An Infectious Disease Medical Policy Simulation and Gaming

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Abstract

This paper analyses a new type of infectious disease by an agent-based simulation and gaming model based on Ebola fever and dengue fever. The mathematical model such as SIR (Susceptible, Infected, Recovered) has been used to model these infectious diseases. Besides, a simulation and gaming model enables to represent the decision-making of each citizen on the computer, and al-so reveals the pandemic by the contact process among people in the model. The study challenges to design an infectious disease model in which some health policies are introduced including vaccine stocks, antiviral medicine stocks, medical staff and so on. Aside from the policies, a gaming simulation of a new type of infectious disease, which has not yet an effective vaccine, is also implemented in the model. We created a medical policy decision game dealing with infections using a serious game approach. As results of experiments, it has been found that preventive vaccine, antiviral medicine stocks and the number of medical staffs are crucial factors to prevent the spread. Besides, a modern city is vulnerable to dengue fever due to commuting by train. It has also been found that self-control and restraint on immigration are essential, and decision-making for vaccine reserve amount and medical support to the partner country where the infection has spread.

Keywords: *Infectious disease, health policy, Ebola haemorrhagic fever, dengue fever*

1. Introduction

Since history, human beings are fearful of infectious dis eases, fighting death. Today, people still have the illusion that they have been released from fear of pathogenic microorganisms. Due to the development of science and technology, pathogenic bacteria have been elucidated, and effective vaccines and therapies have been developed for infectious dis-eases that threatened human society for a long time, such as cholera and plague. Regarding plague, a plague bacterium was discovered in 1894, and in 1943 an antibiotic streptomycin effective for plague and tuberculosis was discovered. To-day, cases of plague have been confirmed, mainly in Africa, but if proper treatment is performed with an antibacterial agent, it will cure.

On the other hand, infectious diseases still have been serious risk factors in the world. Smallpox has been recorded in human history since more than B.C 1100. Many other infectious diseases have imposed the risk to human such as malaria, cholera, tuberculosis, typhus, AIDS, influenza and so on. Although people have tried to prevent and hopefully eradicate them, unknown infectious diseases including SARS, Ebola fever and dengue fever have emerged in our societies.

Infectious disease models, which are SIR (Susceptible, Infected, Recovered) model and SEIR (S, Exposed, I, R) model, have been studied for years, and widely used to analyse diseases using a mathematical model. Although these models are useful to make an infectious spreading estimation, the SIR model has difficulty to find which measures are effective, because it has one parameter β as an infection rate to represent infectiveness. Therefore, it is difficult to evaluate the effect of the temporary closing of stores and school due to the influenza epidemic. The modeler has difficulty in interpreting the β. The agent-based or the individual-based approach, however, has an ability to solve these problems [1-11]. It enables to reveal the spread of an infection because it simulates the contact process among people and also represents the behaviour of each person.

In this study, we developed a model to simulate Ebola fever and dengue fever based on infectious disease studies using agent-based modelling [12, 13]. The purpose of the study is how to prevent an epidemic of infectious diseases not only using mechanisms of the outbreak but also decision making of health policy. Most importantly, we need to decide a policy where people are on the move frequently worldwide in our modern society. Besides, we should minimize the economic and human loss caused by the epidemic.

2. Cases of Infectious Disease

A. Ebola haemorrhagic fever

There is no sign of converging the epidemic of Ebola haemorrhagic fever in West Africa. Over 8000 people died as of January in 2015. Ebola haemorrhagic fever virus has the strong infectivity and toxicity.

A source of Ebola infection is allegedly by eating a bat or a monkey, but it is unknown whether eating these animals is a source of the disease. The current epidemic, which began in Guinea in Dec. 2013, 23 people have died. The authorities of Guinea, Liberia and Sierra Leone have each launched a state committee of emergency and have taken measures to cope with the situation. The prohibition of entry over the boundary of Guinea is included in these measures.

After that, the epidemic spread to Nigeria and Senegal. In September 2014, the president of MSF (Medecins Sans Frontiers) declared that "Six months into the worst Ebola epidemic in history, the world is losing the battle to contain it." Although infection of Ebola haemorrhagic fever is strong, it is not an airborne infection. It is thought that infection is caused by contact with patients' bodily fluids such as vomit, blood, flesh, saliva, mucus, excreta, sweat, tear, breast milk, semen and so forth.

There is a risk that a cough and a sneeze include the virus, so the infection risk is high within 1 meter in length of the cough or sneeze. The incubation period is normally seven days, and then the person gets infected after showing the symptoms. The symptoms in the early stage are similar to influenza. They are fever, a headache, muscular pain, vomiting, diarrhoea, and a stomachache. The fatality rate is very high; 50 to 90 per cent. There is no effective medical treatment medicine confirmed officially and several medicines are currently being tested. According to a guideline of WHO, the serum of a recovered patient is one of the most effective treatments.

B. Dengue fever

Dengue is an infectious disease caused by being bitten by a mosquito having dengue virus (Aedes). There are more than 100 countries where mosquitoes that mediate dengue virus live, mainly in tropical and subtropical regions, and it is said that there are about 100 million people worldwide annually. The first domestic infection in nearly 70 years was reported in Japan in 2014, and attention is needed even in Japan.

a) Cause and infection route: The pathogen are dengue viruses. Dengue virus has four serotypes (type 1, 2, 3, 4). Even if the virus of the same type is re-infected, it is mild by immunity, but if it infects different types, immunity may be excessive and severe. An infection will be established by biting a mosquito carrying a dengue virus. In Japan, the Aedes aegypti has not been confirmed, and domestic infections are caused by Aedes albopictus. It will not infect people directly from humans.

b) Symptoms: Typically, after a latency period of 2 to 15 days (mostly 3 to 7 days) after being bitten by mosquitoes, high fever (38 to 40 degrees Celsius), headache, orbital pain, joint pain, muscle pain, etc. Symptoms will recover in about a week. It rarely becomes severe and may cause dengue hemorrhagic fever that exhibits bleeding symptoms or shock symptoms.

The related disease is Zika fever. It is an illness caused by Zika virus via the bite of mosquitoes. It can also be potentially spread by sex according to recent reports [17, 18]. Most cases have no symptoms and present are usually mild including fever, red eyes, joint pain and a rash [16], but it is believed that the Zika fever may cause microcephaly which severely affects babies by small head circumference.

3. The Health Policy Simulation Model of Infectious Disease

We developed an agent-based simulation model of infectious disease based on Epstein's smallpox model. The model enables to simulate Ebola fever and dengue fever.

Each round consists of interaction with the entire agent population. The call order is randomised, and agents are processed or activated, serially. When an agent is activated, she identifies her immediate neighbours for interaction on each round. Each interaction results in contact, and then, in turn, the contact results in a transmission of the infection from the contacted agent to the active agent with probability.

4. Related work

A. Smallpox and Bioterrorism simulation

Epstein [6, 7] made a smallpox model based on 49 epidemics in Europe from 1950 to 1971. In the model, 100 families from two towns were surveyed. This model was designed as an agent-based model, and simulation of infectious disease was conducted using the model. The results of experiments showed that 1) in a base model in which any infectious disease measures were not taken, the epidemic spread within 82 days and 30 per cent of people died, 2) it was difficult to trace all contacts to patients in an underground railway or an airport, though a trace vaccination measure was effective, 3) although a mass vaccination measure was effective, the number of vaccinations would be huge so it was not be realistic, 4) epidemic quenching was also effective, and reactive household trace vaccination along with pre-emptive vaccination of hospital workers showed a dramatic effect.

B. Individual-based model for infectious diseases

Ohkusa [8] evaluated smallpox measures using an individual-based model of infectious diseases. The model sup-posed a town including 10,000 habitants and a public health centre. In the model, one person was infected with the smallpox virus at a shopping mall. They compared a trace vaccination measure and a mass vaccination measure. As a result of the simulation, it was found that the effect of trace vaccination dropped if the early stage of infection was high and the number of medical staffs is small, while the effect of mass besides was stable.

C. Summary of related work

From these studies, the effectiveness of an agent-based model has been revealed, yet these are not sufficient models to consider a relationship between vaccination and antiviral medicine stocks, and the number of support medical staff and medicine from other countries. In addition, authorities need to decide on the blockade, restrictions on outings including cars and railways while considering the economic loss of the policy.

5. A Health Policy Simulation Model of Infectious Disease

We designed a health policy simulation model of infectious disease based on Epstein's smallpox model. The model includes Ebola haemorrhagic fever and dengue fever.

A. The basic model of Ebola hemorrhagic fever

The family includes two parents and two children; thus, the population is each 400 from each town. All parents go to work in their town during the day except 10 per cent of adults who go to another town. All children attend school. There is a public hospital serving the two towns in which every 5 people from each town work. We assume all individuals to be susceptible which means no background of immunity. One hundred families live in two towns.

Each round consists of interaction through the entire agent population. The call order is randomized where each random and agents are processed or activated, serially. On each round, when an agent is activated, she identifies her immediate neighbours for interaction. Each interaction results in con-tact. In turn, that contact results in a transmission of the infection from the contacted agent to the active agent with probability.

The probability of contact at interaction is 0.3 at a work- place and a school, while 1.0 at home and a hospital. The probability of infection at contact is 0.3 at a workplace and a school, while 1.0 at home and a hospital. In the event the active agent contracts the disease, she turns blue to green, and her own internal clock of disease progression begins.

In the event the active agent contracts the disease, she turns a stage from no-infection to latent infection, and her internal clock of disease progression begins. After seven days, she will turn yellow and begins infecting others. However, her disease is not specified in this stage. After three days, she begins to have vomiting and diarrhoea, and the disease is specified as Ebola. Unless the infected individual is dosed with antiviral medicine within three days of exposure, the medicine is ineffective. This is an imaginary medicine to play the policy game. At the end of day 12, individuals are assumed to hospitalise. After four more days, during which they have a cumulative 90 per cent probability of mortality, surviving individuals recover and return to circulation permanently immune to further infection. Dead individuals are coloured black and placed in the morgue. Immune individuals are coloured white.

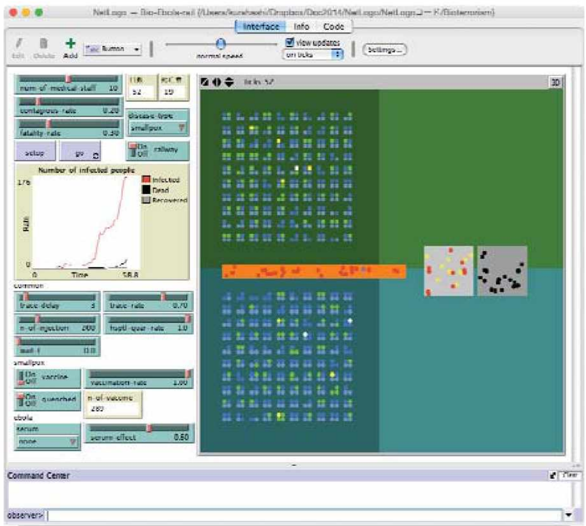

Figure 1. Interface view of a health policy simulation model of smallpox and Ebola fever.

B. The basic model of dengue fever

About 80% of cases have no symptoms which are called latent infection, but the latent patients can transmit dengue virus to other mosquitos. The incubation period of dengue virus disease is not clear, which is likely to be 3 to 9 days. After the incubation period, the symptoms including fever, skin rashes, conjunctivitis, muscle and joint pain, malaise, and headache occur and last for 6 days. Dengue virus dis-ease is relatively mild and requires no specific treatment, so any strategies are not selected in the model [14, 15].

In this model, a mosquito is designed as an agent as well as an inhabitant agent. Dengue virus is transmitted to people through the bite of an infected mosquito from the Ae-des. This is the same mosquito that transmits Zika. There-fore, the model of dengue fever is based on the life and habits of mosquitoes that transmit Zika. Mosquitos bite and thus spread infection at any time of day. Humans are the primary host of the virus, but it also circulates in mosquitoes. An infection can be acquired via a single bite. A mosquito that takes a blood meal from a person infected with dengue fever, becomes itself infected with the virus in the cells lining its gut. About 10 days later, the virus can be spread to other humans. An adult mosquito can live for 30 days with the virus. This model is designed on the assumption that habitats of mosquitos and climate are around south-east Japan in the Asian monsoon region in summer.

Mosquitoes live around each town, office, and school in dengue fever model. The areas they live in overlap with human regions. Therefore, the dengue virus can be trans-mitted between mosquitoes and human. Additionally, mosquitoes also live around a rail station in another dengue fever model where people use a train to commute their offices every day.

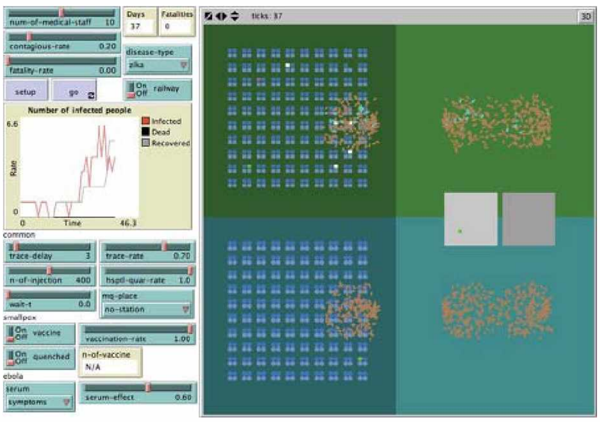

Figure 2. Interface view of a health policy simulation model of dengue fever.

We are concerned about the possibility that mosquitos are infected with dengue virus from people in both towns. Therefore, we conducted an experiment on whether the train station can be the new source of infection or not. A mosquito bite human once per four days. An infection rate from a mosquito to human is set at 0.5 and from human to a mosquito is set at 1.0.

C. Vaccination strategies for Ebola hemorrhagic fever

The vaccination strategies we can select in the model are mass antiviral medicine and trace serum. Each of them has advantages and disadvantages.

1) Mass vaccination: As preemptive vaccination, the mass vaccination strategy adopts an indiscriminate approach. First, all of the medical staff is vaccinated to prevent infection. When the first infected person is recognised, certain per cent of individuals in both towns will be vaccinated immediately. The vaccination rate and the upper limit number of vaccinations per day are set on the model for the strategy.

2) Trace serum or antiviral medicine dosing: All of the medical staff is given serum or antiviral medicine as TAP (Target antivirus prophylaxis). Given a confirmed Ebola hemorrhagic fever case, medical staff traces every contact of the infected person and provides the medicine to that group. In addition to the mass vaccination strategy, the trace rate and the delay days of contact tracing are set according to the model.

6. Experimental results

A. base model of Ebola hemorrhagic fever

The process of infection in an Ebola hemorrhagic model is plotted in Figure 3.

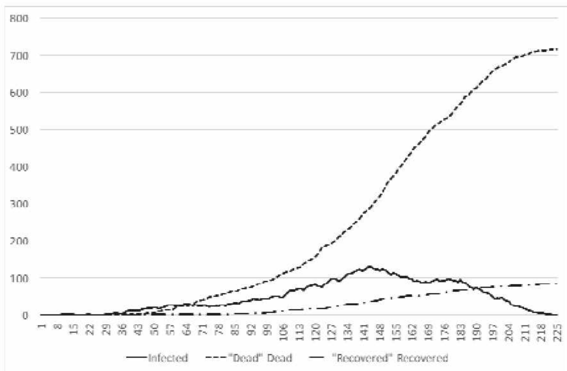

Figure 3. The experimental result of the Ebola base model: non-intervention.

The model employs non-intervention to the disease. A solid line, a dotted line and a line with marker indicate the number of infected, dead and people who have re-covered respectively. When a player adopts non-intervention, it takes approximately 231 days until convergence of the outbreak and more than 716 people have died.

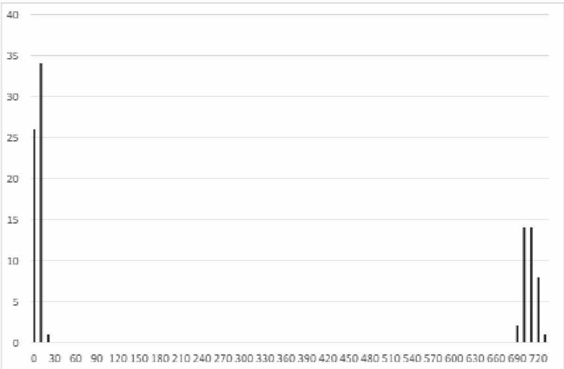

Figure 4. The frequency chart of the Ebola base model: non-intervention.

Figure 4 shows the results of 100 experiments. The number of fatalities under 20 people was 59 times out of 100 experiments, but the number of fatalities over 700 people in 800 in-habitants recorded 39 times. The result indicates that the infection phenomenon is not based on the normal distribution. It means we need to carefully consider all possibilities and risk beyond the scope of the assumption regarding infection spread.

B. Mass vaccination model

The process of infection is plotted with the mass vaccination strategy in which individuals are vaccinated randomly after three days when given a confirmed case. The policy succeeds to prevent the outbreak because the number of vaccinations per day is 600 and three-fourths of inhabitants are vaccinated per day. On the other hand, the low ability of vaccination ends in failure because the number of vaccinations per day is 400 and a half of inhabitants are vaccinated. The ability of vaccination per day bifurcates the results.

C. Trace serum strategy

It was found that the ability of more than 50 serums per day was able to control an epidemic in most cases. In the case of using public transportation to commute, however, it makes a substantial difference. Four hundred serums per day could not prevent the outbreak, while 600 serums per day succeeded to prevent it. Trace vaccination strategy is one of the most effective policies in a town where people commute by car, but a large number of serums per day, at least a half of people, is required if most of the people use public transportation systems like a railway and a bus.

D. Isolated Town model of dengue fever with/without a rail station

The process of infection in dengue model of an isolated town is plotted in Figure 5. It was found that most cases are under 30 fatalities, but a few cases are over 70 fatalities. On the other hand, Figure 6 shows that cases are polarised to different results in a modern city with a railway for a commute. The case under 10 infected people is 15 times, and the case in which all people are infected by mosquitoes is 85 times.

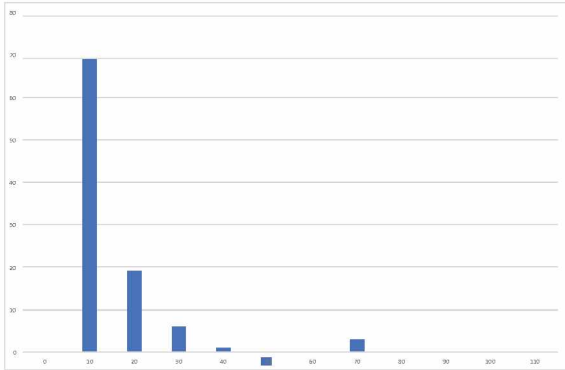

Figure 5. The experimental result of dengue fever model without a railway.

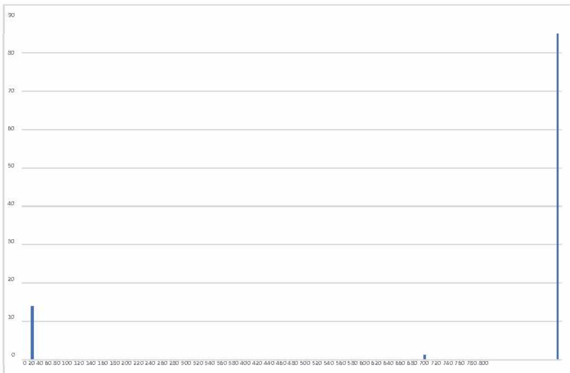

Figure 6. The experimental result of dengue fever model with a railway.

7. Infectious Disease Medical Policy Game

In the experiment so far, we have seen that it is difficult to prevent the spread of infection in areas with many rail-way users. A contemporary society faces the risk of the infection spreading across borders like Ebola hemorrhagic fever and new influenza. In this case, international cooperation of medical policy team is important. The World Health Organisation (WHO) is promoting international co-operation for measures against infectious diseases, and frequently taken up at the G7 Summit and other conferences. Therefore, in order to expand the model so far, we developed a cooperative game for countermeasures against infectious diseases and conducted an experiment to promote cooperation between two countries or regions.

In this game, it is supposed that a new type of infectious disease occurs in which the disease is similar to smallpox and Ebola hemorrhagic fever. Vaccine and antiviral medicine for the disease are already developed and provided to the market in this model. Players as authorities of two countries decide the amount of both medicines' stocks according to their restricted budget. They also need to decide the number of medical staffs, blockade and restrictions on outings. The players should consider giving support medicine and staff to countries to prevent or control its epidemic for his/her own country while taking account of economic cost and loss. Travel restrictions have a huge economic impact, while it is very effective in stopping an outbreak. Supporting to another country means decreasing its own preparations. Thus, this game has a complicated structure of trade-offs among cost, effect, cooperation and defense.

A. Medical policy model

The medical policy leaders of both countries will make decisions on the following policies. 1) Number of vaccines ordered for stockpiling 2) Number of antiviral drug orders for stockpiling 3) Employment of medical staff who can respond to Ebola hemorrhagic fever Discussions on the collaboration of infectious disease countermeasures with neighbouring countries are underway, and policies that support each other can be implemented. 4) Number of vaccine support to neighbouring countries 5) Number of antiviral drugs supported in neighbouring countries 6) Number of supports for medical staffs who can cope with infectious diseases to neighbouring countries. However, since this assistance will reduce the stock and medical staff of their country, the duty of support is exempted if danger is approaching. On the other hand, as an emergency response, it is possible to instruct the residents to go out and to order restrictions on entry and departure with neighbours. 7) The rate of a voluntary ban on leaving home, 8) The rate of restrictions on immigration, 9) Mass vaccination for all residents, 10) Trace vaccination for infected people, 11) A dose of an antiviral drug to a contact with an infected person, 12) A dose of an antiviral drug to a contact getting fever with an infected person

Players can get a report of infection status including her/his own country and a neighbouring country every ten days. Although they decide to avoid pandemic in their own country as they cooperate when they get each report, they have to cope with a difficult situation within a pre-determined budget. They are admitted to using additional budget by the government, but the smaller they use the budget, the more advantage they get to win the game. For the sake of their budget management, the following parameters are pre-defined in a game; budget, the price of the vaccine, the price of the antiviral drug, personal expenses of medical stuff, economical cost of a voluntary ban on leaving home, and economical cost of restrictions on immigration. Figure 7 shows Interface view of a health policy game.

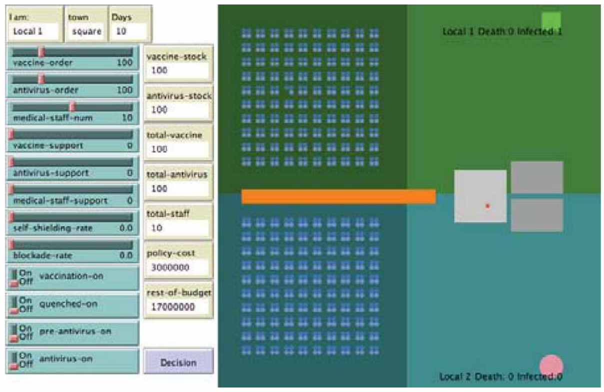

Figure 7. Interface view of a health policy simulation and gaming.

B. First experimental gaming result

Two teams of two people (C country, S country) conducted two games. After performing the briefing, the player got used to the operation of the game with a model without railroad use.

Figure 8. First experimental gaming result.

The first game was conducted with a model with railway use. The purpose of the game was to minimise the number of deaths due to Ebola hemorrhagic fever infection in their country and to minimise policy costs as much as possible. The transition of the first infection in the experiment is shown in Figure 8. The experiment result shows that the death toll in country C was 9 and the death toll in S country was 35. S country was a little delayed to order enough vaccine and supported too much to C country. C country decided to order a plenty of vaccine, antivirus drug corresponding to the epidemic.

C. Second experimental gaming result

As a result of the second experiment, the spread of infection was suppressed, and the number of deaths decreased sharply by one person each. The transition of the first infection in the experiment is shown in Figure 9.

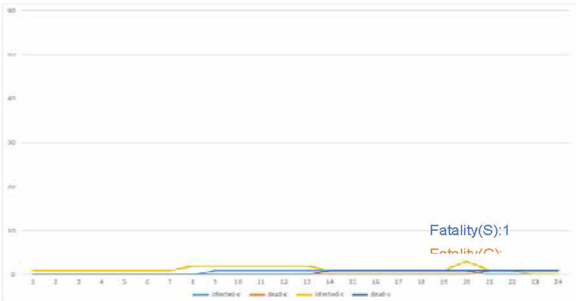

Fig. 9. Second experimental gaming result.

From experience that allowed the spread of infection at the first time, players in the two countries were expected to deepen collaborative relationships, but in fact, the actions taken by both players showed that the level of vaccine and staff support is about the same level as the first or less. Instead, the players of both countries had decided to refrain from going out of their country and early strengthening the blockade of the border. S country ordered vaccine twice as much as the 1st game when the epidemic was found. C country decided to send stuff to S country and a partial voluntary ban on leaving home and blockade.

8. Discussion

The results of these experiments are that 1) trace vaccination strategy is one of the most effective policies to Ebola hemorrhagic fever, but 2) both Ebola hemorrhagic fever and Dengue fever can be affected seriously by the case of train commuters, even if the trace vaccination strategy is adopted for them. This result indicates that a blockade of railways is a more effective alternative strategy in modern cities where most people commute by public transportation system such as a train, subway, bus and so on. Next, we conducted an experiment using a medical policy game considering inter-national collaboration. In this experiment, it is assumed that Ebola hemorrhagic fever infection occurred in two borders, and it is aimed to cooperate and prevent the spread of the virus. As a result of the experiment, the total of 44 deaths were issued in the first experiment, but the second was able to suppress to 2 people. After the first game finished, since the meeting to support each other was voluntarily held, the effect of collaborative learning by the game was seen.

9. Conclusion

In this study, we developed the infection process of Ebola hemorrhagic fever and Dengue fever as a deductive model based on ABM. Symptoms after infection and each parameter were defined based on actual data, and residents and regional models were defined as two simple regional models as possible. Experimental results showed that trace serum administration is most effective in the case of Ebola hemorrhagic fever, and complete suppression of infection is difficult when railway use is assumed for commuting as public transportation.

In addition, this study also conducts the model of Dengue fever to understand the mechanism of spreading Dengue virus via mosquitoes. As a result of experiments, it is crucial for preventing a Dengue epidemic to get rid of mosquitoes from a train station where people use it to com-mute to their office.

Besides, as international cooperation by medical authorities is indispensable today, we have constructed a medical policy game that encourages bilateral coordination and conducted experiments. As a result, experiencing the game prompted a certain degree of cooperative action, plus the prevention of the spread of infections to other countries by forced policies such as self-control and border blockade, these were chosen by the player.

This model can be applied to various institutional evaluations as a deductive model. It also gives ideas that con-tribute to game designers' cooperative behaviour and emergence, educational effectiveness, and medical policy design.

10. Acknowledgements

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