Introspection, Counterplot, and Future Strategic Planning after Epidemics of Infectious Diseases - For the Celebration of the 21st Anniversary of the Epidemiology Bulletin

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A. Introduction

The Epidemiology Bulletin in Taiwan has been in publication for 21 years. During this time, Taiwan's Department of Health has been in cooperation with the USA's Centers for Disease Control and Prevention, and through this association and improvements in our educational systems, we have cultivated professionals capable of meeting the challenges of epidemics of infectious disease. Of equal importance have been the experiences we have had with our own outbreaks of several infectious diseases. Successful or not, our sense of responsibility has been increased, our skills at investigating the pathogens and mechanisms behind epidemics have been honed, our sense of responsibility and dedication to disease prevention has been upgraded professionally, and we now are more capable to provide an array of adequate public health services both domestically and internationally. On the other hand, since Taiwan's withdrawal from the United Nations in 1972, we have not been able to participate in any public health related technical conferences or training workshops held by the World Health Organization (WHO), and have, therefore, forced to rely on our own professionals to meet the challenges of unexpected epidemics and make the necessary timely changes needed to respond to protect the health of our people. Much has occurred in twenty years; thus, twenty years is not an insignificant period of time for a responsible journal to contribute to the protection and betterment of the public health of our society. The Epidemiology Bulletin, founded at the same time Taiwan's public health system began its transformation, has in addition to guiding health professionals on disease prevention and control, has kept the public, policy makers, and the professionals in our health care system well informed on what is happening internationally with regard to disease prevention and control. Hence, in its first 20 years, the Epidemiology Bulletin has provided insights into the epidemiologic characteristics of Taiwan's infectious diseases, has lead the ways to the establishment of different infectious disease surveillance systems, has shown how new diagnostic technologies can help in the timely detection of disease outbreak, and has often thoughtfully discussed on how to plan and implement better public health policies based on epidemiologic results and statistical analysis. With this twenty-year accumulation of experience and a strong desire to protect the health of all people, we are now more than ever prepared and excited about our role in the effective prevention and control of infectious diseases in the future.

B. Historical Lessons of Major Epidemics

From John Snow's field investigation of cholera epidemic in London [1] to the more recent and seriously widespread dengue hemorrhagic fever (DHF) pandemic in South America and Asia, outbreaks have simultaneously sprouted up like bamboo roots after heavy rains [2]. The increased frequency of epidemics and the shortening of epidemic time intervals of Ebola hemorrhagic fever in Africa [3], the burst of severe acute respiratory syndrome (SARS) across countries between 2002 and 2003 [4], and the cross-county and cross-continent spread of the emerging avian influenza virus H5N1 from Asia to Europe and Africa since 2003 [5] demonstrate several important epidemiological characteristics of infectious diseases. First, the epidemics of infectious diseases often spread from the areas where they originate to the places where they do not normally take place. Second, when an epidemiological investigation starts quite late or the outbreak is still bewildering with regard to the continuing presence of both source of infection and mode of transmission, the case numbers and fatalities increase greatly. Third, increased more convenient travel today leads to increase possibility of pandemics, as infectious disease can spread more rapidly to areas undetectable, unfamiliar and unprepared for them. In the past, epidemiologists analyzed the epidemic curves, geographical distributions, and risk/preventive factors *after* epidemics. Many of these methods are reserved for post-epidemic study, after numerous deaths, group health impairment, and economical loss, and can only prevent the next wave of epidemics, but cannot make up for loss of loved ones or be suitably used to study such pathogens as human immunodeficiency virus (HIV) which persistently infect their hosts [6]. Indeed, a large-scale epidemic of any infectious disease greatly impacts the families of the infected and society; the damage is even greater in under-developed areas/countries. Indeed, a large-scale epidemic of any infectious disease creates great impact on the family of a patient and society; the damage is even greater in under-developed areas/countries. Therefore, it is not humane to wait until the increase of case numbers or fatal cases to more than ten thousand people in a major epidemic to start investigating the epidemiological characteristics and associated factors of the infectious disease.

Looking forward, an epidemic can be monitored and controlled at the beginning when there are still very few cases, cross-area/country epidemiological investigation becomes more important. In other words, when case numbers of one infectious disease are less than 10 in one area, it would be easier to discover important clues if we could combine data collected from cases of the same disease in other areas through regional integration or epidemiological linkage. For example, by integrating data from the SARS cases in Hong Kong, Vietnam, Canada, and Singapore in 2003 through international collaboration on the cross-country epidemiological investigation, we were able to prevent further spread of the disease internationally. Therefore, future epidemiological investigation of infectious diseases can be more professional, integrated, and international. In fact, we presented an *"integrated"* approach to human and animal influenza virological surveillance at the *International Symposium on "Options for the Control of Influenza IV"* in Greece in 2001 and also to WHO along with an application for a grant four years ago [7]. Unfortunately, due to political barriers, we were not given the opportunity to contribute our ideas as much as we would have liked to the international community, and nor could we help the urgent needs of avian influenza in mainland China. This vision on integrated surveillance becomes especially important after the quick emerging of the human avian influenza cases in Turkey from 2005 to 2006. Since then, many European and American countries have actively started preparing for pandemic influenza.

C. The Important Epidemics of Infectious diseases in Taiwan and the Counterplots

Taiwan had very comprehensive infectious disease reporting system with detailed records during the Japanese Colonial Period. At that time, several outstanding Japanese parasitologists, who paid careful attention to the prevention of parasitic infections in Taiwan. Therefore, Diphtheria, rabies, plague, and other early human infectious diseases were all eliminated during the Japanese occupation or around the retrocession period of Taiwan from Japan to Republic of

China in 1945. The elimination of malaria was also accomplished by cooperating with American entomologists, who nurtured public health professionals here. In 1965, WHO awarded a certificate confirming malaria had been eradicated in Taiwan. In addition, Dr. Ping-chin Fan, who successfully controlled filariasis by using medicated salt in Kinmen Islet, received international recognition [10]. The control of poliomyelitis became more feasible after the administration of early immunizations strongly recommended by Dr. H. Y. Wei [11]. The public health professionals in 1950s in Taiwan aiming to hold malaria in check showed a spirit and determination comparable to John Snow's efforts to control cholera. Fully dedicating themselves to the health of our people, these brave public health personnel pedaled old-fashioned bicycles carrying heavy insecticide-spraying equipment, entered each house in the backcountry, personally moved the furniture out of people's home, and fumigated every possible corner very carefully. Their hands-on and practical spirit is worthy of today's current public health educators appreciation and gratitude, should make the best role model. Therefore, how to arouse the young generation's passion, to encourage them to serve in the places where it is most needed, and to spur their interests in disease prevention is the future direction for all current public health educators to put more efforts.

Altogether, the successes in control of infectious diseases before and after the restoration of Taiwan were only possible because of the concerted effort of selfless people focused on understanding and controlling the triad of the infectious disease: pathogen, host, and environment. Their approaches to eliminating malaria were very professional for the times and even constantly examined possible pesticide resistance as they sought to eliminate the hosts of the disease. These contributions to the prevention of infectious diseases, in addition to the birth control policies advocated by Mr. K. T. Li and Mr. Tse-chiu Hsu, served as important cornerstones of the Taiwan's great economic growth period in the 1970's which eventually won us the recognition as being one of "the four tigers of Asia."

There have been several important epidemics of infectious diseases in Taiwan over the last 40 years that have attracted public attention: (1) the 1962 island-wide epidemic of cholera, which made the export of bananas, a major export item, to Japan difficult [12]; (2) the 1981 Hsiao-Liu-Chiou Islet epidemic of dengue fever (DF) caused by dengue virus serotype 2, which had an 80% attack rate [13]; (3) the 1982 island-wide epidemic of poliomyelitis resulting in 1031 poliomyelitis cases and 98 fatalities and causing great panic among the Taiwan's parents [14]; (4) the 1983 epidemic of typhoid involving antibiotic-resistant strain of *Salmonella typhi* in Chu-Tung township [15]; (5) the 1987-1988 large-scale epidemic of dengue fever in Kaohsiung and Pingtung caused by dengue virus serotype 1, which caused the overcrowding of hospitals all over southern Taiwan [16]; (6) the 1988-1989 island-wide measles epidemic which went through over-wintering and spread for many months along the train stations [17-18]; (7) the 1998 island-wide epidemic of enterovirus 71, which caused 405 severe cases and 78 fatalities, again striking fear and panic in Taiwan's parents [19]; (8) the 2001-2003 epidemic of dengue/dengue hemorrhagic fever (DHF), caused by dengue virus serotype 2, the most serious epidemic of dengue with a very high case-fatality rate in Taiwan in the recent 60 years, totaling 5388 DF cases, 242 DHF cases, and 13 fatal cases in 2002 based on the documentation from Taiwan-CDC [20,21]; and (9) the outbreak of severe acute respiratory syndrome (SARS) between March and June of 2003, in which the hospitals, themselves, became a important source of infection [22].

From several large-scale epidemics of infectious diseases in Taiwan in past years, our local health bureaus, once directed by military personnel with no medical background, are now led by directors with public health or medical backgrounds. They are not alone; however, the awareness of epidemics still relies on self-motivated physicians with strong social responsibility and a watchful eye for signs of emerging epidemics. Control of every epidemic, too, requires the efforts of many courageous and dedicated public health nurses, primary staff members and section chiefs inspired by their love for humanity and such leaders as Mr. Fu-Chih Lee of Taiwan's Provincial Department of Health, who led field investigations for every reported case of cholera, and Mr. Yin-Chang Wu, who established dengue virus laboratory surveillance and worked very hard in finding the source of infection for every laboratory confirmed positive dengue case. Yet, in an era of finely divided specialties, fewer people are willing to participate in front line field investigation of epidemics, to perform their experiments alone constrained by time, and to intensively seek ways to improve the intelligence of the surveillance systems. Finding people able to do all these three would be even harder. In a time marked by increasing chronic diseases and decreasing infectious diseases, it is even more difficult to find young professionals interested in infectious diseases and willing to work in local health agencies for lower salaries.

Large-scale epidemics of infectious diseases in Taiwan have changed from the frequently seen vaccine preventable infectious diseases [23] to the "infectious diseases without preventive vaccines." In the past, from the 1982 island-wide epidemic of poliomyelitis and the 1988-89 severe epidemic of measles [14,17-18], epidemiological findings have been applied to the standardization, systematic improvement, and routine evaluation of immunization policies. This successfully decreased the case numbers and minimized the number of areas to which the diseases spread, leading to no cases of poliomyelitis being found in Taiwan since 1983 [24]. The frequency of hepatitis A in the uplands has also been greatly reduced [25]. The epidemics of emerging and re-emerging infectious diseases without preventive vaccines are of great concern today. Through the integration of the epidemiological field investigation, experimental examination and public health practice, the dengue research team in Taiwan found that dengue hemorrhagic fever cases appeared only after the cases of dengue fever [26] and occurred more frequently in places with a clustering of dengue cases. In other words, if the less dangerous dengue fever could be controlled properly, the more serious dengue hemorrhagic fever cases could be prevented from fast spreading as fast as it did in South America and Southeast Asia [27]. In addition, using geographical information system (GIS) [28], we found that the range of population movement played an important role in swift dispersion of the cases during the summer of 2002 [29]. Our molecular studies also found that viral titers in the dengue hemorrhagic fever patients were much higher than that of dengue fever patients, particularly at the stage of defervescence [30]. Together, once a dengue hemorrhagic fever patient is found, it needs for fast and comprehensive preventive measures as well as educating the patients to reduce the range of dispersion and to prevent the too fast spread epidemic far from getting out of control. Controlled in this way, public health personnel can be spared the arduous task of extinguishing an epidemic. Otherwise, control efforts might be far behind the increasing case numbers. Another example is the 1998 epidemic of enterovirus 71. Since the time it was first discovered, seroepidemiological studies have found: (1) children less than 3 years old to be a high risk group; (2) the infected siblings of a family to be important sources of infection; and (3) using multivariate analysis, the risk of infection to be higher for those who attending kindergartens or day-care centers [adjusted odds ratio, OR, was 1.8; 95% confidence interval (CI) was 1.3-2.5], having contacts with patients of hand-food-and-mouth disease (HFMD) or herpangina (adjusted OR:1.6, 95%CI: 1.2-2.1); and those living in the countryside (adjusted OR: 1.4%, 95% CI: 1.2-1.6%) and having more family members (adjusted OR: 1.4%, 95% CI: 1.1-1.7) [19]. In the recent years, these data have been applied to the children's health education in day care centers, kindergartens, and the countryside. This has resulted in a dramatic decrease in severe and fatal cases of enterovirus 71 and has shown the importance of epidemiological studies to disease prevention. Altogether, when our surveillance system concerns itself with subclinical infections as well as mild to severe cases, and fatal cases [31-33], epidemiological methods can uncover the interrelationships among these four types of infection outcomes, and help us better understand, for example, what conditions would allow the severe cases of dengue hemorrhagic fever to arise more easily. With an effective surveillance system, important epidemiological factors can be detected earlier rather than later, after the occurrence of many severe cases, as was done in past. These approaches can undoubtedly increase control efficiency and reduce the health threats presented by severe cases of enterovirus infection.

D. The Challenges of Emerging/Re-emerging Infectious Diseases

With the rapid changes and globalization occurring in the world today, different countries/areas are interacting more and more with each other. More noticeable now is the disparity between the economically advantaged countries and the poorer countries, largely due to the fast rise of knowledge, centralization of resources and the industrial planning and management which aims at cost-effectiveness. Unfortunately, severe epidemics of infectious diseases often occur in places with lower educational and economical standards. To make matters worse, they are usually not found until there is already a large number cases or until the diseases are already spreading rapidly. By that time, pathogenic microbes have already been widely spread to many different areas. In an era of global village considering how conveniently people are traveling internationally these days, if we do not handle infectious disease well in the poorer countries, then we are at risk of pandemic public health disaster.

Looking as the macroscopic ecology of microorganisms, the ability of pathogens to cross species barrier greatly influences the ability of other microorganisms such as bacteria, viruses, and other microbes or plasmid with low pathogenicity that have reached "balanced pathogenicity" in their ecological niches to disseminate cross species [34]. It is very likely for a pathogen, after jumping into a different host, to develop into a microorganism with higher virulence or stronger drug resistance through the process of continuing evolution and adaptation with genetic mutations and phenotypic changes of the microbe. This type of variation does not usually take a long time. Knowledge of this is fueling much of nervousness surrounding the occurrence the avian influenza virus and the pandemic threat it poses to public health.

Furthermore, more attention is being paid to possible epidemics resulting from human-made pathogens or re-emerging infectious diseases. The delivery of anthrax-laced mail in Florida and several Northeastern states in the United States in 2001 [35] and the wide dispersal of West Nile virus over the United States (nearly 80%) from 1999 to 2002 [36] has instilled some fear that such "outbreaks" of emerging infectious diseases (EIDs) might become "endemic". Clearly, if the EIDs are not controlled appropriately, they can become annual endemic diseases within several years. Concerning possible epidemics due to bioterrorism attack, these two epidemics of anthrax and West Nile encephalitis have drawn the attention of the public health authorities [37]; the major causes include: (1) infectious diseases with bioterrorism potential can be disseminated to other countries through travel and international transportation within a short period of time; and (2) man-made bioterrorism of infectious diseases may cause increased incidence rate and fatality rate due to the lack of herd immunity and thus lead to unnecessary social panic. For the time being, we can only rely on early detection by public health surveillance system, the high alertness and passion of physicians, or rapid laboratory diagnosis. Taking the index case of the US anthrax outbreak as an example, the rapid dissection of the cadaver integrated with the laboratory examination using immunopathologic techniques indeed prevented numerous subsequent cases. Had this happened in Taiwan, it may have been more difficult obtain early pathological verification for fatal cases during the early period of epidemics. For example, in the 1998 enterovirus 71 epidemic in Taiwan, the traditional social beliefs on keeping the whole body of fatal cases so that parents refused scientists to take pathological examinations for understandings of pathological mechanism and better medical management once severe cases come in. Hence, in Taiwan, a timely and effective surveillance system with further advanced epidemiological methods should be implemented immediately and public education programs should be prepared in advance and even being given at this moment to make everyone a part of the disease prevention network so that possible disasters caused by unknown etiological agent can be minimized.

E. Future Prospects

In the wake of 2003 SARS epidemic [38-42], which made us vigilant and introspective, the former director of Taiwan's CDC, Dr. Ih-Jen Su, encouraged us to establish a "hospital emergency department (ED)-based real-time automated syndromic surveillance system." With such a system we could decrease the risk of nosocomial infection for hospital healthcare workers and also increase the efficiency of public health policy decision-making process. This pilot research has been initiated since July of 2003 through the collaborative efforts between the Institute of Epidemiology, College of Public Health, National Taiwan University (NTU) and other health agencies and academic institutes: the three Divisions of Health Information/ Emerging Infectious Diseases/Surveillance of Taiwan-CDC; the Department of Biostatistics and Bioinformatics of National Health Research Institutes; the four Departments of Emergency/Pediatrics/Health Information/ Laboratory Medicine of the National Taiwan University Hospital; Infectious Diseases Epidemiology Laboratory of the Institute of Biomedical Sciences, Academia Sinica; the Center of Geographic Information System (GIS) Research, Academia Sinica; the Institute of Health Informatics, School of Medicine, National Yang-Ming University; the department of Internal Medicine at Taipei Veterans General Hospital, Jen-Ai Hospital, and Wan-Fang Hospital: Taipei Medical University Graduate Institute of Medical Informatics; Taipei City's Department of Health; and Taipei City Hospital [43]. Although this work is still under research and development, its unique part is to plan together among the academic organizations and government health agencies at the very beginning because a novel influenza virus H5N1 was isolated in Hong Kong from the travelers who came back from Fujian Province of China in February of 2003 [44]; This virus presents challenges, as its genetic recombination has become complicated in both Hong Kong and China since 1997 [45]. Therefore, one major future direction for our collaborative efforts is creating an integrated scheme for public health policy and timely disease surveillance system with systematic and routine mechanisms capable of rapidly detecting outbreaks of epidemics early and reducing tragedies caused by infectious diseases like avian influenza [46-47].

Moreover, past healthcare policies in Taiwan have sought to provide full medical care at the lowest price. Seeking to reduce operating costs, hospitals have increased in size, intensified medical services, shortened the time they attend to each outpatient and overloaded their healthcare workers. At the same time, medical schools do not consider “epidemiology” as an important subject, with many decreasing course credit for such courses to one credit hour or to almost zero by devoting a meager total of ten hours to infectious disease epidemiology. This will no doubt lead to great risk of nosocomial infection. Until the 2003 SARS outbreak, past nosocomial infections were usually concealed or went unreported. Suddenly, at that time the SARS outbreak, our society started realizing infections could occur in hospitals at a great cost to society. At present, our greatest need is to fully integrate vertically and horizontally and closely ally our medical care systems with each other. With unified leadership, this would allow us to adequately manage future crises and reduce the cost of infectious disease to society.

The following are several important directions for future efforts in the control infectious diseases in Taiwan:

1. The rapid spread of information through the internet and increase in air travel by more and more populations bring the nations of the world closer together. With this closeness come awareness that we do indeed live in a global village and prevention of disease in that village in absolutely necessary. We are not only protecting ourselves; we are protecting the inhabitants of this planet. It is our duty to prevent and control local outbreaks as early as possible, which

involves more professionalized efforts and international cooperation.

2. Because the increase interactions between Taiwan and China, it becomes necessary to establish a routine cross-channel talks for the prevention of new and recurring infectious diseases, regardless of where they originate, to avoid the possible reoccurrence of the spread of infectious diseases as we faced the explosive 2003 outbreak of SARS. Less finger-pointing and more partnership are required.
3. Our successful control of SARS shows that it is very possible to rapidly control an emerging infectious disease through a modern functional system of disease prevention if humans are the primary hosts. This experience also demonstrates that strengthening the quarantine of travelers at harbors/airports entry will effectively improve the control of domestic infectious diseases.
4. Leaders in health should thoroughly understand epidemic trends of infectious diseases and seek to employ innovative thoughts and policies that can control several chronic infectious diseases, including tuberculosis and AIDS.
5. The disease prevention should not only involve top-down strategies but bottom-up strategies as well, meaning prevention can also begin at the family level, school-level, hospitals, other population-dense areas, farms, and the places where animals/wild birds gather. Clinical physicians/veterinarians/ pathologists/epidemi- ologists can play a more important role in the prevention and surveillance of disease. Microbiology and immunology, too, should be become more integrated with public health related subjects and clinical/veterinary sciences to help shorten the period of time diseases can be controlled.
6. Health care systems and medical education should be improved step-by-step over time. The education of infectious disease epidemiology should be

strengthened in medical schools and colleges. Only when physicians and nurses have basic knowledge of infection control, they feel happily and responsible to learn the importance of timely surveillance and cooperation with health agencies and save more lives than that of one patient at a time.

The famous microbiologist, Louis Pasteur said, "Success favors the prepared mind." With regard to the challenges presented by infectious diseases and their threat to public health, by systematically and comprehensively preparing for their prevention and control, we will allow ourselves the opportunity to ensure public health, and, as a result, economic growth and national security.

I would like to conclude by offering our sincere congratulations to Taiwan's CDC for its many improvements and innovative programs in our public health system since the SARS attack. In the next 20 years, the Epidemiology Bulletin also looks forward to continuing serving our society and receiving an increasing number of contributions from domestic and international researchers dedicated to the prevention and control of contagion and the health for all men and women.

F. Acknowledgements

Our special thanks to Dr. Ping-Ing Lee from the Department of Pediatrics, National Taiwan University (NTU) Hospital; Dr Clement Hsu from Kaohsiung Yuan's General Hospital; Dr. Chao-Chin Joe Chang from the Department of Veterinary Sciences, National Chung Hsing University; Tsung-Shu Joseph Wu, Ms. Yu-Tseng Chu, and Mr. Pai-Shan Chiang from the Institute of Epidemiology, NTU College of Public Health; Mr. Chuin-Chern Chen from the Institute of Bioinformatics, National Chiao Tung University, HsinChu, Taiwan; Dr. Chi-Tai Fang from the Department of Infection and Dr. Fuh-Yuan Shih from the Department of Emergency Medicine at NTU Hospital; Dr. Solomon Chih-Cheng

Chen from the Department of Health; Dr. Fu-Chiang Hu, Dr. Chin-Yin Ting, Dr. Tony Chiang and Dr. Jung-Der Wang at NTU College of Public Health; Dr. Hui-Lin Yen from Dr. Robert G. Webster Influenza Laboratory at St. Jude Children's Research Hospital; and Dr. Wen-Ju Shieh from the Centers for Disease Control and Prevention in the U.S.A. for their reviews and comments. Most importantly, we would like to thank to many primary and central public health professionals for all their contributions to public health in Taiwan.

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