer treatments by radiotherapy and supporting our energy consumption by the massive energy release from nuclear reaction in power plants. On the other hands, radiation is known as double edged swords. Biologically, ionizing radiation releases local energy deposition and produces ionizing water and highly reactive radicals in our body. It leads to break DNA strands and it leads to cell death, mutation, and carcinogenesis. To prevent the worst scenarios, we have to know well about the characters of radiation and its history. We will discuss here about radiation accidents in Japan and world and radiological decontamination. Then, we will explain the background level radiation exposure and a possible increased cancer cases in Japan by a high usage of medical diagnostic x-ray. Finally radiological casualties and classic and new biomarkers for radiation dosimeters will be discussed.

Basic Radiation Biology

Radiobiology is the study of the action of ionizing radiations on living things. The absorption of energy from radiation in biologic materials may lead to excitation or to ionization locally. Like X-ray, radio waves, radar, radiant heat, and visible light are forms of electromagnetic radiation. They have same velocity, $c=3x10^9$m/s, but they have different wavelengths and frequencies. X-ray and gamma-ray produced extranuclearly or intranuclearly have short frequency and can ionize molecules directly. And neutron, alpha particles, beta-ray, heavy charged particles are also known as particle ionizing radiation. The first step in their absorption is the production of fast recoil electrons. After that, the atoms of target molecules may be ionized directly or indirectly by high reactive free radicals. Since ionizing radiation locally produces ionized free radicals, it easily breaks DNA strands. It is the unique character of ionizing radiation. Broken DNA can be repaired, but un-repaired or mis-repaired broken DNA caused cell death, mutation, and carcinogenesis (1).

Key words: radiation, decontamination, background radiation, acute high dose radiation

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Table 1; Scheme of radiation events.

10^{-15} seconds	Radiation Event
10^{-3} ~10^{-5} seconds	Radical Formation
Minutes Hours	DNA Breaks and Repair
Days	Cell Loss
Weeks Months	Death
Years	Carcinogenesis

Different of doses of radiation will give different modes of death to man. 10Gy of radiation causes gastrointestinal death within 9 days. 3-8 Gy of exposure leads to hematopoietic death about 3 weeks or more. The $LD_{50/60}$ (the dose for half of human death within 60days) for human is 3 to 4 Gy for young adults without medical intervention. The duration time between exposure and death are associated with DNA repair and cell division. The loss of fast growing gastrointestinal cells results in the loss of body fluid from intestine. Radiation damages and kills stem cells and it prevents organs from producing renewal mature functioning cells. In fact, a bone-marrow transplant is effective in small window between 8-10 Gy radiation exposures (1).

Table 2; Acute radiation effects

0.25-1Gy	Subclinical range, minor blood chemistry changes
1-2Gy	White blood cell loss
>2.5Gy	Acute radiation syndrome
>3.5Gy	Hematopoetic syndrome
4.5Gy	LD50/60
>6Gy	Gastrointestinal syndrome
10Gy	LD100/60
>10Gy	Central nervous system syndrome

Not only cell killing, radiation has effect for mutagenesis and carcinogenesis. Radiation carcinogenesis is a stochastic effect, the probability of an effect increases with dose, with no dose threshold. Cataracts are an example of a deterministic effect of radiation. After atomic bombing in Hiroshima and Nagasaki, about 120,000 persons have been followed cancer incidence including about 50,000 received doses in excess of 5mSv. By 1990, there had been 6,000 deaths from cancer of which about 400 were considered to be an excess mortality caused by radiation. The latency of tumorgenesis is dependent on tumors. Leukemia has the shorted latent period (7-12 years), and solid tumors showed a long latency than the leukemia (10-50 years) from the survivors of Hiroshima and Nagasaki.

Radiation Accidents

So many radiation accidents have been reported not only Japan and the world. Some of them extremely damaged and contaminated to human and nature. Others did not as expected. Accidents associated radiation and radioactive materials can be separated into two category open type and closed type. The open type radiation accident is actual release of radionucleotide into nature. In Chernobyl power plant accidents, huge amounts of radionuclides were released to open space and spread onto Europe. The amounts of radioisotope is estimated about 10t including about $1500x10^{15}$Bq of ^{131}I and $80x10^{15}$Bq of ^{137}Cs. Although still 10km radius from power plant is limited to access, there is a real wild life protection area around Chernobyl and many wild lives increases their number. A critical accident occurred in 1999 at a uranium conversion facility in Tokaimura, Ibaraki, Japan. The criticality was unexpectedly initiated when a worker on the platform was leaning over a precipitation tank, pouring a solution of uranyl nitrate enriched in ^{235}U from a stainless steel bucket in the tank through a funnel. Of course, this critical accidents release many radionuclides from the facility like Chernobyl. Only those workers were exposed to significant amount of radiation. Three workers developed acute radiation syndrome and they were transferred to the National Mito Hospital once. And then the patients were transferred to National Institute of Radiological Sciences in Chiba 5 hours after exposure by helicopter to further evaluation and treatment. Based on several methods of dose estimation, three workers were exposed to 16-20 Gy equivalent, 6-10 Gy equivalent, and 1 to 4.5 Gy equivalent.

Table3; Estimated doses in Gray for three workers in Tokai

	Worker A	Worker B	Worker C
Neutron	5.5	2.9	0.81
Gamma-ray	8.5	4.5	1.3

Worker A and B were transferred to the University of Tokyo Hospital for intensive higher care. Worker A died of multiple organ failure on Day 82. And Worker B succumbed to refractory respiration failure on Day 211 (2).

Compared with direct exposure from radiation accidents as mentioned above, indirect exposure from radiation fall out or radiological contamination can be reduced the amount of exposure by radiological decontamination. The primary differences between the mechanics of radiological decontamination and chemical decontamination are the methods of monitoring and timing. Chemical decontamination is an emergency.

Decontamination of casualties is an enormous task. The process requires dedication of both large numbers of personnel and large amount of time with appropriate training and planning. Removal of outer clothing and washing exposed skin and hair removes 95% of contamination.

Radiation Exposure in Medicine

Everyone is exposed to radiation from unperturbed natural sources (cosmic rays, terrestrial radiation, and natural compounds of our body), enhanced natural sources (airplane travel, radon exposure), and sources from human activity such as nuclear medicine. Intensity of cosmic rays arriving

at the earth's surface varies with both latitude and altitude above sea level. Average equivalent dose in the USA is about 0.26mSv/year, but in Denver, Colorado (a mile high city), it is 0.5mSv/year. The biggest source of natural background radiation is radon gas in the USA, which seeps into the basement of houses from rocks underground.

There are several inhabited areas of the world where background radiation is considerably high because of radioactivity in rocks or soil or building materials. In Brazil, about 30,000 people live in coastal areas are exposed to dose rate of 5mSv/yr (20 times higher). The highest background is in Kerala, India, where more than 100,000 people receive an annual dose of about 13mSv (50 times higher). After many researches have been made of these human populations, so far no excess incidence of caner or hereditary abnormalities have been reported by radiation.

In USA, annul effective dose was about 3.6mSv. 55% comes from radon gas. 18% is man made nuclear medicine. Internal was 11%, terrestrial was 8%, and cosmic was 8% in 1987. In Japan, annual effective dose is about 3.75mSv. About 60% comes from nuclear medicine, and contribution of radon is 10%. Nuclear medicine is not natural source of background radiation. One paper published to famous medial journal Lancet in 2004 showed that the usage of medical radiation diagnosis is three times higher in Japan than other western countries and it contributes cancer incidence in Japan. They estimated 3.2% of cancer patients in Japan were caused by x-ray diagnosis, however, it is still unclear and controversy (3).

Table 4; Annual natural background radiation exposures in USA and Japan.

	USA	Japan
Radon	2.0mSv	0.4 mSv
Nuclear Medicine, Diagnose	0.53 mSv	2.25 mSv
Others	1.07 mSv	1.1 mSv
Total	3.6 mSv	3.75 mSv

Table 5: Medical diagnostics and radiation exposure.

Medical Diagnostics	**mSv**
Chest x-ray	0.1
Dental oral exam	1.6
Mammogram	2.5
Lumbosacral spine	3.2
PET	3.7
Bone (Tc-99m)	4.4
Cardiac (Tc-99m)	7.5
Cranial CT (MSAD)	50
Barium contract G-I fluoroscopy (2min)	85
Spiral CT	30-100

Risks in Nuclear Affairs

Acute high dose radiation occurs in three principal situations. A nuclear weapon will result in extremely high dose rates from initial nuclear reaction and the fallout (Hiroshima and Nagasaki). Highly enriched nuclear material is allowed to form a critical mass. Then, nuclear reaction releases the large amount of neutrons and gamma-ray (Chernobyl and Tokai). A radiation dispersal device made form from highly radioactive materials (Dirty bomb).

Nuclear weapons cause not only acute radiation syndrome but also the blast and thermal biological effects. Blast causalities will require evaluation for acute trauma in accordance with advanced trauma life-support standard therapies. Thermal burns will be the most common injuries, subsequent to both the thermal pulse and the fires it ignites. We should not forget the anxiety by radiation stress. The severity of the psychological effects of a dirty bomb will depend on the nature of the material itself and the method of deployment. Although a point source such nuclear weapons targets physical damages and injuries, dirty bombs will produce more detrimental psychological damage to civilians.

Each case, measurement of actual doses for radiation exposure is important to understand the radiological damages and to help the medical and psychological cares. The classic dosimetry assays are based on several biomarkers. Onset of vomiting with in 12 hours indicates the radiation exposure from 2Gy to 20Gy. Depletion of peripheral blood lymphocytes within 10days suggests the doses from 2 to 8 Gy. Cytogenetics techniques, lymphocyte-metaphase spread dicentric and premature chromosome condensation assays can detect doses from 0.2 Gy to 20Gy. Prodromal signs and symptoms and hematological analysis can be quick but not accurate to determine the doses. Although these cytogenetic assays are so sensitive to determine the actual doses, sample blood have to be collected 24 hours after radiation exposure and need time and professional handling for analysis.

Several practical and easy assays are developing for new radiation exposure biomarkers for the high throughput analysis. Recent studies for γ H2AX foci can measure each DNA double strand breaks and estimate actual exposure and handling is easer than conventional cytogenetics. In this technique, isolated lymphocytes can be fixed and stained with antibody against γ H2AX. Actual measurements can be done with microscopic analysis or automated flow cytometer.

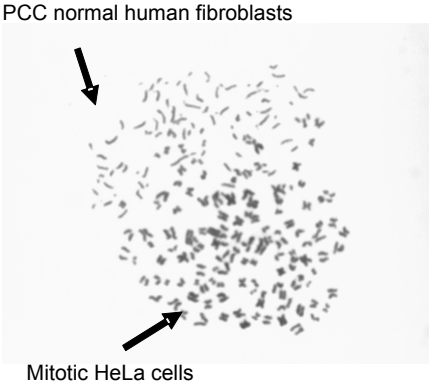

Figure 1; Premature Chromosome Condensation

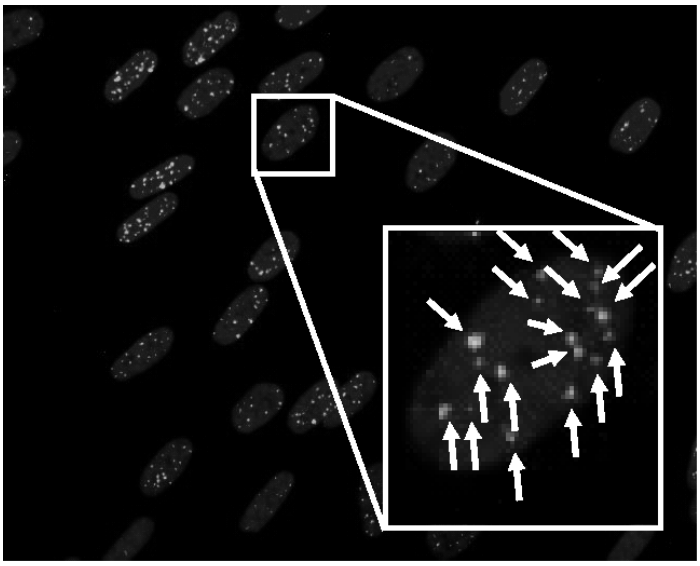

Figure2; γH2AX foci after 1Gy of irradiation.

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An Application of Computer Simulations for People Evacuation Management in a Complex Setting

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Abstract

Natural and man-made hazard does not necessarily result in disaster in an area. It hinges upon: (1) the risk and the strength of the hazard; (2) the population density; (3) the integrity of structures; and (4) the efficiency of hazard management implemented in the areas. From this perspective, Asia Pacific Region is one of the highly risky regions in view of the tremendously growth in the urbanization process. The super high density of population and the super high rise structures in this region pose an immense risk of disastrous consequence just even triggered by a trivial natural or man-made hazard. Recognizing this, a variety of organizations at all levels of government and in the public and private sectors have increased consideration of emergency management.

We understand that absolute prevention of disasters and restricting their spread may be impossible. Evacuation of people from the hazardous region(s) is *per se* a way to reduce the ill effects of disasters and evacuation planning is *prima facie* one of the critical components in emergency management. This article briefly outlines the framework of emergency management and discusses the use of computer simulations for evaluating different people's evacuation strategies for an urban area.

Introduction

Rapid urbanization and concentration of people and facilities in the metropolitan areas cause huge demand of floor space in many cities. Super high-rise and complex buildings and estates are now constructed everywhere, in particular in many metropolitan areas in the Far East. Of all the issues relating to such complex society, safety is one of the major concerns of many people as well as the government. In the circumstance, societies have attempted to establish systems to 'manage' the natural and technological hazards and their impacts on life and property.

It is well-known that absolute elimination of hazard appears impossible. Nevertheless, we should endeavor to minimize the possibility of happening of hazardous events. If unfortunately such an event happens, the system should be able to limit its effect such as in case of a fire incident, controlling the spread of the fire and smoke. Failure to control the spread of the hazards, people in the area should be evacuated immediately, and emergency personnel should be able to gain access to the site to assist the evacuation and perform rescue.

Keywords: Emergency Management, Evacuation, Simulation

This article begins by providing a brief outline of emergency management. A review of the importance of evacuation is then discussed. Particular introduction will be given to the use of a tool – computer simulation for analyzing the pattern of people's movement efficiency of the crowd flow process in evacuation.

Emergency Planning

Natural and man-made hazard does not necessarily result in disaster in an area. It hinges upon: (1) the risk and the strength of the hazard; (2) the population density; (3) the integrity of structures; and (4) the efficiency of hazard management implemented in the areas. From this perspective, the super high density of population and the super high rise structures in the Far East region pose an immense risk of disastrous consequence just even triggered by a trivial natural or man-made hazard. Recognizing this, a variety of organizations at all levels of government and in the public and private sectors have increased consideration of emergency planning and management. Cigler (1987) has described that emergency planning is the process of 'developing and implementing policies and programmes to avoid and cope with the risks to people and property from natural and man-made hazards'.

Managing emergency incidents effectively can be discussed and encapsulated in an emergency event continuum. Table 1 summarises the four stages that an emergency event (a disaster) may pass through.

Table 1: Outline stages in the emergency continuum

Emergency events continuum		**What involved?**	**What to do?**
Pre-event	Mitigation	• Identify hazard and assess the effect • Develop the approach to reduce vulnerability • Verify the scope of risks	• Plan the land use and control mechanism • Formulate building and fire codes • Initial studies relating to emergency management
	Preparedness	• Analyse the consequence of an event • Establish appropriate reaction mechanism, etc. • Identify inter-agencies roles • Determine detection mechanism, etc.	• Establish reaction strategies (including evacuation strategies) and detection system • Train key emergency personnel • Formulate inter-agency cooperation
Post-event	Response	• Establish warning system • Formulate communication structures • Designate emergency control point • Formulate the ways to control/ extinguish the hazardous event	• Initiate warning system • Notify emergency service • Establish control point • Perform control and rescue process • Maintain the functions, as far as practicable, of the community • Support officials empowered for action
	Recovery	• Establish restore programmes • Plan rehabilitation (including buildings, environment, etc) • Mobilise and review the communities resources	• Restore to normality as quickly as possible • Revitalise the destruction

In crisis situations, such as tsunami, nuclear, chemical, terrorist attack emergencies, appropriate decision making holds the core to alleviating the intensity of the ruinous impacts of the disaster. Often speed and accuracy are success determining factors for the decision making. It is therefore, crucial that planning and preparation processes for potential emergencies are carried out in advance. The mitigation and preparedness planning at the pre-event stage are significant. Figure 1 outlines a brief approach.

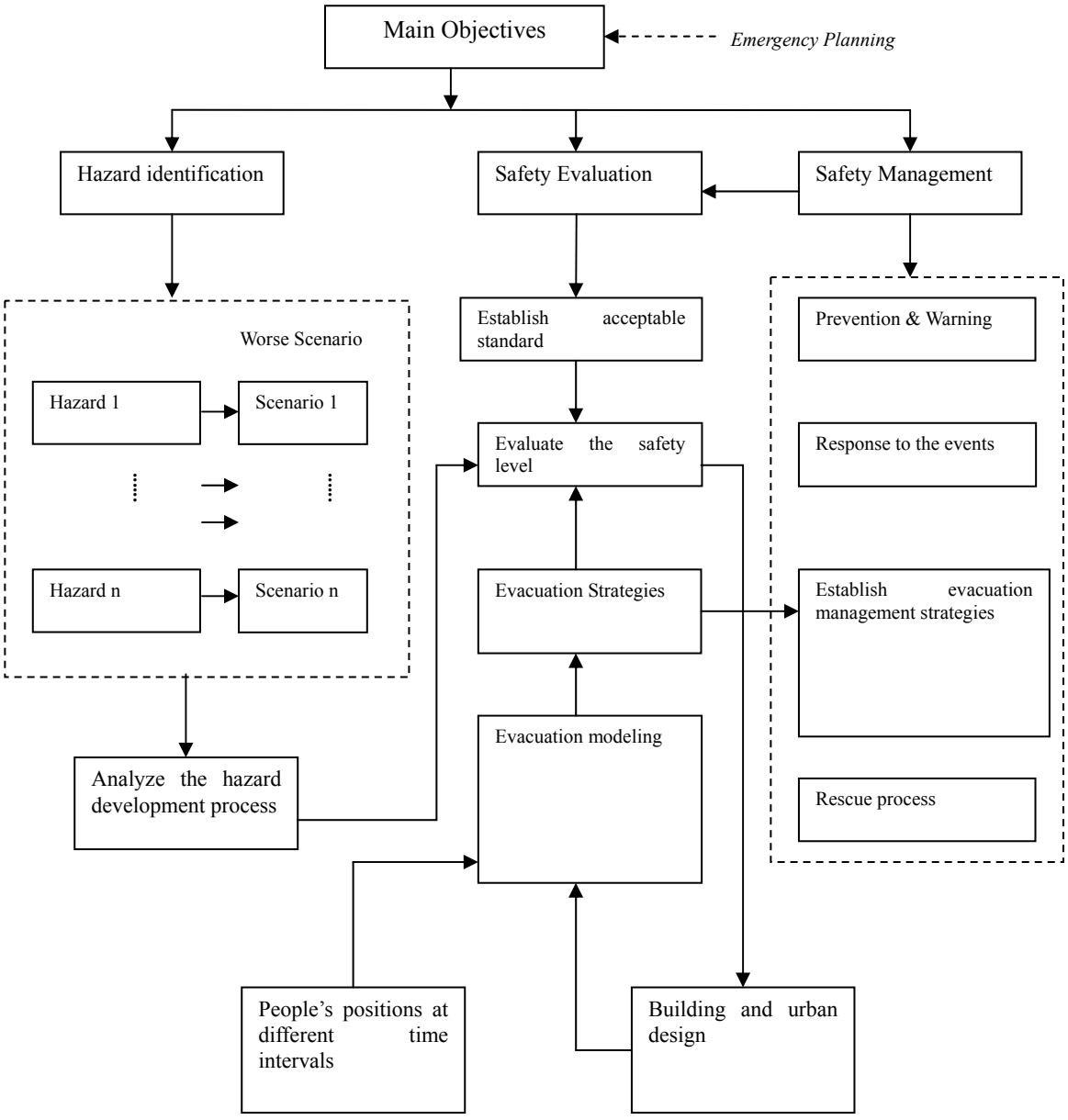

Figure 1: An outline of emergency planning

Evacuation

Evacuation of people from the hazardous region(s) is *per se* a way to reduce the ill effects of disasters and evacuation planning is *prima facie* a critical component in emergency management.

Moving ahead of the danger is the better practice. Some recent disasters caused by the 'attack' of hurricanes have demonstrated that timely evacuation should be a means of mitigation to the ill-effect. It is recognized that two factors have a major impact on evacuation strategies: the timing of evacuation relative to disaster impact, and the amount of time in which evacuees are required to leave the evacuation planning zone. The former component, which is not discussed in this article, requires the development of an effective hazard detection and warning system. Even if an effective detection system has been established, it is useless if the threatened areas cannot be effectively evacuated in the determined time. Thus, the latter issue that involves evacuation planning arouses the interest of many management scientists.

Evacuation planning may be categorized into simulation models approach and analytical models approach. Figure 2 briefly describes the major models adopted for evacuation planning.

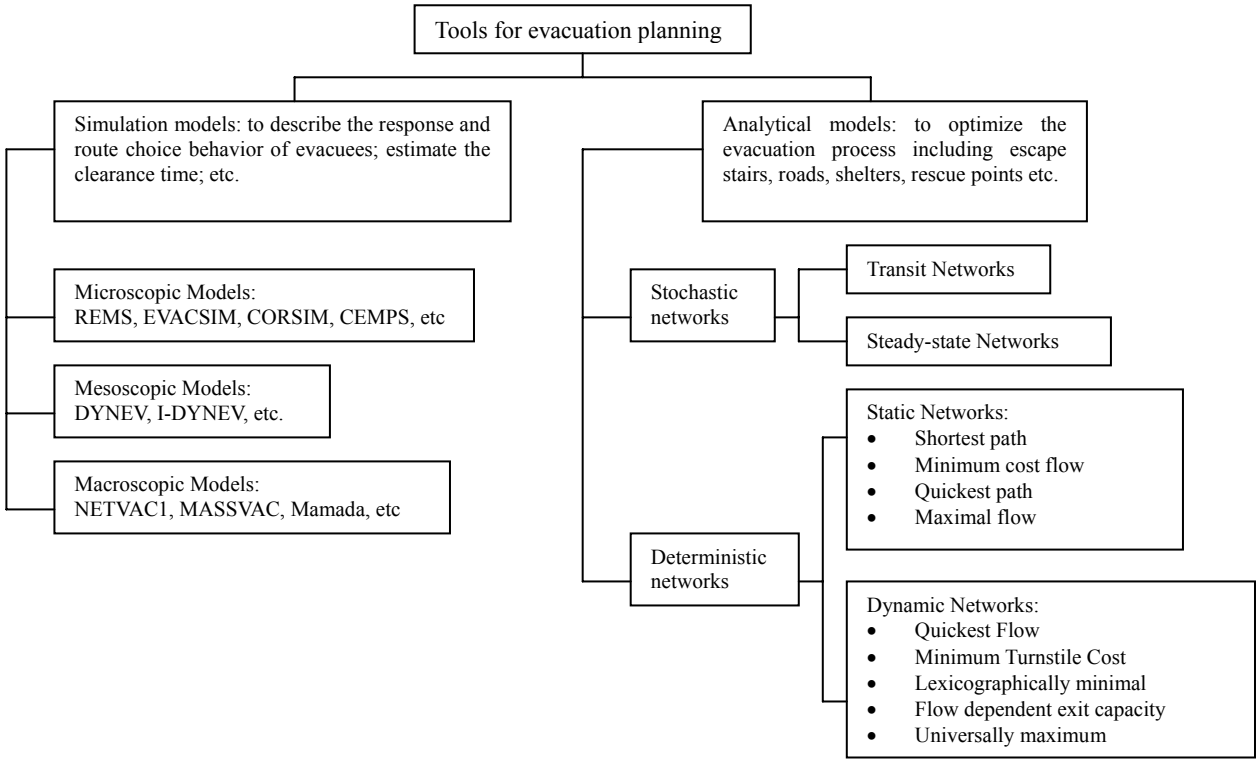

Fig. 2 Major Models for Evacuation Planning

Applications

An important aspect of ensuring safe evacuation in a building or a district is the availability of a sufficient number of adequately sized and safe escape routes for the people to leave the hazardous zone within an appropriate period of time. Normally the time being considered is the time before the zone becomes hazardous to the people. In general, building and fire codes and other planning guidelines provide guidance on the design of egress routes in terms of size and capacity. However, individual components conform to the guidelines, but as a collected whole, they may lack the coordination necessary for the inducement of smooth egress during evacuation, especially in a

complex setting with numerous people and traffic volume.

Apart from the space planning initiated by the building and urban designers, emergency management personnel may also need to understand the possible crowd and traffic flow pattern so that they can plan to control the flow pattern in order to ensure a smooth evacuation.

In order to facilitate the understanding of dynamic crowd flow pattern, researchers in recent years have developed many evacuation models. With the advancement of computer technology, some of the models are so sophisticated that each individual's movement in the concerned area can be traced and their movement path can be visualized, such as the EXODUS (Galea, 1994), SIMULEX (Thompson *et al*, 1995), EGRESS (Ketchell et al, 1993), SGEM (Lo *et al*, 2004), PEDGO (Klupfel, 2004), etc. The simulation process is adopted to build up some kind of artificial model or simplified representation which resembles the real world system.

Evacuation under emergency situation for a complex setting is too complex to be represented by simple flow equations and can hardly be initiated for experiment (fire drill exercise cannot be regarded as a real experiment). Therefore, the simulation model may be an alternative approach to anticipate in advance how the system will react should emergency situation arises. During the implementation stages, a simulation model can be used to experiment with new designs or policies, so as to prepare for what may happen. Valuable insight may be obtained by changing simulation inputs and observing the resulting output.

The following simulation outputs (Figure 3 - 5) are extracted from the model SGEM (Lo, *et al*, 2000, 2004, 2006; Zhi *et al*, 2003) developed by the author at the Department of Building and Construction, City University of Hong Kong. The model is basically a fine grid model which can adopt the spatial information from CAD based architectural plans to perform simulation to generate the crowd movement pattern. The model can provide reasonable results under large population situations. However, in case where only few people located in the area, the people's behavioral reaction will have a significant effect on the evacuation process.

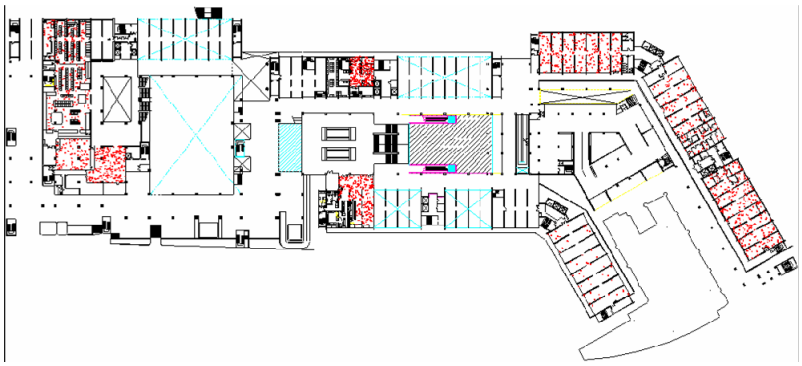

Figure 3: Simulation output of a large shopping mall

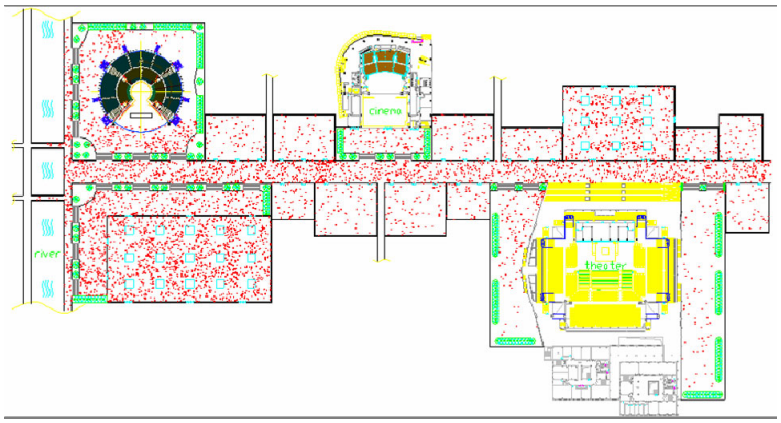

Figure 4: Simulation output of a pedestrian walkway

Figure 5(a): Simulation output of crowd flow in a mass transit station

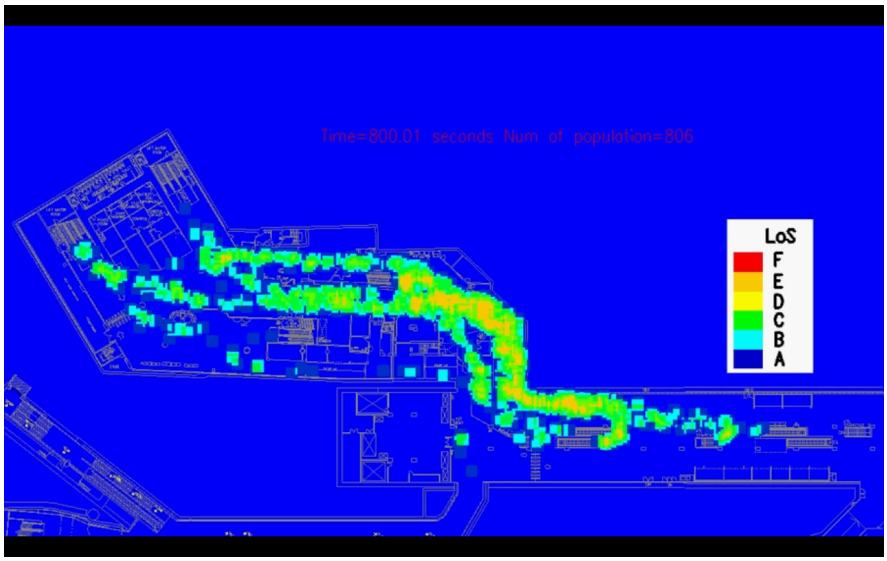

Figure 5(b): Simulation output of the crowd density in a mass transit station

The results given by the simulation outputs (Figure 4-5 refers) can be adopted to analyze the crowd flow pattern. Critical points may be obtained by tracking the dynamic crowd density. Fruin (1971) has pointed out that crowd may crush and endanger the people in the crowd if the density is about or over 5.6 person per square metre. The model can provide the crowd density information at various point of time. If it is greater than the acceptable value, which should be lower than that indicated by Fruin, for some time, the setting adjacent to the critical points should be altered. Control the amount of people flowing to the critical points may also be necessary.

Concluding Remarks

The article presents a brief outline of emergency planning and the use of computer simulation model for evacuation analysis. The simulation output can offer valuable information for evaluating the crowd flow pattern, which can serve as a reference for determining the effective layout at design stage and formulating the crowd management strategies.

Nevertheless, it should be pointed out that social science of emergency egress is also important. People's behavior is partly the result of what threatens them. Evacuations are a function of a system of interactions among characteristics of the hazards, characteristics of the social and cultural organization of an area in case of evacuation for a large district, characteristics of the escape routes and if for a large district, the road and transportation system, and characteristics of the warning and emergency management system.

Different disasters should have different detection systems and different warning modalities. The emergency management system of an area is also not uniform for all hazards, but will be more or less prepared to respond if not mitigate the effects of the various hazards causing the disaster as well as the effects of the disasters. Importantly, often hazards or disasters may block or even destroy the escape routes such as staircase, or road and transportation structures, which must be factored in as the simulation goes forward.

The evacuation simulation models cannot provide the insights for all the components in an emergency management system. An effective emergency management system should be established by considering all aspects including mitigation, preparedness, response and recovery.

Acknowledgments

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医療過誤防止と医薬品品質確保のための製剤設計・製造設計

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1．はじめに

医薬品等における「誤認」「誤薬」は，医療機関の規模に関係なく発生する可能性があるため，各医療機関は職員の啓発・教育のみならず，それぞれ独自の事故防止システムを積極的に導入している．一方，我々医薬品メーカー側においても，医薬品の「誤認」「誤薬」を可能な限り回避できるような製剤設計に努めるとともに，一方では，健康被害の原因ともなりうる製造工程における医薬品の汚染を防止するために，製造システムの設計とさらなる改良にたゆまぬ努力を傾注している．今回は，医薬品メーカーにおけるこれらの製剤設計，製造設計の事例を簡単に紹介する．

一般的に，製剤からの薬物の溶出性とか含量均一性など，医薬品が本来その機能として具備すべき品質に対しては，GMPにもとづいた厳重な管理システムが構築されており，これらの機能性に問題のある製品が出荷されることは考えにくい状況にある．しかしながら，医薬品の汚染とりわけ異物混入に関しては，数百万錠に1錠の発生であっても問題化することがあり，それはもはや統計的品質管理のおよぶ領域ではなくなっている．このため異物に関してはより厳格な対応が必要となる．今回は医療過誤とあわせて，この部分にも焦点をあててみたい．

2．錠剤の識別性の向上

(1)錠剤の大きさについて

日本国内では径が7～8mmで白色の円形錠が好まれる傾向にあり，欧米の大型で毒々しい色に着色された変形錠が多く市販されている状況とはかなり異なった状況にある．このことは，多分に日本の国民性からくるものと思われるが，錠剤の識別性を低下させる原因となっていることは明らかである．

また，直径が 5mm から 6mm 程度の非常に小型の錠剤も市販されているが，これは昭和 50 年ころに主として開発された製剤であり，その主たる目的は患者の服薬性を向上することにあった．しかしながら高齢化社会を迎えた現在においては，服薬性はもちろんであるが，錠剤のハンドリングのしやすさや識別性・調剤鑑査など，多角的な観点から錠剤の形状を議論することが重要となっている．表1は錠剤のつまみやすさの順位と，錠剤の直径との関係を調査した杉原らの研究結果[1)]であるが，素錠では7～8mm辺り，糖衣錠では8～9mm辺りにつまみやすさの評価の分かれ目があることが示されている．一方，図1に示したように服用のしやすさに関しては，素錠・糖衣錠ともに8mm前後で評価が高く，必ずしも小型錠が飲みやすいとは限らない結果となっている．しかも，小型の錠剤では刻印や印刷も相対的に小さくなるため，識別性の点からも問題の生ずる場合がある．このような背景から，最近では直径が 7～8mm の通常サイズの円形状とするのが一般的となっているようである．

このように，白色で円形の錠剤が多数を占めるわが国においては，錠剤間の識別性が重要な問題となる．すなわち，錠剤が包装から取り出された状態になったあとでも，製品名，主薬含有量，メーカーなどが容易に判別できることは，調剤ミス防止や調剤検査・服薬ミス防止の観点から重要な要件であるといえる．

この識別性を錠剤に付与する方法として，素錠の場合には刻印を施すことが一般的である．刻印される情報としては製品名を表わすコード番号やメーカーの社章，主薬含有量を表わす数字などがある．これらの刻印は錠剤の識別を目的とするものであるから，明瞭に判読できることが必須である．この刻印の明瞭さを確保するためには，刻印の設計，錠剤の処方，製造条件などを細かく検討することが必要となるが，このことを論じた文献はほとんどない．そこで，本講演では若干の実例をまじえながら，刻印錠の設計と圧縮成形についてごく簡単に解説を試みてみたい．

（2）字体の大きな刻印錠

刻印の字体を太く大きくし，刻印の判読性を向上させることは，識別性向上に有用である．図2はその一例であるが，字体を大きくすれば刻印の線はそれに比例して太く深いものとするのが通常である．しかしながら，このような刻印を下杵に配置して打錠を行うと，刻印の欠損が高い頻度で認められることがある．この原因は，錠剤と下杵の刻印が嵌合した状態で錠剤に横方向から力を作用させて打錠機から放出させるとき，その衝撃力が刻印部分に集中するためと説明できる．この場合の対策としては，刻印の深さや角度・Rの再検討により，刻印嵌合部からの錠剤の抜けやすさを改善することが必要となるが，一方，上下の杵の運動軌跡を考慮すると，太く深い刻印を上杵に配置することは，最も簡単で有効な対策であることが推察できる．すなわち，圧縮成形後の上杵は錠剤から垂直方向へ離れてゆくため，錠剤は刻印嵌合部分から無理なく開放され，欠損力が作用することはないと考えられる．実際，上杵に同様の大きな字体の刻印を配した場合，欠損のない鮮明な打刻が可能となった．このように大きくて明瞭な刻印錠を安定して製造するためには，刻印の各設計寸法もさることながら，その刻印を上・下杵のいずれに配するかはきわめて重要な問題となることが多い．

（3）刻印の摩損対策

錠剤が平面錠の場合は問題となることは比較的少ないが，R面である場合は刻印の摩損による識別性の低下に注意が必要である．上下杵で打錠用粉粒体を高速圧縮（動的圧縮）する場合，粉粒体内部での応力分布は液体と違って均一ではなく，上下杵間距離の小さい部分に応力が集中する．したがってR面の錠剤においては，錠剤の周辺部分から中央部に向かって，圧縮力が低下する分布となる．もしもR面の錠剤中央部分に刻印が施されていると，刻印部分は周辺部分よりも弱い圧縮力で成形されることになり，刻印部分の脆性が周辺部分よりも増大する．しかも錠剤の除粉，コーティング，包装などの各操作，および輸送中などに生じる摩擦力や衝撃は錠剤R面中央部に集中する場合が多く，これら2つが相乗して刻印を磨耗させ，不鮮明にする原因となる．したがってR面の錠剤の場合は，2段R面とすることなどにより，刻印面のRをできるだけ大きくして平面に近づけることや，錠剤のR面中央部分を避けて刻印を施すなどの配慮が必要である．

(4)異形錠の設計

市販されている錠剤の多くは円形であるが，一方では円形以外に楕円や四角，花形，蝶型などの異形の錠剤も市販されており，識別性の向上に寄与している．

図3に示したのは，市販されている蝶型錠の形状および寸法であるが，その特異な形状は通常の円形状と比較して非常に注意を引く．この形状について前出の杉原らは，60 人のパネラーに対してイメージ調査を実施している [2]．その結果を引用して表2～表4に示したが，若年者では好意的な結果となっているが，全体としての好意的回答は約半分である．好ましい理由には「印象に残る」や「従来にない形」などが多く，このような形状の識別性が高く，誤認・誤薬の防止，調剤鑑査や服薬指導などに有用であることが明らかとなった．

しかし一方，好ましくない理由としては「蝶が嫌い」というものが認められた [2]．また高齢者になると「服用しにくい」という回答が増加する傾向にあり，対象とする患者の年齢層を意識した形状の検討も必要であることが示唆されている．ところで，この蝶型の形状の主目的は識別性以外に分割性の向上という面もある [46]．分割性の正確さも投薬上非常に重要である．この蝶型は従来の円形の割線錠では正確な分割が困難であること，および分割精度における個人差が大きいことなどに着目し [3～7]，割線部分にくびれをつけてより正確な分割ができるよう検討された形状である．表5は，円形で割線のある直径 7mm の通常の錠剤と，ここで述べている蝶型の錠剤を，年齢ごとに男女それぞれ 1 名ずつのパネラーに分割してもらった結果を示したものであるが，明らかに蝶型の形状の分割精度が優れた結果となっている．

分割のしやすさに関する意識調査でも蝶型錠は 100%分割しやすいという結果となっている．また，分割後の錠剤に対して15局質量偏差試験法を適用して判定値を算出した場合，蝶型錠では余裕を持って適合する結果となっているが円形錠では若干不安の残る結果となっている．

(5)刻印とスティッキング対策

刻印を不明瞭とする要因の中で重要なものがスティッキングである．スティッキングとは，錠剤と杵表面との接触面における付着力が大きくなって，錠剤の表面部分が一部はがれて杵面に付着する現象をいう．スティッキングのレベルは，錠剤の光沢がわずかに失われる程度の軽微なものから，錠剤全面が剥離するような重度のものまでさまざまである．このスティッキングが発生するのは，ステアリン酸マグネシウムなどの滑沢剤不足や主薬成分の物理化学的性質，あるいは造粒条件をはじめとする製造条件の不適切に起因する場合が大部分であって，それらの改善が根本的な解決手段となる．しかしながら，スティッキングの発生状態を注意深く観察すると，特定の刻印の特定の位置で発生し始めることが多い．これは，刻印自体にもスティッキングを誘発する要因が存在することを示しているが，具体的には，図4に斜線で示すようなアルファベットのAやB，そして数字の4や8などの中州状態の部分でスティッキングが発生しやすい．この部分は周囲から孤立した状態となっているため，他の部分よりも剥離しやすいことは容易に想像できる．したがって刻印を設計する場合には，数字やアルファットの字体に注意し，できるだけ中州状の部分の面積を広くする工夫などが必要である．

3. 製造工程における医薬品の汚染防止対策

日本においては異物混入についての市場の関心が高く，また製薬企業自身も医薬品は清浄であるべきとの立場に立って，異物混入対策に真剣に取り組んでいるところが多い．

一般に，医薬品製剤への異物混入防止対策は次の3つの原則に要約される．

- 異物を製造工程に持ち込まない
- 製造過程で異物を混入させない
- それでも製品中に混入してしまった異物は除去する

これらについて順番に解説する．

(1)原料，中間品中の異物混入防止対策

一般に固形製剤の場合，液剤とは違って，一旦混入した異物を検知，除去することは相当に困難であるし，手間がかかる．従って，原料メーカーにおける異物混入防止対策が重要なポイントとなる．そのために原料メーカーと購入契約を結ぶ際には，混入している異物の質と量を把握し，品質規格とベンダーオーディットなどに関する条件を契約条項に組み入れ，原料メーカーの工程と品質の確認を定期，不定期に実施することが肝要であり，問題が起これば，その都度，異物の分析結果を原料メーカーに報告し，原因の究明と適切な対策の実施を依頼する必要がある．

しかしながら，賦形剤などの副原料に関しては，食品産業など他用途のものを一部医薬用に転用している場合があり，医薬用としての要求品質が必ずしも満足されているとはいえない場合が起こりうる．この意味においては，医薬品用添加物に対するGMP基準の制定は医薬品の品質向上に繋るものとして大いに期待されてよい．ところが一方，医薬品産業が使用する原料は他用途よりもはるかに少量である場合が多く，原料メーカーにとって医薬品産業は必ずしも重要な顧客ではないということも無視できない事実であって，このことは，原料メーカーが対応できる原料品質と医薬品メーカーが要求する品質に大きな差が生じた場合に問題が起こりうることを示唆するものといえる．

一方，外国においては，たとえ主薬原料といえども概して異物混入に鷹揚な場合が多く，混入異物に対して問題点を指摘しても速やかな解決に至る例は比較的少ない．このことが，安価な医薬品原料を国外に求めにくくし，製造原価低減という企業の基本を犠牲にする原因ともなっており，異物品質に関する国際調和が今後大いに進展することが要望される理由となっている．

(2)篩による異物の除去

固形製剤用の原料粉末や中間製品である製錠用顆粒あるいは製品としての顆粒剤，細粒剤などに混入する異物を除去する方法として篩過処理が通常よく行なわれるが，篩過の原理を考えれば異物除去の効果が原料粉末や中間製品より大きい異物に限定されることは明らかである．また，異物が微細な粒子の集合体である場合，篩を通す過程で微細な粒子にほぐれて，異物汚染を拡散させてしまうことがあるので注意を要する．

異物を除去することを目的とする以上，篩の目開きの選択はできるだけ細かくする必要があるが，その限度は適用する原料粉末や中間製品の粒子サイズと凝集性など篩の通過し易さに関係する特

性と篩過装置の機構に依存する.

図5に2種類の篩過装置を示したが, (a)はスクリーンが振動するタイプの篩過装置であり, 付着凝集性の強い粉末でもスクリーンが目詰まりしにくく, かつ篩過能力が高いという特徴がある. 一方, 筆者らの固形製剤の製造工場では, ブラシで圧篩する方式の篩過装置(b)が多用されており, (a)のタイプと同様に比較的凝集性の強い粉末でも実用的な処理速度が得られ, かつ篩の目開きを細かく選定できる. しかしながら(a), (b)いずれのタイプにせよ, 異物が微細な粒子の集合体である場合は, 上述のとおりかえって異物汚染を拡散させる危険性があることに注意が必要である.

また一方, 篩で異物を除去する場合には, 細長い異物が篩を「縦通過」することを考慮しておく必要がある. たとえば, その典型的な例である毛髪の場合, その径はおよそ100μm であるから, 通常使用される目開き300～500μm の篩を縦に通過してしまう確率は高い. したがって篩による異物除去においては対象とする異物の形状を充分検討しておくことが必要である.

異物除去を目的とする篩過工程では, ロット毎あるいは1日処理毎に, 篩上に捕捉された異物を透明粘着テープに転写・固定して品名・ロット番号・処理量・処理条件などとともに工程管理記録にファイルしておくことが重要で, このことにより異物の増減のトレンドや新規な異物の混入の有無などが確認できる. また, 必要に応じて, 顕微鏡写真やFTIR, EPMA分析を行なえば原料メーカーへのフィードバックや異物の混入経路の推定に大きく役立つ.

以上のように, 篩による異物の除去はある限定された条件下で効果を発揮するものであるから, 篩過装置の形式と条件設定の選定にあたっては篩過対象と除去すべき異物の特性を充分見極めておくことが必要で, 要時, チャレンジテストでその異物除去能力を評価することも肝要と言える.

(3)マグネットによる磁性異物の除去

固形製剤用原料粉末や中間製品中の磁性を有する異物除去の方法として, 製造工程中の粉粒体の通過経路にマグネットを設置し, その磁力によって磁性異物を捕捉する方法が採られる. 具体的には, 図6に示すように, 複数のマグネット棒を粉粒体の通過経路中に設置して, その間に粉粒体を流し, 混入する磁性異物たとえば鉄粉やステンレス摩耗片などをマグネット棒に捕捉する方法である. この方法によれば, 篩過では対応できない非常に細かい磁性異物の除去が可能となる. しかし, この方法には折角捕捉された磁性異物が粉粒体の流れによって削り取られ, 粉粒体中に再混入してしまう問題があり, このことを避けるためには粉粒体の流れの速度を落とすなどの対策が必要となる.

異物除去用に使用されるマグネットの強度は通常 6000～12000 ガウス程度であるが, 強ければ強いほど磁性異物捕捉効果が上昇し, かつ捕捉異物の粉粒体による削り取られも減少するが, マグネットを強くするとその確実な固定方法が必要となるし, マグネット同志の, あるいは磁性を有する機械部品との間の強力な接着力のために, 分解, 組み付けなどのハンドリングにおいて問題が生じる可能性もあるので注意が必要である.

マグネットによる磁性異物除去の日常の管理としては, 篩過の場合と同様にロット毎あるいは1日処理毎に分解して, 捕捉された異物を透明粘着テープに転写・固定して管理記録を作成しておくことが重要で, このことにより磁性異物の混入量の推移を把握でき, 磁性異物が異常に増加した場合

などに，原料メーカーへのフィードバックがタイムリーに実施できるし，自工程の異常の検出もより正確に行える．

この磁石による異物除去方法は相当に微少な異物に対応できる反面，磁性の無い異物に対しては対応できない．一方，前述の篩過方法の場合は非磁性異物には対応できるもののスクリーン目開き以下の異物には対応できない．つまり，それぞれに一長一短がある訳であり，これらを組み合わせて使用すればある程度それぞれの短所を補完し合うことが期待される．換言すれば，異物対策においては適用可能な除去手段を組み合わせて使用することが必要であるといえる．

(4)風篩式異物除去装置による異物の除去

前節において既に述べたことであるが，固形製剤をはじめとする医薬品の製造においては，異物の混在しない原料を確保し医薬品の汚染に対して充分にバリデートされた製造プロセスを確立することが異物対策の原則となる．しかし，輸入原料などでは異物混在の危険性が高い場合もあり，その対策として一般には原料の前処理(篩過)や最終製剤の外観検査が実施されている．しかし混入した可能性のある異物は可能な限り早期に除去する必要があることから，粉粒状の中間製品に混在する異物を除去する目的でシオノギが開発した連続式インライン型異物除去装置[8)]を簡単に紹介してみたい．

(4.1) 異物除去装置の概要

装置の概略を図7に示した．図の(A)は流動層型異物除去装置で，粒度の揃った顆粒剤に混在する異物の除去を目的とし，一方(B)のトンネル型異物除去装置は微粉を含む打錠用あるいはカプセル充填用粉粒体を対象とする装置である．これらの装置は，底面からの流動化空気により供給される粉粒体を流動状態にさせ，粉粒体と混在異物との物性差や磁性などを利用して混在異物を分離除去するものである．具体的には金属，ガラス片等の重質異物は落下捕集，ビニル片等軽質異物は排気除去し，磁性異物は磁石により捕集する．なお，流動化空気速度，粉粒体供給速度，排出口高さは対象とする粉粒体の物性により適宜設定を行い，必要に応じて装置内に仕切板の設置，磁石本数の変更も可能である．

(4.2) 本装置の異物除去原理

(4.2.1) 顆粒と重質異物の流動化開始速度差

流動化開始速度とは，充填された粒子層の下から空気を送風する時，徐々に風速を増加させて粒子が運動しはじめる瞬間の送風速度のことであり，簡易的に(1)式[9,10)]により求めることができる．

$$umf = 0.7\{\rho(\rho_p - \rho)\}^{0.94} Dp^{1.82} / \rho u^{0.88} \qquad (1)$$

ここで ρ および ρ_p は流体と粒子の密度，μ は流体粘度，Dp は粒子径である．異物として金属を想

定し，顆粒との流動化開始速度の違いを(1)式より計算して図8に示した．なお，顆粒および金属(SUS)の密度はそれぞれ 1.0 , 7.8 g/cm^3 とした．図8では両者間の流動化開始速度に大きな差が認められ，この差を利用すれば金属等の重質異物を粉粒状の製剤中間製品から分離除去できると期待される．

(4.2.2) シミュレーションによる異物分離機構の解析

離散要素法を用いた粒子運動の数値シミュレーションは，ドラム混合[11]や錠剤コーティング[12]など固形製剤分野においても現象の解析に広く用いられるようになっている．この手法を用いて流動層内における粒子の運動をシミュレートし，今回開発した異物除去装置の異物分離機構を解析した．

個々の粒子の運動は離散要素法を用いた Lagrange 的な手法により追跡し，また流体に対しては速度，圧力などを空間的に重み付けをして平均化した局所平均量を用いた基礎式を解くことにより，粒子の流動化現象をシミュレートした．具体的には，バネ，ダッシュポットおよび摩擦スライダを用いた Cundall,Strack[13]と同様のモデルにより粒子間の接触力を与え，この接触力と流体から受ける力をもとに個々の粒子の運動を Lagrange 的に計算し，流体の運動については粒子の存在を考慮した連続の式および運動方程式を計算する2way coupling 法[14]を用いた．なお，計算は球粒子を用いた2次元流動層を対象とし，直径が等しく密度の異なる 2 種類の粒子の混合物(軽質:重質=96:4)を，流動層の底面から一様な流動化空気で吹き上げた時の粒子の運動をシミュレートした．計算条件を表1に示したが，特に送風速度は顆粒の流動化開始速度(1.5 m/s)の1.2倍(1.8 m/s)とした．

図9は送風開始からの粒子のスナップショットを経時的に示したものである．黒丸が重質粒子を表し，初期状態では斜めにほぼ整列させて配置した．図9(1)～(6)に示すように流動化が始まるとともに，重質粒子は流動化する軽質粒子の空隙を落下するように移動することがわかる．これは上述の流動化開始速度による推定と一致する現象であり，さらに時間が経過すると重質粒子は図9(7)～(9)に示すように底面近くで周囲の顆粒とともにほとんど静止した状態となった．この時の流動化は粒子層の上層部のみで起こっており，沈降した重質粒子は再び浮遊することはなく，軽質粒子と重質粒子の分離状態が保たれた．これは重質粒子が含まれる部分(下層部)と軽質粒子のみの部分(上層部)の見かけのかさ密度に差が生じ，この差によって流動状態に差違が生じたためであるといえる．以上のように2次元流動層を用いて本装置の異物分離機構をシミュレートした結果，粒子径が等しい場合，軽質粒子と重質粒子とを完全に分離可能であり，本装置の有用性が示唆された．

(4.3) 本装置の異物除去能力の実験的評価

上述のシミュレーションで示された本装置の異物除去能力を実際に確認した結果，図7に示すように顆粒と金属異物との物性差による除去限界は SUS 粒子径 0.1～0.2mm 程度であり，顆粒の供給速度が小さいほど除去能力は向上した．このことからシミュレーション結果で可能性が示唆された密度差を利用する顆粒と金属異物の分離方法が実際に可能であることが実験的に証明されたといえる．そして異物が SUS の場合その分離限界は顆粒の大きさの 1/3～1/2 程度であることがわかった．なお，ここでは省略するがトンネル型についても同様な結果が得られている．

以上の検討結果をもとに 6000 ガウス磁石を標準仕様とした装置を生産ラインに組み込んだ結果，安定した異物除去機能が得られ，その有用性が証明された．図10は生産プロセスでの使用例を示したものであるが，最近はプロセスのクローズド化，省人化を目的とした空気輸送ラインが多く，インラインで使用できる本装置の有用性は大きいといえる．ちなみに，図11は生産ラインで実際に捕集された異物であるが，内部に微小金属を伴った顆粒などもあり，従来の方法(篩過や外観検査機)では除去困難な異物の除去も可能となったことが確認された．以上から，本装置はシオノギの固形製剤工程に標準装備されることとなった[15,16]．

5．外観検査機の導入

以上のように原料や製造工程，中間製品などに細心も注意はらっても，外来異物の混入リスクを完全になくすことは困難であり，錠剤や顆粒剤，カプセル剤など最終の工程が完了した時点で外観検査を実施することが常識となっている．最近では，各メーカーから高性能な外観検査機が市販されているが，これらの装置は錠剤やカプセル剤などの搬送方法は異なるものの，検査の方式そのものはほぼ同じであると言ってよい．検査原理を図12に示す．すなわち，錠剤をカメラで撮像した場合，錠剤表面に異物が存在すると，その部分の明るさや，明るさの差分に変化が生じる．この変化があらかじめ設定されている閾値を越えると，異物であるという判定となり，その錠剤は系外へ排除される．高性能の検査機では一時間あたり 10 万錠以上の検査が可能であり，異物除去や外観品質の確保に大きな威力を発揮している．

しかしながら，最終工程にこのような検査機があるからといって，上述してきた中間工程や原料に対しての異物混入防止の取り組みがおろそかになっては本末転倒であり，最終工程におけるこれらの外観検査機は，製造工程全体が異物混入に対して良好なコントロール状態にあることを検証するものであるという考え方が必要である．

6．おわりに

医薬品の医療過誤防止や健康被害防止について，医薬品メーカー側からの取り組みの一端を紹介させていただいたが，これらの取り組みは合理的な製剤設計およびGMPに則った医薬品製造プロセスと協調していることが重要である．

今回の講演により，別の演者が紹介した包装仕様の問題も含めて，製造，物流，調剤，投薬の各ステップのいずれの段階においても医療過誤や健康被害が起きないよう，我々医薬品メーカーがたゆまぬ努力を続けていることをご理解いただければ幸いである．

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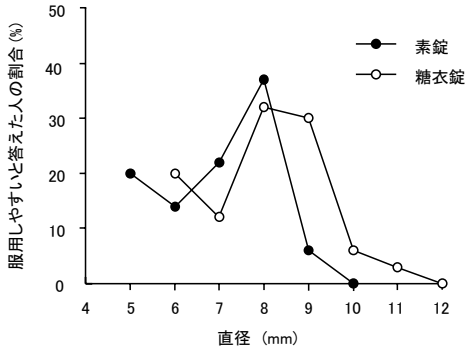


杉原ら「剤形および包装における識別性の検討」 病院薬学 Vol. 12, No.4 (1986)

図 1. 錠剤の服用しやすいサイズ

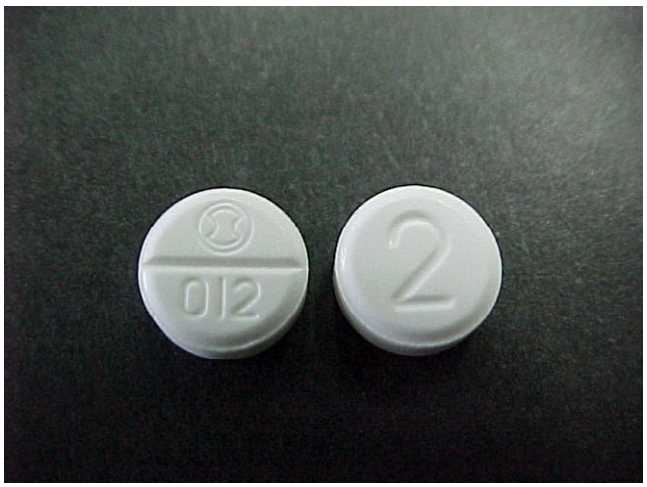


図2 字体の大きな刻印錠

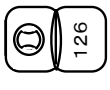
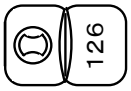
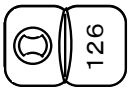
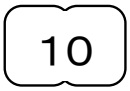
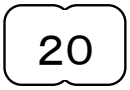
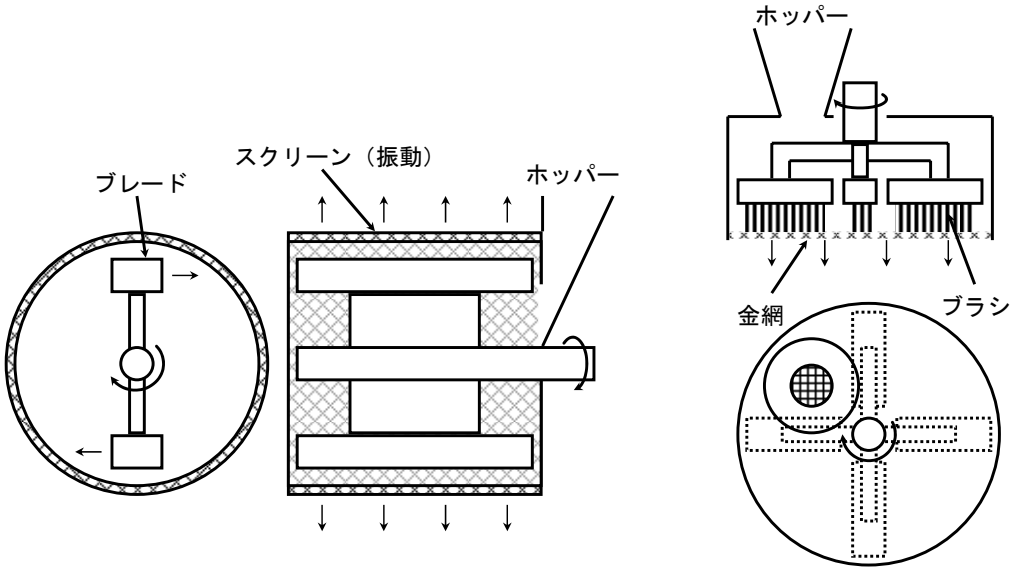
		5mg 錠	10mg 錠	20mg 錠
形状	表面			
	裏面			
	側面			
寸法	長径	約 7.5 mm	約 9.3 mm	約 9.3 mm
	短径	約 4.5 mm	約 5.6 mm	約 5.6 mm
	厚さ	約 2.4 mm	約 3.3 mm	約 3.5 mm

図 3. 蝶型錠の形状と寸法

図 44. スティッキングを誘発しやすい刻印部分



(a) 振動式篩過装置　　(b) 回転ブラシ式篩過装置

図5. 2種類の篩過装置

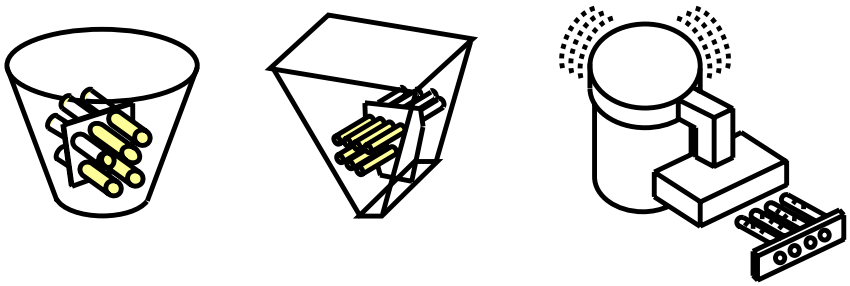


図6　　粒体の通過**経路**に設置したマグトット**棒**

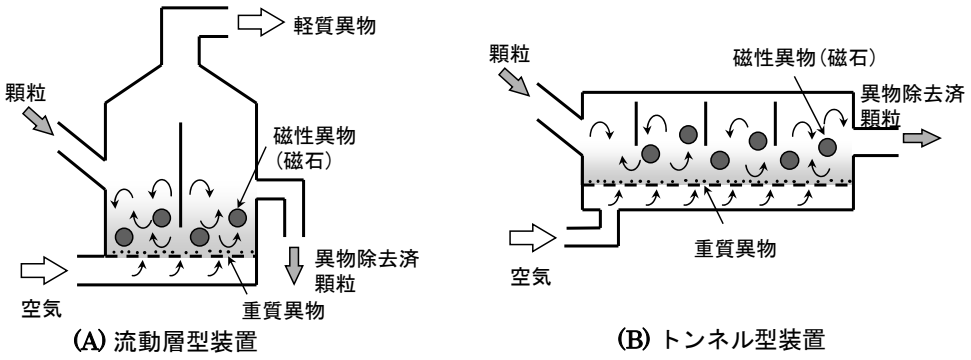


図７　風篩式異物除去装置の概略

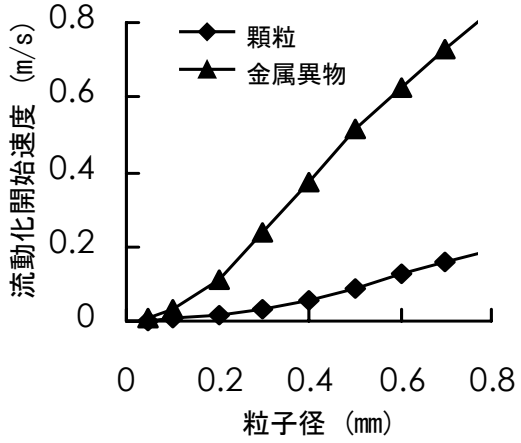


図８　流動化開始速度と粒子径の関係

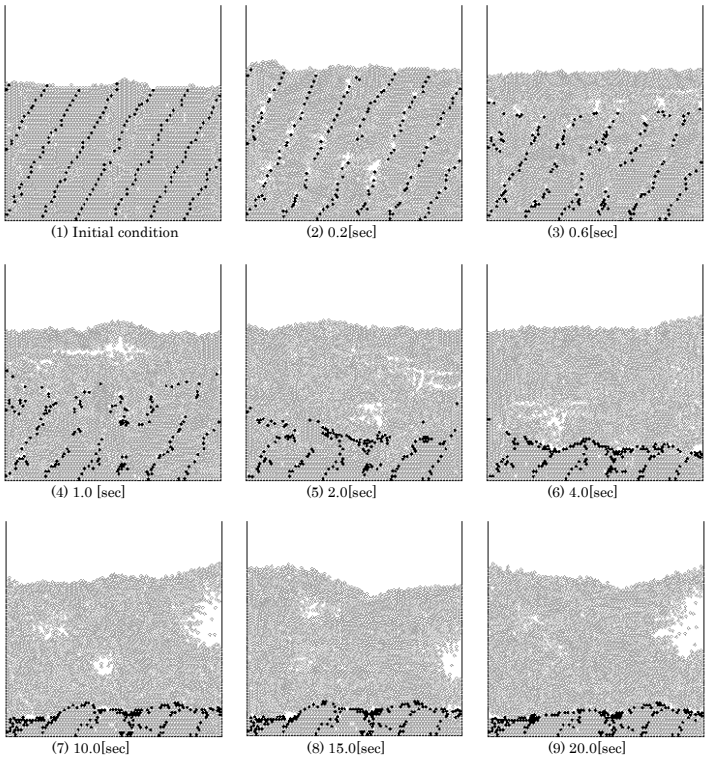
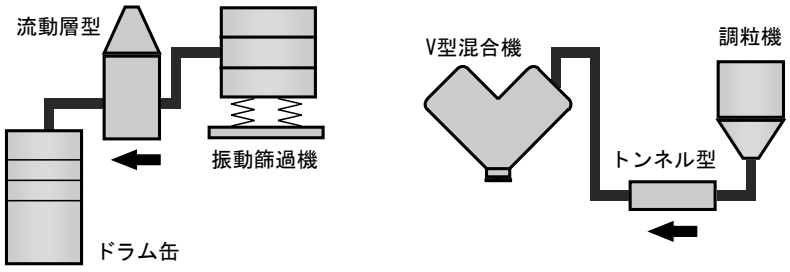


図９ シミュレーション結果



・篩過後の収缶ラインに設置　　・調粒後の空気輸送ラインに設置

図10 生産プロセスでの使用例

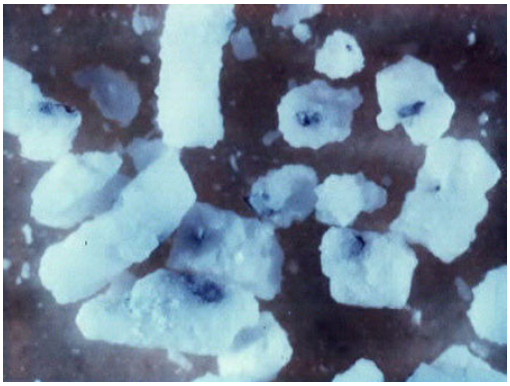


図11 捕集異物の例（異物を伴った顆粒）

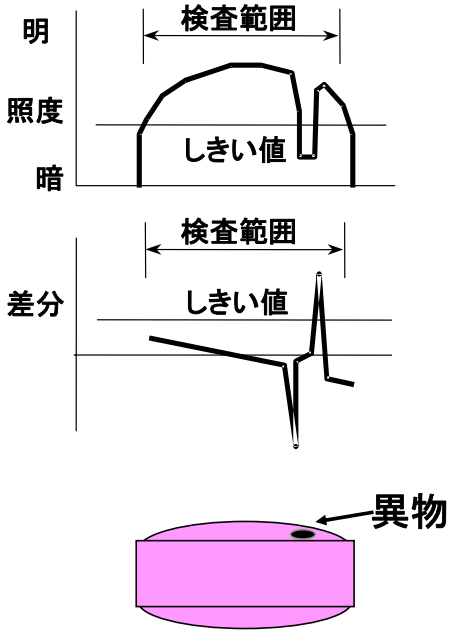


図12. 外観検査機の検査原理

表 1. 錠剤のつまみやすさの順位

素錠		糖衣錠		
直径	平均順位	直径	平均順位	
11 mm	2.4	10 mm	2.4	
10 mm	2.4	11 mm	2.5	
9 mm	2.6	12 mm	2.7	⇧ つまみやすい
8 mm	3.2	9 mm	3.1	
7 mm	4.6	8 mm	4.5	⇩ つまみにくい
6 mm	5.9	7 mm	5.8	
5 mm	6.8	6 mm	6.9	

杉原ら「剤形および包装における識別性の検討」病院薬学 Vol. 12, No.4 (1986) 一部改

表 2 蝶形錠剤のイメージは好ましいか否か

年齢	回答者	好ましい	好ましくない	なんとも言えない
20代	学　生 (10)	6	2	2
	会社員 (10)	4	5	1
	薬剤師 (20)	7	6	7
	合計 (40名)	17	13	10
		42.5%	32.5%	25.0%
30代	薬剤師	2	2	4
	(8名)	25.0%	25.0%	50.0%
40代	薬剤師	0	1	0
	(1名)	0.0%	100.0%	0.0%
50代	薬剤師	0	1	0
	(1名)	0.0%	100.0%	0.0%
60代	薬剤師	2	6	2
	(10名)	20.0%	60.0%	20.0%
合計	60名	21	23	16
		35.0%	38.3%	26.7%

日高ら「変形錠剤の使用性について」病院薬学 Vol. 18, No.4 (1992)

表 3. 蝶形錠剤のイメージの好ましい理由

年齢	回答者	美しい	印象に残る	明るい	従来にない形	その他	その他の内容
20代	学　生 (10)	0	5	0	1	1	形がシンプル
	会社員 (10)	0	2	1	1	0	
	薬剤師 (20)	0	5	2	2	2	分割しやすい 飲むのが楽しい
	合計 (40名)	0	12	3	4	3	
		0.0%	30.0%	7.5%	10.0%	7.5%	
30代	薬剤師	0	1	0	1	1	割線があるので使いやすい
	(8名)	0.0%	12.5%	0.0%	12.5%	12.5%	
40代	薬剤師	0	0	0	0	0	
	(1名)	0.0%	0.0%	0.0%	0.0%	0.0%	
50代	薬剤師	0	0	0	0	0	
	(1名)	0.0%	0.0%	0.0%	0.0%	0.0%	
60代	会社員	0	0	0	1	1	分割服用できる
	(10名)	0.0%	0.0%	0.0%	10.0%	10.0%	
合計	60名	0	13	3	6	5	
		0.0%	21.7%	5.0%	10.0%	8.3%	

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表 4. 蝶形錠剤のイメージの好ましくない理由

年齢	回答者	理由（内容）	
20代	学　生	蝶が嫌い	1
	（10名）		
	会社員	形が変	3
	（10名）	服用しにくい	1
		蝶と関係	1
	薬剤師	蝶が嫌い	2
	（20名）	形が変	3
30代	薬剤師	服用しにくい	1
	（8名）	蝶が嫌い	1
40代	薬剤師	蝶が嫌い	1
	（1名）		
50代	薬剤師	蝶が好きではない	1
	（1名）		
60代	会社員	蝶が嫌い	1
	（10名）	服用しにくい	3
		無関係	2
合計	60名	蝶が嫌い	7
		服用しにくい	5
		形が変	6
		蝶と関係ないから	2
		その他	1

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表 5 錠剤の分割性の比較

		蝶型錠（106mg）		7mmΦ円形割線錠（120mg）	
年齢		男性	女性	男性	女性
20代	$\bar{X}$ (mg)(n=40)	52.82	53.03	59.35	60.07
	max (mg)	56.63	55.18	64.53	67.19
	min (mg)	49.60	50.77	52.92	53.02
	c. v. (%)	3.90	2.22	4.56	6.55
	判定値 (%)*)	4.16, 6.11, 5.25, 6.19	2.62, 2.73, 3.72, 3.22	8.89, 5.78, 6.30, 8.52	8.73, 10.03, 12.60, 9.75
	分割しやすさ	○	○	×	×
30代	$\bar{X}$ (mg)(n=40)	53.13	52.96	59.81	59.62
	max (mg)	56.05	57.34	68.97	67.79
	min (mg)	49.18	48.77	51.10	51.49
	c. v. (%)	3.05	3.55	8.12	7.55
	判定値 (%)*)	4.39, 4.02, 4.55, 4.41	7.25, 3.72, 6.31, 2.77	14.96, 11.63, 11.42, 11.72	8.52, 12.63, 12.10, 14.19
	分割しやすさ	○	○	×	×
40代	$\bar{X}$ (mg)(n=40)	53.03	52.84	59.16	59.24
	max (mg)	58.64	55.04	66.67	64.69
	min (mg)	48.32	50.13	50.53	55.16
	c. v. (%)	3.99	2.57	7.34	3.42
	判定値 (%)*)	3.38, 3.71, 6.95, 6.88	3.91, 2.76, 3.77, 3.21	10.88, 8.75, 12.78, 12.32	4.81, 3.71, 7.38, 6.07
	分割しやすさ	○	○	×	×
50代	$\bar{X}$ (mg)(n=40)	52.91	53.01	58.95	59.30
	max (mg)	57.83	56.16	69.80	67.99
	min (mg)	47.64	49.28	50.84	53.13
	c. v. (%)	4.55	3.26	7.90	6.19
	判定値 (%)*)	6.28, 7.25, 5.16, 6.49	4.44, 5.17, 3.05, 4.59	15.91, 12.36, 12.90, 10.12	11.28, 10.60, 10.36, 8.13
	分割しやすさ	○	○	×	×

*）40個のサンプルを無作為に10個ずつ抽出しそれぞれについてJP15重量偏差試験の判定値を算出した.

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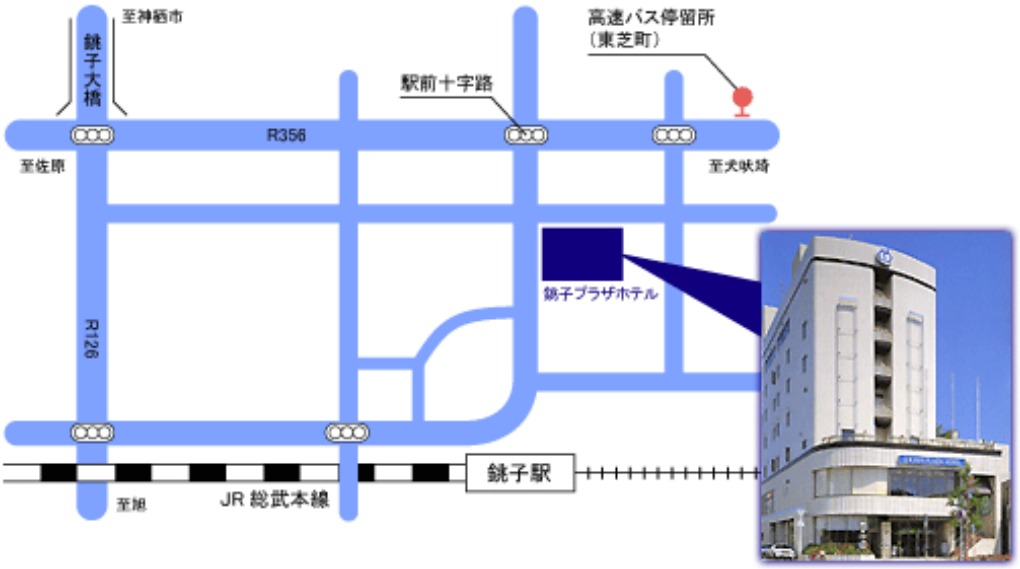

Pre Symposium
Programs and Abstracts

プレシンポジウム

「知っておきたい感染症とその危機管理
～今、私たちにできること」

講演プログラム と 講演要旨

講演プログラム

平成 **20** 年 **9** 月 **13** 日（土曜日）

13:30-17:00　プレシンポジウム　（第 **1** 会場）

座長:　増澤 俊幸（千葉科学大学 教授）
柴原 壽行（千葉科学大学 教授）

13:30−14:00　**[Pre01]**　**岡部 信彦（国立感染症研究所感染症情報センター）**
麻疹が大学生で流行、なぜ？

14:00−14:30　**[Pre02]**　**西尾 治（国立感染症研究所）**
ノロウイルス感染症の現状と予防策

14:30−15:00　**[Pre03]**　**吉川 泰弘（東京大学大学院農学生命科学研究科）**
BSE のリスク評価と危機管理

15:00−15:15　**休憩**

15:15−15:45　**[Pre04]**　**大槻 公一（鳥インフルエンザ研究センター，京都産業大学；鳥由来人獣共通感染症疫学研究センター，鳥取大学）**
日本で発生した鳥インフルエンザとアジアで発生している鳥インフルエンザ

15:45−16:15　**[Pre05]**　**上村 浩一（京都府農林水産部畜産課）**
京都府における高病原性鳥インフルエンザの防疫対応について

16:15−17:00　**総合討論**

18:00-20:00　ウエルカム・レセプション　（カフェ マリーナ）

[Pre01]

麻疹が大学生で流行、なぜ？

岡部 信彦

国立感染症研究所感染症情報センター

麻疹（はしか）は重症な疾患です。約 1/3 に肺炎、中耳炎、急性脳炎など何らかの合併症があり、致死率は 0.1-0.2%です。よい治療法はありません。WHO は、この麻疹を、ワクチンによってコントロール可能な疾患であると位置づけ、各地域におけるゼロ発生、流行の遮断（measles elimination :麻疹排除）を大きな目標として掲げています。

わが国では昭和 53 年から本格的な麻疹ワクチンの接種が始まり、麻疹の患者さんはぐっと少なくなりました。しかし平成 11 年に乳幼児を中心にした流行があり、全患者数は 17 万～33 万人程度と推定されました。なおこのころアメリカでは全患者数は年間数十人の単位でした。この時は、1歳で麻疹のワクチンを受ける人が少なかった主な原因で「1歳のお誕生日にワクチンを」と呼びかけた結果多くの人が受けるようになり、乳幼児の麻疹は大分おさまりました。

ところが昨年には、20 代前後の若者の間での麻疹の流行がみられ、大学の休校、海外旅行中の日本人の発症と感染のひろがりなど、国際的な問題としても取り上げられました。

この流行は、

1)麻疹ワクチン未接種で未罹患者（約 10%）

2)麻疹ワクチン接種したが免疫獲得が出来なかったもの(primary vaccine failure:2-3%)

3)麻疹ワクチンによる免疫が次第に弱くなったもの(secondary vaccine failure:約 10%)、

が学校などで集団生活する中に麻疹ウイルスが入り込んだこと、そして若者たちの行動範囲の広さが流行を拡大させたものと考えらます。

そして今回流行の麻疹には、三つの問題があげられます。

1)免疫を持っていない人が感染すると、年齢に関わらず重症となり、合併症も含め個人にとって危険が高い。致死率も 0.1-0.2% ある。

2)免疫が次第に減弱してきた人は典型的な麻疹にはならないですむが、感染源にはなることである。これは感染拡大ということで、家族や友人そして社会全体に影響を及ぼす。

3)麻疹は世界中で“排除(elimination)”という目標に向けて取り組んでいる中、諸外国にしてみれば「日本ともあろう国がまだ麻疹が？」という思いと、実際に日本から麻疹を持ち込まれるのは非常に迷惑に感じており、「日本の対策は不十分」という声が強い。

というものです。

今回の麻疹流行をきっかけに、遅ればせながらではあります、我が国における麻疹対策は大きくすすめられることになりました。

今回は皆さんの健康に大いに関係のある、麻疹の流行状況と、これからの対策、などについてお話をする予定です。

ノロウイルス感染症の現状と予防策

西尾 治

国立感染症研究所

今日、ノロウイルスは最も患者数の多い感染症であり、食中毒の主要なウイルスでもある。

2004 年には高齢者施設でのノロウイルスによる死亡例が社会的にも大問題となり、2006 年・07 年の初冬には日本を含め欧米でも大流行を起こし、ノロウイルスによる集団発生や食中毒が連日報道された。小児科領域ではノロウイルスによる感染性胃腸炎の患者が、毎年、180 万人程度と推定されているが、2006 年・07 年の初冬は約 2 倍の患者数で、食中毒では、事件数(504 件)の 33%、患者数(27,616 名)の 71%を占め、過去最大となった。

ノロウイルスは 1968 年にアメリカ、ノーウォークで急性胃腸炎患者の糞便から電子顕微鏡で発見された。形態的特徴は小さいことなどから、小型球形ウイルス(SRSV、small round structured virus)と呼称されていたが、2002 年 8 月国際ウイルス命名委員会でカリシウイルス科、ノロウイルス属に命名された。

ノロウイルスは経口感染で、潜伏期間は通常 12～72 時間、主症状は嘔気、嘔吐、下痢、腹痛である。腸管の炎症に伴う下痢症状を呈し、激しい水様性の便が数回続くこともある。嘔吐は突然、急激に強く起こり、その際に腸内容物が逆流し、ウイルスが吐物中に入り込む。これらの症状が 1～2 日続いた後、治癒し、後遺症も残さない。しかし、高齢者や乳幼児等の抵抗力の弱いヒトでは脱水症状を起こすことがあり、時には、嘔吐時の嘔吐物により気管の栓塞、誤嚥性肺炎を起こすことがあるので注意を要する。ノロウイルスに効果のある薬剤は無く、脱水症状が強い時には補液などの対症療法が必要となる。ワクチンは開発されていない。

急性期の患者の糞便には 1g 当たり 1 億個、吐物には 100 万個のウイルスが存在し、糞便からのウイルスの排泄は 2 週間程度続く。

嘔吐物、糞便を消毒せずに放置すると、乾燥し、ウイルスは塵埃となり、口に入り感染する。

ノロウイルスは感染力が強く、ウイルス粒子 10 個から 100 個で感染・発病する。ノロウイルスは乾燥・液中で長期間安定であり、食品を汚染すると食中毒となる。

ノロウイルスに類似のネコカリシウイルスから推測すると物理化学的抵抗性は強く、70%アルコール、低い塩素濃度イオン 3～6ppm、酸(pH3)、アルカリ(pH10)溶液では短時間で不活化されない。熱にも強く、殺滅には 85℃ 1 分間の加熱が必要と考えられている。

今後も、ノロウイルスによる集団発生、食中毒は多発することが予測され、その予防には古くから言われている手洗いと汚染の危険性のあるものは加熱する。また糞便、嘔吐物の感染源を適切な方法で消毒することである。

[Pre03]

BSE のリスク評価と危機管理

吉川 泰弘

東京大学大学院農学生命科学研究科

我が国の BSE の危機管理対応は 3 つの要素からなっている。①特定危険部位（SRM）の食用からの排除と焼却、②と畜場での BSE 検査（法的には 21 か月以上の牛）、③全ての牛の個体識別と農場から小売までのトレーサビリティー体制の確立である。

BSE の人への伝播を止めるには、3 つのレベルがある。①牛から牛への病原体の伝搬を止めること。②牛から人への伝搬を止めること、③人から人への伝搬を止めることである。このうち、牛から牛への伝搬を止めることが最も基本的である。肉骨粉など動物由来蛋白の牛への給与禁止、飼料工場の分離あるいは製造工程の分離による交差汚染の排除、肥料使用の規制などである。牛から人への伝播防止は、BSE 検査による陽性牛の排除、ピッシング規制、安全なと畜方法の導入、特定危険部位の排除・焼却、BSE 陰性国の安全な部位を利用した牛由来材料を用いた医薬品製造などである。人から人への伝播防止は「ハイリスク者」（英国に 1966 年まで英国に 1 日以上滞在した人、EU の BSE 陽性国に半年以上滞在した人）の献血、臓器移植の禁止である。英国では 2003 年以後、献血による変異型 CJD の感染がおこり問題視されている。

わが国は従来、安全性を行政が保証し国民は無批判にそれを受け入れる方式で安全神話を作り上げてきた。また出来上がった安全神話（ゼロリスク）の上に立ってシステムの検証を行うこともしない。したがって、一度安全神話が崩れると、多かれ少なかれパニックを繰り返し、改めてシステムの見直しをすることになる。BSE パニック後に導入されたシステムがリスク分析であり、リスクの評価と管理を分離するため内閣府に食品安全委員会を置くこととなった。プリオン調査専門委員会はその 1 つで、プリオンの専門家、公衆衛生、感染症の専門の医師、獣医師 12 名からなり、プリオンに関するリスク評価を行う責務を負った。BSE は科学的不確実性の多い、また異常に長い潜伏期をもつ感染症である。このような特殊な感染症のリスク評価と我が国の管理措置の有効性評価、および管理対応の難しさを中心に述べる。

日本で発生した鳥インフルエンザとアジアで発生している鳥インフルエンザ

高桑 弘樹[1)]*, 常國 良太*[1)]*、大槻 公一*[1,2)]

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分子遺伝学的研究の進展から、すべてのA型インフルエンザウイルスの本来の宿主は人等の哺乳類ではなく、鳥類、特にカモなどの水鳥であることが知られるようになりました。このような鳥類を固有宿主としてきたインフルエンザウイルスが、何らかの変異を起こすかもしくは親ウイルスとは異なる性質を獲得した遺伝子再集合体ができて、その結果、人に対する病原性を示し、人から人へ容易に伝播できるウイルスが出現して、人類に大流行を引き起こしてきた事実が過去にあった事が分かっています。今、アジア、ヨーロッパ、アフリカで猛威を振るっている H5N1 亜型ウイルスがそのような変異を起こして新型インフルエンザの原因ウイルスになる事が懸念されています。1968 年の香港型インフルエンザウイルスの登場以来新型インフルエンザウイルスが現れていないところに、世界に広く分布してしまった H5N1 亜型鳥インフルエンザウイルスが、多くの人に感染したことが報告されています。このウイルスが新型インフルエンザの原因ウイルスに発展する可能性を可及的速やかに封じ込めることが求められているのです。

鳥インフルエンザウイルスに対して豚が強い感受性を持っている事は良く知られています。したがって、豚の体内で H5N1 亜型鳥インフルエンザウイルスと現在人の間で流行しているインフルエンザウイルスの混合感染が起り、パンデミックを起こし得る「遺伝子再集合体」が出現する可能性も念頭に入れておく必要があります。この場合、ウイルスの亜型は必ずしも H5N1 亜型とは限りません。幸い日本国内では養豚産業と養鶏産業は独立して存在する地域がほとんどです。豚, 鶏, アヒルが一緒に飼育されている中国あるいは東南アジアでの新型インフルエンザの出現を考えておく必要があると思われます。

現在鳥インフルエンザの発生し続けているアジア地域での一刻も早い鳥インフルエンザの撲滅への取組が求められています。私たちも長崎大学熱帯医学研究所と協力しながら、ベトナムにおいて鳥インフルエンザ浸潤状況の把握と防疫対策の確立に向けて鋭意取り組んでいるところです。

[Pre05]

京都府における高病原性鳥インフルエンザの防疫対応について

上村 浩一

京都府農林水産部畜産課

【発生と対応】

平成16年2月29日に20万羽を超える大規模採卵養鶏場において、本病の発生が確認され、直ちに知事を本部長とする対策本部を設置し、連日200名の府職員による鶏の殺処分や消毒作業の防疫作業に着手しました。しかし、3月４日には約5km離れた約1万5千羽飼養する肉用鶏農場でも発生したため、国、他府県及び市町村から応援を得るとともに、大量の鶏の鶏舎からの搬出や埋却処理に自衛隊、機動隊の協力を得て、4月13日にすべての防疫措置を完了することができました。

京都府での事案は、大規模農場での発生という前例のないものであったことから、対応に当たって、ウイルス、土壌などの専門家や医師等9名で構成する専門家会議を設置し、防疫措置の進め方や死亡鶏等の処理方法等について的確な助言をいただきながら防疫作業を進めました。

また、26回開催した府における対策本部会議をすべて公開し、ホームページに即日・詳細な情報提供を行うとともに、人の健康や鶏の病気に関する相談窓口を設置するなど、府民の不安解消に努めました。

【危機管理】

京都府では、発生の経験を踏まえ、予防対策や発生時の対応などをマニュアル化し、府独自の防疫対策要領を策定しました。

発生予防対策については、国内での本病の発生は渡り鳥が感染要因と言われていることから、感染経路の徹底した遮断を図ることが最も重要であり、そのために、すべての養鶏農場に野鳥などの侵入防止のための防鳥ネットの設置や車両消毒、地下水や池の水などを飲用水として利用している農場には水の消毒など、日常の予防対策を徹底し、四半期毎に家畜保健衛生所がすべての農場を巡回し、防鳥ネットの破損の有無や鶏に異常がないかどうかを確認するとともに、併せて巡回時に血液検査を実施してウイルスの侵入を監視しています。また、愛玩として鶏を飼養している飼養者も含め、すべての小規模飼養者に対しても市町村等の協力を得て、予防対策徹底の巡回指導を年1回実施しています。

万一の発生時の対応については、現地での関係機関の役割分担や連携が確実にできるよう養鶏農場や市町村等の関係者を対象に、毎年防疫演習や実地訓練を実施しており、庁内においても、発生時に迅速な対応がとれるよう、危機管理監を中心に、関係部局の緊急連絡体制や役割分担の明確化など、危機管理体制を整備しています。また、京都府以外で本病が発生した場合、例えば、昨年の宮崎県での発生時には、直ちに庁内に警戒本部を設置し、養鶏農場等関係者への正確な情報提供を行うとともに、万一の発生には迅速に対応できるよう、部局連絡調整会議を開催し、情報の共有化と発生時の動員体制や各部局の役割分担について確認しました。

一方、本病の発生による「鶏卵や鶏肉がウイルスに汚染されているのではないか」などの風評被害

への対策として、平素から、府民に鳥インフルエンザについて正しく認識してもらうことが重要であり、講演会の開催などにより京都府産の鶏卵・鶏肉のピーアールと併せて鳥インフルエンザの正しい知識の普及・啓発に取り組んでいます。

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