SEIRS-SEI Model of Malaria Disease with Application of Vaccines and Anti-Malarial Drugs

[*]Resmawan

(Department of Mathematics, Gorontalo State University, Jl. Jenderal Sudirman No. 6, Gorontalo, Indonesian)
Corresponding Author: Resmawan

Abstract: *This article discusses the mathematical model of SEIRS-SEI type malaria disease. Modification of the model is done by giving the treatment in humans, in the form of vaccines and anti-malarial drugstreatment. In this model, the human population is divided into four classes, namely susceptible human, exposed human, infected human, and recovered human. The mosquito population is divided into three classes, namely susceptible mosquito, exposed mosquito and infected mosquito. Furthermore, the analysis of the model to show the effect of treatment given to disease transmission. At the end of this article is provided numerical simulations to show the effectiveness of vaccines and anti-malarial drugs in humans to suppress the rate of transmission of disease. The simulation results show that the increase of vaccines effectiveness and anti-malarial drugs in humans can reduce the reproduction numbers, so that within a certain time the disease will disappear from the population.*

Keywords: *Epidemic Model, Malaria, SEIRS-SEI model, Treatment, Vaccines*

I.   Introduction

Malaria is a disease caused by a parasitic infection of Anopheles mosquito that is very deadly for humans. Malaria can be transmitted through the bites of infected mosquitoes, blood transfusions, use of needles, and congenital. Therefore, it is necessary to take preventive measures to control both the infection rate and the extent of the spread of the disease. Based on several cases of malaria that have occurred, various studies have emerged that construct a mathematical model for malaria. Mathematical modeling can help understand and identify the relationship of malaria transmission with various epidemiological parameters, assist in future planning and consider appropriate control measures.In this study we discussed a malaria transmission model based on [1,2].Modification of the model is done by addition of exposed classes in both populations with reference to [3]. This is necessary because the sporozoid produced from infected mosquito bites requires an incubation period of9-14 days to actually cause the disease, as stated in [4].During this incubation period, populations are grouped into exposed classes.Modification of the model is also done with the addition of parameters in the form of vaccines and anti-malarial drugs in humans.Vaccines given can make susceptible humans who have been bitten can directly move into humans recovered.In this case, it is assumed that humans in the susceptible class (S_h) may move into the recovered class (R_h) due to vaccines at the rate of θ as introduced in [5].Stability analysis is then performed to reveal the effects of treatments on population dynamics. At the end of this article is provided numerical simulations to show the effectiveness of vaccines and anti-malarial drugs in humans to suppress the rate of transmission of malaria disease.

II.   Mathematical Model

In constructing the model we employ the following assumptions.We assume that the human population is divided into four classes, namely susceptible humanS_h, exposed humanE_h, infected humanI_h, and recovered humanR_h, while the mosquito population is grouped into two classes, namely susceptible mosquitoS_m, exposed mosquito E_m, andinfected mosquito I_m. Individuals who are born and migrate to the susceptible class has a constant rate of λ_h. Humans in susceptible class can move into the exposed class due to an infected mosquito bite at a rate of $a\beta_1$ (with a is average number of infected mosquito bites on susceptible human per unit time and β_1 is the chances of disease transmission from infected mosquitoes to susceptible humans). Humans in susceptible class can move into the recovered class due to vaccination at a rate ofθ. Humans in susceptible class (S_h) may die at a rate ofμ_h. A newborn baby can be infected malaria due to congenital with a rate of γ. Human in exposed can move to the infected class after going through the incubation periodat a rate of v_h. Human in exposed class (E_h) may die at a rate of μ_h. Humans in infected class can move to the recovered class due to the use of anti-malarial drugs with a rate of $k\psi$ (with k is the rate of human recovery and ψ is the effectiveness of anti-malarial drugs). Humans in infected class (I_h) can die at a rate of μ_h and death due to malaria at a rate of α. Human in recovered class can move to the susceptible class after immune lose at a rate of ω. Humans in recovered class (R_h) can die at a rate of μh.

Furthermore, mosquitoes are born and migrate to susceptible class with a constant rate of λ_m. Mosquitoes in susceptible class may move into the exposed class for biting infected humans at a rate of $b\beta_2$ (with b is average number of susceptible mosquito bites on infected humans per unit time and β_2 is the chances of disease transmission from infected humans to susceptible mosquitoes). Mosquitos in exposed class can move into the infected class after going through the incubation period at a rate of v_m. Mosquitoes can die because the use of spraying at a rate of δ or can die at a rate μ_m. Compartmental diagram of the model is illustrated in Fig.1 and its dynamical equations are formulated by system (1) as follows:

$$\begin{cases} \dfrac{dS_h}{dt} = \lambda_h + \omega R_h - a\beta_1 I_m S_h - (\theta + \mu_h)S_h \\[2mm] \dfrac{dE_h}{dt} = a\beta_1 I_m S_h - (v_h + \mu_h)E_h \\[2mm] \dfrac{dI_h}{dt} = v_h E_h + \gamma I_h - (\mu_h + \alpha + k\psi)I_h \\[2mm] \dfrac{dR_h}{dt} = k\psi I_h - (\mu_h + \omega)R_h + \theta S_h \\[2mm] \dfrac{dS_m}{dt} = \lambda_m - (b\beta_2 I_h + \mu_m + \delta)S_m \\[2mm] \dfrac{dE_m}{dt} = b\beta_2 I_h S_m - (v_m + \mu_m + \delta)E_m \\[2mm] \dfrac{dI_m}{dt} = v_m E_m - (\mu_m + \delta)I_m \end{cases} \tag{1}$$

III. Stability Analysis

3.1 Equilibrium Points

Equilibrium points can be obtained by simultaneously solving the following equations:

$$\frac{dS_h}{dt} = \frac{dE_h}{dt} = \frac{dI_h}{dt} = \frac{dR_h}{dt} = \frac{dS_m}{dt} = \frac{dE_m}{dt} = \frac{dI_m}{dt} = 0$$

System (1) has two types of equilibrium points, namely disease-free equilibrium point x_{dfe} and endemic equilibrium point x_{ee}. It is easy to verify that:

$$\boldsymbol{x}_{dfe}(S_h, E_h, I_h, R_h, S_m, E_m, I_m) = (S_h^*, 0, 0, R_h^*, S_m^*, 0, 0) \tag{2}$$

where

$$S_h^* = \frac{\lambda_h(\omega + \mu_h)}{\mu_h(\mu_h + \omega + \theta)}, \qquad R_h^* = \frac{\theta\lambda_h}{\mu_h(\mu_h + \omega + \theta)}, \qquad S_m^* = \frac{\lambda_m}{\delta + \mu_m}$$

and

$$\boldsymbol{x}_{ee}(S_h, E_h, I_h, R_h, S_m, E_m, I_m) = (S_h^{**}, E_h^{**}, I_h^{**}, R_h^*, S_m^{**}, E_m^{**}, I_m^{**}) \tag{3}$$

where

$$S_h^{**} = \frac{\lambda_h + \omega R_h}{a\beta_1 I_m + \theta + \mu_h}, E_h^{**} = \frac{a\beta_1 I_m Sh}{v_h + \mu_h}, I_h^{**} = \frac{v_h E_h}{\alpha - \gamma + \mu_h + k\psi}, R_h^{**} = \frac{\theta S_h + k\psi I_h}{\omega + \mu_h}$$

$$S_m^{**} = \frac{\lambda_m}{b\beta_2 I_h + \delta + \mu_m}, E_m^{**} = \frac{b\beta_2 I_h S_m}{v_m + \delta + \mu_m}, I_m^{**} = \frac{v_m E_m}{\delta + \mu_m}$$

3.2 Reproduction Number

Reproductive number $\mathcal{R}_0$ is denoted by the expectation value of the number of infections per unit time. This infection occurs in a susceptible population produced by one infected individual. To determine the basic reproduction number we use the next ge neration matrix approach [6,7]. Based on system (1), we may define matrices F and V as follow:

$$F = \begin{bmatrix} 0 & \dfrac{a\beta_1\lambda_h(\omega + \mu_h)}{\mu_h(\mu_h + \omega + \theta)} \\ \dfrac{b\beta_2\lambda_m}{\delta + \mu_m} & 0 \end{bmatrix} \text{ and } V = \begin{bmatrix} \mu_h + \alpha + k\psi - \gamma & 0 \\ 0 & \mu_m + \delta \end{bmatrix}$$

Reproductive number $\mathcal{R}_0$ is the largest positive eigen values of the matrix $K = FV^{-1}$, from which we obtain:

$$\mathcal{R}_0 = \sqrt{K_1 K_2} \qquad (4)$$

Where

$$K_1 = \frac{b\beta_2\lambda_m}{(\delta + \mu_m)(\mu_h + \alpha + k\psi - \gamma)} \text{ and } K_2 = \frac{a\beta_1\lambda_h(\omega + \mu_h)}{\mu_h(\mu_h + \omega + \theta)(\mu_m + \delta)}$$

Equation (4) is an epidemic threshold value that will be the benchmark for transmission of malaria disease in the population. The possible conditions of the reproduction number as introduced in [6] are:
1. If $\mathcal{R}_0 < 1$, then the number of infected individuals will decrease with each generation, so that the disease will not spread, and
2. If $\mathcal{R}_0 > 1$, then the number of infected individuals will increase with each generation, so that the disease will spread.

IV. Simulation
4.1 Parameters values
In this simulation, the population dynamics are observed in conditions such that $\mathcal{R}_0 < 1$. Thus we would like to show the effect of vaccination and anti-malarial drug in a situation where the disease doesn't spread. The selection of parameters is relied on the studies conducted by various reliable sources. Based on [8] we use the following values $a = 4.30$ and $v_h = 0.10$. According to [9] we have $b = 0.33$ and $v_m = 0.083$ and from [1], we have $k = 0.611$. Next we refer to [10] to obtain each parameter values $\lambda_h = 0.027, \mu_h = 0.004, \mu_m = 0.04,$ $\omega = 1/730,$ and $\alpha = 0.005$. The following parameter values are assumed based on the most common situation $\lambda_m = 0.13, \delta = 0.01, \theta \in [0.10, 0.50], \gamma = 0.005, \psi \in [0.10, 0.50], S_h(0) = 300, E_h(0) = 50, I_h(0) = 10,$ $R_h(0) = 0, S_m(0) = 2000, E_m(0) = 100,$ and $I_m(0) = 10$.

4.2 Dynamics of population in a disease-free condition
By linearization and calculation of the system (1) around the disease-free equilibrium point, jacobian matrix and eigenvalues are obtained for disease-free equilibrium point. The jacobian matrix and the disease-free equilibrium point are obtained from the numerical solution of the system (1) with the value of the reproduction number $\mathcal{R}_0 = 0.53$. The disease-free equilibrium point is
$$x_{dfe} = (0.34, 0, 0, 6.41, 2.60, 0, 0)$$
The system is said to be stable if all eigenvalues obtained are negative. Based on parameter values, Jacobi matrix is obtained around fixed point, that is:

$$J_{X_{dfe}} = \begin{pmatrix} -0.104 & 0 & 0 & 1/730 & 0 & 0 & -0.015 \\ 0 & -0.104 & 0 & 0 & 0 & 0 & 0.015 \\ 0 & 0.1 & -0.065 & 0 & 0 & 0 & 0 \\ 0.1 & 0 & 0.0611 & -0.0054 & 0 & 0 & 0 \\ 0 & 0 & -0.062 & 0 & -0.05 & 0 & 0 \\ 0 & 0 & 0.062 & 0 & 0 & -0.13 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0.083 & -0.05 \end{pmatrix}$$

From the matrix, the following eigenvalues are obtained:

$\xi_1 = -0.15$ $\xi_5 = -0.05$
$\xi_2 = -0.11$ $\xi_6 = -0.03$
$\xi_3 = -0.09 - 0.04i$ $\xi_7 = -0.004$
$\xi_4 = -0.09 + 0.04i$

This indicates that the system is in a stable state around the disease-free equilibrium point.

The dynamics of population with some initial values given in this case are shown in Fig. 2. Based on this figure, it is shown that the solution of the system approaches the disease-free equilibrium point under condition $\mathcal{R}_0 < 1$.

Fig. 2 shows the dynamics of population from baseline to disease free condition. Each class of the population undergoes the dynamics of the initial condition toward the point around the disease-free equilibrium point. Humans in susceptible classes experience a decrease due to exposure to infected mosquitoes. Likewise,

mosquitoes in susceptible classes have decreased because of exposure by infected humans. This condition causes an increase in exposed and infected classes of both species. This increase occurs from the first day until about the 13th day. After passing the 13th day, the population in the exposed and infected class of both species decreased toward the disease-free equilibrium point. This coincides with the increase of human beings in the recovered class, so the disease will disappear from the population.

4.3 Simulation of the effectiveness of the use anti-malarial drugs

In this section, simulation is performed to demonstrate the effectiveness of the use of anti-malaria drugs (ψ) to suppress the rate of disease transmission. In this case, it will be shown that change the value of the parameter ψ can change the reproduction number $\mathcal{R}_0$ defined in (4). There are three observed ψ values, taken on hose [0.10,0.50] with step 0.20. The change of parameter ψ value causing the change of reproduction number value can be seen in Table 1 and dynamics of the population are shown in Fig. 3 and Fig. 4.In the human population, as shown in Fig. 3,if the effectiveness of the use of anti-malarial drugs is increased, then it decreases the number of exposed humans and the number of infected humans, but it increased the number of recovered humans.Anti-malarial drugs given to humans also affect mosquito populations, as shown in Fig. 4.If the effectiveness of the use of anti-malarial drugs is increased, then the population of mosquitoes in the exposed and infected class decreases. This causes the number of mosquitoes in the susceptible class to increase.

The change in the number of humans and mosquitoes in each class tends to differ for each increase in the effectiveness of the use of anti-malarial drugs on humans.A maximum number of humans and mosquitoes are exposed at around the 9th days, while the maximum number of humans and infected mosquitoes occurs on the 20th and 15th days.This is consistent with the theory that the exposed human will experience an incubation period of approximately 14 days later is completely infected. On the 20th day, with an increase in the effectiveness of the use of anti-malarial drugs on humans by 40% can reduce the infected human population by 13.88% of the human population and on the 15th day can decrease the population of infected mosquitoes by 1.43% of the mosquito population.

The effectiveness of the use of anti-malarial drugs in suppressing the rate of transmission of disease is indicated by the dynamics in each class of the population. Based on the assumption of the initial value given, it appears that the increased in the use of anti-malarial drugs do not significantly affect the susceptible class.This is because the use of anti-malarial drugs is not done directly in the susceptible class of population.Significant changes occur in an infected human population where increased the use of anti-malarial drugs effectiveness accelerate the rate of decline in infected humans.The same situation occurs in mosquito populations where increased effectiveness of the use of anti-malarial drugs on humans can reduce the number of infected mosquitoes in a faster time.This is shown that increased effectiveness of the use of anti-malarial drugs can accelerate the loss of disease in the population.

4.4 Simulation of the Effectiveness of the Use Vaccine

In this section, simulation is performed to demonstrate the effectiveness of the use of vaccines (θ) to suppress the rate of disease transmission. In this case, it will be shown that change the value of the parameter θ can change the reproduction number $\mathcal{R}_0$ defined in (4). There are three observed θ values, taken on hose [0.10,0.50] with step 0.20. The change of parameter θ value causing the change of reproduction number value can be seen in Table 2 and dynamics of the population are shown in Fig. 5 and Fig. 6.In the human population, as shown in Fig. 5, if the effectiveness of the use of vaccines on humans is increased, then the number of human exposed and infected decreases, while human recovered from the disease have increased.This is because the use of vaccines causes humans susceptible immune from disease.The use of vaccines in humans also has an impact on mosquito populations, as shown in Fig. 6.If the effectiveness of the use of vaccines on humans is increased, then the population of mosquitoes in the exposed and infected class decreases. This is because the use of vaccines will reduce the human population in the infected class.Thus, the chance of mosquitoes will be exposed by infected humans is also reduced.The change in the number of humans and mosquitoes in each class tends to differ for each increase in the effectiveness of the use of vaccines on humans.A maximum number of humans and mosquitoes are exposed at around the 10th days, while the maximum number of humans and infected mosquitoes occurs on the 20th day.On the 20th day, an increase in the effectiveness of the use of vaccines on humans by 40% can decrease the infected human population by 12.50% of the human population and decrease the infected mosquito population by 0.47% of the mosquito population.This is shown that increase of the use of vaccines onhumans can accelerate the loss of disease in the population.The effectiveness of the use of vaccines in suppressing the rate of transmission of disease is indicated by the dynamics in each class of the population. Based on the assumption of the initial value given, it appears that the increased in the use of vaccines do not significantly affect the mosquito population.This is because the use of the vaccines does not directly affect the mosquito population.Significant changes occur in human populations where increased effectiveness of the use of vaccines accelerates the rate of decreased in the number of susceptible, exposed, and infected humans and accelerates the increased in human recovered. This dynamic occurs because humans given the vaccine will

move to the human recovered class after being bitten by an infected mosquito. Thus, increasing the effectiveness of the use of vaccines can accelerate the loss of disease in the population.

V.   Figures And Tables
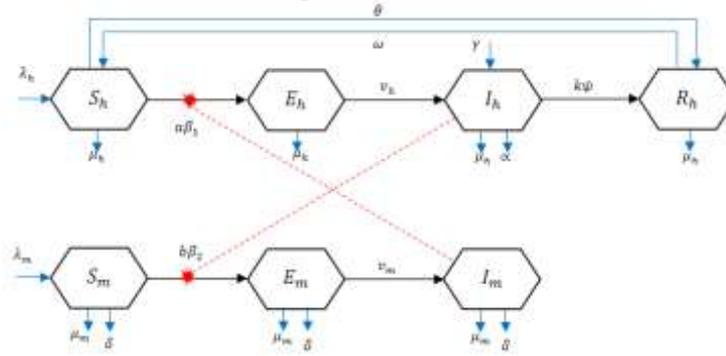
Fig. 1:Compartmental diagram of malaria disease
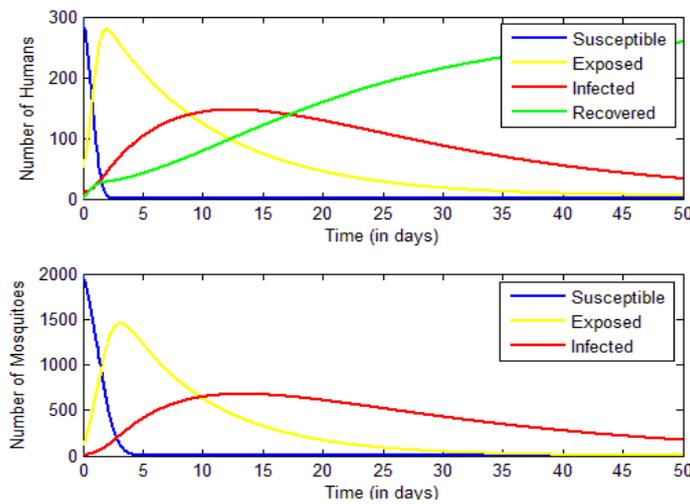
Fig. 2:Dynanics of population at condition $\mathcal{R}_0 < 1$
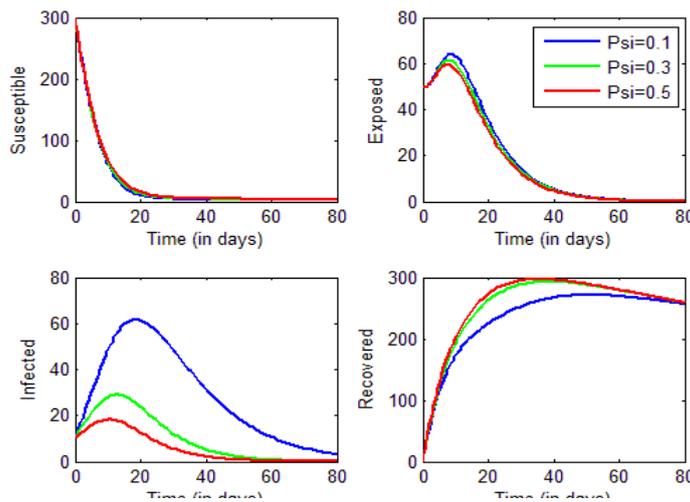
Fig. 3:Dynamics of human population under the treatmentofanti-malarial drugs
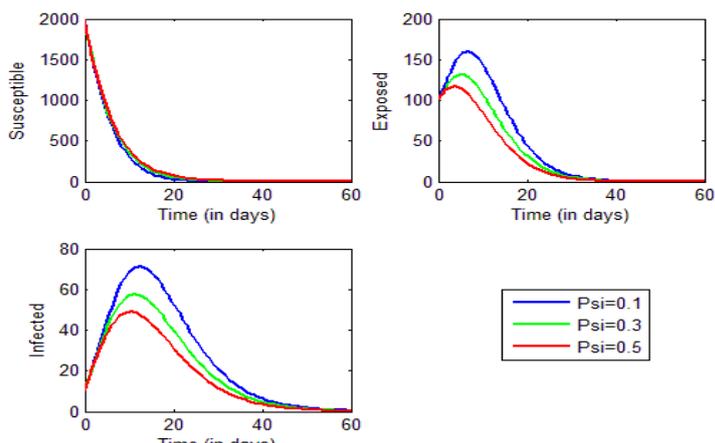
Fig. 4:Dynamics of mosquito population under the treatmentofanti-malarial drugs
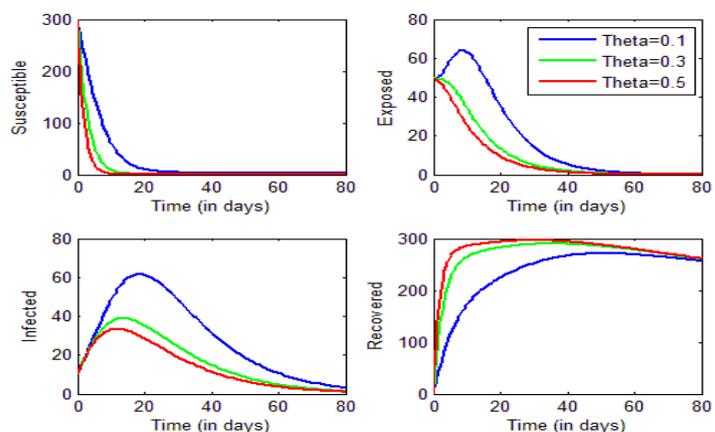

Fig. 5:Dynamics of human population under the treatmentofvaccines
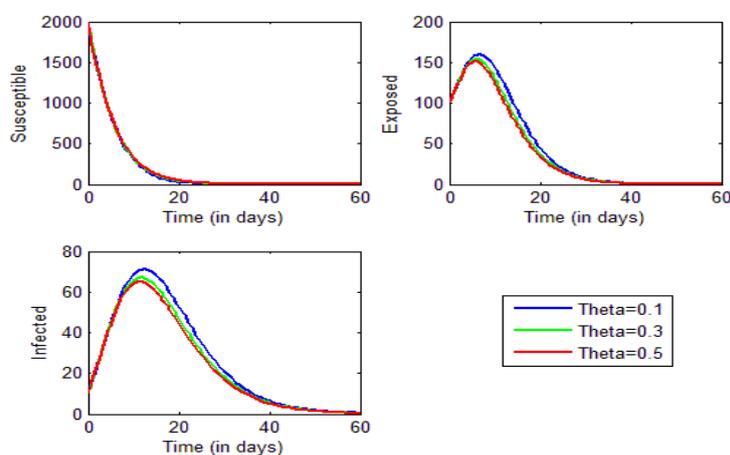

Fig. 6: Dynamics of mosquito population under the treatmentofvaccines

Table 1: Parameter values used for simulation of the effectiveness of anti-malarialdrugs

Parameter ψ	Reproduction number
$\psi = 0.10$	$\mathcal{R}_0 = 0.53$
$\psi = 0.30$	$\mathcal{R}_0 = 0.31$
$\psi = 0.50$	$\mathcal{R}_0 = 0.24$

Table 2: Parameter values used for simulation of the effectiveness of vaccine

Parameter θ	Reproduction number
$\theta = 0.10$	$\mathcal{R}_0 = 0.53$
$\theta = 0.30$	$\mathcal{R}_0 = 0.31$
$\theta = 0.50$	$\mathcal{R}_0 = 0.24$

VI. Conclusion

We have presented an SEIRS-SEI model of malaria transmission equipped with treatments namely the use of vaccines and anti-malarial drugs. This model have disease-free and endemic equilibrium points. we perform a stability analysis characterized by a reproduction number. The simulation results shown that the system is stable around the disease-free equilibrium point at condition $\mathcal{R}_0 < 1$. The simulation results also shown that the effects of treatments with different levels affect to human and mosquito populations.

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