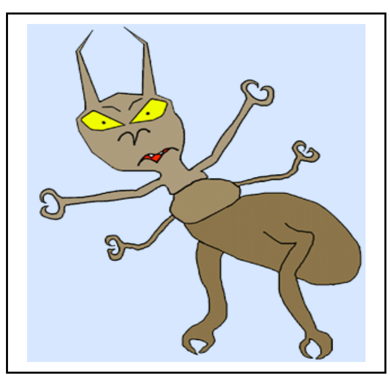
Choose Focus Analyze Exercise

Topic:

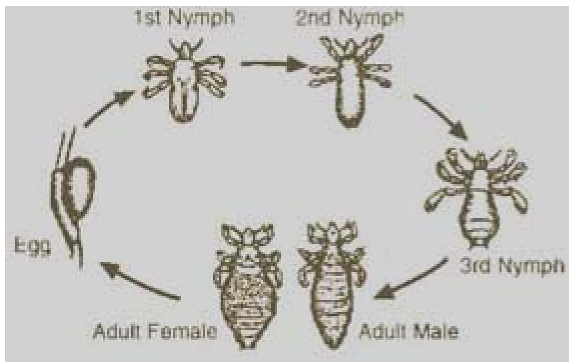
- **Modeling of head lice growth**
- **Examination of effects due to sucking of blood**
- **Anti-lice treatment effectiveness**



Introduction

Some facts about lice…

Head lice (Pediculus humanus) are tiny wingless insects, which are ectoparasites specific to humans. They feed on human blood 3-4 times a day and cannot survive for more than 2 days away from the host. They lay eggs close to the scalp on hair shafts where the temperature is ideal for incubation. Usually temperatures between 75 and 98.6˚F are optimum for lice. The eggs are glued to the hair shaft and it is difficult to dislodge them. Lice insert their mouthparts into human skin to draw blood and inject their saliva that prevents blood from clotting and also causes irritation and subsequent itching. Excessive scratching can lead to secondary infections and inflammation. Head louse can spend its whole life on human head.
The details of life cycle of lice are as follows-



courtesy- www.healthhappiness.com/lifecycle.jpg

- One full life cycle of louse has a span of about 33-35 days.
- The eggs of the louse called nits take 7-9 days to hatch.
- The hatched ones go through 3 nymph stages and mature into adult by the 17th day.
- Adult females mate with adult males and start laying eggs three days after fertilization.
- An adult female can lay 6 eggs per day on an average.

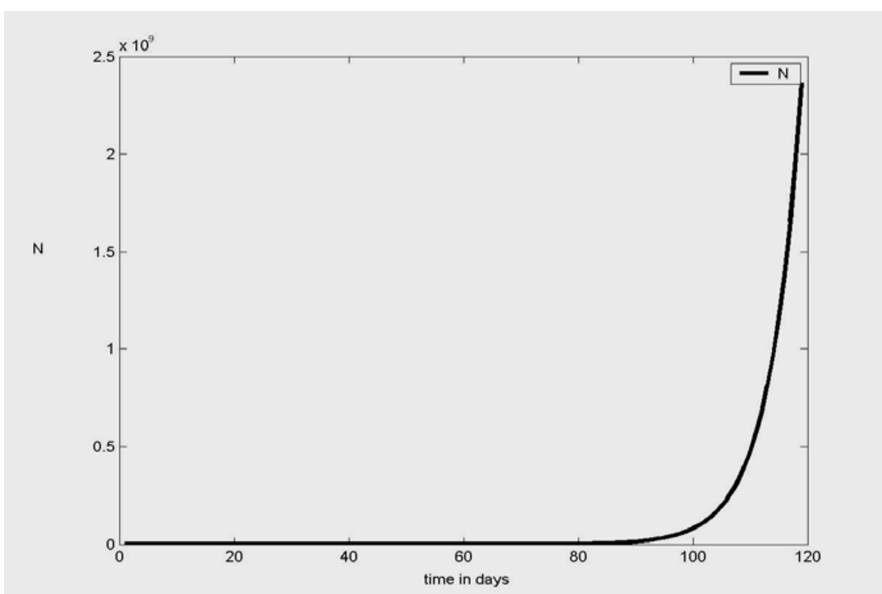
Statement of the problem

Lice can spend their whole lifetime as ectoparasites feeding on an infested person’s blood. They suck blood from skin capillaries painlessly. Usually people get it treated because of itching, secondary infections and inflammation. But the amount of itching caused varies from person to person depending on their sensitivity. A person might have been infested with lice months before any itching is noticed. In cases where no itching is observed it is left untreated. In India in many rural areas people don’t get any treatment done for lice infestation. The children in such families may also be malnourished and on the borderline of becoming anemic. So I shall attempt to find the time required for lice infestation to significantly affect a person due to blood suction (anemic effects) by finding the number of lice on head as a function of time from the first infestation. I shall also try to verify the claims of Mediker (antilice treatment) that it ensures freedom from lice in 4 weeks.

Assumptions and Analysis

- The life span of louse is 35 days from the time egg is laid.
- The time for hatching of the nit is taken as 8 days.
- The mating time is taken as the 16^{th} day and so the adult female lays eggs 19^{th} day onwards.
- The number of eggs laid per day by each adult female is taken as 6.
- Since each adult male can mate several times and one fertilization is sufficient to fertilize the eggs to be laid by the female for the rest of its lifetime. So it can assumed that all the adult females undergo mating and fertilization of eggs.
- It has been found that the ratio of males to the total number of lice is conserved over 100 years to be 0.4.This ratio is found to be independent of intensity of infestation.

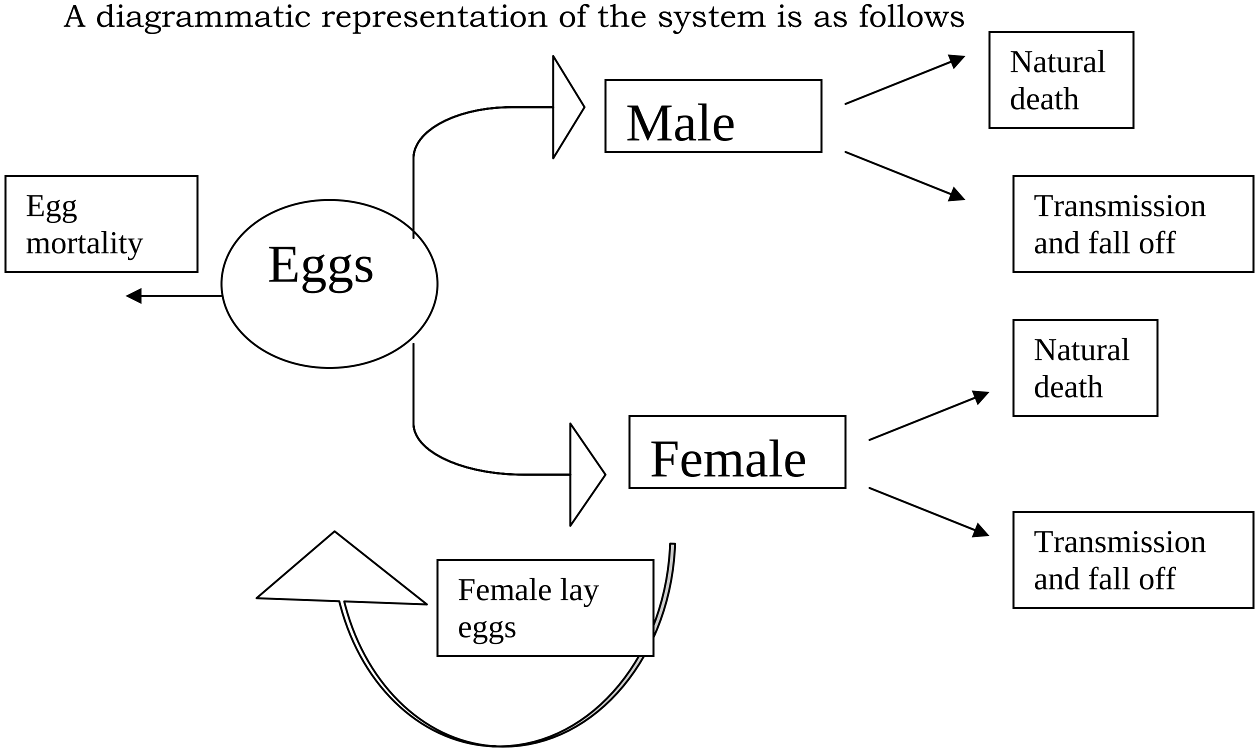
Based on the above considerations I tried to calculate the number of lice with time for about 120 days. To start with I assumed that one adult female louse which is ready to lay eggs (on its 19^{th} day) infects the person on the first day. Initially the data was generated considering only natural death and neglecting the effect of transmission to other persons or rate at which the lice fall off while grooming hair etc. and also the unproductiveness of the eggs i.e it was assumed that all eggs will hatch to produce nymphs.
The data generated (attached at the end of the report) predicted an exponential increase in the number of lice with the number of days.



The data was fit into an exponential growth model
y= 1.4594 exp (0.1782x) with R^2 =0.9956 which is a good fit.
This gives a specific growth rate of 0.1782.
But it is very unrealistic as the number of lice on head may utmost be 100 even in severe cases of infestation. (This information was given by Dr Sharad Nadig, Skin and hair specialist,Bangalore). This indicates that the rate of decrease in the number of lice due to transmission to other people and falling off while combing, taking a head bath etc is not only significant but also quite large. So in order to make the model realistic the rates of transmission and falling off as well as the egg mortality rate should be considered.

System representation

A diagrammatic representation of the system is as follows



Here I am assuming natural death only after the completion of life cycle i.e nymph death is not considered. The rate of transmission and fall off depends on two factors

– Crowding or the total number of lice per unit area at a particular point of time.
- Density and length of hair. People with long and dense hair can support more lice and therefore transmission rate is low in such cases.

The above system can be represented by differential equations as follows-

Differential equations

$$dF/dt = ko*(1-a)*E - kd*F - kt*F^2$$

$$dM/dt = ko*(a)*E - kd*M - kt*M^2$$

$$dE/dt = k1*F - k2*E - ko*E$$

where F,M and E are the number of female, male and eggs respectively.
The rate constants are for

ko= hatching of eggs
kd=natural death
kt=transmission and fall off
k1=egg generation or laying of eggs
k2=egg mortality
and
a=fraction of male population

Here first order rate constants were assumed as a good approximation of the real situation as with nonlinear terms the estimation of coefficients is difficult without any experimental details. First I tried using first order even for the rate of transmission and fall off but it did not give a good picture of actual situation. Second order in case of transmission and fall off indicates that under crowded conditions the rate of decrease due to such effects is very significant.

Estimation of parameters

The parameters are determined assuming equal distribution of the lice and egg population over various phases and ages through the life cycle.

- The rate constant for hatching of eggs is given by ko+k2 =1/8 in an equal distribution as it takes 8 days for an egg to hatch. It has been found that 88% is the maximum hatch rate i.e 12% of the eggs turn out to be unproductive. (ref: http://www.thebestcontrol.com/lice-chapter/about_lice.htm). So the rate of egg mortality is 88% of the rate of generation of eggs. Therefore ko=0.88(1/8)=0.11
  k2=0.12(1/8)=0.015

- A female in its lifetime of 27 days (excluding 8 days of egg stage) lays eggs for the last 17days. So the ratio of number of egg laying female to the total number of females is 17/27.

  k1*N=rate of generation of eggs=6*f per day
  therefore k1=6*f/N=102/27=3.778

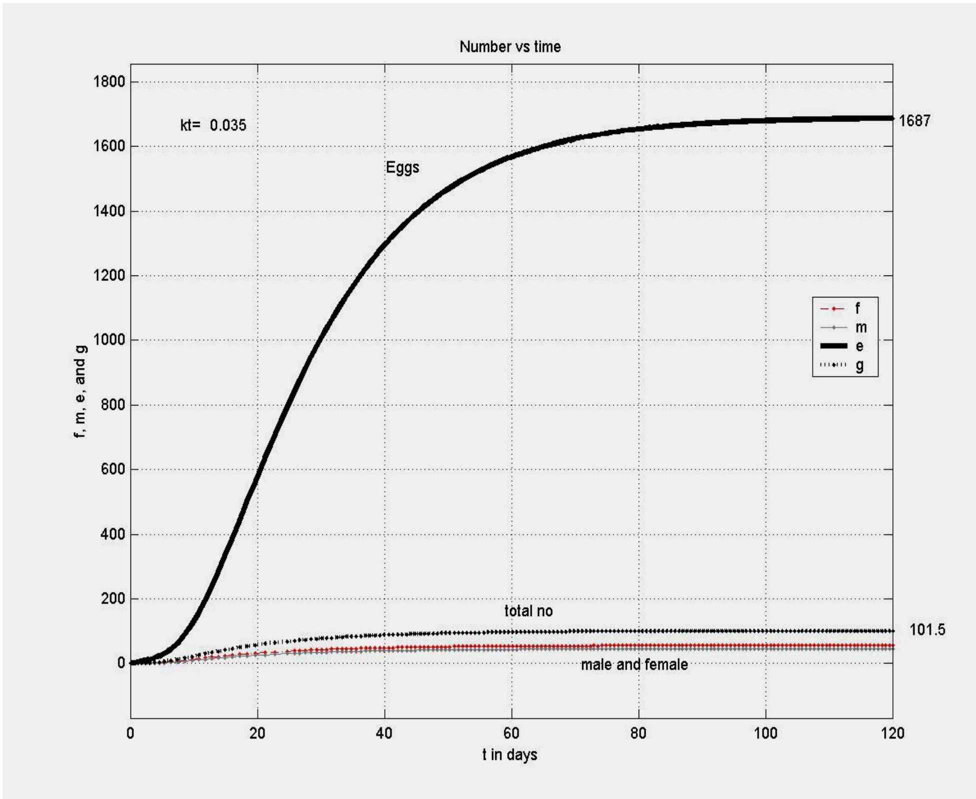
- Since the population is distributed equally over different ages the death rate constant kd is given by 1/27=0.037

- The fraction of male population is found to be 0.4 (ref: M Alejandra Perotti and Silvia S Catala, BMC genetics 2004, 5:10) and hence a=0.4

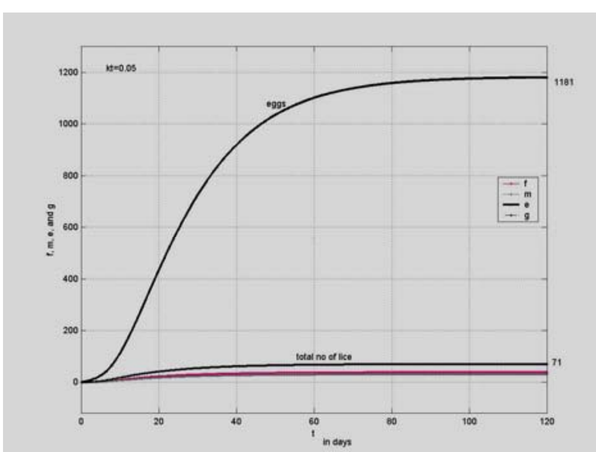
- The rate constant for transmission and fall off varies from person to person depending on the length and density of hair, surface area as it determines the number of lice per unit area. Depending on kt the severity of the infestation also varies. So different values of kt were tried out to find the kt for the case of severe infestation where the total number of lice usually saturates at about 100.

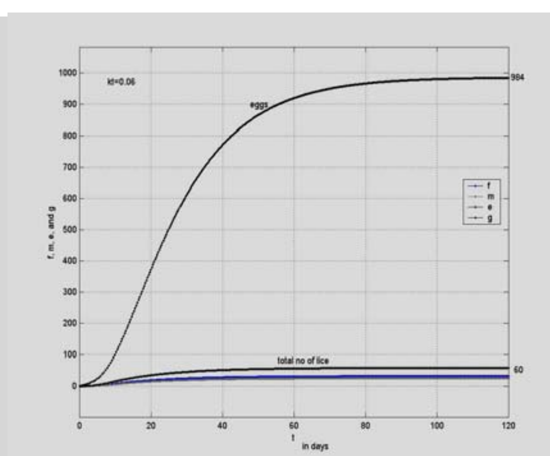
Solution of differential equations

The differential equations were solved using ode solver in MATLAB and the plots of the number of eggs, female lice, male lice and total number of live lice were obtained against time.



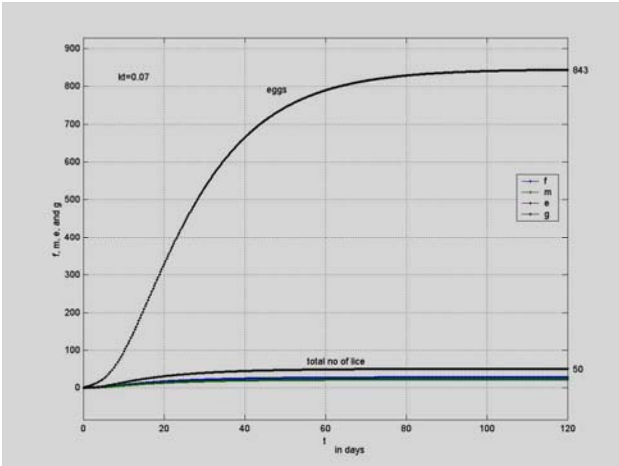
The above graph for kt=0.035 gives the total no of lice that saturates at about 100 which is the real situation in cases of severe infestation. The following graphs show the variation of total no of lice and eggs with respect to time for different values of kt(varying levels of infestation).A saturation of value of number of lice at about 20 is considered to be moderate infestation.



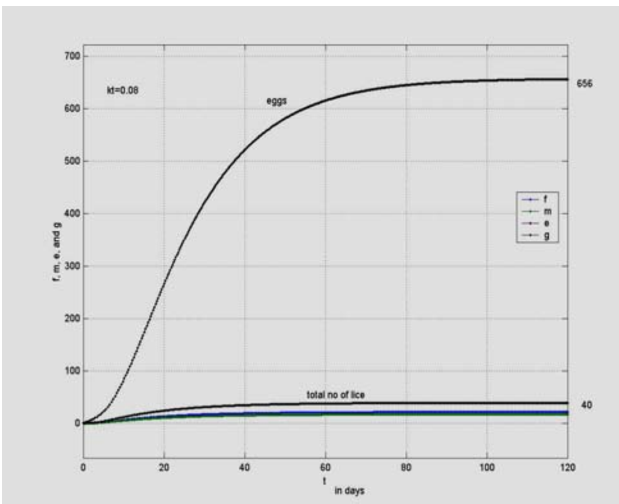


kt=0.05,E=1181,L=71 kt=0.06,E=984,L=60

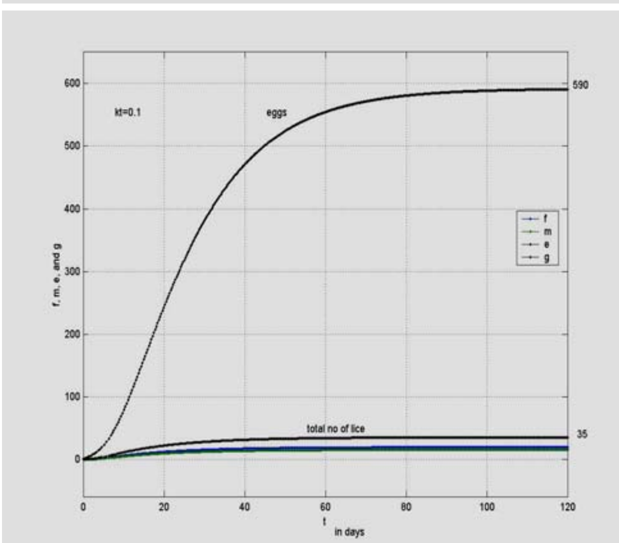
where E is total no of eggs, L is total no of live lice.



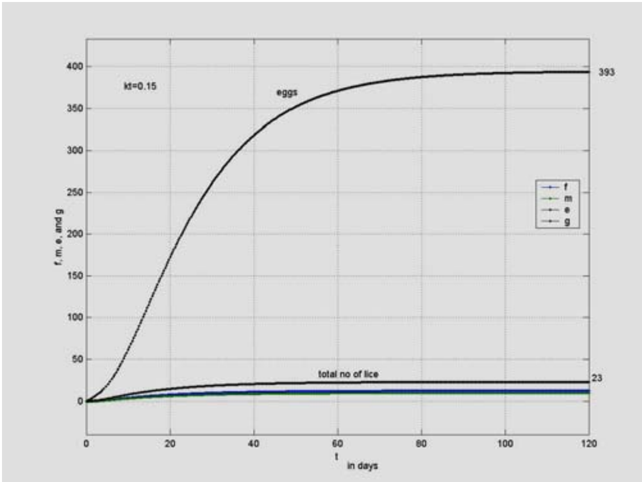
kt=0.07,E=843,L=50



kt=0.08,E=656,L=40



kt=0.1,E=590,L=35



kt=0.15,E=393,L=23

<u>How much blood is sucked?</u>

Head lice are very tiny organisms about 2-3mm long and 4-8µl in volume. They take 3 blood meals per day and each meal is for duration of about 15 min. At a time they can suck about 1 µl of blood. So the rate of blood sucking is 3*L µl per day where L is the total number of lice.(This information was provided by Dr. Waclaw Szybalski, Professor of Oncology, University of Wisconsin Medical School through email)

When we write a material balance equation for the RBC cells in the body

$$\dot{I}+\dot{G}-\dot{O}-\dot{C}=dX/dt$$

Since the system consists of both the lice on the head and the blood in the body, both the terms for rate of input and output go to zero.

$$\dot{I}=0 \quad \dot{O}=0$$

Here the assumption is that during the time considered there is no loss of blood by any other means.

I shall not consider the effect of erythropoetins that are involved in regulating the count of erythrocytes or RBC in the body. This is because it has been found that louse feeding does not have any effect on erythropoesis. (ANN. ACAD. MED. GEDAN, 1974, 4, 19-51 STEFAN KRYNSKI, EUGENIUSZ BECLA, MARIAN MACHEL)

From sources reliable (The new complete Medical and health encyclopedia Vol2) it is found that there is a dynamic equilibrium between the rate of generation and natural destruction of RBC in the body. The lifespan of RBC in the body is 120 days. About 200 billion RBC are synthesized and destroyed everyday in the body. The total volume of blood in the human body is about 5 l.

Here we have

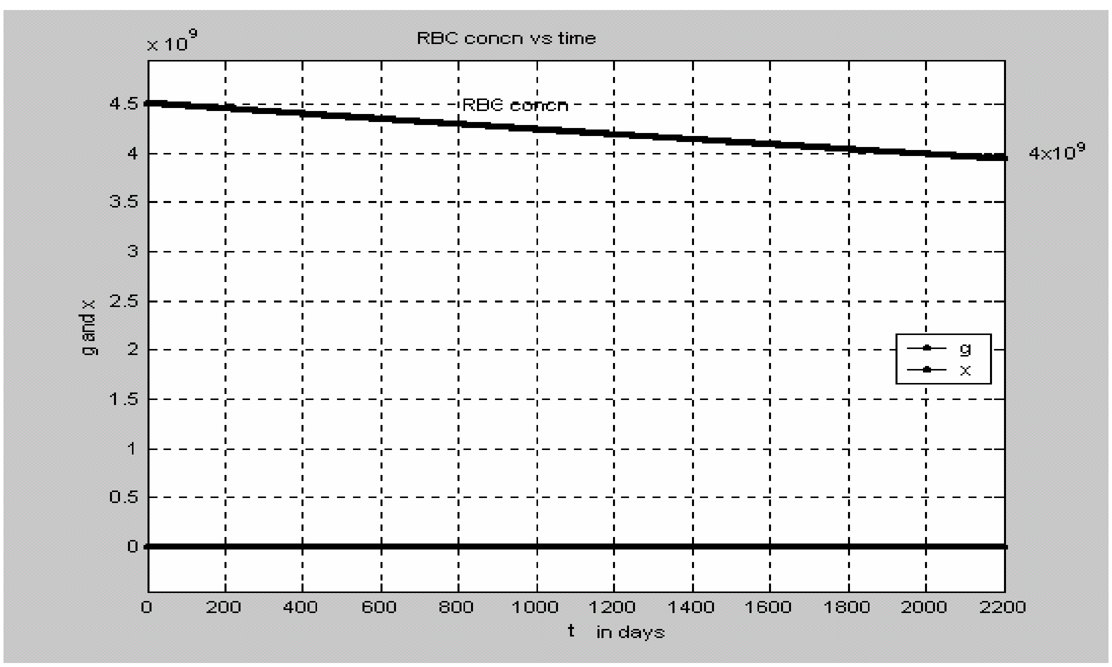
$\dot{C}$ = Natural destruction rate of RBC + rate of sucking of blood*concentration of RBC in the blood

But we know rate of natural destruction of RBC is equal to rate of generation of RBC and hence the term cancels with Generation term. So we finally have

$$- L(t)*v*X(t) = V*dX/dt$$

Here L(t) is the total number of lice as a function of time
v=Amount of blood sucked by one louse per day = 3*10^-3 ml
X(t)=concentration of RBC in the blood as a function of time
V=volume of blood in the body=5000ml

The normal count of RBC is 4.5*10^9 cells/ml and when this count goes below 4*10^9 cells/ml the person becomes anemic.
So the differential equation is solved taking 4.5*10^9 cells/ml as the initial concentration.



Thus it can be observed that it takes approximately 6 years for the RBC count to significantly go down which is highly unlikely. It can be inferred that lice cannot cause significant harm. It is also known that head lice do not transmit infections. The only problem is due to itching, which may lead to loss of sleep and secondary infections due to excessive scratching. So they cannot cause anemia because loss of any blood is made up by synthesis.

Mediker (antilice treatment)

Mediker, which contains permethrin, is used for treating lice but the eggs are not killed by it. Therefore it is recommended that it should be used for 4 consecutive weeks and should not be discontinued till the course is complete. An attempt to analyze this process is made here. (4 Sundays to freedom!)

Initially the egg population is distributed over all ages and only lice are killed by the first application.
For people with severe infestation the saturation number of eggs is about 1690 and total number of lice is about 100. On the first Sunday all the 100 lice are killed and 1690 eggs remain. Using the differential equation for the rate of accumulation of eggs (still applicable as equal distribution still exists)

$dE/dt=k1*F-k2*E-ko*E$

here since all lice are dead, the first term goes to zero.

$dE/dt= -k2*E-ko*E =-0.125E$

After one week, on the second Sunday
$E = Eo \exp(-0.125*7) = 704.49$ eggs remain.

For the second week the eggs are not equally distributed but all are synchronized that is they all hatch on the 8th day giving rise to lice, which are killed by the treatment on third Sunday.
Though freedom from lice is ensured in three Sundays itself it is recommended for 4 weeks to make provision for inefficiency in killing all the live lice at the time of treatment and also variations in the time of hatching of eggs which may sometimes take two weeks.
Thus Mediker is an effective treatment against lice and can indeed provide freedom from lice provided it is used for 4 consecutive weeks.

Results and inferences

- ✓ Lice do not increase in number indefinitely but are limited due to crowding effects and lack of area. So the rate of transmission or fall off is significant.
- ✓ When a model based on equal distribution is assumed, the total number of lice as a function of time indicates that there are no chances of a person becoming anemic due to blood sucking effects of lice.
- ✓ The claim of Mediker to ensure freedom from lice in 4 weeks is quite authentic.

Drawbacks and scope for improvement

- ❖ Due to insufficiency of data and experimental results first order rate constants were assumed in the differential equation. Probably more accurate representations of the system can be obtained by considering non-linear models.
- ❖ As I was unable to find the age distribution data for the egg and lice population equal distribution was assumed as a reasonably good approximation.
- ❖ The equal distribution may hold good only after a certain lag period and not right from the beginning. So if the data for age distribution is obtained better growth model can be achieved.
- ❖ Biological systems are highly dynamic. Randomness is always an inherent part of such systems. So it is difficult to obtain very good representative mathematical models without experimental data.

Acknowledgement

I would like to thank my professor Dr G K Suraishkumar for inspiring me to think originally and develop analyzing power. I might not have reached amazing heights in innovative and creative work but I have definitely made an attempt. I am very thankful to Dr G K S for providing me this opportunity.

I would also like to thank Dr Sharad Nadig and Dr. Waclaw Szybalski for helping me in the completion of my CFA by providing me certain necessary information.

I would also like to thank almighty for providing me courage through the ups and downs that I faced while doing my CFA.

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Thank you

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