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MATHEMATICAL QUEUEING MODEL TO FIND THE TRIIODOTHYRONINE REPLETION IN INFANTS DURING CBP FOR CHD USING NORMAL DISTRIBUTION

M. Vasuki* & A. Dinesh Kumar**

* Assistant Professor, Department of Mathematics, Srinivasan College of Arts & Science, Perambalur, Tamilnadu

** Assistant Professor & Head, Department of Mathematics, Dhanalakshmi Srinivasan Engineering College, Perambalur, Tamilnadu

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Abstract:

Cardiopulmonary bypass suppresses circulating thyroid hormone levels. Although acute triiodothyronine repletion has been evaluated in adult patients after cardiopulmonary bypass, triiodothyronine pharmacokinetics and effects have not previously been studied in infants undergoing operations for congenital heart disease. We hypothesized that triiodothyronine deficiency in the developing heart after bypass may adversely affect cardiac function reserve postoperatively. From the system with Poisson input flows the generating function of the unique stationary queue length distribution, (i.e) in the $M^X/M^R/1/\infty$ queueing system is used to find the effect triiodothyronine repletion in infants during cardiopulmonary bypass for congenital heart disease.

Key Words: Triiodothyronine, Cardiopulmonary Bypass (CBP), $M^X/M^R/1/\infty$ Queueing System, Congenital Heart Disease (CHD) & Normal Distribution

1. Introduction:

Circulating levels of the thyroid hormones, triiodothyronine (T_3) and thyroxine (T_4), decrease substantially during and after cardiopulmonary bypass (CPB) [8]. Possible responsible mechanisms include blood dilution during CPB, alterations in peripheral T_3 metabolism, and central disruption of hypothalamic – pituitary – thyroid - control included by nonpulsatile flow [11]. Regardless of the operative mechanisms, depression of serum T_3 and T_4 levels persists for several days after CPB in both adults and children. Several investigators have postulated that thyroid hormone deficiencies can contribute to myocardial depression observed after cardiac surgery and CPB T_3 or T_4 supplementation after coronary artery bypass provides short term increases in cardiac performance in adults, which result from a direct inotropic effect on the heart and decrease in systemic vascular resistance. The developing heart normally undergoes thyroid promoted maturation of physiologic and metabolic processes, which can increase cardiac contractile function and reserve [9] & [10]. However, operation for congenital heart disease accompanied by CPB can theoretically disturb this maturation at least temporarily by decreasing circulating thyroid hormone levels. Thus, depression of thyroid hormone levels could limit cardiac contractile responses during the vulnerable postoperative period. Accordingly, we postulated that T_3 repletion in the immediate postoperative period should improve hemodynamic parameters in infants undergoing cardiac surgery with CPB. This current study represents the initial phase in evaluation of T_3 repletion in infants undergoing CPB. We study in this paper, single channel queueing system with renovation. The solutions for the queues with Poisson input flow are discussed. In the $M^X/M^R/1/\infty$ queueing system, the generating function of the ordinary Poisson is given by $\pi(z) = \frac{1-z^*}{z-z^*}$ where z^* is the root of the equation $\lambda z^2 - (\lambda + \mu)z + p\mu = 0$ is used to evaluate T_3 repletion in infants undergoing CPB.

2. Notations:

CPB	-	Cardiopulmonary Bypass
PRP	-	Pressure Rate Product
NT	-	Control Patients
ND	-	Normal Distribution

3. Ergodicity Conditions:

Consider a single channel queueing system with FIFO discipline and the following modification. After each customer is serviced, all the others leave the queue with probability q. Only a customer who has been serviced leaves the system with probability $p = 1 - q$. The probability q, which we call renovation probability, is essential to our analysis. This probability defines many important features of our model. This model is a generalization of the classical single server system. Below we present a short review of previous results concerning only the queues with general distribution of the input flow. The results related to such cases as Markovian input or deterministic input are well known and are described in many books and papers [1] & [4].

The case of general input flow and exponentially distributed service times was considered in [4]. It is shown that if $N < \infty$, the Laplace transform of the stationary queue length distribution can be expressed through the roots of certain equations. A similar expression can be written down in the case $N = \infty$, but there is only one root to be found. More general results, such as ergodicity and heavy traffic limit theorems, were considered by [2] & [3].

Our aim is to generalize the results concerning the "classical" model to the case of the queueing systems $M/M^R/1/N$ and $GI/M^R/1/N$ with renovation. These queueing systems are of significant interest for our applications. The first publications to study such models were papers by [6] & [13]. The motivation of these models is given below. If [6] deals with a model of a so called "prefetch instruction buffer". The prefetch buffer provides a pipeline mechanism in the most recent processors and Microprocessors for systems with a single instruction flow. This architectural element improves the performance when the linear part of a program is running by allowing the simultaneous processing of independent parts of different instructions. If the recent instruction is "branch" (or "go to"), then the processor loses the content of the prefetch instruction buffer and renovates it.

Another example of a renovation mechanism is considered by [13]. They studied the probabilistic models of buddy protocols for fault tolerant systems. This model [13] leads to priority queues with renovation which does not depend on the service process. Consider a queueing system with renovation and general interarrival and service time distributions. Assume that the customers arrive from the outside at moments $t_1, t_2, \ldots$ and form a recurrent flow with interarrival times $I_n = t_{n+1} - t_n, n = 0, 1, \ldots$ Thus, the sequence $\{I_n\}$ forms a family of independent, identically distributed, random variables with a common distribution function $F(x)$.

$$\text{Assume } 0 < EI = \int_0^\infty x dF(x) < \infty$$

Let S_n be the service time of the n[th] customer. Assume that $\{S_n\}$ are independent and identically distributed random variables with $ES_1 < \infty$. Denote by ξ_t, the queue length at time $t, (t \geq 0)$. Assume that the initial queue length is finite with probability 1.

3.1 Proposition:

If $0 < p < 1$, then for each initial state ξ_0 of the queue satisfying the condition $Pr\{\xi_0 < \infty\} = 1$, the queueing system with renovation has a unique stationary distribution

$$\pi_j = \lim_{t\to\infty} Pr\{\xi_t = j\}, j = 0, 1, \ldots$$

which does not depend on the initial state of the queue length process.

Proof:

Denote by $A_t = \{inf_{0\leq s\leq t} \xi_s = 0\}$the event that the queue once became empty during $[0, t]$. The process ξ_t has a renovating event $\{\xi_t = 0\}$ [3]. For all finite values of ξ_0, the probability of the complementary event

$$B_t = \bar{A}_t = \{inf_{0\leq s\leq t} \xi_s > 0\} \text{ tends to zero}$$

$$P_t = Pr\{B_t\} \to 0$$

As $t \to \infty$. Indeed, let $N(t, t+T)$ be the number of customers served without renovation of the queue. Then for each $\in > 0$ and for each integer M, there exists T sufficiently large, such that for every $t > 0, Pr\{N(t, t+T) > M\} < \epsilon$. Thus, the probability of the event A_t tends to 1 as $t \to \infty$. The existence of the renovating event provides the ergodicity of the queueing system. This results shows that the renovation probability is a critical parameter for the stability domain. Indeed, if $q > 0, EI_1 < \infty$ and $ES_1 < \infty$, the system is stable. In the case $q = 0$, the system is stable if and only if the inequality $EI_1 > ES_1$ is satisfied.

4. System with Poisson Input Flow:

Consider a queueing system with renovation. We assume that the system has only one queue with FIFO discipline and one input flow of customers. The input flow is assumed to be Poisson. Denote by λ the input flow intensity. Service times are mutually independent and exponentially distributed random variables with parameter μ. After a customer is serviced, all others can leave the queue with probability q. Only a customer who receives service leaves the system with probability $p = 1 - q$. Below we consider two classes of queues with renovation, Poisson input flow, and exponential service time distribution.

4.1 $M/M^R/N$ Queueing System:

Denote by N the size of the waiting room. Let ξ_t be the number of customers in the system at moment t. Then $\xi_t \leq N$. Denote $\pi_j(t) = Pr\{\xi_t = j\}, j = 0, 1, \ldots, N$

The stationary distribution of the queue length is given by the following assertion.

4.2 Proposition:

If $0 < p < 1$ and $\mu > 0$, then for each initial state of the queue satisfying the condition

$$\pi_j = \lim_{t\to\infty} Pr\{\xi_t = j\}, j = 0, 1, \ldots, N$$

The generating function of this distribution satisfies the equation

$$\pi(z) = \frac{\mu p(1-z)\pi_0 - q\mu z - \lambda \pi_N (1-z) z^{N+1}}{Q(z)}$$

where $Q(z) = \lambda z^2 - (\lambda + \mu)z + p\mu$, and the probabilities π_0 and π_N are given by the formulas

$$\pi_0 = 1 - \frac{z^{*N} - z_*^N}{z^{*N+1} - z_*^{N+1}}$$

$$p_N = \frac{z^* - z_*}{z^{*N+1} - z_*^{N+1}}$$

with z^* and z_* being the roots of the equation $Q(z) = O$.

Proof:

The process ξ_t is a Markov chain. It is easy to verify that for $0 < p < 1$ and $\mu > 0$ this Markov chain is ergodic. The stationary distribution $\{\pi_j\}_{j=0}^{\infty}$ of ξ_t satisfies the equations

$$(\lambda + \mu)\pi_k = \lambda p_{k-1} + \mu p \pi_{k+1}, k = 1, 2, \dots, N-1$$
$$\lambda \pi_{N-1} = \mu \pi_N \qquad (1)$$
$$\lambda \pi_0 = \mu \pi_1 + \mu q \sum_{j=2}^{N} \pi_j$$

and the normalization condition

$$\sum_{j=0}^{N} \pi_j = 1$$

Then, from (1) after standard calculations we obtain

$$\pi(z) Q(z) = \mu p (1 - z)\pi_0 - q\mu z - \lambda \pi_N (1 - z) z^{N+1}$$

The equation $Q(z) = 0$ has two roots z^* and z_*. Both roots are real and positive. The generating function $\pi(z)$ is a polynomial. The stationary probabilities π_0 and π_N must satisfy the equations

$$\mu p \pi_0 (1 - z_*) - \lambda \pi_N z_*^{N+1} (1 - z_*) = \mu q z_* \qquad (2)$$
$$\mu p \pi_0 (1 - z^*) - \lambda \pi_N z^{*N+1} (1 - z^*) = \mu q z^* \qquad (3)$$

From (2) and (3), we obtain the relations for π_0 and π_N. Proposition 2 is proved.

4.3 Corollary:

If the renovation probability $q = O$, then the stationary distribution of the queue length is given by

$$\pi_k = \pi_0 p^{k-1}, k = 1, 2, \dots, N$$
$$\pi_0 = \frac{1-\rho}{1-\rho^N}$$

where $\rho = \lambda/\mu$. If the renovation probability $q = 1$, then the stationary distribution of the queue length is given by

$$\pi_k = \frac{\mu}{\lambda+\mu}\left(\frac{\lambda}{\lambda+\mu}\right)^k, k = 0, 1, 2, \dots, N-1$$
$$\pi_N = \left(\frac{\mu}{\lambda+\mu}\right)^N$$

Proof:

The first part of the corollary is well known [1] & [5]. The second part follows directly from the equations (1) for the equilibrium distribution of the queue length process.

4.4 $M^X/M^R/1/\infty$ Queueing System:

Let us study now the case $N = \infty$. We consider a more general situation of bulk input. Assume that the customers arrive in groups of random size, and interarrival times are mutually independent, exponentially distributed random variables with parameter λ. This arrival flow is usually called a compound Poisson process. Denote

$$p_k = Pr\{l = k\}, k = 1, 2, \dots$$

where l is the size of an arrival group of customers. We denote by $p(z)$ the generating function of this distribution. Thus,

$$p(z) = \sum_{k=0}^{\infty} p_k z^k$$

where $|z| \le 1$. The average size of the arriving groups is assumed to be finite. Then the function $p(z)$ is regular in the unit disc $D = \{z: |z| \le 1\}$ and the average size of the arrival group is equal to $El = p'(1)$.

4.5 Proposition:

If $0 < p < 1$, $El < \infty$ and $\mu > 0$, then for each initial state, the queueing system has a unique stationary queue length distribution. The generating function of this distribution is given by the formula

$$\pi(z) = \frac{\mu p (1-z)\pi_0 - q\mu z}{Q_p(z)}$$

where $$Q_p(z) = \lambda z p(z) - (\lambda + \mu) z + p\mu, \pi_0 = \frac{q z_*}{p(1 - z_*)}$$

and z_* is a unique root of the equation $Q_p(z) = 0$, that satisfies the inequality $0 < z_* < l$.

Proof:

Denote by $q_m, (m = 1, 2, 3, \dots)$the number of customers in the system at the arrival epoch τ_m of the m[th] customer. Using the standard technique it is not difficult to verify that $\{q_m\}$ is a positive supermartingale. On the other hand, the queue length ξ_t at the moment t, $\tau_m < t \le \tau_{m+1}$ satisfies the inequality $0 \le \xi_t \le q_m$ for $m \ge 0$. The last inequality implies that the process t has a stationary distribution $\pi_n = \lim_{t\to\infty} Pr\{\xi_t = n\}$ that satisfies the equations

$$(\lambda + \mu)\pi_k = \lambda \sum_{n=1}^{\infty} \pi_{k-n} p_n + \mu p \pi_{k+1}, k = 1, 2, \dots \qquad (4)$$

$$\lambda\pi_0 = \mu\pi_1 + \mu q \sum_{j=2}^{N} \pi_j \quad (5)$$

Then from (4) and (5) we have

$$\pi(z) = \mu \frac{p(1-z)\pi_0 - qz}{\lambda zp(z) - (\lambda+\mu)z + p\mu} \quad (6)$$

The generating function $\pi(z)$ is regular in the unit disc D. By Rouche's theorem, the equation

$$\lambda zp(z) - (\lambda+\mu)z + p\mu = 0$$

has only one root, $z_* \in D$. Therefore, the numerator of the fraction in (6) should be equal to 0 at $z = z_*$. Hence,

$$\pi_0 = \frac{qz_*}{p(1-z_*)}$$

Therefore, the generating function of the stationary distribution satisfies the relation

$$\pi(z) = \mu q \frac{z-z_*}{z_*-1} \frac{1}{Q_p(z)}$$

4.6 Corollary:

If the input flow of customers is ordinary Poisson $(p(z) = z)$, then

$$\pi(z) = \frac{1-z^*}{z-z^*} \quad (7)$$

where z^* is the root of the equation $\lambda z^2 - (\lambda+\mu)z + p\mu = 0$, satisfying the inequality $z^* > 1$.

5. Example:

Infants less than 1 year old undergoing ventricular septal defect or tetralogy of Fallot repair were randomized into 2 groups. Group T $(n = 7)$ received triiodothyronine $(0.4\ \mu g/kg)$ immediately before the start of cardiopulmonary bypass and again with myocardial reperfusion. Control $(NT, n = 7)$ patients received saline solution placebo or no treatment. Heart rate, systolic and diastolic blood pressure and peak pressure rate product (PRP) were generally maintained at steady levels in the control group over the first 24 hours postoperatively. In our study heart rate is examined first 24 hours. Times in hours are taken as x axis and the heart rate in beats/min as y axis. Heart rate after CPB for the patients receiving $T_3(T)$ and control patients (NT). Time indices hours after termination of CPB. There are significant differences between groups occur at 1 and 3 hours after CPB [7-12].

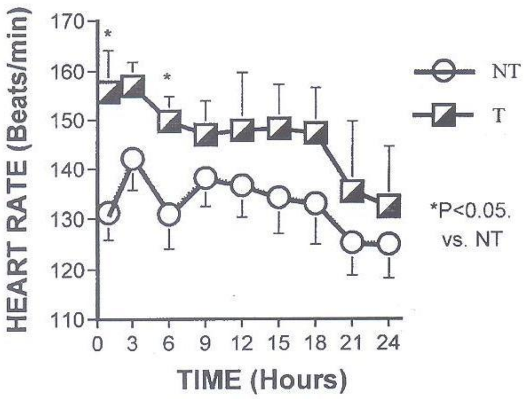

Figure 1: Heart rate after CPB for the patients receiving $T_3(T)$ and control patients (NT). Time indicates hours after termination of CPB. Significant differences between groups occur at 1 and 3 hours after CPB.

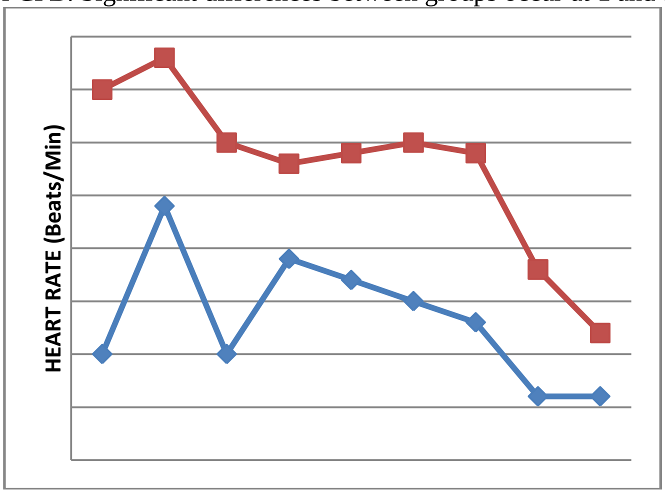

Figure 2: Heart rate after CPB for the patients receiving $T_3(T)$ and control patients (NT). Time indicates hours after termination of CPB. Significant differences between groups occur at 1 and 3 hours after CPB (Using Normal Distribution)

6. Conclusion:

These data imply that (1) triiodothyronine in the prescribed dose prevents circulating triiodothyronine deficiencies and (2) triiodothyronine repletion promotes elevation in heart rate without concomitant decrease in systemic blood pressure. The $M^X/M^R/1/\infty$ queueing system with renovation gives same result as the medical report mentioned above. By using normal distribution (ND) the mathematical model gives the result as same as the medical report. The medical reports {Figure (1)} are beautifully fitted with the mathematical model {Figure (2)}; $(i.e)$ the results coincide with the mathematical and medical report.

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