

M. Lisi – S. Totaro

ANALYSIS OF AN AGE-STRUCTURED MSEIR MODEL

Abstract. In this paper we study the properties of an age-structured MSEIR epidemic model. Existence, uniqueness and positivity of the strict solution of the problem are proved by using semigroup techniques. Moreover, the expression of the total population density by means of a suitable nonlinear semigroup is given. Finally, a simplified system of ODE is proposed and the equilibrium solutions with stability results are analyzed.

1. Introduction

In the framework of epidemic models, many kinds of mathematical models have been investigated: the most common ones are the so called SIR and SIS models. The first type analyzes the theoretical number of people infected by a contagious illness. In the modeling transmission dynamics of a communicable disease, it is common to divide the population into distinct classes whose sizes change with time. The name SIR is due to the fact that this kind of models involves ordinary differential equations for the number of Susceptible, Infected and Recovered individuals: one the simplest examples is the Kermack-McKendrick model, proposed to study London's cholera of 1865 and Bombay's plague of 1906, [6]. Talking about the second type, SIS models take into consideration a group of diseases for which infection does not confer immunity (e.g., gonorrhoea); a Susceptible can become Infective and Susceptible again, [8].

In most of cases, the set of individuals studied in SIR and SIS models depends only on time t , whereas the variable age a does not effect the epidemic dynamics. However, since many diseases, such as measles or chickenpox, are primarily diseases of children (see, for instance, [2], [3] and [4]), only subdividing the population into differing age-classes we can be able to capture age-structured transmission in more detail.

In this work, we shall study an age-structured MSEIR epidemic model, where, besides Susceptibles ($S(a,t)$), Infectious ($I(a,t)$) and Removed ($R(a,t)$), a class of individuals protected by Maternal antibodies after their birth ($M(a,t)$) and a class of individuals Exposed to the disease but not yet infected ($E(a,t)$) are considered. This last choice is due to the fact that many diseases, such as measles and mumps, are characterized by a latent period. Literature in the framework of MSEIR models is not wide: an example is given by [13] (see also the references quoted therein), where existence and uniqueness of positive steady states for an age-structured MSEIR epidemic model, similar to that proposed here, is proved. Our model is improved considering the total population N not only depending on the age variable a , but also on the time variable t . Moreover, whereas in [13] many manipulations to the model are made and the authors used the positive invariant sets theory, we study the problem simply as a semilinear problem, by using the classical semigroup theory, ([1],[9]). Moreover, we prove that the nonlinear term of the system is Frechet differentiable and the expression of the total

population density, by means of a suitable nonlinear semigroup, is given.

The paper is organized as follows: after the epidemic model description, in Section 2, by using semigroup techniques ([1],[9]), we study global existence and uniqueness of the model solution and we prove that M, S, E, I, R (i.e., the densities of individuals protected by maternal antibodies, susceptibles, exposed, infective and removed, respectively) are positive and regular functions. The results provide the explicit form of the total population density and also a priori estimates of the functions S, E, I , which allow to get positivity and global existence results. Finally, under some homogeneity assumptions, last Section is devoted to derive a system of ordinary differential equations for the total number of individuals protected by maternal antibody, susceptibles, latents, infectives and removed ones; the equilibrium solutions and their stability are also analyzed. Note that the results of this paper agree with those present in literature (see, for instance, [11]).

A further work will be dedicated to the study of an MSEIR model with vaccination effects: the idea is that of using mathematical techniques similar to those used in the present paper (see [12], for numerical simulation).

2. The epidemic model

Assume an isolated population of individuals of age a , at time t (no immigration or emigration process is considered), can be divided into a set of five disjoint classes, dependent upon their experience with respect to a given disease. Related to each group we consider:

1. $M = M(a, t)$: density of individuals protected by maternal antibodies;
2. $S = S(a, t)$: density of susceptibles;
3. $E = E(a, t)$: density of people exposed to the disease but not yet infectious (latents);
4. $I = I(a, t)$: density of infectives;
5. $R = R(a, t)$: density of removed (or immunes).

The total population density $N = N(a, t)$ will be such that:

$$(1) \quad N = M + S + E + I + R, \quad 0 \leq a \leq r_m, t \geq 0,$$

with $r_m < +\infty$ the highest age attended.

The spread of disease can be described by the following system of partial integro-differential equations:

$$(2) \quad \begin{cases} M_t + M_a = -(\mu + \delta)M, \\ S_t + S_a = \delta M - (\mu + \lambda)S, \\ E_t + E_a = \lambda S - (\mu + \alpha)E, \\ I_t + I_a = \alpha E - (\mu + \gamma)I, \\ R_t + R_a = \gamma I - \mu R, \end{cases}$$

where

$$H_t = \frac{\partial}{\partial t}H(a,t), \quad H_a = \frac{\partial}{\partial a}H(a,t), \quad H = M, S, E, I, R, \quad a \in (0, r_m), t > 0,$$

the constants $\delta^{-1}, \alpha^{-1}, \gamma^{-1}$ represent the mean period protected by maternal antibodies, the mean latent period and the mean infectious period, respectively, whereas with $\mu = \mu(a)$ we indicate the instantaneous death rate at age a . In order to have attainable finite age, we assume that:

Hp1: μ is a nonnegative locally integrable function, such that $\int_0^{r_m} \mu(a)da = +\infty$.

Finally, the term $\lambda = \lambda(a,t)$ represents the so-called force of infection and it is given by the following function:

$$\lambda(a,t) = \int_0^{r_m} \beta(a,\sigma)I(\sigma,t)d\sigma,$$

where $\beta(a,\sigma)$ is the probability, per unit of time, that a susceptible of age a meets an infectious of age σ and the first becomes latent: this means that, at time t , the probability a susceptible became latent during the interval $(a, a + da)$ is given by $\lambda(a,t)da$. It is reasonable to assume:

Hp2: $\beta(a,\sigma)$ is an essentially bounded function over the interval $(0, r_m) \times (0, r_m)$: $0 \leq \beta \leq \bar{\beta}$.

System (2) is supplemented with the boundary conditions:

$$M(0,t) = q > 0, \quad H(0,t) = 0, \quad H = S, E, I, R$$

and the initial conditions:

$$H(a,0) = H_0(a) > 0, \quad H = M, S, E, I, R.$$

REMARK 1. From now on, we often use the following definition:

$$\tilde{H} = HI(a), \quad H = N, M, S, E, I, R,$$

with

$$l(a) = \exp\left[\int_0^a \mu(s) ds\right].$$

and the following notations:

$$\tilde{H}_t = \frac{\partial}{\partial t} \tilde{H}(a, t), \quad \tilde{H}_a = \frac{\partial}{\partial a} \tilde{H}(a, t), \quad \tilde{H} = \tilde{N}, \tilde{M}, \tilde{S}, \tilde{E}, \tilde{I}, \tilde{R}, \quad a \in (0, r_m), t > 0,$$

$$\tilde{H}_0(a) = H_0(a)l(a), \quad \tilde{H} = \tilde{N}, \tilde{M}, \tilde{S}, \tilde{E}, \tilde{I}, \tilde{R}, \quad a \in [0, r_m].$$

By summing all equations of system (2) and taking into account definition (1), we have the following system:

$$(3) \quad \begin{cases} \tilde{N}_t + \tilde{N}_a = 0, \\ \tilde{N}(0, t) = q, \\ \tilde{N}(a, 0) = N_0(a)l(a) = \tilde{N}_0(a), \end{cases}$$

where $N_0(a) = M_0(a) + S_0(a) + E_0(a) + I_0(a) + R_0(a)$ (see also Remark 1).

Let us consider the Banach space $X = L^1(0, r_m)$, with norm

$$(4) \quad \|f\| = \int_0^{r_m} |f(a)| da, \quad \forall f \in X,$$

and positive cone ([7], [10])

$$X^+ = \{f \in X, f(a) \geq 0, \text{ a.e. in } (0, r_m)\}.$$

It is easy to prove that the solution of system (3) has the form:

$$(5) \quad \tilde{N}(a, t) = \begin{cases} \tilde{N}_0(a-t), & a \geq t, \\ q, & a < t. \end{cases}$$

If \tilde{N}_0 is a bounded function, a suitable $k > 0$ exists such that $|\tilde{N}_0(a)| \leq k$, for any $a \in [0, r_m]$ and

$$(6) \quad |\tilde{N}(a, t)| \leq K, \quad \forall t \geq 0, a \in [0, r_m],$$

with $K = \max(k, q)$.

Since the first equation of system (2) is similar to the first one of (3), the solution of

$$\begin{cases} \tilde{M}_t + \tilde{M}_a = -\delta \tilde{M}, \\ \tilde{M}(0, t) = q, \\ \tilde{M}(a, 0) = M_0(a)l(a) = \tilde{M}_0(a), \end{cases}$$

is given by:

$$(7) \quad \tilde{M}(a, t) = \begin{cases} \tilde{M}_0(a-t) \exp(-\delta t), & a \geq t, \\ q \exp(-\delta a), & a < t. \end{cases}$$

REMARK 2. Note that $\tilde{M} \in X^+$, provided that $\tilde{M}_0(a) \geq 0$ for $a \in [0, r_m]$. Moreover, since it is reasonable to assume $|\tilde{M}_0(a)| \leq k$, then \tilde{M} satisfies estimate (6).

Since from definitions (1) and Remark 1

$$\tilde{R} = \tilde{N} - \tilde{M} - \tilde{S} - \tilde{E} - \tilde{I},$$

system (2) will be completely solved, if we find the solutions of the following system :

$$(8) \quad \begin{cases} \tilde{S}_t + \tilde{S}_a = \delta \tilde{M} - \lambda \tilde{S}, \\ \tilde{E}_t + \tilde{E}_a = \lambda \tilde{S}, \\ \tilde{I}_t + \tilde{I}_a \alpha \tilde{E} = \gamma \tilde{I} \\ \tilde{S}(0, t) = \tilde{E}(0, t) = \tilde{I}(0, t) = 0, \\ \tilde{S}(a, 0) = \tilde{S}_0(a), \tilde{E}(a, 0) = \tilde{E}_0(a), \tilde{I}(a, 0) = \tilde{I}_0(a), \end{cases}$$

where \tilde{M} is given by (7) (see also Remark 1).

Define the operator:

$$(9) \quad Lf = -f', \quad D(L) = \{f \in X, f' \in X, f(0) = 0\}, \quad R(L) \subset X.$$

Note that L is a linear operator, because its domain contains the homogeneous boundary condition. We prove it generates a linear C_0 -semigroup, [1].

In order to study system (8), we prove three preliminary lemmas.

LEMMA 1. *The operator L satisfies the following properties:*

i) $\|(\lambda I - L)^{-1}g\| \leq \frac{1}{\lambda} \|g\|, \quad \forall g \in X;$

ii) $D(L)$ is dense in X ;

iii) L is closed.

Proof. Consider the equation

$$(\lambda I - L)f = g$$

where the unknown f must be sought in $D(L)$. Hence the solution of

$$f' = -\lambda f + g, \quad f(0) = 0,$$

is given by:

$$f(a) = \int_0^a g(s) \exp[-\lambda(a-s)] ds, \quad 0 < a < r_m.$$

Moreover, from (4):

$$\|f\| \leq \int_0^{r_m} e^{\lambda s} |g(s)| ds \int_s^{r_m} e^{-\lambda a} da \leq \frac{1}{\lambda} \|g\|.$$

Thus, f belongs to $D(L)$. Property ii) follows from the fact that $D(L) \supset C_0^\infty(0, r_m)$, which is dense in X . Finally, since $D((\lambda I - L)^{-1}) = X$ and $(\lambda I - L)^{-1}$ is a bounded operator, $(\lambda I - L)^{-1}$ is a closed operator. Hence, also $L = -(\lambda I - L) + \lambda I$ is a closed operator, [5]. \square

REMARK 3. Lemma 1 proves that the operator $(\lambda I - L)^{-1}$ exists, it is defined on the whole space X and is a bounded operator; hence, it is the resolvent operator $R(\lambda, L)$ of L , [5].

LEMMA 2. L is the generator of a C_0 -semigroup $Z(t) = \{\exp(tL), t \geq 0\}$, such that

$$\|Z(t)f\| \leq \|f\|.$$

The semigroup $Z(t)$ maps the positive cone X^+ into itself.

The proof of the theorem follows directly from the Hille Yosida Theorem, [5], [9].

Define the operator

$$Jf = \int_0^{r_m} \beta(a, \sigma) f(\sigma) d\sigma, \quad D(J) = X, \quad R(J) \subset X.$$

The following lemma holds.

LEMMA 3. J is a bounded operator and $\|J\| \leq \bar{\beta}r_m$. Moreover, $Jf \in L^\infty(0, r_m)$, for any $f \in X$, and $\|Jf\|_\infty \leq \bar{\beta}\|f\|$, where $\|\cdot\|_\infty$ is the norm in $L^\infty(0, r_m)$.

To study system (8), consider the Banach space

$$X^* = X \times X \times X,$$

with norm

$$\|\mathbf{f}\|_* = \left\| \begin{pmatrix} f_1 \\ f_2 \\ f_3 \end{pmatrix} \right\| = \sum_{i=1}^3 \|f_i\|, \quad \forall \mathbf{f} \in X^*,$$

where $X = L^1(0, r_m)$ and $\|f_i\|$ is given by (4), with $f_i \in X, i = 1, 2, 3$.

Define the following operators

$$L^*\mathbf{f} = \begin{pmatrix} Lf_1 & 0 & 0 \\ 0 & Lf_2 - \alpha f_2 & 0 \\ 0 & 0 & Lf_3 - \gamma f_3 \end{pmatrix},$$

$$D(L^*) = D(L) \times D(L) \times D(L), \quad R(L^*) \subset X^*,$$

$$(10) \quad F\mathbf{f} = \begin{pmatrix} -f_1 J f_3 \\ f_1 J f_3 \\ \alpha f_2 \end{pmatrix}, \quad D(F) = X^*, \quad R(F) \subset X^*.$$

By using operator L^* and F , the abstract version of (8) becomes:

$$(11) \quad \begin{cases} \frac{d}{dt} \mathbf{u}(t) = L^* \mathbf{u}(t) + F \mathbf{u}(t) + \mathbf{g}(t), & t > 0, \\ \mathbf{u}(0) = \mathbf{u}_0, \end{cases}$$

where

$$(12) \quad \mathbf{u}(t) = \begin{pmatrix} u_1(t) \\ u_2(t) \\ u_3(t) \end{pmatrix} = \begin{pmatrix} \tilde{S}(.,t) \\ \tilde{E}(.,t) \\ \tilde{I}(.,t) \end{pmatrix}; \quad \mathbf{g}(t) = \begin{pmatrix} \delta\tilde{M}(.,t) \\ 0 \\ 0 \end{pmatrix}; \quad \mathbf{u}_0 = \begin{pmatrix} \tilde{S}_0 \\ \tilde{E}_0 \\ \tilde{I}_0 \end{pmatrix}.$$

LEMMA 4. *The linear operator L^* is the generator of a C_0 -semigroup $\{\exp(tL^*), t \geq 0\}$, given by*

$$\exp(tL^*) = \begin{pmatrix} \exp(tL) & 0 & 0 \\ 0 & \exp(-\alpha t)\exp(tL) & 0 \\ 0 & 0 & \exp(-\gamma t)\exp(tL) \end{pmatrix},$$

with L given by (9). Moreover,

$$\|\exp(tL^*)\| \leq 1.$$

Let r be a given positive number, the following subset of X^* can be defined

$$D_r = \{\mathbf{f} \in X^*, \|\mathbf{f}\|_* \leq r\}.$$

LEMMA 5. *F satisfies a Lipschitz condition on D_r and*

$$(13) \quad \|F(\mathbf{f}) - F(\mathbf{g})\|_* \leq \bar{l}\|\mathbf{f} - \mathbf{g}\|_*,$$

with $\bar{l} = 2\bar{\beta}r + \alpha$.

Proof.

$$\begin{aligned} \|F(\mathbf{f}) - F(\mathbf{g})\|_* &= \|f_1 J f_3 - g_1 J g_3\| + \|f_1 J f_3 - g_1 J g_3\| + \|\alpha f_2 - \alpha g_2\| \leq \\ &\leq 2\|f_1 J f_3 - f_1 J g_3\| + 2\|f_1 J g_3 - g_1 J g_3\| + \alpha\|f_2 - g_2\|, \quad \forall \mathbf{f}, \mathbf{g} \in D_r. \end{aligned}$$

From Lemma 3, we have:

$$\|F(\mathbf{f}) - F(\mathbf{g})\|_* \leq 2\bar{\beta}r\|f_3 - g_3\| + 2\bar{\beta}r\|f_1 - g_1\| + \alpha\|f_2 - g_2\| \leq (2\bar{\beta}r + \alpha)\|\mathbf{f} - \mathbf{g}\|_*.$$

□

LEMMA 6. *F is Fréchet differentiable in X^* and the derivative $F_{\mathbf{f}}$ is continuous with respect to $\mathbf{f} \in X^*$.*

Proof. The following equality must be proved, for any given $\mathbf{f}, \mathbf{h} \in X^*$:

$$F(\mathbf{f} + \mathbf{h}) - F(\mathbf{f}) = F_f(\mathbf{h}) + G(\mathbf{f}, \mathbf{h}),$$

where F_f is a linear bounded operator which depends on $\mathbf{f} \in X^*$ and $G(\mathbf{f}, \mathbf{h})$ is such that

$$\lim_{\|\mathbf{h}\|_* \rightarrow 0} \frac{G(\mathbf{f}, \mathbf{h})}{\|\mathbf{h}\|_*} = 0.$$

Since

$$F(\mathbf{f} + \mathbf{h}) - F(\mathbf{f}) = \begin{pmatrix} -f_1 J h_3 - h_1 J f_3 - h_1 J h_3 \\ f_1 J h_3 + h_1 J f_3 + h_1 J h_3 \\ \alpha h_2 \end{pmatrix},$$

by defining

$$F_{\mathbf{f}}(\mathbf{h}) = \begin{pmatrix} -f_1 J h_3 - h_1 J f_3 \\ f_1 J h_3 + h_1 J f_3 \\ \alpha h_2 \end{pmatrix}, \quad G(\mathbf{f}, \mathbf{h}) = \begin{pmatrix} -h_1 J h_3 \\ h_1 J h_3 \\ 0 \end{pmatrix},$$

we have that

$$\lim_{\|\mathbf{h}\|_* \rightarrow 0} \frac{\|G(\mathbf{f}, \mathbf{h})\|_*}{\|\mathbf{h}\|_*} = \lim_{\|\mathbf{h}\|_* \rightarrow 0} 2\bar{\beta}\|\mathbf{h}\|_* = 0.$$

Since

$$\|F_{\mathbf{f}}(\mathbf{h})\|_* = 2\|f_1 J h_3 + h_1 J f_3\|_1 + \alpha\|h_2\|_1 \leq (4\bar{\beta}\|\mathbf{f}\|_* + \alpha)\|\mathbf{h}\|_*,$$

$F_{\mathbf{f}}$ is linear and bounded. Moreover, since

$$\begin{aligned} \|f_1 J h_3 + h_1 J f_3 - g_1 J h_3 - h_1 J g_3\| &\leq \|(f_1 - g_1) J h_3\| + \|h_1 (J f_3 - J g_3)\| \leq \\ &\leq \bar{\beta}\|h_3\| \|(f_1 - g_1)\| + \bar{\beta}\|h_1\| \|f_3 - g_3\| \leq 2\bar{\beta}\|\mathbf{h}\|_* \|\mathbf{f} - \mathbf{g}\|_*, \end{aligned}$$

the continuity of $F_{\mathbf{f}}$ with respect to $\mathbf{f} \in X^*$ is proved, i.e.,

$$\lim_{\|\mathbf{f} - \mathbf{g}\|_* \rightarrow 0} \|F_{\mathbf{f}}(\mathbf{h}) - F_{\mathbf{g}}(\mathbf{h})\|_* = 0.$$

□

THEOREM 1. *System (11) has a unique strict solution $\mathbf{u} = \mathbf{u}(t)$ defined on a suitable interval $[0, T]$.*

The proof of the theorem follows directly from Lemmas 4, 5, 6 and by the definition of \mathbf{g} , given by (12), [1]. Such a solution can be found by using a successive approximation procedure for the integral equation

$$(14) \quad \mathbf{u}(t) = \exp(tL^*)\mathbf{u}_0 + \int_0^t \exp[(t-s)L^*][\mathbf{g}(s) + F(\mathbf{u}(s))]ds.$$

Since we proved that $\tilde{N}(a, t)$ is a bounded and positive function (see (6)), it is quite reasonable to think that also the solution of (11) (or equivalently the solution of the integral equation (14)) has bounded and positive components. In order to prove this, let us introduce the space

$$X_{\infty}^* = X_{\infty} \times X_{\infty} \times X_{\infty} = L^{\infty}(0, r_m) \times L^{\infty}(0, r_m) \times L^{\infty}(0, r_m),$$

with norm

$$\|\mathbf{f}\|_{\infty} = \sum_{i=1}^3 \|f_i\|_{\infty}, \quad \forall \mathbf{f} \in X_{\infty}^*,$$

where $\|f_i\|_\infty = \sup\{f_i(a), a \in (0, r_m)\}, \forall f_i \in X_\infty, i = 1, 2, 3$. For a suitable $\hat{m} > 0$, define the set:

$$S(\hat{m}) = \{\mathbf{f} \in X^* \cap X_\infty, \|\mathbf{f}\|_\infty \leq \hat{m}\}.$$

It can be proved that $S(\hat{m})$ is a not empty closed set of X^* (see Example 1.23 of [1]).

LEMMA 7. *If $\mathbf{f} \in S(\hat{m})$, then $\exp(tL^*)\mathbf{f} \in S(\hat{m})$ and $F(\mathbf{f}) \in S(2\bar{\beta}\hat{m}^2 + \alpha\hat{m})$.*

The proof of the lemma follows from Lemmas 3, 4, definition (10) and the properties of $S(\hat{m})$.

Define the space

$$X_c^* = C([0, T]; X^*),$$

(T will be chosen in the sequel), with the norm

$$\|\mathbf{f}\|_c = \max\{\|\mathbf{f}(t)\|_*, t \in [0, T]\}, \quad \forall \mathbf{f} \in X_c^*.$$

Consider the following closed subset of X_c^* :

$$\Delta(\hat{m}) = \{\mathbf{f} \in X_c^*, \mathbf{f}(t) \in S(\hat{m}), t \in [0, T]\}.$$

The nonlinear Volterra integral equation (14) can be written as

$$\mathbf{u} = Q\mathbf{u},$$

where:

$$(15) \quad Q(\mathbf{f}(t)) = \exp(tL^*)\mathbf{u}_0 + \int_0^t \exp[(t-s)L^*] [\mathbf{g}(s) + F(\mathbf{f}(s))] ds,$$

with $D(Q) = X_c^*, R(Q) \subset X_c^*$.

LEMMA 8. *If $\mathbf{u}_0 \in S(\hat{n})$, with \hat{n} a given positive constant, then:*

- i) $Q\mathbf{f} \in \Delta(\hat{n}p(T))$, for $\mathbf{f} \in \Delta(\hat{n})$;
- ii) $\|Q(\mathbf{f}) - Q(\mathbf{g})\|_c \leq p(T)\|\mathbf{f} - \mathbf{g}\|_c$, for $\mathbf{f}, \mathbf{g} \in \Delta(\hat{n})$,

where

$$p(T) = \left[\frac{\hat{n} + \exp T - 1}{\hat{m}} (\delta K + 2\hat{m}^2\bar{\beta} + 2\hat{m}^2\bar{\beta}r_m + \alpha\hat{m}) \right].$$

Proof. From definitions (15), we have:

$$\|Q(\mathbf{f}(t))\|_\infty \leq \hat{n} + (\delta K + 2\bar{\beta}\hat{m}^2 + \alpha\hat{m}) \int_0^t \exp(t-s) ds \leq \hat{m}p(T).$$

Moreover, if $\mathbf{f}, \mathbf{g} \in \Delta(\hat{n})$, from Lemma 5, we have:

$$\|Q(\mathbf{f}) - Q(\mathbf{g})\|_c \leq \int_0^t \exp(t-s) \|F(\mathbf{f}(s)) - F(\mathbf{g}(s))\|_c ds \leq p(T)\|\mathbf{f} - \mathbf{g}\|_c.$$

□

REMARK 4. If we choose $\hat{n} < \hat{m}$, then $\lim_{T \rightarrow 0} p(T) = \hat{n}/\hat{m} < 1$, i.e., a suitably small T exists, such that $p(T) < 1$. This means that Q maps $\Delta(\hat{m})$ into itself and is strictly contractive on $\Delta(\hat{m})$. Note that the relevance of this result is due to the fact that, even if T could be really small, after finding an a priori estimate of the norm of the solution, it permits to prove the existence and uniqueness of the solution for each $t \geq 0$ (see in the sequel and [9], Theorem 1.4, Chapter 6).

THEOREM 2. If $\mathbf{u}_0 \in S(\hat{n})$ and $\hat{m} > \hat{n}$, then system (11) has a unique strict solution $\mathbf{u} = \mathbf{u}(t)$ defined on a suitable interval $[0, T]$ and such that $\mathbf{u}(t) \in S(\hat{m}), t \in [0, T]$.

Choose $\mathbf{u}_0 = \begin{pmatrix} \tilde{S}_0 \\ \tilde{E}_0 \\ \tilde{I}_0 \end{pmatrix} \in S(\hat{n})$ and $\hat{m} > \hat{n}$. From system (11), we have:

$$u_1(t) = \exp(tL)e^{-\hat{m}t}\tilde{S}_0 + \int_0^t \exp[(t-s)L]e^{-\hat{m}(t-s)}\delta\tilde{M}(s)ds + \\ + \int_0^t \exp[(t-s)L]e^{-\hat{m}(t-s)}u_1(s)(\hat{m} - Ju_3(s))ds,$$

$$(16) \quad u_2(t) = \exp(tL)e^{-\alpha t}\tilde{I}_0 + \int_0^t \exp[(t-s)L]e^{-\alpha(t-s)}u_1(s)Ju_3(s)ds,$$

$$u_3(t) = \exp(tL)e^{-\gamma t}\tilde{E}_0 + \int_0^t \exp[(t-s)L]e^{-\gamma(t-s)}\alpha u_2(s)ds.$$

THEOREM 3. Each component $u_i(t), i = 1, 2, 3$, of $\mathbf{u}(t)$ belongs to X^+ , for any t u_i is defined.

It is possible to prove the theorem by a successive approximation procedure.

From Theorem 3, since it can be easily proved that $M, R \in X^+$, from (6) we have that $\|\mathbf{u}(t)\|_* \leq Kr_m$. This a priori estimate proves the existence of a unique strict solution $\mathbf{u}(t)$ of the Eq. (14), for each $t \geq 0$ (see [1] and [9], Theorem 1.4, Chapter 6). From Lemma 6 and the regularity properties of the known term $\mathbf{g}(t)$, follows the differentiability of $\mathbf{u}(t)$. It is easy to prove that also \tilde{M} and \tilde{R} are differentiable functions both with respect to a and t . Hence, the following result holds (see [9], Theorem 1.5, Chapter 6).

THEOREM 4. System (8) has a unique classical solution defined for each $t \geq 0$ and whose components belong to X^+ , provided that the initial conditions belong to X^+ .

REMARK 5. Defining the nonlinear operator

$$Af = -f', \quad D(A) = \{f \in X, f' \in X, f(0) = q\},$$

it can be easily proved that A generates a nonlinear semigroup of contractions $\{W(t), t \geq 0\}$ given by (5) and the solution of the evolution problem is given by $w(t) = W(t)N_0, t \geq 0$. Note that the operator A is nonlinear because of its domain.

3. A simplified model

The aim of this section is to derive a system of ordinary differential equations which simplify system (2) and to study the stability properties of its equilibrium solutions. In order to make this section more readable and less boring, we introduce some notations and omit to write many calculations.

Define the following quantities:

$$(17) \quad \tilde{\mu}_H = \frac{\int_0^{r_m} \mu(a)H(a,t)da}{\|H(t)\|}, \quad H = M, S, E, I, R,$$

$$m = \frac{\int_0^{r_m} p(a)S(a,t)da}{\|S(t)\|}, \quad \text{with } p(a) = \frac{\int_0^{r_m} \beta(a, \sigma)I(\sigma,t)d\sigma}{\|I(t)\|}, \quad a \in (0, r_m).$$

To get a simplified model, we make the following assumption:

Hp3: the quantities defined in (17) are constant and such that:

$$\tilde{\mu} = \tilde{\mu}_M = \tilde{\mu}_S = \tilde{\mu}_E = \tilde{\mu}_I = \tilde{\mu}_R.$$

Even if Hp3 seems very restrictive, estimates found in Section 2 can be used to evaluate $\tilde{\mu}_H, H = M, S, E, I, R$.

Integrating equations of system (2) with respect to a in the interval $[0, r_m]$, taking into account the properties of M, S, E, I, R , and using the notation $\|H\|_t = \frac{d}{dt}\|H\|, H = M, S, E, I, R$, we have:

$$(18) \quad \left\{ \begin{array}{l} \|M(t)\|_t = q - (\tilde{\mu} + \delta) \|M(t)\|, \\ \|S(t)\|_t = \delta \|M(t)\| - \tilde{\mu} \|S(t)\| - M \|S(t)\| \|I(t)\|, \\ \|E(t)\|_t = m \|S(t)\| \|I(t)\| - \tilde{\mu} \|E(t)\| - \alpha \|E(t)\|, \\ \|I(t)\|_t = \alpha \|E(t)\| - \tilde{\mu} \|I(t)\| - \gamma \|I(t)\|, \\ \|R(t)\|_t = \gamma \|I(t)\| - \tilde{\mu} \|R(t)\|, \\ \|H(0)\| = \|H_0\| \quad H = M, S, E, I, R. \end{array} \right.$$

Solving the first equation of (18), we get

$$(19) \quad \|M(t)\| = e^{-(\tilde{\mu}+\delta)t} \|M_0\| + \frac{q}{\tilde{\mu} + \delta} (1 - e^{-(\tilde{\mu}+\delta)t}).$$

Note that

$$\lim_{t \rightarrow +\infty} \|M(t)\| = \frac{q}{\tilde{\mu} + \delta} = \bar{M},$$

where \bar{M} is the equilibrium solution and it results asymptotically stable.

By summing all equations of system (18), and using (19), it is easy to prove that

$$\lim_{t \rightarrow +\infty} (\|S(t)\| + \|E(t)\| + \|I(t)\| + \|R(t)\|) = \frac{q}{\tilde{\mu}} - \frac{q}{\tilde{\mu} + \delta} = \frac{q\delta}{\tilde{\mu}(\tilde{\mu} + \delta)}.$$

In order to simplify (18), we shall consider the system for large time, and we put $\|M(t)\| = \bar{M}$:

$$(20) \quad \left\{ \begin{array}{l} \|S(t)\|_t = \frac{\delta q}{\tilde{\mu} + \delta} - (\tilde{\mu} + m\|I(t)\|)\|S(t)\|, \\ \|E(t)\|_t = m\|S(t)\|\|I(t)\| - (\tilde{\mu} + \alpha)\|E(t)\|, \\ \|I(t)\|_t = \alpha\|E(t)\| - (\tilde{\mu} + \gamma)\|I(t)\|, \\ \|R(t)\|_t = \gamma\|I(t)\| - \tilde{\mu}\|R(t)\|, \\ \|H(0)\| = \|H_0\| \quad H = S, E, I, R. \end{array} \right.$$

The equilibrium solution $(\bar{S}, \bar{E}, \bar{I}, \bar{R})$ of (20) satisfies the following system:

$$(21) \quad \left\{ \begin{array}{l} 0 = \frac{\delta q}{\tilde{\mu} + \delta} - (\tilde{\mu} + m\bar{I})\bar{S}, \\ 0 = m\bar{S}\bar{I} - (\tilde{\mu} + \alpha)\bar{E}, \\ 0 = \alpha\bar{E} - (\tilde{\mu} + \gamma)\bar{I}, \\ 0 = \gamma\bar{I} - \tilde{\mu}\bar{R}. \end{array} \right.$$

From the last two equations of (21), we get

$$(22) \quad \bar{R} = \frac{\gamma}{\tilde{\mu}}\bar{I}, \quad \bar{E} = \frac{\tilde{\mu} + \gamma}{\alpha}\bar{I}.$$

Hence, by substituting (22) into the first two equations of (21), we have

$$(23) \quad \left\{ \begin{array}{l} 0 = \frac{\delta q}{\tilde{\mu} + \delta} - \tilde{\mu}\bar{S} - m\bar{S}\bar{I}, \\ 0 = m\bar{S}\bar{I} - \frac{(\tilde{\mu} + \alpha)(\tilde{\mu} + \gamma)}{\alpha}\bar{I}. \end{array} \right.$$

$\bar{I} = 0$ is a solution of the second equation of (23); since from (22), we get $\bar{R} = \bar{E} = 0$, from the first of (23):

$$(24) \quad \bar{S} = \frac{\delta q}{\tilde{\mu}(\tilde{\mu} + \delta)}.$$

If we define:

$$(25) \quad S(t) = \|S(t)\| - \bar{S}, \mathcal{E}(t) = \|E(t)\|, I(t) = \|I(t)\|,$$

system (20) becomes:

$$(26) \quad \begin{cases} S_t = -(\tilde{\mu} + mI)S - \frac{m\delta q}{\tilde{\mu}(\tilde{\mu} + \delta)}I, \\ \mathcal{E}_t = [mS + \frac{m\delta q}{\tilde{\mu}(\tilde{\mu} + \delta)}]I - (\tilde{\mu} + \alpha)\mathcal{E}, \\ I_t = \alpha\mathcal{E} - (\tilde{\mu} + \gamma)I, \\ S(0) = S_0, \mathcal{E}(0) = \mathcal{E}_0, I(0) = I_0. \end{cases}$$

Since the Jacobian matrix of the right hand side of (26), evaluated in the equilibrium solution $(0, 0, 0)$ is

$$J(0, 0, 0) = \begin{pmatrix} -\tilde{\mu} & 0 & -\frac{m\delta q}{\tilde{\mu}(\tilde{\mu} + \delta)} \\ 0 & -(\tilde{\mu} + \alpha) & \frac{m\delta q}{\tilde{\mu}(\tilde{\mu} + \delta)} \\ 0 & \alpha & -(\tilde{\mu} + \gamma) \end{pmatrix},$$

its eigenvalues are given by:

$$\lambda_1 = -\tilde{\mu}, \quad \lambda_{2,3} = \frac{-(\tilde{\mu} + \alpha) - (\tilde{\mu} + \gamma) \pm \sqrt{(\alpha - \gamma)^2 + 4\alpha m\delta q / \tilde{\mu}(\tilde{\mu} + \delta)}}{2}.$$

Whereas λ_1 is always a negative real number, $\lambda_2 \neq \lambda_3$ are negative real numbers if

$$(\tilde{\mu} + \alpha)(\tilde{\mu} + \gamma) > \frac{\alpha m\delta q}{\tilde{\mu}(\tilde{\mu} + \delta)}.$$

With this assumption, the equilibrium solution $(0, 0, 0)$ is asymptotically stable; the number of susceptibles $\|S(t)\|$ tends to \bar{S} , whereas both the number of latents and the number of infectives tend to zero. Moreover, it can be shown that also the number of removed individuals tends to zero, for large time. Note that, if

$$(27) \quad (\tilde{\mu} + \alpha)(\tilde{\mu} + \gamma) = \frac{\alpha m\delta q}{\tilde{\mu}(\tilde{\mu} + \delta)},$$

one of the eigenvalues of $J(0, 0, 0)$ is zero; hence the stability of $(0, 0, 0)$ has to be analyzed in another way. For example, by summing all equations of (26) with the fourth of (20) and defining $\mathcal{R}(t) = \|R(t)\|$, since

$$S(t) + \mathcal{E}(t) + I(t) + \mathcal{R}(t) = (S_0 + \mathcal{E}_0 + I_0 + \mathcal{R}_0)e^{-\tilde{\mu}t},$$

we get

$$(28) \quad \lim_{t \rightarrow +\infty} S(t) + \mathcal{E}(t) + I(t) + \mathcal{R}(t) = 0.$$

If $S_0, \mathcal{E}_0, I_0, \mathcal{R}_0 \in \mathbb{R}^+$, ($\|S_0\| > \bar{S}$ from (25)), hence $S(t), \mathcal{E}(t), I(t), \mathcal{R}(t) \in \mathbb{R}^+$, $t \geq 0$ and (28) implies that each term of the sum tends to 0. In particular, if $\|S_0\| > \bar{S}$ (for instance, δ or q or both are small quantities), the number of susceptibles decreases to \bar{S} , whereas the number of latent, infectious and removed individuals tends to zero.

In a similar way, if $S_0 < 0$ ($\|S_0\| < \bar{S}$ from (25)), $\mathcal{E}_0, I_0, \mathcal{R}_0 \in \mathbb{R}^+$, hence $S(t) < 0$, $\mathcal{E}(t), I(t), \mathcal{R}(t) \in \mathbb{R}^+$, $t \geq 0$. In fact, with (27), system (26) becomes:

$$\begin{cases} S_t = -(\tilde{\mu} + mI)S - [(\tilde{\mu} + \alpha)(\tilde{\mu} + \gamma)I]/\alpha, \\ \mathcal{E}_t = m[S + (\tilde{\mu} + \alpha)(\tilde{\mu} + \gamma)/\alpha]I - (\tilde{\mu} + \alpha)\mathcal{E}, \\ I_t = \alpha\mathcal{E} - (\tilde{\mu} + \gamma)I, \\ \mathcal{R}_t = \gamma I - \tilde{\mu}\mathcal{R}, \\ S(0) = S_0, \mathcal{E}(0) = \mathcal{E}_0, I(0) = I_0, \mathcal{R}(0) = \mathcal{R}_0. \end{cases}$$

Since by summing the second, the third and the fourth equations of the previous system

$$\begin{cases} (\mathcal{E} + I + \mathcal{R})_t = m[S + (\tilde{\mu} + \alpha)(\tilde{\mu} + \gamma)]I/\alpha - \tilde{\mu}(\mathcal{R} + \mathcal{E} + I), \\ \mathcal{E}(0) + I(0) + \mathcal{R}(0) = \mathcal{E}_0 + I_0 + \mathcal{R}_0, \end{cases}$$

by applying Gromwall's inequality, we get:

$$\mathcal{E}(t) + I(t) + \mathcal{R}(t) \leq (\mathcal{E}_0 + I_0 + \mathcal{R}_0) \exp[(m\bar{S} - \tilde{\mu})t],$$

where we used (24) and (27). As a consequence, if

$$(29) \quad \bar{S} < \frac{\tilde{\mu}}{m},$$

the sum $\mathcal{E}(t) + I(t) + \mathcal{R}(t)$ goes to zero, as $t \rightarrow +\infty$. Since $\mathcal{E}, I, \mathcal{R} \in \mathbb{R}^+$, it results that $\lim_{t \rightarrow +\infty} \mathcal{E}(t) = \lim_{t \rightarrow +\infty} I(t) = \lim_{t \rightarrow +\infty} \mathcal{R}(t) = 0$. Hence, from (28), we get that $\lim_{t \rightarrow +\infty} S(t) = 0$, that is $\lim_{t \rightarrow +\infty} \|S(t)\| = \bar{S}$. Thus, if (27) holds and (29) is fulfilled (for instance, if the latent period or the force of infection or both are small), the equilibrium $(\bar{S}, 0, 0, 0)$ is such that \tilde{S} tends to \bar{S} .

Finally, if

$$(30) \quad (\tilde{\mu} + \alpha)(\tilde{\mu} + \gamma) < \frac{\alpha m \delta q}{\tilde{\mu}(\tilde{\mu} + \delta)},$$

one of the eigenvalues of $J(0, 0, 0)$ is positive and the equilibrium solution $(0, 0, 0)$ is unstable.

Let us come back to system (23); if $\bar{I} \neq 0$ the solutions are given by

$$(31) \quad \hat{S} = \frac{(\tilde{\mu} + \alpha)(\tilde{\mu} + \gamma)}{m\alpha}, \quad \hat{I} = h, \quad \hat{E} = h \left(\frac{\tilde{\mu} + \gamma}{\alpha} \right), \quad \hat{R} = h \frac{\gamma}{\tilde{\mu}},$$

where

$$(32) \quad h = \frac{\delta q \alpha}{(\tilde{\mu} + \delta)(\tilde{\mu} + \alpha)(\tilde{\mu} + \gamma)} - \frac{\tilde{\mu}}{m}.$$

Values in (31) have biological meaning if $h > 0$. Since this agrees with (30), we have that the condition which makes the equilibrium solution $(\bar{S}, 0, 0, 0)$ unstable, provides also the existence of the biological equilibrium solution $(S, \mathcal{E}, I, \mathcal{R})$. Moreover, $h = 0$ represents (27) and yields to the equilibrium solution $(\bar{S}, 0, 0, 0)$ again.

Assuming $h > 0$, let us analyze the stability of $(\hat{S}, \hat{E}, \hat{I}, \hat{R})$. Since, by using definitions (31) and the following notation

$$\hat{\mathcal{H}}(t) = \|H(t)\| - \hat{H}, \quad H = S, I, R,$$

system (20) becomes:

$$(33) \quad \begin{cases} \hat{S}_t = -m\|S\|\hat{I} - (mh - \tilde{\mu})\hat{S}, \\ \hat{E}_t = m(\|S\|\hat{I} + h\hat{S}) - (\tilde{\mu} + \alpha)\hat{E}, \\ \hat{I}_t = \alpha\hat{E} - (\tilde{\mu} + \gamma)\hat{I}, \end{cases}$$

the unique equilibrium solution is $(0, 0, 0)$ and the Jacobian matrix of the right hand side is:

$$J(0, 0, 0) = \begin{pmatrix} -(mh + \tilde{\mu}) & 0 & -m\hat{S} \\ mh & -(\tilde{\mu} + \alpha) & m\hat{S} \\ 0 & \alpha & -(\tilde{\mu} + \gamma) \end{pmatrix}.$$

Since the characteristic equation of $J(0, 0, 0)$

$$(34) \quad \lambda^3 + \lambda^2(a + b + h + \tilde{\mu}) - \lambda(a + b)(h + \tilde{\mu}) + abh = 0,$$

(with $a = \tilde{\mu} + \alpha, b = \tilde{\mu} + \gamma$) has three solutions whose product is given by the known term $abh > 0$, it follows that the matrix $J(0, 0, 0)$ has at least one positive eigenvalue. In fact, if (34) admits only one real solution, it must be positive, because the product of the other two complex conjugate solutions is positive. On the other hand, if there are three real solutions, by examining all the possibilities, we find that at least one of these is positive. This means that the equilibrium point $(0, 0, 0)$ is unstable for system (33) and thus the equilibrium solution $(\hat{S}, \hat{E}, \hat{I}, \hat{R})$ is unstable for system (20).

Note that the stability analysis is quite similar to that made for other epidemic models (see, for instance, the more complicated model presented in [11]). In particular,

we can conclude that if the coefficient m is very small or the mortality coefficient $\tilde{\mu}$ is very high, the number of susceptibles tends to the equilibrium value $\bar{S} \neq 0$, whereas the number of latent, infective and removed individuals tends to zero. In this case, as in the simpler Kermack Mc Kendrick model, the disease stops because there are not yet infectives and there are some individuals who do not become infective in any case. On the other hand, if $h > 0$ (see (32)), i.e., if the mortality coefficient $\tilde{\mu}$ is small or m is high, there is a non trivial equilibrium solution, (endemic steady state solution) $(\hat{S}, \hat{E}, \hat{I}, \hat{R})$, which is unstable (see [11]).

All the results of this section can be summarized in the following theorem.

THEOREM 5. *The simplified system (20) has two equilibrium solutions $(\bar{S}, 0, 0, 0)$ and $(\hat{S}, \hat{E}, \hat{I}, \hat{R})$. The first solution is asymptotically stable if $h > 0$ and is unstable if $h < 0$, with h given by (32). The second solution has biological meaning if $h > 0$ and it is unstable. If $h = 0$, only the equilibrium solution $(\bar{S}, 0, 0, 0)$ exists and it is such that $\mathcal{E}, \mathcal{I}, \mathcal{R} \rightarrow 0$ and $s(t) \rightarrow \bar{S}$, provided that $\bar{S} < \tilde{\mu}/m$.*

Acknowledgments This work was partially supported by PAR 2006 - Research Project “Metodi e modelli matematici per le applicazioni” of the University of Siena, Italy, as well as by M.U.R.S.T. research funds.

References

- [1] BELLENI MORANTE A. AND MCBRIDE A. C., *Applied Nonlinear Semigroups*, John Wiley & Sons, Chichester 1999.
- [2] BUSEMBERG S., IANNELLI M. AND THIEME H. R., *Global behaviour of an age-structured epidemic model*, SIAM J. Math. Anal. **22** (1991), 1065–1080.
- [3] CHA Y., IANNELLI M. AND MILNER F. A., *Existence and uniqueness of endemic states for the age-structured S-I-R epidemic model*, Math. Biosci. **150** (1998), 177–190.
- [4] EL-DOMA M., *Analysis of an age-dependent SIS epidemic model with vertical transmission and proportionate mixing assumption*, Math. Comput. Modelling **29** (1999), 31–43.
- [5] KATO T., *Perturbation theory for linear operators*, Springer Verlag, 1984.
- [6] KERMACK W.O. AND MCKENDRICK A. G., *A contribution to the mathematical theory of epidemics*, Proc. Roy. Soc. Lond. A **115** (1927), 700–721.
- [7] KRASNOSEL'SKII M., *Positive solutions of operator equations*, P. NoordHoof, Groningen 1964.
- [8] MANFREDI P. AND WILLIAMS J. R., *Realistic population dynamics in epidemiological models: the impact of population decline on the dynamics of childhood infectious diseases. Measels in Italy as an example*, Math. Biosci. **192** (2004), 153–175.
- [9] PAZY A., *Perturbation theory for linear operators*, Springer Verlag, 1984.
- [10] SCHAEFFER H. H., *Banach lattices and positive operators*, Grund. Math. Wissenschaften, Band 215, Springer Verlag, New York 1974.
- [11] SHUETTE M. C., *A qualitative analysis for the transmission of varicella-zoster virus*, Math. Biosci. **182** (2003), 113–126.
- [12] SHUETTE M. C. AND HETHCOTE H. W., *Modeling the effects of varicella vaccination programs on the incidence of chickenpox and shingles*, Bull. Math. Biol. **61** (1999), 1031–1064.
- [13] LI X., GUPUR G. AND ZHU G., *Existence and uniqueness of endemic states for the age structured MSEIR epidemic model*, Acta Math. Appl. Sinica **18** (2002), 441–454.

AMS Subject Classification: 47D06, 47H20, 92B05.

Meri LISI, Silvia TOTARO, Dipartimento di Scienze Matematiche ed Informatiche "Roberto Magari",
Università degli Studi di Siena, Pian dei Mantellini 44, 53100, Siena, ITALY
e-mail: lisi7@unisi.it, totaro@unisi.it

Lavoro pervenuto in redazione il 27.11.2007 e, in forma definitiva, il 19.02.2008.