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Mini-Thesis

Effect of Breakthrough Infection on the Spread of COVID-19 Evaluated by a Flexible Compartment Model

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ABSTRACT

Vaccination causes not only a decrease in the number of su tible als in the community but also an increase in the number of individuals who ar resista to COVID-19 infection, causing a marked decrease in the total number of infected in viduals. Ad tionally, when vaccination is continued until the day when the sum of the numb recovered individuals and the number of vaccinated individuals exceeds an 'expedient herd i munity reshold', the total number of infected individuals is significantly reduced, with a considerably shorten duration of infection. However, vaccine-induced immunity in vaccinated ind duals decreases gradually, and when it decreases to below a certain threshold several weeks after vaccina ion, vaccinated individuals substantially get back to susceptible individuals and ca be infected ith COVID-19. Namely, breakthrough infection can occur. The number of suscepti individual s affected not only by the change in the number of infected individuals but also by the ge in the number of vaccinated individuals and, additionally, by the change in the mber of individuals who get back to susceptible individuals from vaccinated individuals. As a sult, th ss of the spread of COVID-19 is complicated. Using a flexible compartment model ecific to COVID-19, changes in the number of individuals infected with breakthrough infection we calculated. The model includes, as independent variables in the calculation equation the ccinati rate, the duration of vaccine-induced immunity, which indicates the validity peri d of th effectiven ss of vaccine-induced immunity, and the 'back to rate', which indicates the ra of the number of individuals who get back to susceptible individuals from vaccinated individuals in day to the number of vaccinated individuals who were vaccinated on the same day. Ch ges in the mber of infected individuals and the duration of mass vaccination to avoid the oc ence of breakthrough infection were examined in relation to the duration of vaccine-induc immu ity. The results revealed that when mass vaccination was continued until a certain day, which was d mined by the duration of vaccine-induced immunity, the vaccination rate and the start date of vaccination, breakthrough infection did not occur. However, when mass vaccina on end before that day, breakthrough infection occurred several weeks after the end of the mass ccinati program. The occurrence of breakthrough infection caused not only 'breakthrough infection' which are infections occurring in susceptible individuals who had got back from vaccinated individuals and also 'normal infections', which are infections occurring in the 'original' susceptible individuals, with severe increase in the number of infected individuals together with a markedly long durati n of infection. However, even if breakthrough infections occur, if the second mass vaccination is p formed immediately after the occurrence of breakthrough infection, outbreaks of infections, including breakthrough infections and normal infections, will be controlled.

Keywords: Breakthrough infection; Compartment model; COVID-19; Duration of infection; Duration of vaccine-induced immunity; Infection during the latent period; Isolation; Mass vaccination duration; Recovered; Susceptible; Symptomatic rate

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INTRODUCTION

Individuals infected with COVID-19 should be isolated from the community when they become symptomatic after the latent period ends, and when the isolation period ends, they become 'recovered' individuals who have infection-induced immunity (disease-induced immunity) and then return to the community. In a community mixed with infected individuals, susceptible individuals and recovered individuals, the contact rate between infected individuals and susceptible individuals is reduced by the contact of infected individuals with recovered individuals when the number of recovered individuals increases, resulting in a decrease in the number of infected individuals.

Vaccination reduces not only the number of susceptible individuals in the community but also the contact rate between infected individuals and susceptible individuals with an increase in the number of vaccinated individuals, just as recovered individuals do. Since the contact rate decreases with an increase in the number of vaccinated individuals, the earlier the start date of mass vaccination is, the smaller the total number of infected individuals becomes, and the longer the mass vaccination duration is, the smaller the total number of infected individuals becomes. Additionally, when vaccination is continued until the day when the sum of the number of recovered individuals and the number of vaccinated individuals exceeds an 'expedient herd immunity threshold', the total number of infected individuals is markedly reduced, and the duration of infection is also considerably shortened [1-3]. Therefore, vaccination practically/strongly controls the spread of COVID-19.

However, the effectiveness of the immunity acquired through vaccination does not continue permanently but decreases gradually until it is below a certain threshold, which indicates a loss of effectiveness. Namely, although the threshold level mainly depends on the properties of the COVID-19 virus and its new strains, vaccine-induced immunity has a duration that indicates the 'validity period of effectiveness of vaccine against SARS-CoV-2 infection and/or COVID-19 disease'. The duration of vaccine-induced immunity has been discussed in terms of the extent to which vaccines are effective [4-13]. For the protection effect/prevention effect (effectiveness against symptomatic COVID-19)/effectiveness against hospitalization (protection effect against severe disease), different durations are reported for different vaccines and/or for different ages of infected individuals; for example, "the vaccine effectiveness persists/decreases by 1 month and/or 6 months and/or 9 months, although antibody response levels vary across demographics such as age, sex, occupation and others". Specifically, the quantity of antibodies in vaccinated individuals decreases gradually and several weeks and/or several months after vaccination, the quantity of antibodies might decrease to below a certain threshold of immunity level at which vaccinated individuals could get infected. What happens when the immunity of vaccinated individuals drops below the threshold after a mass vaccination program ends?

When the quantity of antibodies decreases to below a certain threshold, vaccinated individuals substantially get back to susceptible individuals and can be attacked by breakthrough infection. Ohmori, showed an example that when a half of vaccinated individuals get back to susceptible individuals at once on the 151st day, the occurrence of breakthrough infection can prolong the duration of infection, with a large number of individuals infected [1].

However, as it was pointed at that time, since vaccination usually continues almost every day after the start of mass vaccination, the number of vaccinated individuals increases daily. In response to changes in the number of vaccinated individuals, the number of individuals who get back to susceptible individuals also changes daily and does not reach 0 easily until there are no more vaccinated individuals in the community. Although all susceptible individuals who have got back from vaccinated individuals will not always become infected, since susceptible individuals who have got back from vaccinated individuals will join the number of existing 'original' susceptible individuals, a long duration of infection could be induced, accompanied by a serious increase in the number of infected individuals. When does breakthrough infection occur after the end of a mass vaccination program? How do breakthrough infections affect the spread of COVID-19? How long should mass vaccination continue to prevent outbreaks of infections, including breakthrough infections, after the end of mass vaccination?

The model used here for calculating the number of infected individuals is the flexible compartment model specific to COVID-19 proposed by Ohmori [1-3]. Since the model uses the vaccination rate which can be given each day as an independent variable, the number of vaccinated individuals can be calculated each day. Since the model contains, as independent variables, the start date of mass vaccination and the duration of vaccine-induced immunity, which indicates the validity period of the effectiveness of vaccine-induced immunity, when and how many individuals whose vaccine-induced immunity decreases to below a certain threshold can be calculated. Moreover, since the 'back to rate', at which vaccinated individuals with vaccine-induced immunity get back to susceptible individuals is included as an independent variable in the model, the number of individuals who get back to susceptible individuals from vaccinated individuals can also be calculated each day. As a result, the number of individuals including not only individuals who were infected with breakthrough infections which indicate infections occurred in susceptible individuals who had got back from vaccinated individuals but also individuals who were infected with 'normal infections' which indicate infections occurred in the 'original' susceptible individuals, can be calculated.

The impact of breakthrough infections is assessed by comparing the total number of infected individuals calculated during different durations of vaccine-induced immunity, different durations of mass vaccination and different vaccination start and end dates. The revealed conditions for outbreaks of breakthrough infections could offer reference materials for medical and/or political measures.

Framework of the flexible compartment model used here

The flexible compartment model proposed by Ohmori consists of six categories: 'susceptible (remainder): RM'; 'vaccinated: V'; 'recovered: RI, RT, RAS'; 'infected ('infectious', 'patient'): P'; 'isolated: I, PI'; and 'death: DAS, DTI, DT', as shown in Figure 1 [1-3]. 'Susceptible' is the number of susceptible individuals who are not infected but could become infected. 'Vaccinated' is the number of vaccinated individuals who have been vaccinated, who have immunity and who live and work in the real community, as shown in Figure 1. 'Recovered' are individuals who were isolated from the real community to the isolation community when they were symptomatic after the end of the latent period and returned to the real community after the infectious period (the recovery period/isolation period) ended. They recovered from the disease and have immunity. 'Infected' are individuals who have been infected and are capable of infecting susceptible individuals.