A RENEWAL REWARD PROCESS AND A WEIBULL MODEL FOR THE FAILURE ON CORTISOL
CHAPTER VI

A RENEWAL REWARD PROCESS AND A WEIBULL MODEL FOR THE FAILURE ON CORTISOL

6.1 INTRODUCTION

In Chapter VI two models have been described. The first model, is “Stochastic Model for Cost of Adaptation Due to Acute Stress, Memory, Attention and Cortisol”[105] and the second model deals with “Stochastic Model for Cortisol Secretion of Asthmatic Children Due to Stress”[71].

The Cortisol responses to acute stressors are thought to be highly adaptive to the organism, ensuring physiological, affective, cognitive, and behavioral changes. Assessments were conducted during a non-exam and exam period. The results revealed that the exam period was associated with an increase in perceived levels of stress, but also a significant reduction in levels of salivary Cortisol, compared with the non-exam period.

There are now a myriad of research avenues under exploration in the quest to better understand the causes and consequences of psychological stress. Among the most compelling areas of enquiry, is the literature devoted to the effects of stress and concomitant stress hormones on cognitive performance. This work has taken many forms, but in the main has chosen to explore the effects of acute/experimentally induced alterations or chronic/naturally occurring alterations in glucocorticoids on a variety of cognitive parameters.
We have offered only a cursory overview of this now extensive literature, however, investigators have drawn a number of conclusions based on the available data. Firstly, it is evident that both endogenous and exogenous based increases in glucocorticoids are associated with deficits in both memory and attention [96][79]. Secondly, evidence that glucocorticoids can compromise the functioning of the hippocampus [84], has led investigators to speculate that hippocampal-based. Cognitive functions may be at particular risk from the deleterious effects of glucocorticoids [79][137]. Finally, in their review of the human and animal literature on the acute effects of glucocorticoids, [77] concluded that and inverted U-shaped relationship is evident between glucocorticoids and the nature and magnitude of cognitive dysfunction.

The formula for general random minimal repair cost is utilized for the cost of adaptation. By using the theory of renewal reward process, expected long run cost per unit time is obtained and compared with the average length of cycle during relaxation period. It was concluded that the results support the view that Cortisol can modulate cognitive processes and that the effects of corticosteroids on cognitive function are selective.

We have attempted to further existing knowledge on the effects of glucocorticoids on cognitive function. Thus, the aim of this investigation was to examine whether acute changed in corticosteroids during an acute and naturalistic stressor, namely examinations, also modulate cognition.
MODEL I

6.2 NOTATIONS

\( F \) - The life distribution of a new system with density \( f \).

\( r(t) \) - The failure rate function of the system.

\( R(t) \) - Cumulative failure rate function.

\( C(y) \) - Age dependent random part

\( C_1(y) \) - Deterministic part which depends on the age.

\( g \) - A positive non decreasing and continuous function.

\( Y_1, Y_2, \ldots \) - Be the Cortisol symptoms.

\( M(t) \) - Renewal function associated with \( F_p(y) \)

\( T, T_0 \) - Are unknown parameters which determine the replacement policy.

\( p(y) \) - A continuous and non-decreasing function.

\( h(z) \) - Expectation with respect to the random variables \( c(z) \) and \( w(z) \).

\( r, p, \) and \( h \) are continuous functions.

\( J(T_0, T) \) - Total expected long-run cost per unit time

6.3 RESULTS

The formula for modified block replacement with two variables and general random minimal repair cost is utilized for the cost of adaptation \([11][28][30][88][89]\). That is, for each and every stress effect (Cortisol) it is measured. Under such a policy, an operating system is preventively replaced by
new ones at times $kT$ ($k=1,2,\ldots$) independently of its failure history \cite{10,87,88,126,127}. (This is possible because of relaxation).

### 6.4 THE THEORY OF RENEWAL REWARD PROCESS

The model with two variables is transformed into a model with one variable and the optimum policy is discussed.

The policy, which minimized

$$ J(T_0, T) = \frac{E[K(T; T_0, T)]}{T} \quad (6.1) $$

$$ J(T_0, T) = \frac{B(T_0) + Q(T_0, T) + C_2}{T} \quad (6.2) $$

Where

$$ B(T_0) = E[K((0, T_0); T_0, T); Y_1 > T_0] + E[K((0, T_0); T_0, T); Y_1 \leq T_0] $$

$$ B(T_0) = F_p(T_0) \int_0^{T_0} h(z) q(z) r(z) \, dz + C_1 F_p(T_0) \int_0^{T_0} [F_p(z) - F_p(T_0)] h(z) q(z) r(z) \, dz + \int_0^{T_0} B(T_0 - y) d F_p(y) \quad (6.3) $$

Thus $B(T_0)$ satisfies a renewal equation

$$ \dot{B}(T_0) = b(T_0) + \int_0^{T_0} B(T_0 - y) d F_p(y) \quad (6.4) $$
\[ B(T_0) = b(T_0) + \int_0^{T_0} B(T_0 - y) \, dM(y) \]

\[ B(T_0) = C_1 M(T_0) + \int_0^{T_0} F_p(y) h(y) q(y) r(y) \, dy \]
\[ + \int_0^{T_0} M(T_0 - y) F_p(y) h(y) q(y) r(y) \, dy \]  \hspace{1cm} (6.5)

where \( F_p(y) = \exp \left[ - \int_0^{y} p(x) r(x) \, dx \right] \)

\( M(t) \) is the renewal function associated with \( F_p(y) \) and
\[
\frac{h(y)}{h(y)} = \frac{E_{w(y)} [ E_{n(y)} [ g ( C(y), c_{w(y)+1} (y)) ]]}
\]

Where \( \{ w(y), y \geq 0 \} \) is a non-homogeneous Poisson process with intensity \( q(y) r(y) \)

We Obtain
\[
Q(T_0, T) = E[K((T_0, T); T_0, T)]
\]
\[
Q(T_0, T) = \int_{T_0}^{T} F_p(y) h(y) q(y) r(y) \, dy
\]
\[
+ \int_0^{T_0} \int_{T_0}^{T} F_p(x - y) h(x - y) q(x - y) r(x - y) \, dx \, m(y) \, dy
\]
\[
+ C_3 \int_0^{T - T_0} F_p(T_0 + t) - \int_0^{T_0} F_p(T_0 + t - y) m(y) \, dy \, dt \]  \hspace{1cm} (6.6)
Then we get the total expected long-run cost per unit time.

\[
J(T_0, T) = \frac{1}{T} \left[ C_2 + C_1 M(T_0) \right]
\]

\[
+ \int_0^{T_0} F_p(y) h(y) q(y) r(y) dy
\]

\[
+ \int_0^{T_0} M(T_0 - y) F_p(y) h(y) q(y) r(y) dy
\]

\[
+ \int_{T_0}^{T} \int_0^{T_0} F_p(x - y) h(x - y) q(x - y) r(x - y) dx \, m(y) dy
\]

\[
+ \int_{T - T_0}^{T_0} F_p(T_0 + t) - \int_{0}^{T_0} F_p(T_0 + t - y) m(y) dy \, dt \quad (6.7)
\]

Put \( T_0 = 0 \), we obtain

\[
J(0, T) = \frac{1}{T} \left( C_2 + \int_0^{T} F_p(y) h(y) q(y) r(y) dy + C_3 \int_0^{T} F_p(t) dt \right) \quad (6.8)
\]

Put \( q(y) = 1 \), \( c = g(C(y), C_1(y)) \).

Letting \( T_0 = 0 \), \( q(y) = 1 \),

and \( h(y) = E_{w(y)} \left[ E_{C(y)} \left[ g \left( C(y), C_{w(y)+1}(y) \right) \right] \right] = c \).

Therefore \( J(0, T) = \frac{1}{T} \left( C_2 + C \int_0^{T} r(y) dy \right) \quad (6.9) \)

This is the cost function of the periodic replacement model with minimal repair at failure introduced by [4].
6.5 MEDICAL RESULTS OF CORTISOL IN EXAM AND NON-EXAM PERIOD

Undergraduate and postgraduate students who were known to have a period of examinations within the second term of the English academic year were approached regarding the study. The resultant sample consisted of 60 students with a mean age of 22 years. There were 36 male participants and 24 female participants, all of whom were due to embark upon an examination period within six months of enrolment into the study.

All participants were asked to provide five saliva over two consecutive days during both the non-exam and exam periods. The samples were collected using salivates and were used to determine levels of Cortisol. Salivary Cortisol has been shown to correlate well with plasma Cortisol [112]. Participants were asked to provide samples between: 7-8 h; 60 min after the first sample; 12-13h; 16-17h and 23-24 h; to avoid meals within 60 min of providing each sample and to avoid caffeine-containing products during the two days of sampling.
Fig. 6.1 Difference between exam and non-exam period

Fig. 6.2 Exam Period, Mean = 9.47
The results from the first model if the study has demonstrated changes in cognitive performance related to significant changes in levels of salivary Cortisol and self-reported levels of stress. However, our data have also shown that examination stress does not reliably produce increase in Cortisol. Indeed, the increase in self reported levels of stress during the examination period was associated with an unexpected decrease in levels of Cortisol. By using the theory of renewal reward process, expected long-run cost per unit time is obtained and compared with the average length of cycle during relaxation period. When the time increases the salivary Cortisol level decreases. The time and Cortisol levels are compared with exam and non-exam periods Fig. (6.2) and Fig. (6.3) show that these are a vast difference between the time periods in both the cases. The results coincide with the medical report.
MODEL II

6.6 A STOCHASTIC MODEL TO FIND THE TIME FACTORS IN CORTISOL DUE TO STRESS

The second model deals with the following; Atopy is defined by the individual predisposition to develop a group of inflammatory disorders in responses to a food or environmental substances that are otherwise innocuous for the host. The important immune regulatory role of the HPA axis aspect under stress this observation could be of clinical relevance and may at least partly explain stress-induced exacerbation of atopic dermatitis present study was designed to investigate whether attenuated responsiveness of the HPA axis to stress represents a character feature of atopic dermatitis or whether it can also be found in other chronic manifestations of Atopy. Awakening in the morning accompanied by a significant rise at Cortisol levels on all three experimental days in allergic asthma and control subjects was not different between two groups. Since the time factor is more important for cumulative stress effects due to allergy which are cause & effects of the disease Asthma. These findings suggest that a blunted adrenocortical response to stress represent a common feature of chronic allergic inflammatory processes that may be relevant in different forms of the manifestation of Atopy. Atopy is a genetically and environmentally determined condition predisposing to different forms of Atopy such as atopic dermatitis (AD), allergic asthma (AA), and allergic rhinitis (AR) [90]. The main symptoms of AA are episodic occurrence of coughing, dyspnea, wheezing and chest tightness, while AD is characterized
by dry skin, erythematous papules, lichenification, and an intense pruritus [85][97][100][135]. Immunological abnormalities group has demonstrated reduced Cortisol levels in responses psychosocial stress in AD children pointing to a dysfunction of the HPA axis [18]. In fact in a more recent study we observed attenuated Cortisol responses to stress in additional sufferers are accompanied by district atopy–relevant in psychological changes and exacerbation of symptomatology [17].

Here use have used a Stochastic model to find the time factors, if

\[ S_n = \sum_{i=1}^{n} (X_i + Y_i) \quad \text{for } n \geq 1 \]

and \( S_0 = 0 \) and let \( N(t) = \sup \{n \geq 0: S_n \leq t\} \)

Then the total downtime is denoted by \( D(t) \) [5][44][48][86][94][120][125].

The mean value of \( E(D(t)) \) is obtained here.

6.7 NOTATIONS

\( X_i \) is the failure time during the magnitude of secretion of Cortisol visit to the \( i^{th} \) state.

\( Y_i \) is the repair time during the \( i^{th} \) visit to that state.

\( F_n \) is the cumulative distribution function \( \sum_{i=1}^{n} X_i \)

\( G_n \) is the cumulative distribution function at \( \sum_{i=1}^{n} Y_i \)

\( F^* \)– Laplace – Stieltjes transform of a cumulative distribution function of \( F \)
**H**^*^ - joint cumulative distribution function of H

Φ(ω) is a simple point measure on E.

Z(t) is right continuous.

D(t) is mean of the total downtime.

M^* - Laplace Stieltjes transform of m(t).

X_i is exponentially distributed with parameter λ+γ.

Y_i is exponentially distributed with parameters μ+γ.

α and β are positive integers.

T_n – The sequences of partial sums of the variables U_i.

N(t) be the delayed renewal process.

### 6.8 RESULT

Cortisol secretion occurs when a Asthma children [3] is affected by a stress. Here we have assumed that during every stimuli, certain amount of Cortisol secretates. Increased Cortisol secretion is in fact potentially dangerous.

Let (X_i) and (Y_i), i ≥ 1 denote the time spent in the states 1 and 0 respectively during the i^{th} visit to that state [124].

We assume that the sequence (X_i, Y_i) of random vectors is independent and identically distributed (i.i.d) with strictly positive components.

X_i and Y_i to be Dependent

Let \( S_n = \sum_{i=1}^{n} (X_i + Y_i) \) for \( n \geq 1 \) and

\( S_0 = 0 \) and \( N(t) = \sup \{ n \geq 0 : S_n \leq t \} \)
Then the total downtime $D(t)$ can be expressed as

$$
D(t) = \begin{cases} 
\sum_{i=1}^{N(t)} Y_i & \text{if } S_{N(0)} \leq t < S_{N(0)} + X_{N(0)+1} \\
\sum_{i=1}^{N(t)+1} X_i & \text{if } S_{N(0)} + X_{N(0)+1} \leq t < S_{N(0)+1}
\end{cases}
$$

(6.10)

Denote the state of the system at time $t$ by $Z(t)$.

If $Z(t)$ is right continuous, then the total down time is $D(t)$ can also be expressed as

$$
D(t) = \int_0^t 1_{(0)}(Z(s)) \, ds
$$

\[\text{where} \quad F(x) = P(X_1 \leq x), \quad G(y) = P(Y_1 \leq y), \quad H(x,y) = P(X_1 \leq x, Y_1 \leq y), \quad K(\omega) = P(X_1 + Y_1 \leq \omega)\]

We write $F_n$ and $G_n$ for the CDFs of $\sum_{i=1}^n X_i$ and $\sum_{i=1}^n Y_i$, respectively.

The Laplace-Stieltjes transforms of a Cumulative distribution function $F$ and a joint Cumulative distribution function $H$ will be denoted by $F^*$ and $H^*$ respectively for $\alpha, \beta > 0$

$$
F^*(\alpha) = \int_0^\infty e^{-\alpha x} \, dF(x)
$$

$$
H^*(\alpha, \beta) = \int_0^\infty \int_0^\infty e^{-(\alpha x + \beta y)} \, dH(x,y)
$$

(6.11)
We will use point process for the derivation of the distribution of the total downtime \( D(t) \). Let \( (\Omega, F, P) \) be the probability space on which the i.i.d. sequence \( (X_i, Y_i) \) is defined and also an i.i.d. sequence \( (U_i, i \geq 1) \) of exponentially distributed random variables with parameter 1 such that the sequences \( (U_i) \) and \( (X_i, Y_i) \) are independent. Let \( (T_n, n \geq 1) \) be the sequence of partial sums of the variables \( U_i \). Then the map

\[
\Phi : \omega \mapsto \sum_{n=1}^{\infty} \delta(T_n(\omega), X_n(\omega), Y_n(\omega)),
\]

where \( \delta(x,y,z) \) is the Dirac measure in \((x,y,z)\), defines a Poisson point process on \( \mathbb{E} = \mathbb{R}^3 \) with intensity measure \( \nu(dt \, dx \, dy) = dt \, dH(x,y) \). Note that, for almost all \( \omega \in \Omega \), \( \Phi(\omega) \) is a simple point measure on \( \mathbb{E} \) such that there is at most one point from the support of \( \Phi(\omega) \) on each set \( \{t\} \times [0, \infty) \times [0, \infty) \). Let \( M_p(\mathbb{E}) \) be the set of all point measures on \( \mathbb{E} \). We will denote by \( P_\nu \) the distribution of \( \Phi \) over \( M_p(\mathbb{E}) \).

For \( t \in [0, \infty) \), define \( M_p(\mathbb{E}) \) the functionals

\[
A_X(t)(\mu) = \int_{\mathbb{E}} x 1_{[0,t]}(s) \mu(ds \, dy),
\]

\[
A_Y(t)(\mu) = \int_{\mathbb{E}} y 1_{[0,t]}(s) \mu(ds \, dx \, dy),
\]

And

\[
A(t)(\mu) = A_X(t)(\mu) + A_Y(t)(\mu).
\]
So, for example, \( A(t)(\mu) \) is the sum of the \( x \) – and the \( y \) – co ordinates of the points in the set of \( \text{supp } \mu \cap [0,t] \times [0, \infty) \times [0, \infty) \),

where \( \text{supp } \mu = \{ (s,x,y) : \mu \{ (s,x,y) \} > 0 \} \). In the sequel we will write \( A_X(t)(\mu) \) for \( A_X(t)(\mu) \) and similarly \( A_Y(t)(\mu) \) and \( A(t)(\mu) \). Defines also for \( t \geq 0 \)

\[
B(t)(\mu) = \int_E \{1_{[0,x]}(t - A(s,\mu))A_Y(s,\mu)
+ 1_{[x,x+y]}(t - A(s,\mu))[t - A_X(s+,\mu)]\} \mu(\text{d}xdy),
\]

Where

\[
A_X(s+,\mu) = \int_E \{1_{[0,\bar{x}]}(r)\mu(\text{d}rdxdy).
\]

In the next lemma we explain the meaning of \( B(t) \)

**6.1 Lemma.** With probability 1,

\[
D(t) = B(t)(\Phi)
\]

**Proof:** Let \( \omega \in \Omega \) such that \( \Phi(\omega) \) is a simple point measure on \( E \) with at most one point of \( \text{supp } \mu \) on each set \( \{t\} \times [0, \infty) \times [0, \infty) \).

\[
B(t)(\Phi(\omega)) = \sum_{i=1}^{\infty} \{1_{[0,\bar{x},(\omega)]}(t - A(T_i(\omega), \Phi(\omega)))A_Y(T_i(\omega), \Phi(\omega))
+ 1_{[X_i(\omega) X_i(\omega)+Y_i(\omega)]}(t - A(T_i(\omega), \Phi(\omega)))[t - A_X(T_i(\omega) + \Phi(\omega))]\}
\]
Note that
\[ 1_{[0,X_t(\omega)]}(t - A(T_{\omega}(\omega), \Phi(\omega))) = 1 \]

Implies that \( i = N(t, \omega) + 1 \). Similarly, if

\[ 1_{(X_t(\omega), X_{t+1}(\omega))}(t - A(T_{\omega}(\omega), \Phi(\omega))) = 1 \]

Implies that \( i = N(t, \omega) + 1 \). Since the intervals

\[ \{ [S_{i-1} + X_i, S_{i+1} + X_{i+1}, S_{i+1} + X_{i} + Y_i) : i \geq 1 \} \]

Partition \([0, \omega)\), for any \( t > 0 \) one and only one of the indicators in the sum will be nonzero.

So, if

\[ 1_{[0,X_t(\omega)]}(t - A(T_{\omega}(\omega), \Phi(\omega))) = 1 \]

Then \( i = N(t, \omega) + 1 \) and

\[ B(t)(\Phi(\omega)) = A_{Y}(T_{N(t, \omega) + 1(\omega), \Phi(\omega))} \]

\[ = \begin{cases} 
0 & \text{if } N(t, \omega) = 0 \\
\sum_{j=1}^{N(t, \omega)} Y_j(\omega) & \text{if } N(t, \omega) \geq 1
\end{cases} \]

and if

\[ 1_{(X_t(\omega), X_{t+1}(\omega))}(t - A(T_{\omega}(\omega), \Phi(\omega))) = 1 \]

Then

\[ B(t)\Phi(t) = t - A_{X}(T_{N(t, \omega) + 1(\omega) + 1)(\omega)}, \Phi(\omega)) \]

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The following theorem gives the distribution of the total downtime $D(t)$ in the form of a double Laplace transform.

### 6.9 APPLICATION TO FUBINI’S THEOREM IN MEASURE THEORY

For $\alpha, \beta > 0$,

$$
\int_0^\infty E[e^{-\alpha D(t)}]e^{-\beta t} dt = \frac{\alpha [1 - F^*(\beta)] + \beta [1 - H^*(\beta, \alpha + \beta)]}{\beta (\alpha + \beta) [1 - H^*(\beta, \alpha + \beta)]}
$$

**Proof:** By Lemma 6.1 and using Fubini’s theorem, we obtain that

$$
\int_0^\infty E(e^{-\alpha D(t)})e^{-\beta t} dt \\
= \int_0^\infty dt \int_{M_\nu(E)} P_\nu(d\mu) \exp \left\{ - \alpha \int_E \mu(dsdxdy) \left[ 1_{[0,x]}(t - A(s, \mu)) A_\nu(s, \mu) + 1_{[x,x+y]}(t - A(s, \mu)) - A_\nu(s+\mu) \right] \right\} e^{-\beta t}
$$

$$
= \int_{M_\nu(E)} P_\nu(d\mu) \int_E \mu(dsdxdy) \int_0^\infty dt \left[ 1_{[0,x]}(t - A(s, \mu))e^{-\alpha(t - A_\nu(s, \mu))} + 1_{[x,x+y]}(t - A(s, \mu))e^{-\alpha(t - A_\nu(s, \mu))} \right] e^{-\beta t}
$$

$$
= \frac{1 - F^*(\beta)}{\beta [1 - H^*(\beta, \alpha + \beta)]} + \frac{F^*(\beta) - H^*(\beta, \alpha + \beta)}{\beta (\alpha + \beta) [1 - H^* (\beta, \alpha + \beta)]}
$$

(6.12)
\[
\int_0^\infty E[e^{-\alpha D(t)}]e^{-\beta t} \, dt = \frac{\alpha[1 - F^*(\beta)] + \beta[1 - H^*(\beta, \alpha + \beta)]}{\beta(\alpha + \beta)[1 - H^*(\beta, \alpha + \beta)]}
\]

(6.13)

taking derivatives w.r.t \(a\) in (6.13) and setting \(a=0\).

We get

\[
\int_0^\infty E[D(t)]e^{-\beta t} \, dt = \frac{F^*(\beta) - H^*(\beta, \beta)}{\beta^2[1 - H^*(\beta, \beta)]}
\]

(6.14)

Then we get

\[
m^*(\beta) = \frac{K^*(\beta)}{1 - K^*(\beta)}
\]

(6.15)

\(m^*\) is the Laplace-Stieltjes transform of \(m(t)\).

And solving we get

\[
\int_0^\infty E[D(t)]e^{-\beta t} \, dt = \frac{F^*(\beta) - K^*(\beta)}{\beta^2[1 - K^*(\beta)]}
\]

(6.16)

Which is in agreement with (6.14) since

\[K^*(\beta) = H^*(\beta, \beta)\]

6.10 SPECIAL CASE

The failure time \(X_i\) and the repair time \(Y_i\) have a joint bivariate exponential distribution given by

\[
P(X_1 \leq x, Y_1 \leq y) = e^{-(\lambda x + \mu y + \gamma \text{max}(x,y))} \quad x, y \geq 0 \text{ and } \lambda, \mu, \gamma > 0
\]

Both \(X_1\) and \(Y_1\) are exponentially distributed with parameters

\(\lambda + \gamma\) and \(\mu + \gamma\) respectively,
We have

\[ \mu_x = \frac{1}{\lambda + \gamma} \]

\[ \mu_y = \frac{1}{\mu + \gamma} \]

\[ \sigma_x^2 = \frac{1}{(\lambda + \gamma)^2} \]

\[ \sigma_y^2 = \frac{1}{(\mu + \gamma)^2} \]

\[ \rho_{xy} = \frac{\gamma}{\lambda + \mu + \gamma} \]

We can also calculate explicitly the mean of the total downtime \( D(t) \). We get

\[
\int_0^\infty E[D(t)]e^{-\beta t} dt = \frac{(2\lambda + \gamma)\beta + (\lambda + \gamma)(\lambda + \mu + \gamma)}{\beta^2[2\beta^2 + (3\lambda + 3\mu + 4\gamma)\beta + (\lambda + \mu)(\lambda + \mu + 3\gamma) + 2\gamma^2]}
\]

\[
\text{6.11 MATHEMATICAL MODEL FOR THE SECRETION OF CORTISOL IN CONTROL AND ASTHMATIC CHILDREN}
\]

Children with asthma 17 females and 9 males aged 7 to 12 years were recruited in the allergy unit of the department of pediatrics of the general hospital. All children were classified as having moderate allergic asthma as indicated by social history and physical examination by the pediatrician. The
children viewed AA symptoms occasionally and in these cases bronchodilator use was commended. The children minimum history of Asthma was 5 years.

To assess Cortisol levels, saliva samples were obtained every 10 minutes before and after the Trier Social Stress – Test for children using the salivette sampling device, while heart rate was monitored continuously. Additionally saliva Cortisol was determined in the morning on three consecutive days on awakening and 10, 20 and 30 minutes after waking up respectively.

**Fig. 6.4 Mean Value of Cortisol in Control and Asthma Children**

Substitute the values of \( \lambda=5.81, \mu=5.44, \gamma=9 \), we get

\[
L^{-1} \left( \frac{20.62\beta + 300}{2\beta^2[\beta^2 + 34.88\beta + 296.2]} \right) = \frac{e^{-24t}}{100} + \frac{t}{20} + \frac{43}{1000} \tag{6.18}
\]
6.12 CONCLUSION

The results from the second Mathematical model also stress the same cumulative effects of asthmatic conditions which are beautifully fitted with Weibull distribution and the corresponding hazard rate average is obtained (See Fig.6.4 and Fig.6.5). Basal Cortisol concentrations and morning Cortisol levels did not differ between AA children and nonatopic controls. The finding of an aberrant HPA axis functioning in asthmatics may be of clinical relevance. It is well accepted that a hypo responsive HPA axis is linked to increase susceptibility to chronic inflammatory disorders [26], [38],[122]. In this model it is assumed that the failure to render an adequate HPA axis response increases the risk for aberrant immune functions that may lead to the aggravation and chronification of inflammatory disease. This may be especially relevant under stressful conditions when both systems the HPA axis and the immune system are activated.