基調講演

Keynote Speech

長崎大学 学長／医学博士・片峰 茂
Shigeru KATAMINE, MD, PhD, President of Nagasaki University

That was a very kind introduction, good morning everybody. I am Shigeru Katamine from Nagasaki University and it is my great pleasure and honor to be here to give a lecture on the occasion of the opening of The Second International Conference on Animal Care in Kobe 2012. I would like to state my appreciation to the conference organizers for inviting me to this very meaningful and exciting meeting. In particular I am very grateful to the Secretary General and to today's chair, Ms. Kayoko TOMINAGA. She has strongly and continuously approached and encouraged me to mount this platform. Thank you.

Currently, I am involved in administrative work at the headquarters of Nagasaki University, but I am basically a scientist. My field of research is virology, studying the viruses that cause various diseases in mankind. So the topic I will be talking about this morning concerns infectious diseases caused by viruses. As you know reducing the risk of infectious diseases is one of the major global issues in the 21st century. Many people are dying due to infectious diseases and, in recent years, so many new pathogens have emerged within human communities and have propagated all around the world.

My talk will consist of two stories.

First I will talk about and briefly summarize the global issue of infectious diseases. Then I will move to my second story about intervention on mother to child transmission of HTLV-1, the virus causing Adult T-cell Leukemia, ATL. It is a very nice example of the battle leading to the successful control of a particular infectious disease.

As the chairman mentioned, my talk will be a very unique and extraordinary. I will talk in English but the slides I will show will be mainly written in Japanese. Here is one such slide and I hope it will help you understanding my Japanese English. I also hope that my talk today will somehow help to strengthen your understanding of infectious diseases and provide ideas on how we can control them.

So, let me start with the global issues. You can see here that infectious diseases are the most prominent cause of death around the world. We can estimate the total number of deaths in the world to be 50 million and, of these, 40% or about 20 million people are dying due to infectious diseases. For example diarrhea caused by various viruses (such as noroviruses, rotaviruses or enterobacteria) is killing about 5 million people every year. Most of them are children, including new born babies. A similar number of people are killed by pneumonia, followed by AIDS (2 million people), tuberculosis (2 million) and measles and malaria (1.5 million each).

The most important point is that these diseases are common in the world. In the developed countries, including United States, the EU and Japan, these diseases are curable by post-hospitalization, by drug treatment and also preventable by inoculating vaccines. Even with AIDS, while a significant number of AIDS patients are dying even in the developed countries, recent advances in anti-HIV therapy can greatly prolong the incubation periods of the HIV-infected individual. (The incubation period refers to the time interval between HIV infection and the onset of the disease). So this means that most of these 20 million people killed by infectious diseases are residing in developing

countries - in the tropic and sub-tropic areas in the world, including sub-Sahara Africa.

The situation in developing countries in the tropical areas is very bad. They have very bad nutrition, very bad sanitary systems. Therefore various infectious diseases easily propagate in human communities. Moreover there are few hospitals and no public care system to distribute vaccines and drugs. And the people have no money to be hospitalized or to buy drugs and vaccine. People in developing countries, in these regions, have barely received any of the benefits of modern medical science. As a consequence, there is a very high prevalence and high mortality by infectious diseases in developing countries. This really reflects the social, political and economic inequality between the north and south of the world.

In addition to the common diseases, there are so many other infectious diseases specifically present in the tropical areas. We call them "Neglected Tropical Diseases" (NTD) and these include sleeping diseases, scistosomiasis and Changes diseases by parasites, Dengue fever and Japanese encephalitis caused by viruses, and cholera and diphtheria caused by bacteria.

The important point is that these diseases are restricted to the tropical and sub-tropically areas. There are no diseases like these in developed countries. For this reason researchers and pharmaceutical companies have not given any attention to these kinds of diseases, the NTDs. As a consequence the pathogenic mechanisms remain to be elucidated, and the therapeutic or preventive measures to combat them still remain to be developed. So far, these particular infectious diseases have been neglected by global societies.

Additionally, over the last 30 years, mankind has begun to face a global risk from newly emerging infectious diseases, such as Ebola, SARS, AIDS and pandemic flu, which have all been breaking out within human societies in recent years. In some cases pathogens persistent in restricted small geographical areas have spread into new geographic areas. For example, in the 1980s, AIDS which had been present in some small isolated rural areas of Western Africa, spread to urban areas and then rapidly propagated all over the world. Many other cases broke out through an invasion of animal pathogens into human communities. The Ebola virus came from monkeys, the Nipavirus from fruit bats, BSE and mad cow disease from cattle, SARS from a kind of domestic cat, and influenza viruses from fowl and pigs. Changes in the genomes of pathogens are also involved in the emergence of new strains of influenza viruses and also drug resistant bacteria.

Many things are responsible for their emergence, such as socio-economic factors, changes of environments and changes in human behavior. For example, the reclaiming of woodland has increased the chances to link between humans and animals. Modern transportation systems have made the emergence of pathogens and their rapid propagation around the world far easier.

So far, I have briefly summarized the global issues relating to infectious diseases. The most important point is that the main focus of this global issue exists in tropical and sub-tropical regions. People in those regions need the help of the world.

Now I will move to the second story. The story is about Nagasaki prefecture-wide intervention in the mother to child transmission of HTLV-1, a causative virus of adult T-cell leukemia, ATL. I myself have been involved in this project for a very long time, more than 20 years.

As you know, cancer is the most important cause of death in Japanese people. About one third of Japanese people die with cancer. Of these, about 25% of cancer

cases are closely related to infection by viruses. Most hepatic cancers, cervical cancers and those of adult T-cell leukemia, ATL are closely associated with infection by hepatitis B / C viruses, human papilloma viruses and HTLV-1, respectively. And the Burkitt Lymphoma (prevalent on the Africa continent) and the Nasopharyngeal Carcinoma (in China) are closely associated with the infection by the Epstein-Barr virus, EB virus. Theoretically, by successful prophylaxis - by successfully preventing infections by these viruses - the human community can overcome these cancers.

What you are seeing here are some cells of adult T-cell leukemia surrounded by many small red blood cells. You can see very characteristic, irregular shaped nuclei in cells. Sometimes cells look as if they have two nuclei. This is a very unique, morphological feature of adult T-cell leukemia cells. This can be distinguished from any other leukemia.

ATL, adult T-cell leukemia was first described by Professor Uchiyama and Takatsuki in Kyoto University in 1977. In addition to their very unique morphological appearance, they are distinguishable from other leukemia by the presence of the frequent skin lesions and also high levels of blood calcium. ATL cells are also very resistant to any chemotherapeutic agent.

Therefore the prognosis of a patient with ATL is extremely poor and most will die within two years after diagnosis. A very important finding is that most of the patients themselves appear to have resided or were born in a particular area of Japan, namely southwestern Japan including Nagasaki, Kagoshima and Okinawa

prefectures. And if they were not, the patients' parents or grandparents appear to have been born in those areas. There are also so many reports of familial cases, that is, more than two patients in the same family. These finding strongly suggested a prevalence in southwestern Japan, and the involvement of infectious pathogens in the development of ATL. As you can see [in the slide] the blue colors referring to Nagasaki, Kumamoto, Kagoshima and Okinawa prefectures show a very high incidence of adult T-cell leukemia.

In 1981, four years after the discovery of ATL, Professor Yorio Hinuma of Kyoto University identified the virus that causes ATL, namely the Human T-lymphotropic virus Type I, in short HTLV-1. HTLV-1 are found to be the first human retroviruses and is capable of immortalizing human T-lymphocyte in vitro. And also importantly, worldwide survey showed that there is a prevalence of HTLV-1 infections in some particular areas of the world including southwestern Japan, the Caribbean basin and African continent. Importantly those prevalent areas completely match and overlap with areas having a high incidence of ATL.

Also later clinical studies show that about 5% of HTLV-1 infected individuals develop Adult T-cell Leukemia, ATL, and that every ATL patient was infected with HTLV-1. And also HTLV-1 is later shown to be associated with some other diseases including a kind of myelopathy, rheumatoid arthritis and other autoimmune diseases.

As I mentioned, HTLV-1 belongs to the retroviruses. Retroviruses have a unique life cycle by the presence of a unique enzyme, reverse transcriptase. Once infected, this kind of virus genome integrates into the genome of the host cells and persists into the cells. Once infected, you cannot remove the virus from the infected host, and after infection, the individual stays healthy for a long time, usually for their whole lifetime, with no disease.

However, some infected individuals develop the disease after a long incubation period during which the infected individual releases the viruses and behaves as a source of further infection. This is the problem. We know of

two kinds of virus in human retroviruses. One is the HTLV-1 and the other is HIV. Both of these two kinds of virus infect the human T-cell T-lymphocytes but the disease outcomes are completely different. HTLV-1 immortalizes the infected T-cells leading to leukemia and T-cell leukemia. In contrast, HIV destructs the infected T-cell finally leading to the immunodeficiency syndrome AIDS.

This slide shows the relationship between the HTLV-1 infection and the outcome of the disease. In the case of rheumatoid arthritis, some patients appear to be infected with HTLV-1 but most of other patients are not infected. In contrast, in the case of ATL only a small proportion, about 5% of infected individuals, develop ATL but conversely every ATL patient is infected with HTLV-1. So we can conclude that if we can successfully control the HTLV-1 infection, we can overcome ATL, the highly malignant and fatal cancer.

This slide shows the situation of Nagasaki Prefecture in the late 1980s. As you see, the total population is about 1.5 million. Within this population 4% were infected with HTLV-1 which is a very high rate of infection. In people above 50-years of age, the infection rate was 10% - very high indeed. And, more importantly, in the areas of remote islands including Goto Island, Hirado, Iki and the Tsushima there was an extremely high prevalence of HTLV-1 infection. There, more than 20%, 30% and sometimes 40% of people were infected with HTLV-1. The annual incidence of ATL in Nagasaki Prefecture was about 100. This corresponded to roughly 1% of total deaths in the prefecture. So the control of HTLV-1 infection is a very important public health issue in the prefecture.

Let's think about prophylactic measures for HTLV-1. When you consider prophylactic methods (meaning, the method for preventions), there is a very important concept - three essential factors behind infections. One of the factors is the host, usually this host is an individual yet to be infected. A second factor is the source of the infection and in the case of HTLV-1 the source of the infection is an infected individual. A third factor is the route of the infection that connects the source with hosts. These three factors are essential for the infection. In other words, without one of the three, infection will no longer be established. So if you think about prophylactic measures for a particular infectious disease, you can focus on one of them, one of the three.

Vaccination giving a host resistance against a particular pathogen is the trendy measure of the prophylaxis. But, in the case of HTLV-1, effective vaccines are not available so far, which is also the case in HIV. How about the source of the pathogens? As I mentioned, once infected you cannot remove HTLV-I from the host. The virus persists in the infected individual for an entire lifetime and most of the infected people stay healthy. You cannot separate them from the general population due to human rights, so the remaining focus should be to address the third factor, the root of the infections. This prompted us to look for the major root of HTLV-1 transmissions. A very important finding was that ATL patients clustered within a family. In the same way many members in a family were infected with HTLV-1, which suggested that the route might be very close contact between family members, such as a mother to child, or husband to wife, and so on. This was important data in our early studies and first provided evidence for the presence of mother to child transmission of HTLV-1. When children born to 78 infected mothers were tested, 17 children appeared to be infected, an infection rate of 22%. This is significantly higher than the control of age-matched children, 2.6%. Conversely if the mothers of infected children are tested, 12 out of 13 appear to be infected, 92% in comparison with the age-matched female, 5.5%. There is a highly significant difference. Similarly when 12 mothers of infected pregnant women were tested,

10 appeared to be infected, or 83%. This is, again, significantly higher than age-matched control of 6.4%. So these epidemiological studies clearly show the presence of a mother to child transmission as a route for HTLV-1.

From mother to child, the virus can transmit by three possible pathways. One is perinatal, that is, the virus transmits to the babies in the uterus. We call this, intrauterine infection. Secondly, the infection can occur during delivery, perinatal infection. Thirdly, postnatal transmission – the virus infects from mother to child mainly via breast milk, breast feedings.

To look for the route of mother to child transmission of HTLV-1 we followed the children born to infected mothers, and found that the infection of the children can be diagnosed very late after birth, later than one year after birth. We thought that the postnatal pathway is the most probable cause of mother to child HTLV-1 transmission so we decided to examine the breast milk of infected mothers. We asked infected mothers to give us their breast milk and we tested it. First we found that there are many cells in the breast milk and in these cells we could find many HTLV-I-infected cells. So breast milk can be a source of infection for everyone.

Next we inoculated the breast milk into experimental animals. We used the common marmoset as the experiment animal. We inoculated the cells from the breast milk of the infected mothers via the oral cavity of the marmoset, and inoculated about 6.8 x 108 cells in the oral cavity. That included about 7 x 105 infected cells.

This slide shows the time course of the experiment. We followed the inoculated marmoset, 1 month, 2 months, 3 months, 4 months, 5 months, 6 months, even 7 months after the inoculation and tested the presence and levels of the antibody against HTLV-1 in the blood. The presence of serum antibody is evidence for infection with HTLV-1.

As you see, two months after the inoculation, the antibody titer begins to elevate and reach the peak level three months after birth. This results clearly showed that the breast milk of infected mother has an infection potential when drunk by babies. So we can speculate that mother to child transmission by breast feeding is the major route of HTLV-1 infections.

Clinical studies at that time gave us very important information. Other than the mother-to-child transmission, HTLV-1 can also transmit horizontally by blood or sexual contact. But clinical data showed no ATL cases developed from this population infected with HLTV-1 at adult age. All the ATL cases without exceptions had developed in the population infected very early in life. So we knew that to overcome ATL in the community we had to control this mother-to-child infection route.

In 1987 we started a prefecture wide project namely the "ATL Prevention Program – Nagasaki" (APP Nagasaki), 25 years ago. One purpose of this project was to finally confirm the idea that breast milk was the major route of ATL transmission from mother to child. If the mother could refrain from breast feeding, the infection rate could dramatically decline. If it would be the case, the idea could be confirmed. Secondly, by having the infected mothers refrain from breast feeding, we could overcome ATL in the communities.

So the first step of the program consisted of screening all the pregnant women in Nagasaki Prefecture whether or not they were infected with HTLV-1. In the second step of the program, when an infected mother was identified, we explained the risk of breast feeding to her, asking her to refrain from breast feeding. Thirdly, we followed up on the children born to infected mothers. This program was conducted through a very close collaboration between the prefectural government, the doctors association, (pediatricians, obstetricians) and also Nagasaki University and it has continued to date for more than 25 years.

This slide shows the details of the program. Once a woman becomes pregnant she consults with the office of obstetricians where she is asked to have a test for the antibody against HTLV-1. The cost for the antibody

test is supported by the prefectural government. If the results are positive, the pregnant woman is informed on her next visit to the office. If infected with HTLV-1 the risks associated with breast feeding are explained so she can select another nursing method. She can refrain from breast feeding and change to bottle feeding and her secretion of breast milk is stopped by drug treatment. However some mothers do still select breast feeding and we ask them the length of their breast feeding period afterwards, for six months or less, or for more than six months. The children born to infected mothers received follow up 6 months, 12 months, 18 months, 24 months, and 36 months after birth in a pediatrician's registered office.

This is the project summary. So far, for over 23 years, from 1987 to 2009 we have tested 255,340 pregnant women. This corresponds to far more than 80% of the total pregnant women in the prefecture. We found about 8,500 infected pregnant women. So the infection rate of the pregnant women in Nagasaki prefectures was computed to be 3.3%. These infected mothers selected by themselves how to nurse their children. Most of them, more than 90%, decided to refrain from breast feeding and nursed their children with bottle milk.

This slide shows the representative results and their interpretation. We can see three important findings. The first is that when infected mothers refrained completely from breast feeding and the children were nursed by bottle instead, the infection rate was 2.7%. In contrast, for those children fed with breast milk the infection rate appears to be 17.6%. This is a highly significant difference and clearly confirms that breast milk is a major source of mother-to-child transmission with HTLV-1.

The second important finding is that if you look at the length of the breast feeding periods, in those children whose mothers gave them breast milk for less than six months the infection rate was 6.7%. In contrast, in those children fed breast milk for a very long time, for more than six months, the infection rate appeared as 26%. This is a highly significant difference. It means that the risk of transmission with HTLV-1 also depends on the length of breast feeding.

The third important finding was that, in spite of refraining from breast feeding, there was still a significant number of mothers who unwittingly transmitted the virus to their children, albeit a very low rate of 2.7%. This indicates the presence of an unidentified route other than the breast milk from mother to child.
So the project can conclude that breast milk is a major source of the mother to child of HTLV-1 transmission, and that the risk of infection depends on the length of the breast feeding, and that there may also be an unknown route of mother-to-child transmission. Ultimately, the project can conclude that refraining from breast feeding is the most effective measure to prevent mother to child transmission of HTLV-1.

The figures shown on this slide are estimations. So far we have tested 255,000 pregnant women including 8,500 infected mothers. More than 90% of the infected mothers agreed to refrain from breast feeding while the risk of infection from long-term breast feeding was 26% compared to the 2.7% risk of infection from bottle feeding. So we can calculate that this program has so far prevented 1,770 cases of mother to child transmission. As 5% of them would develop ATL in the future, this project can be said to have so far prevented 88 future ATL cases.

Another estimation is that if the current population of Nagasaki has a 3.2% infection rate, then in the annual age population (meaning the population of each age fixed as 25,000), there are 800 infected people of each age in Nagasaki Prefecture. From this 800, in the future 40 of them will develop ATL. Then for next generation after that, if the mothers in that population feed their children by breast feeding, and the infection rate is 26%, we can calculate that the affliction rate will be 0.8%. If the mothers in this population also refrain from breast feeding, then we can expect that the infection rate over the next generation to be only 0.1%. Now, this corresponds to 200 and 25 infected people in each age. Among them 10 and 1 ATL cases will develop. As

I mentioned, this is only our estimation, so this value may be much lower.

Nagasaki Prefecture readily expects the rate of infected pregnant women – those born after the start of the program - will be dramatically declined and the annual incidence of ATL will be less than one person. The annual incidence means that the annual number of patients with ATL will be less than one in the next generation or at least by the next-next generation. So Nagasaki Prefecture will overcome this fatal and highly malignant cancer in the future.

However, some issues remain to be challenged. The first one, as I mentioned, is that the program indicated the presence of an unidentified mother to child transmission route. We are very sorry that there were even a few but a significant number of mothers who unwittingly transmitted the virus to their children in spite of refraining from breast feeding. So firstly we have a duty to identify the unidentified transmission route.

Secondly, we are also responsible to the more than 8000 mother who were informed that they were infected. We can easily presume that from these 8000 mothers, 5% of them (equivalent to about 400 people) will develop ATL. But unfortunately we have no measures to prevent the development of ATL in the infected individuals. That is the second issue to be challenged.

The third issue is complicated. This concerns the balance between the advantages and disadvantages of infected mothers refraining from breast feeding. As you well know, breast milk has a huge great benefit for children. It provides the children with nutrition, and of course, antibodies and natural immunity against various pathogens. But the skin-ship interaction between mother and baby also seems to be very important for the child's future development. So this is a complicated problem to be challenged.

Finally I would like to point out the need for an extension and popularization of the APP success to a national level. The prevalence of HTLV-1 in other areas of Japan is very low - less than 0.1% - but the total number of infected individuals nationwide is still estimated to be 1 million people. This means that, in order to overcome ATL, the Nagasaki system has to be popularized and expanded to a national level.

In December 2010, the Ministry of Health, Labor and Welfare in Japan concluded a general counter plan for HTLV-1. Under this plan the Ministry decided to support the cost of conducting the HTLV-1 antibody test on every pregnant woman all over Japan. So this is a giant step towards "ATL Zero" in Japan.

I am confident that the success of APP in Nagasaki has strongly pushed the Ministry's decision. Today, in my lecture, I have given you an introduction to APP Nagasaki, a long-term prefecture-wide intervention and shown you that the success of the program has been a consequence of the dedicated collaboration of many people in Nagasaki. This of course includes the many mothers and their children, as well as all those officials and healthcare workers in the prefectural government, and the many pediatricians and obstetricians as well as many young researchers.

I would like to close my talk by expressing my heartfelt gratitude to all the people involved in this program. Thank you very much for your attention.

How we can control infectious diseases: Intervention in the mother-to-child transmission of HTLV-I in Nagasaki, Japan, for 24 years.

Nagasaki University
Shigeru Katamine, MD, PhD

【Slide1】

Infectious diseases are the most important cause of death in the world

年間死亡総数：約5,000万人

感染症による死亡総数：約2,000万人（40%）

1） 下痢症：500万人
2） 肺炎：500万人
3） エイズ：200万人
4） 結核：200万人
5） 麻疹：150万人
6） マラリア：150万人

【Slide2】

顧みられない熱帯病
(NTD: neglected tropical diseases)

- 寄生虫疾感染症
  トリパノソーマ（睡眠病）、住血吸虫症、シャーガス病など
- ウイルス感染症
  デング熱、日本脳炎など
- 細菌感染症
  コレラ、ジフテリアなど

【Slide3】

新興感染症
Emerging Infectious Diseases

(1)地方に限局していたウイルスが世界的大流行をおこした
：AIDSウイルス（HIV）、西ナイルウイルス
(2) 動物種間で維持されていたウイルスがヒトの世界に侵入
：エボラウイルス、ニパウイルス、BSE（プリオン）、SARSウイルス、インフルエンザウイルス（トリ、豚）
(3) 既存の病原体の遺伝子変異に基づく大流行
：インフルエンザウイルス、薬剤耐性菌

【Slide4】

The 25-year-long intervention on mother-to-child HTLV-I transmission in Nagasaki, Japan

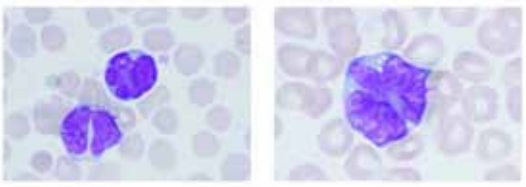
【Slide5】

The viruses cause cancers in the mankind

がんの種類	原因ウイルス
肝がん	B型及びC型肝炎ウイルス
子宮頸がん	パピローマウイルス
バーキット・リンパ腫／上咽頭がん	EBウイルス
成人T細胞白血病（ATL）	HTLV-I

【Slide6】

成人T細胞白血病
(Adult T-cell Leukemia; ATL)



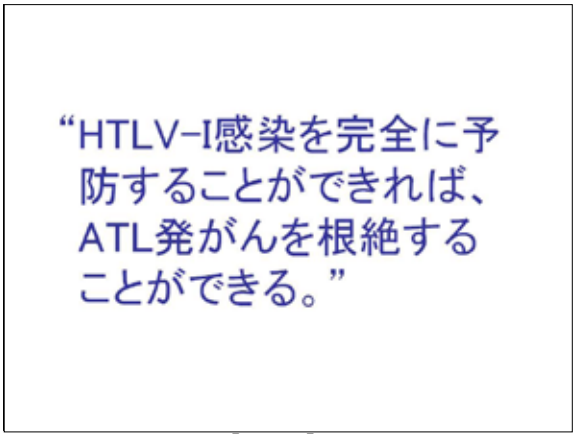
【Slide7】

成人T細胞白血病（内山、高月ら；1977）
Adult T-cell Leukemia; ATL

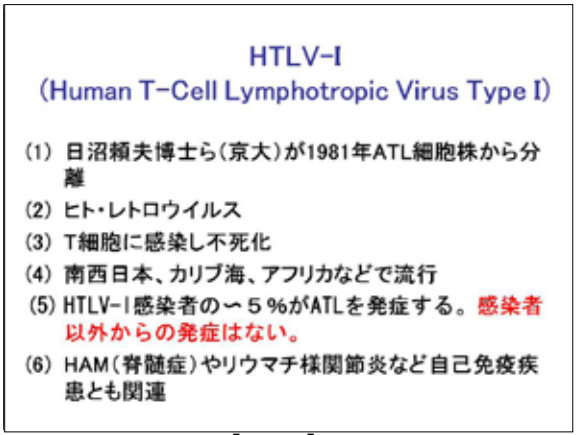
(1) 白血病細胞の独特の形態（核の切れ込み）
(2) 皮膚病変
(3) 高カルシウム血症
(4) 化学療法剤が効かない
(5) 治療成績はきわめて悪く，ほとんどの患者が発病2年以内に死亡する。
(6) 南西九州・沖縄出身者に多い
(7) 家族内発症例

【Slide8】

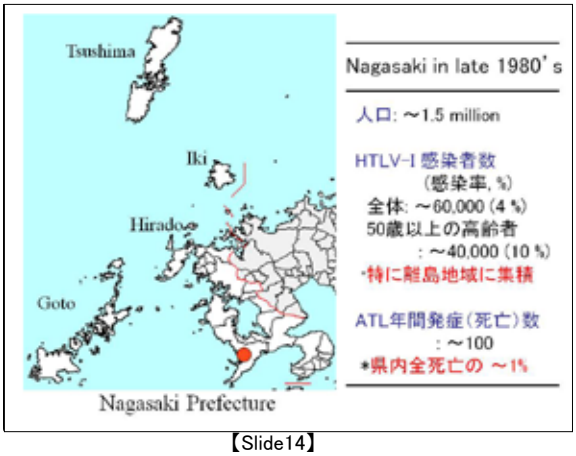
【Slide9】



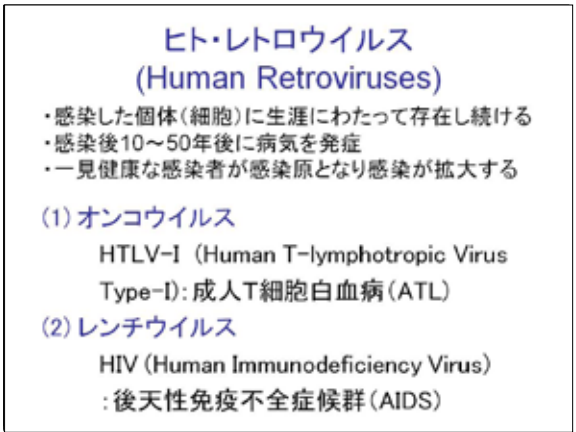
【Slide13】



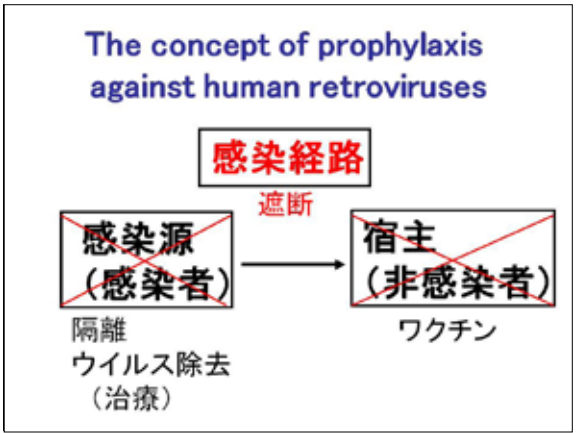
【Slide10】



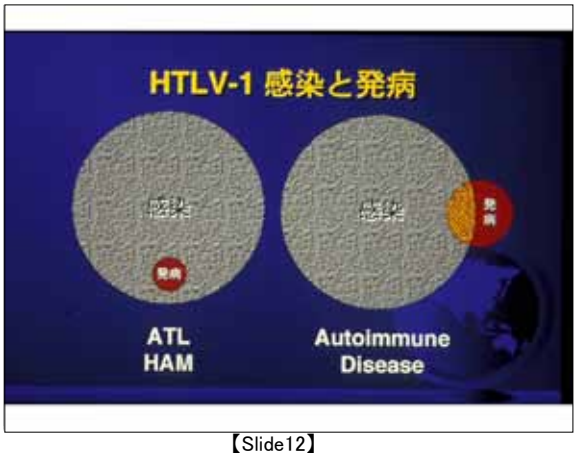
【Slide14】



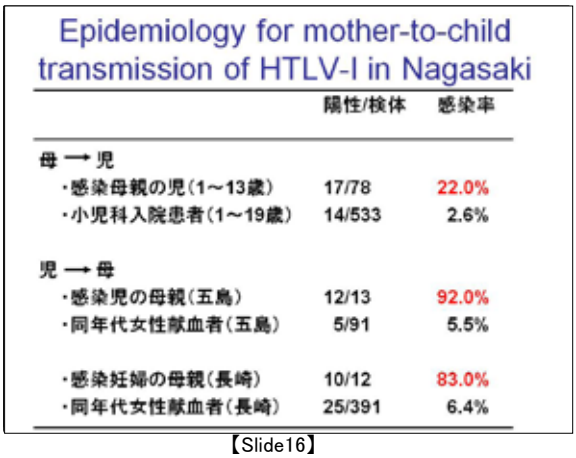
【Slide11】



【Slide15】



【Slide12】



【Slide16】

Mother-to-child transmission of viruses

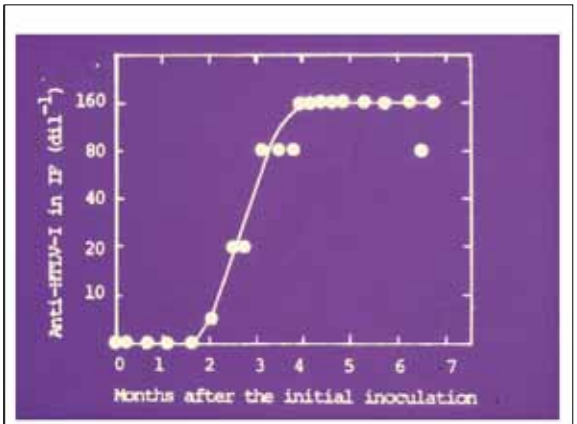
・子宮内感染（経胎盤感染）

・産道感染（周産期感染）

・母乳感染（出生後感染）

【Slide17】

【Slide18】



【Slide19】

Transmission pathways of HTLV-I and ATL

水平感染 ✗→ ATL

Blood

Sex

垂直（母子）感染 → ATL

Breast milk

【Slide20】

ATL Prevention Program (APP)-Nagasaki

～目的～

- HTLV-I 母子感染経路が母乳を介した生後感染であることを最終的に確定すること
- HTLV-I 母子感染の頻度を減らし、最終的に長崎県の年間ATL 発症を1例以下にすること。

【Slide21】

APP-Nagasaki since 1987

- 県下の全妊婦を対象とした血清HTLV-I 抗体検査
- HTLV-I 感染妊婦への母乳栄養回避の勧奨
- 出生児の追跡調査
- 長崎県を挙げた介入研究（Intervention）
  協力機関：長崎大学、長崎県産婦人科医及び小児科医会、長崎県

【Slide22】

ATL Prevention Program Nagasaki '87

産科

1.妊婦HTLV－1抗体検査説明
↓同意を得られた方について
2.HTLV－1抗体検査（妊娠後期）
↓陽性者
3.結果告知、ATL・栄養方法の選択などについて説明
↓
4.妊婦の自己決定による栄養方法の選択
＊人工栄養 ＊ 母乳（＜or＞ 6ヶ月）
↓
母乳分泌抑制（薬剤）
5.フォローアップについての説明

小児科 児のフォローアップ
＊17指定病院小児科
＊6. 12. 18. 24. 36ヶ月採血

【Slide23】

Summary of APP Nagasaki 1987-2009

HTLV-I 抗体検査妊婦の総数
：255,340*
*県内全妊婦の 80％ 以上に相当

うち HTLV-I 感染妊婦
：8,502 *
*感染妊婦比率: 3.3％

【Slide24】

HTLV-I 母子感染率
Bottle- vs Breast-Feeding

	出生児総数	感染児数	感染率(%)	P values
Bottle-Feeding	1,001	27	2.7	P<0.01
Breast-Feeding	311	55	17.6	P<0.01
短期（≦6ヶ月）	134	9	6.7	P<0.01
長期（>6ヶ月）	177	46	26.0	P<0.05

【Slide25】

CONCLUSION

1. 母乳が母子感染の主要ルートである
2. 感染のリスクは母乳の授乳期間の長さに依存する。
3. 未知の母子感染ルートが存在する
4. 完全断乳が最も有効な母子感染予防方策である

【Slide26】

Estimation (1)

- APP Nagasaki は、これまでに1,800例以上の HTLV-I 母子感染と90例以上の将来のATL発症を予防した

・血清スクリーニングで判明した感染妊婦総数: 8,500
・うち、人工栄養に同意妊婦数: 7,600 (90%)
・母乳(長期)による母子感染確率: 26.0%
・人工栄養による母子感染確率: 2.7%

7,600 x (0.260−0.027) = 1,770

・感染者からのATL発症確率: 5.0%

1,770 x 0.05 = 88

【Slide27】

Estimation (2)

感染率(%)	HTLV-I感染者数（年間予測）	ATL発症数（年間予測）
親世代		
3.2	800	40
次世代		
0.8 （母乳）	200	10
0.1 （断乳）	25	1

各年齢人口: 25,000
母乳による感染率: 0.26
母乳以外による感染率: 0.03
HTLV-I感染者の生涯ATL発症リスク: 0.05

【Slide28】

“長崎県における年間ATL 発症数は、次世代もしくは次々世代において1以下になる。”

【スライド 29】

The issues remained to be challenged

1. 母乳以外の未知の母子感染経路は何か？
2. 感染を告知した女性（母親）のATL発症予防方策が未開発
3. HTLV-I感染予防効果か、母乳の効用か？
4. 長崎など流行地以外の地域（東京など）における母乳回避介入の必要性：HTLV-I総合対策（2010年12月厚生労働省）

【Slide30】

Thank you very much for your attention.

【Slide31】

お互いの存在に「感謝」し…

We need to ‘appreciate’ their each and every existence

感謝（マハロ）
mahalo (Appreciation)