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

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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

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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

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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 カ国に広がった。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の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

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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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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もの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 一看護師の立場から

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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фек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り組んでいる。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り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—

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社団法人 地域医療振興協会 医療安全推進室

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、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

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Recently radiation has been contributing to our society from several aspects. Especially radiation generators and radioisotope is essential tools in medical 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 Radiation Exposure and its Risk Management

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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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重粒子医科学センター 放射線医学総合研究所 日本

大線量放射線に対する危機管理は、外部からの大線量被曝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曝をした。6Sv(シーベルト)以上の被曝者では、長期生存の可能性は極めて少ないが、4Sv以下の被曝の場合、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曝をしたのかは、距離だけではなく、周りの環境に大きく左右され、被曝量を調べるには、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、より簡便な被曝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

Japanese Disaster Medical Compendium Compiling Team, Tokyo, Japan

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 serious 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

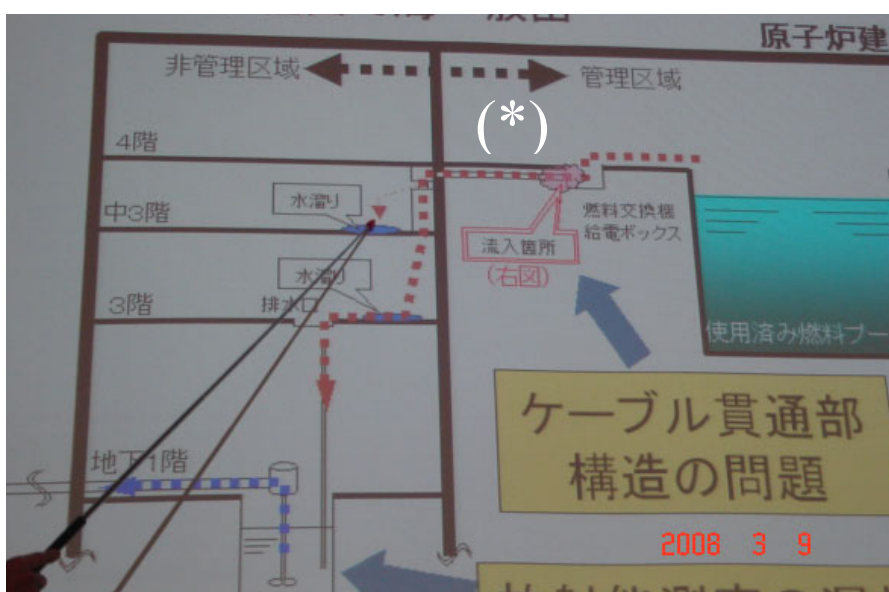


Figure: Minimal leakage of water contaminated with radioactive substance occurred from the asterisk(*) through the pointed route toward the basement level.

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 planned. 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.

人獣共通感染症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症である。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。

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

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[L16]

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

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The Anthrax events of 2001/2002 caused the USA and others to re-assess their 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 reagents. Additionally, lessons were 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 acetylcholinesterase 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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Research on Analytical Algorithm of Chemical Agent Gas Using RGB Value of Reaction Surfaces as an Index






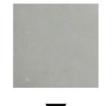

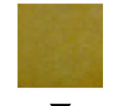

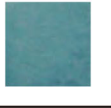

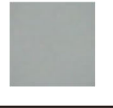



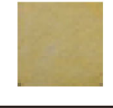
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In recent years, threat of the terrorism using chemical agent is on the rise on a global scale and each country proceeds research. We also have been studying a portable automatic detector for gaseous chemical agent. For the detector, we focused on 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

| Reaction Surface A | | Reaction Surface B | | Reaction Surface C | | Reaction Surface D | |
|---|---|---|---|---|--|---|---|
| Test Area | Comparison Area | Test Area | Comparison Area | Test Area | Comparison Area | Test Area | Comparison Area |
|  |  |  |  |  |  |  |  |
| ▼ | ▼ | ▼ | ▼ | ▼ | ▼ | ▼ | ▼ |
|  |  |  |  |  |  |  |  |

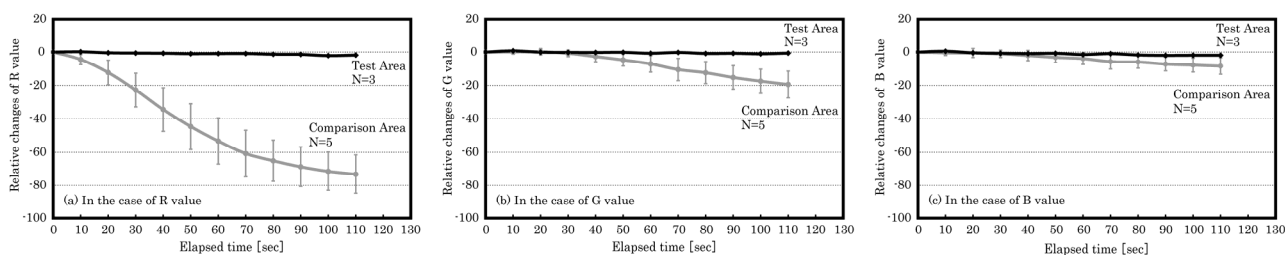


Figure 2 The changes of RGB values of "Reaction Surface A"

[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

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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

TOHO University Medical Center, OHASHI Hospital, Japan

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

Tadatsugu TANINO

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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.

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.

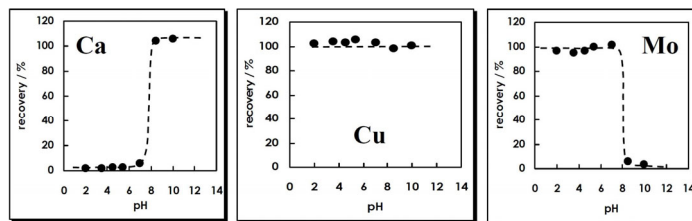
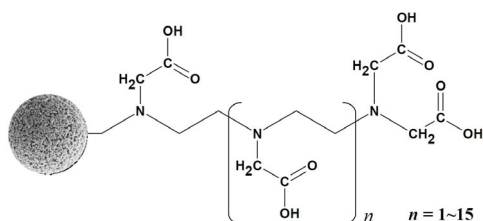


Fig.1 Chemical structure of CM-PEI resin Fig. 2 Extraction behaviors of elements on CM-PEI resin

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

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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.

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 $\mu\text{gAs/l}$, 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

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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。バツ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。

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