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Chairman, Board of Directors: Kenichi Ishibashi, MD, PhD

Editors: K. Ito, MD, PhD, T. Kondo, MD, PhD,
K. Ichihashi, MD, PhD, T. Murakami, PhD, R. Nagai, MD, PhD,
I. Taniguchi, MD, PhD, and T. Yamazaki, MD, PhD

3F MK Sangenjaya Building, 1-15-3 Kamiyama, Setagaya-ku, Tokyo 154-0011, Japan.
TEL 03(5486)0601 FAX 03(5486)0599 E-mail: imsj@imsj.or.jp <http://www.imsj.or.jp/>

The 448th International Symposium on Therapy

The 448th International Symposium on Therapy was held by the Zoom Webinar on March 18, 2021. Dr. Ko Ichihashi, Director of the International Medical Society of Japan (IMSJ), presided over the meeting.

Changes to and problems with vaccinations

Introductory Message from the Chair

Ko Ichihashi, MD, PhD
Director, IMSJ

The theme of the 448th International Symposium on Therapy is "Changes to and problems with vaccinations". Vaccination is one of the most useful methods for preventing diseases; however, there are various problems regarding vaccination in Japan and it is inadequately performed compared to other countries. In recent years, it has become possible for multiple vaccines to be regularly given, and rules on giving simultaneous vaccinations and restrictions on vaccination time-intervals have been relaxed. Currently, vaccination against COVID-19 has started, so the general public is more and more interested in the effects and side reactions of vaccines.

In Lecture I, Mahito Mine, MD and the Director of the Mine Pediatric Clinic will give us a lecture on the "Circumstances of vaccination in Japan". He will explain the current vaccination situation, as well as various problems in the history of vaccination in Japan. He will also mention the COVID-19 vaccination situation.

In Lecture II, we will ask Ryo Konno, MD, PhD and Professor in the Department of Obstetrics and Gynecology at Jichi Medical University Saitama Medical Center to give a lecture titled "the HPV (Human papillomavirus) vaccine - Light and shadow in Japan and the world". He will talk about the effectiveness of the HPV vaccine, how its inoculation rate is still low, as well as problems with it in Japan, from the perspective of world standards.

Lecture I

Circumstances of vaccination in Japan

Mahito Mine MD
Director
Mine pediatric clinic

Until a few years ago, the control status of VPD (Vaccine Preventable Disease) by vaccines in Japan was not sufficient. Measles was recognized as an excluded country by the WHO in March 2015, but rubella has been prevalent every few years, especially among men in their late 30s and 50s. Before October 1, 2014, when two vaccinations were scheduled, chickenpox occurred in about 1 million patients each year. Around 2013, hepatitis B was expected to cause more than 5,000 new infections each year, including mild and latent infections. Until October 1, 2020, when the rotavirus vaccine was routinely inoculated, rotavirus gastroenteritis was the most common gastrointestinal infection in children. Mumps is still prevalent every few years.

Here, I will summarize the characteristics of infectious diseases in recent children in Japan. First of all, the number of infectious diseases has decreased significantly, and the number of diseases targeted for routine immunization has decreased dramatically. On the other hand, the mumps epidemic continues every few years. As gastrointestinal infections, rotavirus infections are rare and norovirus infections are high. Influenza in children is endemic almost every year. It is characterized by many respiratory tract infections caused by RS virus, human metapneumovirus, mycoplasma, adenovirus, etc. In other words, it can be seen that the incidence of VPD is greatly reduced by regular vaccination in infectious diseases in which the vaccine exists.

Certainly, the "vaccine gap" between Japan and other countries has improved considerably in more than 10 years. However, despite the fact that it is a

regular vaccination in other countries, the vaccines that are voluntarily vaccinated in Japan are the mumps vaccine, meningococcal vaccine, and pediatric influenza vaccine. Is done.

In addition, the inoculation interval between different vaccines was also significantly different from the international standard until October 1, 2020. Under the Japanese vaccination system, until now, when different vaccines are given after inactivated vaccination, there is an interval of 6 days or more. If different vaccines were given after all live vaccinations, there would be an interval of 27 days or more. From October 1, 2020, it has been changed to an interval of 27 days or more only when a different live vaccine is given after the injection of the live vaccine, which has been common in other countries for a long time. This is expected to reduce the number of cases of incorrect vaccination intervals, which had to be reported as incorrect vaccinations, by half.

In addition, even with the COVID-19 vaccine, which is currently being inoculated, it is necessary to devise ways to inform medical personnel because the inoculation procedure is intramuscular injection rather than subcutaneous injection, which is commonly performed in Japan. Normally, the main focus is on sharing information on the effectiveness and safety of vaccines and how to respond when adverse reactions occur, but in Japan, explanations of intramuscular injection techniques and precautions and practical training are also required. Also, at the inoculation site, many vaccines are given individually at medical institutions in Japan, so mass inoculation to inoculate many people in a short period of time, such as pandemic vaccines such as COVID19 vaccine, inexperienced, information sharing and training are required for these as well.

In this way, the situation regarding vaccines in Japan still has many parts that differ from international standards, and there are many problems in terms of controlling VPD by vaccines. It

may be necessary to regard the current situation in Japan as the perfect time to approach international standards at this time when the interest and expectations for vaccines are increasing due to the COVID19 epidemic.

Lecture II

HPV (Human papillomavirus) vaccine - Light and shadow in Japan and the world

Ryo Konno MD, PhD.

Professor

Department of Obstetrics and Gynecology,
Jichi Medical University Saitama Medical Center

What is National immunization program (NIP)? Vaccination is for individuals and families, is resulted to protect life and health in the country, then the mission should be more efficient and effective for use of financial resources.

Recently, in Japan, the numbers of cervical cancer incidence and deaths increase, especially in young generation. In 2011, about 400 women under the age of 44 died. Among the developed countries, Japan has the highest number of cervical cancer incidence and mortality, but this is because of the low screening coverage. Among Asian countries, Japan was used to be a country with lower incidence and mortality owing to the early start of cancer screening, but current incidence is the same as India (14.7 per 100,000 population) and worse than China (10.7) and South Korea (8.4), respectively.

The natural history of cervical cancer has been well elucidated. Most cervical cancers are caused by HPV infection. The four steps of cervical cancer are HPV infection, the development and persistence of precancerous lesions, progression to cancer and invasion. Most women and men are infected with HPV at least once in their lifetime, but only few infected people will develop precancerous lesions and cancer. If you can get the HPV vaccine and

prevent the infection, the subsequent steps will not progress, and you can prevent the cancer.

(1) The efficacy of a domestic clinical trial and (2) the effectiveness of the HPV vaccine, which we conducted for the cervical cancer screening examinees of the Japan Cancer Society are shown below. Both are comparisons of HPV vaccinated and non-vaccinated women. (1) vaccine efficacy was evaluated on TVC naive (HPV uninfected women in the total vaccine cohort) including 20-25 years old (vaccinated 254, unvaccinated 251) women, who progressed CIN2 or more and CIN3 or more, respectively 74% (95% CI 1.1-95.3) and 100% (95% CI -417.0-100.0). On the other hand, (2) vaccine effectiveness was investigated on 3,770 vaccinated women and 30,511 unvaccinated women, who progressed to CIN2 more and CIN3 or more, respectively, 76% (95% CI 0.10-0.60) and 91% (95% CI 0.00-0.42). These results are as good as (or better than) previous reports abroad, suggesting a sharp decline in the number of cervical cancer patients if vaccination continues in the future. In addition, recent our studies suggested possible herd immunity. Herd effects are seen not only in unvaccinated women, but also in men in previous foreign reports. Then HPV vaccine is recommended for both men and women up to the age of 45 in the United States, and preventable cancers including anal and oropharyngeal cancers.

In April 2016, even before the regular vaccination of the HPV vaccine, just FAKE NEWS was taken up by the media, and it caused the drastic decrease of HPV uptake from 70% down to 0.1%. The reason is that the delay of governance of vaccine administration without internationalization, and it resulted not to make decisions based on the medical and scientific grounds presented by WHO and others. The term of side reactions (effects) in Japan and in Japanese are used with confusion of adverse events. Japan has not registration program of NIP and does not grasp the background incidence of prior to the vaccine program. The concerns of HPV vaccination program were the inaction of the crime

and will cause the worst tragedy due to the failure of vaccination governance.

Conclusion

HPV vaccine is highly effective and highly safe. There is no reason to hesitate to be vaccinated because of FAKE NEWS with so-called side reaction. Resurrection of proactive recommendation as soon as possible. Relief for women up to the age of 26 who have missed or have not completed vaccination (catch-up as regular vaccination). Expanded regular vaccination to gender neutral aged 12-26 persons. We should learn a lot of lessons from HPV and COVID-19 vaccination and reform the national immunization program.

Discourse

Introduction of the speaker of discourse

Ko Ichihashi, MD, PhD
Director, IMSJ

Takahiko (TK) Sakanoue, CEO & President of HIYA Pharmaceutical Co., Ltd. will give us a lecture entitled "How to carry on 400 years of traditional business". It will be very interesting to listen to stories about the roots of the well-known Hiya Kiogan and the reason why they were able to continue their business for 400 years.

Discourse: 400 Years of Traditional Business & Key Points of Continuation

Takahiko Sakanoue
CEO & President
Hiya Pharmaceutical Co., Ltd.

Our company has 400-year history of the household medicine "Hiya Kiogan" since our foundation in 1622 (Genna 8).

I would like to talk about how this family business has been continued in a changing era as well as the historical background.

1.400-year History and Hiya Kiogan

First of all, our location has never changed at Temma, Osaka for these 400 years. Why didn't it change?

In old times, people who finished their business at the Dojima Rice Exchange, visited and worshiped at Osaka Temmangu shrine, drank glasses of Temma's sake with the eel from the Yodo River as a side dish, crossed the Temmabashi bridge and took passenger boats called "Sanjikkoku-bune" from the pier at Hachikenya-hama to go to Kyoto. Hiya Kiogan used to be sold for souvenirs before boarding the boat on the back approach of Osaka Temmangu. Small, expensive and precious medicines were ideal for souvenirs. So, many people visited our shop to buy Hiya Kiogan from all over Japan, just like "Explosive Buying" by the borderless visitors from overseas today. Therefore, our service and dedication to Osaka Temmangu has been an indispensable task.

The product name "Hiya Kiogan" consists of two parts. One part is "Hiya". In the Edo period, our shop had a rain gutter on the roof-end to prevent customers from getting wet in the rain. "Hiya" with the meaning of "shop with rain gutter" became our trade name. "Kiogan" was named by expressing how to improve symptoms. It means "medicine with outstanding and satisfactory effects for various diseases and symptoms. The original formulation of Kiogan was said to be brought to Japan by a priest Ganjin (Jianzhen) in the 8th century.

The formulation consists of natural plants and animals, based on a Chinese medicinal theory. "Musk" is the secreted material of musk deer, which is also used in perfumes such as Chanel #5. "Oriental Bezoar" is gallstone of cattle only fed with natural pasture. In these days, its supply has become very tight due to the expected effectiveness on the aftereffects of intracerebral hemorrhage in the Chinese medical industry. "Bear Bile" is bile acid of Brown Bear or Asian Black Bear bile acid, which is also a main ingredient of Toyama's traditional medicines "Yutan-en" and "Hangontan" which became famous in the 1690 Edo Castle Abdominal Pain Incident. As herbal ingredients, "Ginseng" is

widely used in health foods and "Agarwood" is famous as a high-class incense.

2. What is the Key to Continuation?

In Japanese society, the birth rate has declined significantly in these 75 years after World War II. The birth rate of 1947 in the baby boom was more than 4 points (2.7 million births), but nowadays it stays 1.44 (0.94 million), decreased to 1/3. It would have been difficult to continue the business if we had just kept doing the same thing.

Accordingly, we have made structural changes of our company by clarifying "What should be changed" and "What should NOT be changed".

For instance, we have changed followings:

- 1) New product development
 - Widen product categories based on "Hiya Kiogan" brand
 - Cold medicine, Chewable tablet for cough, Antipyretic suppository, Syrup medicine for cold & cough, etc.
 - Hiya Kiogan Gold for adults
 - Heart tonic pill for adult, "HIXINGAN" characterized by Oriental Bezoar
- 2) New application development
 - Widen indications from current Hiya Kiogan (Night crying / Peevishness)
 - Clinical trial by Chinese medicine clinic in Taiwan
 - ex) Insomnia, Phobia (Panic, Anxiety), Hyperactivity disorder, etc.
 - Clinical trial by E-da Hospital in Taiwan
 - ex) Improving impaired consciousness and shortening recovery period in patients with ischemic stroke
- 3) New Method of Information Provision & PR.
 - Newspaper, Magazine >> TV, Radio >> Internet, SNS
- 4) New Route of Information Provision & Supply
 - Sales in our Shop (Temma, Osaka)
 - >> Sales through Distributors (Domestic Drug Stores)
 - >> Sales in internet / Cross-border e-commerce

"What should NOT be changed" is brand and reliability.

3. Conclusion

400 Years of Traditional Business & Key Points of Continuation

→ Business operation by classifying "What should be changed" and "What should not be changed".

What should be changed:

- Practical aspects such as products, uses, contents & means of information, supply system, etc.

What should not be changed:

- Traditional brand business of "Hiya Kiogan"
 - Keep building reliability for the brands
 - Thanks and gratitude to the received favors

I believe the above-mentioned is a basic principle for every type of industry, and sincerely hope it will be helpful to everyone at International Medical Society of Japan.