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Modeling and Analysis of an SEIR Epidemic Model with a Limited Resource for Treatment

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Abstract - In this paper an SEIR epidemic model with a limited resource for treatment is investigated. It is assumed that the treatment rate is proportional to the number of patients as long as this number is below a certain capacity and it becomes constant when that number of patients exceeds this capacity. Mathematical analysis is used to study the dynamic behavior of this model. Existence and stability of disease-free and endemic equilibria are investigated. It is shown that this kind of treatment rate leads to the existence of multiple endemic equilibria where the basic reproduction number plays a big role in determining their stability.

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I. Introduction

There is a long and distinguished history of mathematical models in epidemiology, going back to the eighteenth century (Bernoulli 1760). Since that time, theoretical epidemiology has witnessed numerous developments. Some of these studies can be found in Baily (1975), Anderson and May (1991), and Hethcote (2000). A tremendous number of models have been formulated, analyzed and applied to a variety of infectious diseases qualitatively and quantitatively. Mathematical models have become important tools in analyzing the spread and control of infectious diseases. Furthermore, mathematical models now plays a key role in policy making, including health-economic aspects, emergency planning and risk assessment, control-program evaluation, and optimizing various detection. One of the fundamental results in mathematical epidemiology is that most mathematical epidemic models usually exhibit "threshold" behavior stated as follows: if the average number of secondary infections caused by an average infective, called the basic reproduction number, is less than one the disease will die out, while if it exceeds one there will be an endemic (see Driessche and Watmough, 2002, Brauer et all., 2008).

Most of the models in mathematical epidemiology are compartmental models, with the population being divided into compartments with the assumptions about the nature and time rate of transfer from one compartment to another. In this paper, an SEIR model is presented where there is an exposed period between being infected and becoming infective. Some of the research done on SEIR models can be found for example in (Zhang et all., 2006, Yi et all., 2009, Sun and Hsieh, 2010, Zhou and Cui, 2011, Shu et all. 2012). Treatment plays an

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important role in controlling or decreasing the spread of diseases such as measles, flue and tuberculosis (see Hyman and Li, 1998, Fang and Thieme, 1995, Wu and Feng ,2000). More recent work on the effect of treatment on the dynamic behavior can be found in (Wang, 2006, Zhang and Liu, 2008, Kar and Baeabyal, 2010, Zhou and Cui, 2011, Wang et all., 2012). In classical epidemic models, the treatment rate is assumed to be proportional to the number of infectives, which is almost impossible in reality. In this paper, the treatment rate is assumed to be proportional to the number of infectives when the capacity of treatment is not reached, and otherwise, takes the maximal capacity (See Wang, 2006, Kar and Baeabyal, 2010).

The organization of this paper is as follows: In the next section, the mathematical model is formed and the basic reproduction number is calculated. In section 3, Equilibria of the system are found and their existence conditions are presented. In section 4, stability of equilibria is investigated. Section 5, is devoted for the discussion of the results.

II. The Mathematical Model and the Basic Reproduction Number

To construct the SEIR model, we will divide the total population into four epidemiological classes which are succeptibles (S), exposed (E) infectious (I) and recovered (R). The model to be studied is of the following form:

$$\begin{aligned} \frac{dS}{dt} &= A - \beta SI - \mu S \\ \frac{dE}{dt} &= \beta SI - (\mu + \varepsilon) E \\ \frac{dI}{dt} &= \varepsilon E - (\mu + r + d) I - T(t) \\ \frac{dR}{dt} &= rI - \mu R + T(t) \end{aligned} \tag{1}$$

where A is the recruitment rate, β is the infection rate, μ is the natural death rate, ε is the progression rate to symptoms development(the rate at which an infected individual becomes infectious per unit time), r is the removal rate(the rate at which an infectious individual recovers per unit time), d is the disease-related death and $T(t)$ is the treatment rate function. In this paper the treatment function is defined by

$$T(I) = \begin{cases} cI & \text{if } 0 \leq I \leq I_o \\ k & \text{if } I > I_o \end{cases}$$

where $k = cI_o$. This means that the treatment rate is proportional to the number of infected people as long as the number of infectives is less than or equal to a fixed value I_o but after that the treatment rate becomes constant. This type of treatment is more realistic when patients have to be hospitalized and the number of beds is limited. This is also true for the case where the medications are not sufficient.(See Wang, 2006, Kar and Batabyal, 2010)

The variable R does not appear in the first three equations of (1), so it is enough to analyze the following reduced system

$$\frac{dS}{dt} = A - \beta SI - \mu S$$

$$\begin{aligned} \frac{dE}{dt} &= \beta SI - (\mu + \varepsilon) E \\ \frac{dI}{dt} &= \varepsilon E - (\mu + r + d) I - T(t) \end{aligned} \tag{2}$$

It follows from system (2) that $(S+E+I)' = A - \mu(S+E+I) - T(t) \leq A - \mu(S+E+I)$

Notes

Then $\lim_{n\to\infty} \sup(S+E+I) \leq \frac{A}{\mu}$. So the feasible region for system (2) is

$\Omega = \{(S,E,I) : S+E+I \leq \frac{A}{\mu}, S > 0, E \geq 0, I \geq 0\}$

The region Ω is positively invariant with respect to system (2). Hence, system (2) is considered mathematically and epidemiologically well posed in Ω.

Now, the basic reproduction number R_o will be found by using the method of next generation matrix found in Driessche and Watmough, 2002.

System (2) always has the disease-free equilibrium $X_o = \left(\frac{A}{\mu}, 0, 0\right)$. Near this disease free equilibrium I has to be less than I_o, so system (2) becomes

$$\begin{aligned} \frac{dS}{dt} &= A - \beta SI - \mu S \\ \frac{dE}{dt} &= \beta SI - (\mu + \varepsilon) E \\ \frac{dI}{dt} &= \varepsilon E - (\mu + r + d + c) I \end{aligned} \tag{3}$$

Let $X = (E, I, S)^T$. System (3) can be written as

$\frac{dX}{dt} = \mathcal{F}(X) - \mathcal{V}(X)$

where

$$\mathcal{F}(X) = \begin{pmatrix} \beta SI \\ 0 \\ 0 \end{pmatrix}, \mathcal{V}(X) = \begin{pmatrix} (\mu+\varepsilon) E \\ -\varepsilon E + (\mu + r + d + c) I \\ -A + \beta SI + \mu S \end{pmatrix}$$

The Jacobian matrices of $\mathcal{F}(X)$ and $\mathcal{V}(X)$ at the disease free equilibrium X_o are, respectively,

$$D\mathcal{F}(X_o) = \begin{pmatrix} F & 0 \\ 0 & 0 \end{pmatrix}, D\mathcal{V}(X_o) = \begin{pmatrix} V & 0 \\ J_1 & J_2 \end{pmatrix}$$

$$\text{where } F = \begin{pmatrix} 0 & \frac{\beta A}{\mu} \\ 0 & 0 \end{pmatrix} \text{ and } V = \begin{pmatrix} \mu+\varepsilon & 0 \\ -\varepsilon & \mu+r+d+c \end{pmatrix}$$

$FV^{-1} = \begin{pmatrix} \frac{\varepsilon\beta A}{\mu(\mu+\varepsilon)(\mu+r+d+c)} & \frac{\beta A}{\mu(\mu+r+d+c)} \\ 0 & 0 \end{pmatrix}$ is the next generation matrix of system (2). The spectral radius of FV^{-1} is

$\rho\left(FV^{-1}\right) = \frac{\varepsilon\beta A}{\mu(\mu+\varepsilon)(\mu+r+d+c)}$

Hence, the basic reproduction number of system (2) is given by

$R_o = \frac{\varepsilon\beta A}{\mu(\mu+\varepsilon)(\mu+r+d+c)}$

III. Equilibria

In this section, equilibria of system (2) will be found and discussed.

First of all, the disease-free equilibria $X_o = \left(\frac{A}{\mu}, 0, 0\right)$ always exists when $I \leq I_o$.

An endemic equilibria of system (2) satisfies

$$\begin{aligned} A - \beta SI - \mu S &= 0 \\ \beta SI - (\mu + \varepsilon) E &= 0 \\ \varepsilon E - (\mu + r + d) I - T(I) &= 0 \end{aligned} \tag{4}$$

When $0 < I \leq I_o$, system (4) becomes

$$\begin{aligned} A - \beta SI - \mu S &= 0 \\ \beta SI - (\mu + \varepsilon) E &= 0 \\ \varepsilon E - (\mu + r + d + c) I &= 0 \end{aligned} \tag{5}$$

When $I > I_o$, system (4) becomes

$$\begin{aligned} A - \beta SI - \mu S &= 0 \\ \beta SI - (\mu + \varepsilon) E &= 0 \\ \varepsilon E - (\mu + r + d) I - k &= 0 \end{aligned} \tag{6}$$

If $R_o > 1$, system (5) admits a unique positive solution $X^* = (S^*, E^*, I^*)$ given by

$S^* = \frac{A}{\mu+\beta I^*} = \frac{A}{\mu R_o}$

$E^* = \frac{A}{\mu+\varepsilon} - \frac{\mu(\mu+r+d+c)}{\beta\varepsilon} = \frac{\mu(\mu+r+d+c)}{\beta\varepsilon}\left(R_o - 1\right)$

$I^* = \frac{\mu}{\beta}\left(R_o - 1\right)$

$I^* \leq I_o$if and only if $R_o \leq 1 + \frac{\beta I_o}{\mu} \triangleq P_o$

So, X^* is an endemic equilibrium of system (2) if and only if $1 < R_o \leq P_o$.

In order to obtain positive solutions of system (6), we solve S from the first equation of (6) to get $S = \frac{A}{\mu+\beta I}$. We also solve E from the thirds equation to get $E = \frac{\mu+r+d}{\varepsilon} I + \frac{k}{\varepsilon}$. Substitute into the second equation of (6), we have

Notes

$$aI^2 + bI + c = 0 \tag{7}$$

where

$a = \beta(\mu+\varepsilon)(\mu+r+d) > 0$

$b = (\mu+\varepsilon)(\mu(\mu+r+d)+\beta k) - \varepsilon\beta A$

$= (\mu+\varepsilon)(\mu(\mu+r+d)+\beta k - \mu(\mu+r+d+c)R_o)$

$c = \mu k(\mu+\varepsilon) > 0$

Let the discriminant of (7) be $\Delta = b^2 - 4ac$.

If $b \geq 0$, then (7) has no positive solution. Also if $\Delta < 0$, then (7) has no real solution. So we see that if $b < 0$ and $\Delta \geq 0$, than (7) has two positive solutions.

$\Delta \geq 0$ is equivalent to $[(\mu+\varepsilon)(\mu(\mu+r+d)+\beta k - \mu(\mu+r+d+c)R_o)]^2$

$\geq 4\mu\beta k(\mu+\varepsilon)^2(\mu+r+d)$

i.e., $R_o \leq 1 + \frac{\beta k-\mu c}{\mu(\mu+r+d+c)} - 2\frac{\sqrt{\mu\beta k(\mu+r+d)}}{\mu(\mu+r+d+c)}$

or $R_o \geq 1 + \frac{\beta k-\mu c}{\mu(\mu+r+d+c)} + 2\frac{\sqrt{\mu\beta k(\mu+r+d)}}{\mu(\mu+r+d+c)} \triangleq P_1$

Note that $b < 0$ is equivalent to $R_o > 1 + \frac{\beta k-\mu c}{\mu(\mu+r+d+c)}$

Therefore, (7) has two positive solutions I_1 and I_2 if $R_o \geq P_1$ where

$I_1 = \frac{-b-\sqrt{\Delta}}{2\beta(\mu+\varepsilon)(\mu+r+d)}$ and $I_2 = \frac{-b+\sqrt{\Delta}}{2\beta(\mu+\varepsilon)(\mu+r+d)}$

Set $S_1 = \frac{A}{\mu+\beta I_1}$ and $S_2 = \frac{A}{\mu+\beta I_2}$

$E_1 = E_2 = \frac{A}{\mu+\varepsilon} - \frac{\mu(\mu+r+d+c)}{\beta\varepsilon} = \frac{\mu(\mu+r+d+c)}{\beta\varepsilon}(R_o - 1)$

Then $X_i = (S_i, E_i, I_i)$, $i = 1, 2$ are endemic equilibria of (2) if $I_i > I_o$.

$I_1 > I_o$ if and only if $-b - \sqrt{\Delta} > 2\beta(\mu+\varepsilon)(\mu+r+d)I_o$

This implies that $b + 2\beta(\mu+\varepsilon)(\mu+r+d)I_o < 0$

It follows from the definition of b that

$R_o > 1 + \frac{\beta k-\mu c}{\mu(\mu+r+d+c)} + \frac{2\beta(\mu+r+d)I_o}{\mu(\mu+r+d+c)} \triangleq P_2$

By a similar argument we see that $I_2 < I_o$ if and only if $R_o < P_2$.

We summarize the above discussion in the following theorem

Theorem 1 *Let* $P_o = 1 + \frac{\beta I_o}{\mu}$, $P_1 = 1 + \frac{\beta k-\mu c}{\mu(\mu+r+d+c)} + 2\frac{\sqrt{\mu\beta k(\mu+r+d)}}{\mu(\mu+r+d+c)}$ *and* $P_2 = 1 + \frac{\beta k-\mu c}{\mu(\mu+r+d+c)} + \frac{2\beta(\mu+r+d)I_o}{\mu(\mu+r+d+c)}$.

1. *System (2) always have the disease-free equilibrium* $X_o = \left(\frac{A}{\mu}, 0, 0\right)$.
2. *The endemic equilibrium* $X^* = (S^*, E^*, I^*)$ *of system (2) exists if and only if* $1 < R_o \leq P_o$
3. *Two more endemic equilibria* $X_i = (S_i, E_i, I_i)$, $i = 1, 2$ *of system (2) exist if and only if* $R_o \geq P_1$ *and* $R_o > P_2$

IV. Stability of Equilibria

By analyzing the eigenvalues of the Jacobian matrices of system (2), we get results about the local stability of these equilibria.

a) Disease-free equilibrium X_o

The Jacobian matrix evaluated at X_o is

$$J(X_o) = \begin{pmatrix} -\mu & 0 & -\frac{\beta A}{\mu} \\ 0 & -(\mu+\varepsilon) & 0 \\ 0 & \varepsilon & -(\mu+r+d+c) \end{pmatrix}$$

and the eigenvalues are $-\mu$, $-(\mu+\varepsilon)$ and $-(\mu+r+d+c)$ which are all negative. So we have the following result

Lemma 2 *The disease-free equilibrium* X_o *is locally asymptotically stable.*

To investigate the global stability of X_o, consider the Lyapunov function $L = \varepsilon E + (\mu+\epsilon) I$

$$\frac{dL}{dt} = \varepsilon \frac{dE}{dt} + (\mu+\epsilon)\frac{dI}{dt} = (\epsilon\beta S - (\mu+\epsilon)(\mu+r+d+c)) I$$

$$\leq \left(\frac{\epsilon\beta A}{\mu} - (\mu+\epsilon)(\mu+r+d+c)\right) I = (\mu+\epsilon)(\mu+r+d+c)(R_o - 1) I \leq 0 \text{ if } R_o < 1.$$

The maximal compact invariant set in $\{(S, E, I) \in \Omega : \frac{dL}{dt} = 0\}$ is the singleton $\{X_o\}$. Using Lasalle's invariance principle (Edelstein-Kesher, 2005), we have the following theorem

Theorem 3 *If* $R_o < 1$, *the disease-free equilibrium* X_o *is globally asymptotically stable and the disease dies out. But if* $R_o > 1$, *then* X_o *is unstable.*

b) Endemic equilibrium X^*

The Jacobian matrix evaluated at X^* is

$$J(X^*) = \begin{pmatrix} -\beta I^* - \mu & 0 & -\beta S^* \\ \beta I^* & -(\mu+\varepsilon) & 0 \\ 0 & \varepsilon & -(\mu+r+d+c) \end{pmatrix}$$

$$= \begin{pmatrix} -\mu R_o & 0 & -\frac{\beta A}{\mu R_o} \\ \mu(R_o - 1) & -(\mu+\varepsilon) & 0 \\ 0 & \varepsilon & -(\mu+r+d+c) \end{pmatrix}$$

Notes

The characteristic polynomial of $J(X^*)$ is given by

$$\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0$$

where

$$a_1 = 2\mu + r + d + c + \varepsilon + \mu R_o$$

$$a_2 = (\mu + \varepsilon + \mu R_o)(\mu + r + d + c) + \mu R_o(\mu + \varepsilon)$$

$$a_3 = \mu(\mu + \varepsilon)(\mu + r + d + c) R_o + \varepsilon\beta A\frac{(R_o - 1)}{R_o}$$

$$= 2\mu(\mu + \varepsilon)(\mu + r + d + c) R_o - \mu(\mu + \varepsilon)(\mu + r + d + c)$$

Clearly, $a_1 > 0$ and if $R_o > 1$ then $a_3 > 0$.

$a_1a_2 - a_3 = (2\mu + r + d + c + \varepsilon + \mu R_o)((\mu + \varepsilon + \mu R_o)(\mu + r + d + c) + \mu R_o(\mu + \varepsilon)) + \mu(\mu + \varepsilon)(\mu + r + d + c) - 2\mu(\mu + \varepsilon)(\mu + r + d + c) R_o > 0.$

Therefore, by Routh-Herwitz criteria, we conclude that the eigenvalues of $J(X^*)$ are all negative when $R_o > 1$. So, we have the following result

Lemma 4 *If $R_o > 1$, then the endemic equilibrium X^* is locally asymptotically stable.*

Now, we will investigate the global stability of X^*. To do so, we consider the following Lyapunov function

$$L = \left(S - S^* - S^* \ln \frac{S}{S^*}\right) + \left(E - E^* - E^* \ln \frac{E}{E^*}\right) + \frac{\mu+\varepsilon}{\varepsilon}\left(I - I^* - I^* \ln \frac{I}{I^*}\right)$$

Thus

$$\frac{dV}{dt} = \left(1 - \frac{S^*}{S}\right)\frac{dS}{dt} + \left(1 - \frac{E^*}{E}\right)\frac{dE}{dt} + \frac{\mu+\varepsilon}{\varepsilon}\left(1 - \frac{I^*}{I}\right)\frac{dI}{dt}$$

Substituting the expressions of the derivatives from system (2) and using the relation

$$A = \beta S^* I^* + \mu S^*$$

we get

$$\frac{dV}{dt} = \left(1 - \frac{S^*}{S}\right)[-\mu(S - S^*) + \beta S^* I^* - \beta SI] + \left(1 - \frac{E^*}{E}\right)[\beta SI - (\mu + \varepsilon) E]$$

$$+\frac{\mu+\varepsilon}{\varepsilon}\left(1 - \frac{I^*}{I}\right)[\varepsilon E - (\mu + r + d + c) I]$$

$$= -\mu\frac{(S - S^*)^2}{S} + \beta S^* I^* - \beta S^* I^* \frac{S^*}{S} + \beta S^* I - \beta SI\frac{E^*}{E} + (\mu + \varepsilon) E^* - (\mu + \varepsilon) E\frac{I^*}{I}$$

$$-\frac{\mu+\varepsilon}{\varepsilon}(\mu + r + d + c) I + \frac{\mu+\varepsilon}{\varepsilon}(\mu + r + d + c) I^*$$

Note that $$\varepsilon E^* = (\mu + r + d + c) I^*$$

This implies that

$$\beta S^* I - \frac{\mu+\varepsilon}{\varepsilon}(\mu + r + d + c) I = \beta S^* I - (\mu + \varepsilon) E^* \frac{I}{I^*} = [\beta S^* I^* - (\mu + \varepsilon) E^*]\frac{I}{I^*} = 0$$

So

$$\frac{dV}{dt} = -\mu\frac{(S-S^*)^2}{S} + 3(\mu+\varepsilon)E^* - \beta S^* I^* \frac{S^*}{S} - \beta S I \frac{E^*}{E} - (\mu+\varepsilon)E\frac{I^*}{I}$$

$$= -\mu\frac{(S-S^*)^2}{S} + (\mu+\varepsilon)E^*\left(3 - \frac{S^*}{S} - \frac{SE^*I}{S^*EI^*} - \frac{EI^*}{E^*I}\right) \leq 0$$

since the arithmetic mean is greater than or equal to the geometric mean of the quantities $\frac{S^*}{S}, \frac{SE^*I}{S^*EI^*}, \frac{EI^*}{E^*I}$. i.e., $\frac{S^*}{S} + \frac{SE^*I}{S^*EI^*} + \frac{EI^*}{E^*I} - 3 \geq 0$.Then $\frac{dV}{dt} = 0$ holds only when $S = S^*$, $E = E^*$ and $I = I^*$. So the maximal compact invariant set in $\{(S,E,I) \in \Omega : \frac{dL}{dt} = 0\}$ is the singleton $\{X^*\}$. Using Lasalle's invariance principle, we have the following theorem

Theorem 5 *If $R_o > 1$, the endemic equilibrium X^* is globally asymptotically stable*

c) Endemic equilibria X_1 and X_2

By analyzing the Jacobian matrix at these equilibria we find that

$$J(X_1) = \begin{pmatrix} -\beta I_1 - \mu & 0 & -\beta S_1 \\ \beta I_1 & -(\mu+\varepsilon) & 0 \\ 0 & \varepsilon & -(\mu+r+d) \end{pmatrix} = \begin{pmatrix} -\frac{A}{S_1} & 0 & -\beta S_1 \\ \beta I_1 & -\frac{\beta S_1 I_1}{E_1} & 0 \\ 0 & \varepsilon & \frac{k-\varepsilon E_1}{I_1} \end{pmatrix}$$

The second additive compound matrix of $J(X_1)$ is given by

$$J(X_1)^{[2]} = \begin{pmatrix} -\beta I_1 - \mu - (\mu+\varepsilon) & 0 & \beta S_1 \\ \varepsilon & -\beta I_1 - \mu - (\mu+r+d) & 0 \\ 0 & \beta I_1 & -(\mu+\varepsilon) - (\mu+r+d) \end{pmatrix}$$

For the local stability of X_1 we need the following lemma (See Arino et all., 2003, McCluskey and Driessche, 2004, Cai et all., 2008)

Lemma 6 *Let M be a 3×3 real matrix. If $tr(M)$, $\det(M)$ and $\det(M^{[2]})$ are all negative, then all of the eigenvalues of M have negative real parts.*

Now clearly $tr(J(X_1)) < 0$

$\det(J(X_1)) = -\frac{1}{E_1}(A\beta\varepsilon E_1 - Ak\beta + \beta^2\varepsilon E_1 I_1 S_1) < 0$ since $\varepsilon E_1 - k > 0$

$\det(J(X_1)^{[2]}) = [-\beta I_1 - \mu - (\mu+\varepsilon)][-\beta I_1 - \mu - (\mu+r+d)][-(\mu+\varepsilon) - (\mu+r+d)] + \varepsilon\beta^2 S_1 I_1$

We can see that $\det(J(X_1)^{[2]}) < 0$ if $\beta^2 I_1^2(\varepsilon + 2\mu + r + d) > \varepsilon\beta^2 S_1 I_1$

The same argument can be used for X_2 as well.

So, we have the following result

Theorem 7 *The endemic equilibria X_i $i = 1,2$ are locally asymptotically stable if $\frac{S_i}{I_i} < 1 + \frac{2\mu+r+d}{\varepsilon}$*

Notes

V. Discussion

In this paper an SEIR epidemic model is proposed to simulate the limited resources for the treatment of patients, which can occur as a consequence of lack of medications or limited beds in hospitals. This model was studied theoretically, and it was found that the dynamic behavior of the model can be determined by its basic reproduction number R_o. When $R_o < 1$, there exists no positve equilibrium and the disease-free equilibrium is globally asymptotically stable, that is the disease dies out. But when $R_o > 1$ the disease-free equilinrium becomes unstable and the disease persists. It was shown that this kind of treatment rate results in the existence of multiple endemic equilibria. An endemic equilibrium X^* exists when $1 < R_o \leq P_o$ in which case it will be globally asymptotically stable. Two more endemic equilibria X_1 and X_2 exist when $R_o \geq P_1$ and $R_o > P_2$. These equilibria are locally asymptotically stable if the ratio $\frac{S_i}{I_i}$ is less than the quantity $1 + \frac{2\mu+r+d}{\varepsilon}$.

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Notes