IJISET - International Journal of Innovative Science, Engineering & Technology, Vol. 3 Issue 7, July 2016
ISSN (Online) 2348 – 7968 | Impact Factor (2015) - 4.332
www.ijiset.com

Modeling The Physiologically-Based Variations For Inhalational Anthrax

[1]Kamalu, C.I.O.; [2]Nwakaudu M.S.; [3]Opebiyi, S.O.; *[4]Obijiaku, J.C.; [5]Oghome, P.; [6]Okwara A.C.; and [7]Uzondu F.N.

[1,2,3,4,5,6,7] Department of Chemical Engineering, Federal University of Technology, P.M.B. 1526, Owerri, Nigeria.
*[4]Phone: +234(0)7062810295; *[4]E-mail: obijiakujudec@gmail.com

ABSTRACT

Four different models were developed to describe the activity of anthrax-caused disease in human beings. Data for validating the models were obtained from the internet. The result showed that the models developed are very good as models 1, 2, 3 and 4 gave correlation coefficients of 0.9968, 0.9999, 0.9952, and 0.9999 respectively. These models can be used to predict the variation of the disease with time. The knowledge of the findings of this work can be applied in the medical fields by medical doctors and nurses in the treatment of anthrax diseases.

Keywords: Physiologically-based, inhalation, anthrax, modeling, spore, dose.

1.0 INTRODUCTION

1.1 Background Study

Bacillus anthracis, the bacterium that causes anthrax, is one of the most dreaded bio-weapons as identified by the Working Group on Civilian (WGC) biodefense. Several countries are believed to have offensive biological weapons programs, as some independent terrorist groups have intended to use them. Because the possibility of a terrorist attack using bio-weapons is difficult to predict, detect, or prevent, it is among the most feared terrorism scenarios (Lew, 1995). In September 2001, *B. anthracis* spores were sent to several locations via the US postal service: 22 confirmed or suspected causes of anthrax infection resulted. 11 of these were inhalation anthrax cases, in which 5 died; eleven were cutaneous cases, in which 7 were confirmed dead (Kennedy, 2001).

The problem of nuclear, biological, chemical (NBC) weapon usage in warfare has become rampant these years (Monterey, 2001). It is important, therefore, to have an existing model(s) for forecasting any disease variation with time or any other variable in human body. This will go a long way in arresting some early death cases.

The objective of this work is to develop models that will relate and forecast:

a. The number of bacteria as a function of time.
b. Percentage infection as a function of percentage dose.

c. Percentage deposition of spores in the alveoli as a function of spore particle size.

d. The number of spores in the lung as a function of clearance time.

These will go a long way in helping the medical world to determine the variation of certain sicknesses and the extent to which they have deteriorated.

1.2 Epidemiology of Anthrax

Natural occurring anthrax in humans is a disease acquired from contact with anthrax infected animals or animal products. The disease most commonly occurs in herbivores, which are infected after ingesting spores from the soil to leaves. Larger anthrax epizootics in herbivores have been reported (Kohout *et al.,* 1964). A published report states that anthrax killed one million sheep in Iran in 1945 (Titball *et al.,* 1991); this number is supported by an unpublished Iranian governmental document (Pienaar, 1967). However, *B. anthracis* spores remain prevalent in soil samples throughout the world and causes anthrax cases among herbivores annually (Titball *et al.,* 1991).

Anthrax infection occurs in humans by three major routes: Cutaneous, gastrointestinal and inhalational.

1.2.1 Cutaneous Anthrax

Cutaneous anthrax is the most commonly, naturally occurring form, with an estimated 2000 cases reported annually worldwide (Brachman and Friedlander, 1999). The largest reported epidemic occurred in Zimbabwe between 1979 and 1985, when more than 10,000 human cases of anthrax were reported; nearly all of them were of cutaneous (Myenye *et al.,* 1996).

1.2.2 Gastrointestinal Anthrax

Although gastrointestinal anthrax is uncommon, outbreaks are continually reported in Africa and Asia, following ingestion of insufficiently cooked contaminated meat (Brachman and Friedlander, 1999). Two distinct syndromes are oral-pharyngeal and abdominal (Sirisanthana *et al.,* 1988). Littlie information is available about the risks of direct contamination of food or water with *B. anthracis* spores. Experimental efforts to infect primates by direct gastrointestinal instillation of *B. anthracis* spores have not been successful (Lew, 1995). Gastrointestinal infection could occur only after consumption of large numbers of vegetative cells such as what might be found in raw undercooked meat from an infected herbivore, but, experimental data is lacking.

1.2.3 Inhalational Anthrax

Anthrax spores have the potential for use in biological warfare because of their ability to survive and because they spread easily in air and can be inhaled. Once the spores are inside the lungs, the bacteria develop and begin to multiply. Naturally occurring inhalational anthrax is now rare.

Eighteen cases of inhalational anthrax cases were reported in the United States from 1900 to 1976; none was identified or reported thereafter. Most of these cases occurred in special-risk groups including goat hair mill or wool or tannery workers; two of them were laboratory associated (Brachman and Friedlander, 1980).

Inhalational anthrax is expected to account for most serious morbidity and most mortality following the use of *B. anthracis* as an aerosolized biological weapon. Given the absence of naturally occurring cases of inhalational anthrax in some Western countries since 1976, the occurrence of a single case is now a cause for alarm (Bradford *et al.*, 2008).

1.3 Microbiology

B. anthracis is an aerobic, gram-positive, spore-forming, and no motile Bacillus species. Spore size is approximately 1µm and grows readily on all ordinary laboratory media at 37^{o}C, with a "jointed bamboo-rod" cellular appearance and a unique "curled- hair" colonial appearance. *B. anthracis* spores germinate when they enter an environment rich in amino acids, nucleoside and glucose, such as that found in the blood tissue of an animal or human host. The rapidly multiplying vegetative *B. anthracis* bacilli, on the contrary, will only form spores after local nutrients are exhausted, such as when anthrax-infected body fluid are exposed to ambient air (Titball *et al.*, 1991). Vegetative bacteria have poor survival outside of an animal or human host. This contrasts with the environmentally hardy properties of the *B. anthracis* spore, which can survive for decades in ambient conditions (Druitt *et al.*, 1995).

1.4 Pathogenesis and Clinical Manifestation

Inhalational anthrax follows deposition into alveolar spaces of spore-bearing particles in the 1 to 5µm range (Kohout *et al.*, 1964), macrophages then ingest the spores, some of which are lysed and destroyed. Surviving spores are transported via lymphatic to mediastinal lymph nodes, where germination occurs after a period of spore dormancy of variable and possible extended duration (Myenye *et al.*, 1996). The trigger responsible for the transformation of *B. anthracis* spores to vegetative cells is not fully understood (Brachman and Friedlander, 1999; Hodges, 1965). Viable spores were demonstrated in the mediastinal lymph nodes of 1 monkey 100 days after exposure (Dragon and Ronnie, 1995).

Once germination occurs, clinical symptoms follow rapidly. Replicating anthracis bacilli release toxins that lead to hemorrhage, edema and necrosis (Friedlander, 1997). Extrapolations from animal data suggest that the human LD 50 (i.e., dose sufficient to kill 50% of inhaled persons exposed to it) is 2,500 to 55,000 inhaled *B. anthracis* spores (Regis, 1999). Recently published

extrapolations from primate data suggest that as few as 1 to 3 spores may be sufficient to cause infection (Regis, 1999).

The antibiotic treatment or post exposure prophylaxis for anthrax among those who are immunosuppressed has not been studied in human or animal models of anthrax infection.

1.5 Infection Control

There are no data to suggest that patient to patient transmission of anthrax occurs and no person to person transmission of anthrax occurred following the anthrax attacks of 2001 (Meselson, 1994). There is no need to immunize or provide prophylaxis to patients, contacts (e.g. household contacts, friends, coworkers) unless they were exposed to the aerosol or surface contamination at the time of the attack. A number of disinfectants used for standard hospital control, such as hypochlorite, are effective in cleaning environmental surface contaminated with infected bodily fluid (Titball *et al.*, 1991; Christopher *et al.*, 1997).

Proper burial or cremation of humans and animals that have died of anthrax infection is important in preventing further transmission of the disease. Embalming of bodies could be associated with special risks (Kohout *et al.*, 1964). If autopsies are performed, all related instrument and materials should be autoclaved or incinerated.

If an environmental surface is proved to be contaminated with *B. anthracis* spores in the immediate area of spill or close proximity, working group believes that decontamination of that area would likely decrease the risk of acquiring anthrax by secondary aerosolizaton (Alibek and Handelman, 1999).

2.0 DEVELOPMENT OF MODELS

2.1 Bacterial Number as a Function of Time

The rate of change of bacteria number in a host $\frac{dB_n}{dt}$ is directly proportional to the decreasing bacteria number itself.

The number of bacteria is also directly proportional to the time of bacterial infection i.e.

$$\frac{dB_n}{dt} \alpha B_n \; or \; \frac{dB_n}{dt} = -K_1 B_n \; or \; B_n = B_{no} \ell^{-K_1 t} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \; \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (1)$$

$$\text{and } B_n \, \alpha t \; or \; B_n = k_2 t \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (2)$$

Combining equation (i) and (ii) as a joint variation gives

$$B_n = ktB_n{}^{o} \ell^{-K_1 t} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (3)$$

2.2 Percentage Infection as a Function of Percentage Dose

The general model for natural resource depletion for natural phenomenal variation (Kamalu, 2010) can be modified as shown below;

$$\begin{pmatrix}\text{Change in actual natural phenomenal variation during a period of time}\end{pmatrix} = \begin{pmatrix}\text{Actual phenmenon in insitu}\end{pmatrix} - \begin{pmatrix}\text{Caused natural phenomenon variation}\end{pmatrix} + \begin{pmatrix}\text{Imigrant natural phenominal variation}\end{pmatrix} - \begin{pmatrix}\text{Emigrant natural phenomenal variation}\end{pmatrix} \quad \text{..... (4)}$$

The phenomenal variation herein can be any natural occurrences, sickness inclusive. If equation (4) is adopted for infection, then the term on the (L.H.S) represent infection (I) as dependent variation.

The first term on the (R.H.S) which is in situ natural phenomenon term represents the maximum infection (*Im*) which is a constant, the second term on the (R.H.S.) is to be computed (caused natural phenomenon variation). The third and fourth terms are assumed to be zero since there is no inflow or outflow in this model, so that the equation can be re-written as;

$$\begin{pmatrix}\text{Change in actual natural phenomenal variation during a period of time}\end{pmatrix} = \begin{pmatrix}\text{Actual phenmenon in insitu}\end{pmatrix} - \begin{pmatrix}\text{Caused natural phenomenon variation}\end{pmatrix} \quad \text{..... (5)}$$

Caused natural phenomenon variation:

The composite dose rate of change of infection $\frac{dI}{dD}$ is directly proportional to the increasing infection (I) itself.

$$\frac{dI}{dD} \alpha I \quad \text{..... (6)}$$

Where, the composite dose (D) is proportional to the actual dose (d) raised to a constant power.

$$D \alpha d^n \quad \text{..... (7)}$$

Solving (6) and (7) respectively yields

$$I = \ell^{-K_1 D} \quad \text{..... (8)}$$

$$D = k_2 d^n \quad \text{..... (9)}$$

So that combing equations (8) and (9) gives

$$I = \ell^{-K_1 K_2 d^n} = \ell^{-ad^n} \quad \text{..... (10)}$$

Where, a = k_1 k_2 are constants.

Note that the product of equation (10) and the maximum infection, *Im*, i.e. ($I_m \ell^{-ad^n}$) is the third and last term of equation (4). Substituting all these into equation (5), give:

$$I = I_m - I_m \ell^{-ad^n} = I_m (I - \ell^{-ad^n}) \quad \text{..... (11)}$$

2.3 Percentage Spore Deposition in Alveoli as a Function of Spore Particle Diameter

Here, the rate of percentage deposition of spores in alveoli with respect to the spore particle size $\frac{dy}{dx_p}$ is a sum of variations which is: 1, partly proportional to the square of the spore particle size; 2, partly proportional to the spore size of the particle; and 3, partly constant, i.e.

$$\frac{dy}{dx_p} = p_{1x^2p} + p_2 x_p \quad p_3 \quad \text{..... (12)}$$

Solving the ODE by direct integration of equation (i) gives

$$y = \frac{1}{3} p_1 x_p^{\ 3} + \frac{1}{2} p_2 x_p^{\ 2} + p_3 x_p + p4 \quad \text{..... (13)}$$

or $y = ax_p^{\ 3} + bx_p^{\ 2} + cx_p + d$ ..... (14)

Where, a = $\frac{p_1}{3}$, $b = \frac{p_2}{2}$, $c = p_3$, $d = p_4$

2.4 Number of Spore in Lung as a Function of Time

The difference between the time of accumulating and the initial time (t - to) in the lung is always proportional to the natural logarithm of the difference between the reciprocals of the accumulating number of spores $\ln\left(1/s - 1/s_o\right) i.e.$.

$$\Delta t \alpha \ln \Delta \frac{1}{s} \text{ or } (t - to) \alpha \ln\left(1/s - 1/s_o\right)$$

Error! Not a valid link., such that $\ln\left(1/s - 1/s_o\right) = \frac{t - to}{t}$

If c = $1/s_o$ and a = to, then, $\frac{1}{s} = \ell^{(t-a)/b} + C$

$$s = \frac{1}{\ell^{(t-a)/b} + C} \quad \text{..... (15)}$$

3.0 COLLECTION OF DATA

Data for (a) number of bacteria as a function of time, (b) Infection as a function of dose (c) percentage alveoli deposition as a function of particle diameter and (d) number of spores in the

lungs as function of time were all obtained from the works of Bradford *et al.* (2008) and are shown below.

Table 1a: Bacterial number as a function of time

Bn X 10^{-6} (spore)	0	0.63	1.28	2.46	3.3	4.1	4.47	4.50	3.89	3.20	2.83
Time (hr.)	0	0.15	0.32	0.70	1.10	1.5	2.5	4.16	5.28	6.4	7.0

Table 2a: Percentage infection as a function of percentage dose

Infection (I) (%)	0	0.4	1.3	2	3	4.4	5.1	5.2	5.5
Dose (D) (%)	0	0.5	1.3	2	3.2	4.0	5.2	5.8	7.6

Table 3a: Percentage deposition in alveoli as a function of spore particle diameter

Pab. (%)	18	15	12.5	15.0	18.75	10
Xp (μm)	0.1	0.325	1.0	3.2	5.0	7.5

Table 4a: Number of spores in lung as a function of time

Sn (Spores)	14,500	15,000	11,670	7500	3340	1600
Time (hr.)	0	5	10	15	20	25

5.0 RESULTS AND DISCUSSION

5.1 RESULTS

The data obtained from the internet (literature) for anthrax caused- disease variations are plotted as scatter diagrams. The respective models were super-imposed on the scatter diagrams to confirm their goodness of fit using MATLAB toolbox 7.0.

The results of the computation in section 4.0 are shown here below in Figures 1- 4 and Tables 1b - 4b.

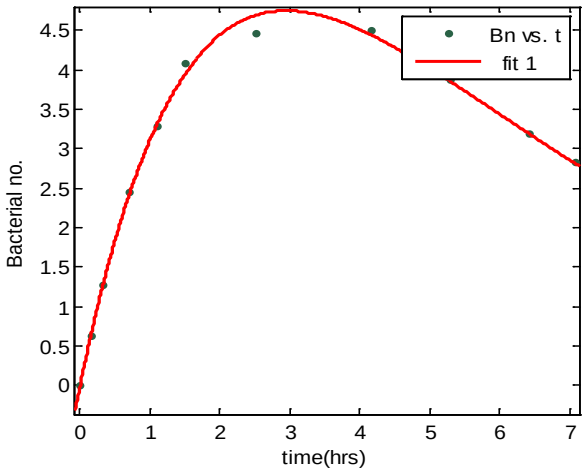

Figure 1a: Bacteria number in the host versus time

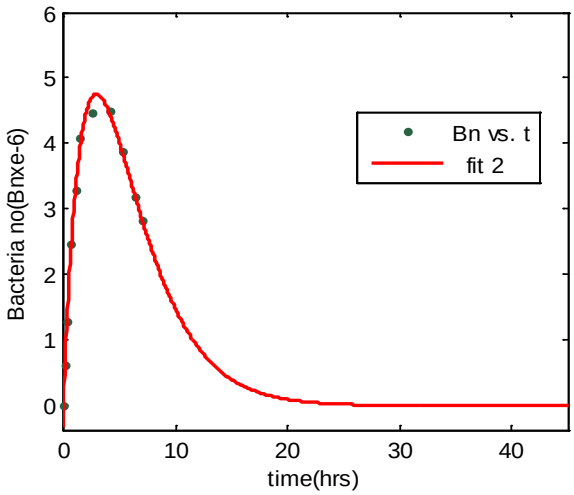

Figure 1b: Bacteria number in the host versus time (predicting the future)

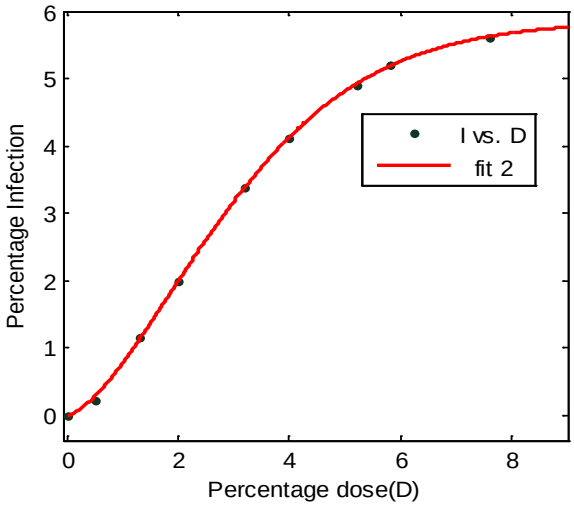

Figure 2a: Percentage Infection versus Percentage Dose

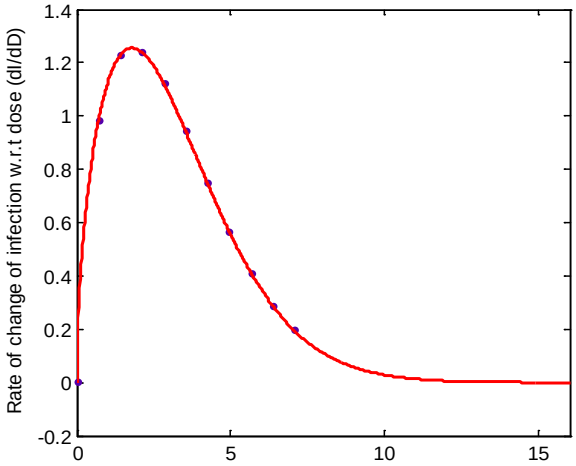

Figure 2b: Rate of Change of Infection with respect to Dose versus Percentage Dosage

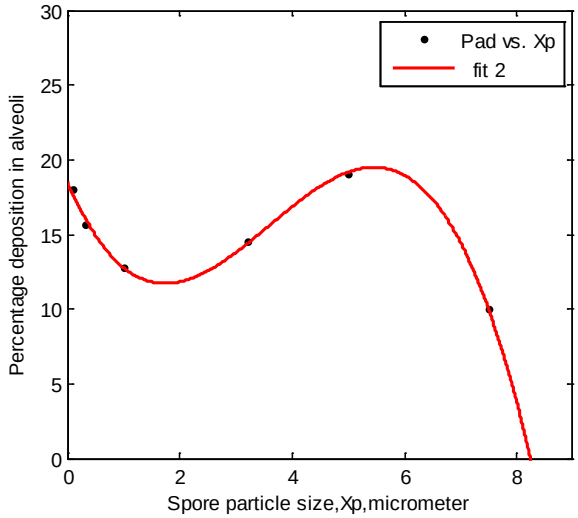

Figure 3: Percentage Deposition in alveoli versus Spore Particle Size

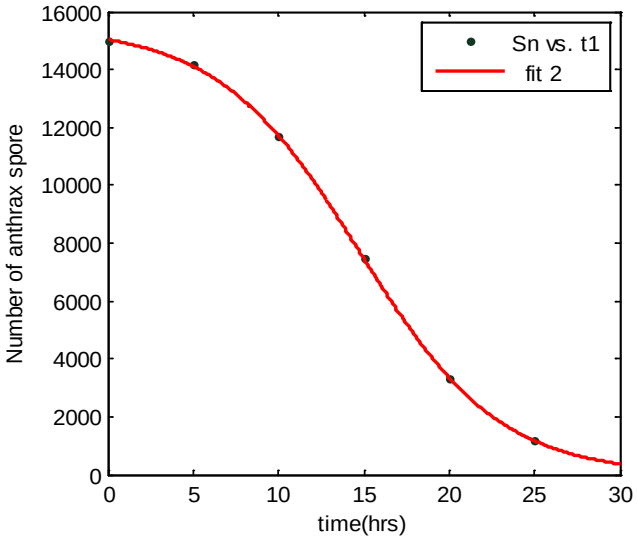

Figure 4: Number of Anthrax Spores in the Lung versus Clearance Time

Table 1b: Co-efficient and Goodness of Fit for Model 1

Bn_o =4.376 (4.203, 4.546)	Goodness of fit

K1 = 0.3387(0.3289, 0.3485)	SSE : 0.7767
F(2.9524) = 4.75291	R-square : 0.9968
K = 1.00	Adjusted R-square : 0.9964
	RMSE : 0.0929

Table 2b (i): Coefficient and Goodness of Fit for Model 2

lm = 5.838 (5.736, 5.939)	Goodness of fit
	SSE : 0.003873
a = 0.1431 (0.1366, 0.1495)	R-square : 0.9999
	Adjusted R-square : 0.9999
b = 1.551 (1.501, 1.60)	RMSE :0.02541

Table: 2b (ii) Derivative of 2nd Graph or Model Data

Dx	0	0.706	1.412	2.118	2.824	3.53	4.236	4.942	5.648	6.354	7.06
DI/dD (DI)	0.0014	0.984	1.23	1.24	1.1214	0.9433	6.7494	0.56780	0.4129	0.2894	0.196

Table (3b): Coefficient and Goodness of Fit for Model 3

$Y= p_1 x^3 + p_2x^2 + p_3x + p_4$	Goodness of fit
$Y = ax^3 + bx^2 + c\,x + d$	SSE: 0.2706
a = 0.3028 (- 0.3806, -0.2251)	R-square : 09952
b = 3.278 (2.372, 4.184)	Adjusted R-square : 0988
c = -8688 (-11.36, -6.016)	RMSE: 0.3678
d = 1851 (17.1,19.92)	

Table 4b: Coefficient and Goodness of Fit for Model 4

a = 54.5 (52.82, 56.19)	Goodness of fit
b = 4.124 (3.942, 4.307)	SSE : 1.168×10^{-4}
c = 6.468×10^{-5} (6.372×10^{-5}, 6.564×10^{-5})	R-square: 0.9999 Adjusted R-square: 0.9999

	RMSE :62.4

5.2 DISCUSSION

From Figure 1a and Table 1b, it is seen that the data obtained from the internet (literature) fitted the model of number of bacteria as a function of time with R-square (coefficient of correlation) of 0.9968. Figure 1b is the same as Figure 1a profile but adjusted for predicting the future. The number of bacteria will exhaust at 25 hours. The pick of bacteria number is 4.7529×10^{-6} at 2.95024 hours.

Figure 2a shows a natural phenomenal kind of sigmoidal profile. It is a logistic profile that will give the ultimate infection and time of occurrence. The differentiated form is shown in Figure 2b as dose rate of infection. The coefficient of correlation of model 2 is 0.9999 which shows that the model is very good in relating infection as a function of dosage. The pick infection of 1.2555 occurs at a percentage dosage of 1.8. The ultimate percentage infection occurs as 5.8 % infection at 9 % dose. The rate of change of infection becomes zero at 12.5 % dosage.

In the third model of percentage deposition of spores in alveoli as a function of spore particle size, the model fitted very well again with R-square of 0.9952.

In Figure 4, the model fitted the collected data very well again with coefficient of correlation of 0.9999. The entire models (1 - 4) fitted the collected data very well from the various values of R-square seen. Hence inhalation anthrax is predictably modelable.

6.0 CONCLUSION

Four different models were developed to describe the activity of anthrax-caused disease in human beings. Data for validating the models were obtained from the internet and are used in validating the models. The results show that the models developed are very good fits of the raw collected data and give correlation coefficient of 0.9968, 0.9999, 0.9952 and 0.9999 respectively.

These models can be used to predict the variation of disease and time. The knowledge of the findings of this model work can be applied in the medical field by medical doctors and nurses in the treatment of anthrax and anthrax caused diseases.

REFERENCES

Alibek K. and Handelman S. (1999), "*The chilling True Story of the Largest Convert Biological Weapons Program in the World*", New York, Random House, pp. 184-196.

Brackman P. and Friedlander A. (1980), "*Inhalational Anthrax*", Ann N.Y. AeadSci, MEDLINE, pp 96 - 101.

Brackman P. and Friedlander A. (1999), "*Anthrax as Biological Weapon*", 3rd ed., Philadelphia, WB Sauders C O., pp. 32 – 46.

Bradford W. G., Stephen R. C. and Alan E. B. (2008), "I*nhalational Anthrax"*, New York, pp. 73 – 78.

Christopher G., Cieslak T., Pavlin J. and Eitzen E. (1997), "*Biological Warfare*: *A Historical Perspective"*, Janna, MEDLINE, pp. 77 – 33.

Dragon D. and Ronnie R. (1995), "*The Ecology of Anthrax Spores"*, Can Vet J. MEDLINE, pp. 52 – 64.

Druitt H., Henderson D., Packman L. and Peacock S. (1995), "*Studies on Respiratory Infection*", New York, Grash Co., pp. 280 – 296.

Friedlander A. (1997), "*Medical Aspect of Chemical and Biological Warfare*", Washington DC, Nelk Press Ltd., pp. 78 – 88.

Hodges D., Klein F., (1965), "*Role of the Lymphaties in the Pathogenesis of Anthrax*", J. Infect Dis MEDLINE.

Kamalu C.I.O. (2010), "*Prediction and Analysis of Nigeria Crude Oil and Gas Resource Depletion*", Ph.D. Thesis, Post-graduate School, Federal University of Technology, Owerri, Nigeria, pp. 80 – 81.

Kennedy H. (2001), "*Daschle Letter of Bombshell Billions of Anthrax Spores*", New York Daily News, October 31:5.

Kohout E., Sehat A. and Ashrat M. (1964), "*Anthrax: A Continuous Problem is South West Iran*", Am J Med. Sci., pp. 56 – 76.

Lew D. (1995), "*Principles and Practice of Infections Disease*", New York, Churchill Livingstone Inc., pp. 185-188.

Meselson M., Guillemin J. and Hugh- Jones M. (1994), "*The Sverdlovsk Anthrax Outbreak of 1979*", Science MEDLINE.

Monterey I. (2001), "*Chemical and Biological Weapon Resource*", Accessed September 27, 2012 from http.//cns.Miis.Edu/research/chw/possess.htm.

Myenye K., Siziya S. and Peterson D.I. (1996), "*Factors Associated with Human Anthrax Outbreak in Central Africa"*, Zimbabwe, MEDLINE, pp. 145 – 152.

Pienaar U. (1967), "*Epidemiology of Anthrax in Wild Animals and Control on Anthrax Epizootics in the Kruger National Park*, South Africa.

Regis E. (1999), "*The History of America's Secret Germ Warfare Project*", New York, Random House.

Sirisanthana T., Nelson K., Ezzell J. and Abshir T. (1988), "*Serological Studies of Patients with Cutaneous and Oral-pharyngeal Anthrax from Northern Thailand*, MEDLINE.

Titball R., Trunbull P. and Hutson R. (1991), "*The Monitoring and Detection of Bacillus Anthracis in the Environment", MEDLINE (20:9S-18S).*