A Mathematical Model on Transmission Dynamics of Meningococcal Meningitis

MURITALA A. AFOLABI[1], KAMORUDEEN S. ADEWOYE[2], ADEYINKA I. FOLORUNSO[3], MUSIBAU A. OMOLOYE[4]

[1, 2] *Department of Science and Social Sciences, Osun State Polytechnic, Iree. Osun State.*

[3] *Department of Statistics, Osun State Polytechnic, Iree. Osun State.*

[4] *Department of Statistics, Federal Polytechnic Offa Kwara State.*

Abstract- ***Meningococcal meningitis is a contagious and severe bacterial disease caused by meningococcus (Neisseria meningitidis). It is spread by human through respiratory droplets of infected-infectious individual in close contact environment. Due to the threat posed by meningococcal meningitis, four compartmental meningitis model was formulated to gain more insight on transmission dynamics of meningococcal meningitis. The next generation matrix (NGM) method was used to obtain the basic reproduction number*** (R_0) ***. The model was epidemiologically and mathematically well posed. Both disease free equilibrium (DFE) point and endemic equilibrium point (EEP) of model were obtained. Analysis of the stability of the disease-free equilibrium (DFE) was done using linearization of the Jacobian matrix method. The result showed that the disease-free equilibrium (DFE) point of the model was locally asymptotically stable as threshold*** $R_0 < 1$ ***and effective contact rate increase the basic reproduction number*** R_0 ***. Sensitivity analysis result value showed that effective contact rate is the most sensitive parameter with value of 1.0000 which propel the reproduction number*** R_0 ***. The increment in basic reproduction number makes it more difficult to have disease free environment.***

Indexed Terms- ***Meningococcal meningitis, Reproduction number, Numerical simulation, Sensitivity analysis, Stability analysis.***

I. INTRODUCTION

Meningitis is an inflammation of the meninges which are membranes that surround the brain and the spinal cord. The purpose of meninges and the cerebrospinal fluid is to protect and provide nourishment to the central nervous system [9]. According to [17], the meninges are made of three layers. They are dura mater, the arachnoid mater and pia mater. The pia mater is the membrane closet to the brain and the arachnoid mater is the middle of the meninges. These two are quite delicate and are separated by subarachnoid space which is small gap that contains cerebrospinal fluid. This fluid acts as a shock absorber within nervous system. The dura mater is thick and durable and closet to the skull, it surrounds the other two parts of the meninges and protects the brain and spinal cord. There are thirteen (13) different types of " Sero groups" of disease, only five (5) of them A, B, C, Y, W135 are globally responsible for the disease [5,3,6,15].

Meningitis is often caused by infection (bacterial, viral, fungal parasitic), but can also be produce by chemical irritation, subarachnoid haemorrage, cancer and other condition [4,12]. Bacterial meningitis is rare but can be very serious if not treated while viral meningitis is the most common and least serious type. Fungal and parasitic meningitis are non-infectious. Bacterial meningitis is generally caused by different types of bacteria such as Neisseria meningitidis, Streptococcus pneumoniae, Haemophilus influenza (most often caused by type b, Hib), Mycobacterium tuberculosis. Neisseria meningitidis which causes meningococcal meningitis occurs most frequently among the three. Bacterial meningitis is common among children and young adults. Humans are the sole hosts of Neisseria meningitidis and it has been responsible for its outbreak [3,7,14,16,15].

Some viral and bacterial meningitis are contagious. They can be transmitted by coughing, sneezing or close contact. It spreads by person to person contact

through respiratory droplets of infected-infectious individual in communities/societies that live in close contact [11,9]. The bacterial enter the bloodstream of an infected person, it may invade and multiply in the cerebrospinal fluid, in most people, antibodies kill the bacteria to preventing them from causing disease. However, it is possible to carry meningococcal while it does not showing any symptoms of infection to the exposed class. Meningococcus, another term for Nesseiria meningitidis naturally resides in the human nasopharynx (throat, area behind mouth). The bacteria can gain entrance into the blood stream by way of the nasopharynx [2]. Once bacteria are inside the blood, they have the ability to defeat the body's defense mechanisms that would fight off infection in other to find its way to cerebrospinal fluid and end up in the meninges, Hence, causes the meninges to become inflamed. The inflammation of the cervical nerves causes Nuchal rigidity. This is the ability to move the head forward and is often used for diagnosis. It takes about 4 days for the bacteria to go from the nasopharynx to the meninges [10,1].

Not everyone with meningitis will have the same symptoms. It depends on the cause but any of the following are possible with bacterial meningitis. They are severe headache, high temperature, vomiting, sensitivity to light (Photophobia), joint pains, drowsiness, irritability, purple areas of skin that resembles bruises, lethargy, confusion and stiff neck. Typically, symptom of bacterial meningitis develop within few hours of few days after exposure (usually within 3-7 days) [3,6,14]

Meningococcal disease can be difficult to diagnosis because the sign and symptoms are often similar to those of other illnesses. Blood or cerebrospinal fluid samples (through lumbar puncture) of suspected patients will be collected for testing to see if there is an infection and, if so, what germ is causing. If Neisseria meningitidis are in the samples, the laboratorians can grow (culture) the bacteria in other to known the specific type of bacteria that is causing the infection. Knowing this will help the Doctor to decide which antibiotic will work best. Also, computerized Tomography (CT) scan do employ. Other tests can sometimes detect and identify the bacteria if the cultures do not [3].

There are vaccines to protect people at risk from contacting meningitis. In the event of outbreak, antibiotics can be given to all those that might have been affected even before people develop symptoms [7,11].

Once a successfully diagnosis is made, the antibiotics treatment must be started as soon as possible. Empirical therapy includes ceftriaxone or cefotaxime, and vancomycin for Streptococcus pneumonia [4].

Even with appropriate antibiotics treatment around 10% of the patients die. The case fatality rate can be between 3% to 10% in developed countries and high as 20% in Africa countries especially in the 26 countries known as African Meningitis Belt. Most people make full recovery from meningitis but can sometimes cause serious long-term problems and be life threatening. About 11% to 19% of the survivors will have long-term disabilities such as loss of limbs, deafness, epilepsy, nervous system or brain damage [3,7,11,15].

A number of factors make people more susceptible to meningitis. Those at high risk are babies and young children.

II. MODEL FORMULATION

The total homogeneous population at time t, denoted by N(t), is partitioned into four (4) compartments of Susceptible S(t) individuals, Carrier C(t) individuals, infected $I(t)$ individuals and recovered R(t) individuals. So that, $\mathrm{N(t)} = \mathrm{S(t)} + \mathrm{C(t)} + \mathrm{I(t)} + \mathrm{R(t)}.$

The susceptible population is increased by the recruitment of individuals (either by birth or immigration) into the population, all recruited individuals are assumed to be susceptible at rate π. This population is decreased by transmission individuals that acquired meningococcal infection following effective contact with infectious individuals in the carrier C(t) and infected I(t) at a rate λ given by:

$$\lambda = \beta . \frac{I}{N} \qquad (1)$$

In (1) β represents the effective contact rate (contact capable of leading to meningococcal infection). This population later decrease due to natural death of susceptible individuals at the rate μ and later increase by recovered individual without disabilities at the rate θ. Thus the rate of change of the susceptible population is given by: $\frac{dS}{dt} = \pi - \lambda S - \mu S + \theta R$ (2)

The population of carrier individuals increased by fraction that developed infectious meningococcal at the rate $(1-\rho)\lambda S$. This population is decreased by the progression of carrier individuals to active stage at the rate κ and by natural death at rate μ.

Thus: $\frac{dC}{dt} = (1-\rho)\lambda S - \mu C - \kappa C$ (3)

The population of infected individuals increased by the remaining fraction of the carrier individuals that developed infectious meningococcal at the rate $\rho\lambda S$. It is further increased by the progression of carrier individuals to active stage at the rate κ. This population is decreased by natural death of meningococcal patient at rate μ and later by disease induced death rate δ. This is further reduced by natural immunity rate σ and treatment rate τ of infected individuals. Hence,

$$\frac{dI}{dt} = \rho\lambda S - \mu I - \delta I + \kappa C - \sigma I - \tau I \quad (4)$$

The population of recovered individuals is increased by natural immunity rate σ and treatment rate τ of infected individuals. This population is reduced by natural death rate μ and recovery without disabilities at the rate θ.Thus,

$$\frac{dR}{dt} = \tau I - \mu R + \sigma I - \theta R - \delta R \quad (5)$$

In view of the above equations, the meningitis transmission model is given by the following system of non-linear differential equations:

$$\begin{aligned}
\frac{dS}{dt} &= \pi - (\lambda + \mu)S + \theta R \\
\frac{dC}{dt} &= (1-\rho)\lambda S - (\mu + \kappa)C \\
\frac{dI}{dt} &= \rho\lambda S + \kappa C - (\mu + \delta + \sigma + \tau)I \\
\frac{dR}{dt} &= \tau I + \sigma I - \mu R - \theta R
\end{aligned} \quad (6)$$

Table A Definition of Variables

Variables	Definition
S(t)	Population of susceptible at time t.
C(t)	Population of Carrier individuals at time t
$I(t)$	Population of Infected individuals at time t
R(t)	Population of Recovered individuals at time t
N(t)	Total population i.e.($S + C + I + R$) at time t

Table B Definition of Parameters used in the model

Parameters	Definition
π	Recruitment rate of individuals
β	Effective contact rate
μ	Natural death rate
δ	Meningitis induced mortality rate
σ	Natural immunity rate
ρ	Probability of developing meningococcal infection rate
κ	Progression rate from carrier to infected class
τ	Treatment rate
λ	Force of infection
θ	Recovered individual without disabilities

A. Positivity of Solution

Theorem 1: The closed set $D = \left\{(S,C,l,R) \in \Re_+^4 : N \le \frac{\pi}{\mu}\right\}$ is positively invariant and attracting with respect to the model equation (6) above.

Proof: Consider the biologically-feasible region D, the rate of change of the total population is obtained by adding all the sub-equations in equation (6) which gives:

$$\frac{dN}{dt} = \pi - \mu S - \mu C - \mu I - \delta I - \mu R \quad (7)$$

Where $N = S + C + I + R$

Then, $\frac{dN}{dt} = \frac{dS}{dt} + \frac{dC}{dt} + \frac{dI}{dt} + \frac{dR}{dt}$ (8)

$$\frac{dN}{dt} = \pi - \mu N$$

Equation (7) becomes $\frac{dN}{dt} = \pi - \mu N$ (9)

In the absence of infection, equation (9) implies:

$$\frac{dN}{dt} + \mu N = \pi \quad (10)$$

using the integrating factor $I.F = e^{\int \mu dt}$

$$I.F = e^{\int \mu dt} = e^{\mu t} \quad (11)$$

Multiply both sides of equation (10) by equation (11), it implies:

$$e^{\mu t}\left\{\frac{dN}{dt}\right\} + \mu N e^{\mu t} = \pi e^{\mu t} \quad (12)$$

$$= \left\{\frac{d}{dt}(Ne^{\mu t})\right\} = \pi e^{\mu t}$$

Integrate both sides with respect to t

$$Ne^{\mu t} = \frac{\pi}{\mu} e^{\mu t} + K \quad (13)$$

Multiply both sides of equation (12) by $e^{-\mu t}$

It becomes:

$$N(t) = N(0)e^{-\mu t} + \frac{\pi}{\mu}(1 - e^{-\mu t}) \quad (14)$$

$$N \to \frac{\pi}{\mu} \ as \ t \to \infty$$

Therefore, $\frac{dN}{dt} < 0$ whenever the total population $N > \frac{\pi}{\mu}$. Hence, for all t>0, all the solutions of the model with the initial conditions in region D will remain in the region D (where the model can be considered as being epidemiologically and mathematically well posed). Thus, the biologically feasible region D is positively-invariant and attracting.

B. Stability of the Critical Point

The DFE of the model equation (6) can be obtained by setting

$\frac{dS}{dt}, \frac{dC}{dt}, \frac{dI}{dt} and \frac{dR}{dt} = 0$ which gives

$$\varepsilon_0 = (S_0, C_0, I_0, R_0) = \left\{\frac{\pi}{\mu + \lambda}, 0, 0, 0, 0\right\} \quad (15)$$

while the endemic equilibrium equations at the steady-state was $\varepsilon_1 = (S^*, C^*, I^*, R^*)$

where

$$S^* = \frac{\lambda}{K_1}, C^* = \frac{(1-\rho)\lambda S^*}{K_2}, I^* = \frac{\kappa((1-\rho) + \rho K_2)\lambda S^*}{K_2 K_3}, R^* = \frac{(\sigma + \tau)[\kappa(1-\rho) + \rho K_2]\lambda S^*}{(\mu + \sigma)K_2 K_3} \quad (16)$$

For

$$K_1 = \lambda + \mu, K_2 = \mu + \kappa, K_3 = \mu + \delta + \tau + \sigma \quad (17)$$

and ε_0 and ε_1 represent disease free equilibrium point (DFE) and endemic equilibrium point (EEP) respectively.

C. Reproduction number Ro

The basic reproduction number for this model was calculated by using the next generation matrix method (NGM) as described by [13]. Consider the next generation matrix G which made up of two parts F and V^{-1}, where F = $\left[\frac{\partial F_i(x_i)}{\partial x_i}\right]$ and V = $\left[\frac{\partial V_i(x_i)}{\partial x_i}\right]$.

The non-negative matrix F are the new infection terms and the non-singular matrix V shows the transfer of infections terms from one compartment to another are derived from equation (6). Thus

$$F = \begin{pmatrix} 0 & (1-\rho)\beta \\ 0 & \beta\rho \end{pmatrix} \quad and \quad V = \begin{pmatrix} K_2 & 0 \\ -\kappa & K_3 \end{pmatrix} \tag{18}$$

It follows that the associated reproduction number denoted by $R_0 = \rho(FV^{-1})$ where ρ denotes the spectral radius (dominant Eigen values in magnitude) of the next generation matrix FV^{-1}. Therefore,

$$V^{-1} = \begin{pmatrix} \frac{1}{K_2} & 0 \\ \frac{\kappa}{K_2 K_3} & \frac{1}{K_3} \end{pmatrix}$$

$$R_0 = \frac{\beta(\rho K_2 - \kappa\rho + \kappa)}{K_2 K_3} \tag{19}$$

Where

$$K_2 = (\mu + \kappa) \quad K_3 = (\mu + \delta + \sigma + \tau)$$

D. Stability Analysis of Disease-Free Equilibrium

The stability of disease-free equilibrium here was done by linearization. The characteristics roots of the equation (6) were examined as follows:

$$\frac{dS}{dt} = -\mu S + \theta R$$
$$\frac{dC}{dt} = -(\mu + \kappa)C$$
$$\frac{dI}{dt} = \kappa C - (\mu + \delta + \sigma + \tau)I$$
$$\frac{dR}{dt} = (\sigma + \tau)I - (\mu + \theta)R \tag{20}$$

The Jacobian matrix of equation (20) was corresponding to equilibrium point ε_0 and was computed at critical point (0.0,0,0), Thus gives:

$$J(o) = \begin{pmatrix} -\mu & 0 & 0 & \theta \\ 0 & -(\mu+\kappa) & 0 & 0 \\ 0 & \kappa & -(\mu+\delta+\sigma+\tau) & 0 \\ 0 & 0 & (\sigma+\tau) & -(\mu+\theta) \end{pmatrix} \tag{21}$$

Each element (aij$^{(s)}$) where $1 \le i, \ j \le 4$ were determined from partial differential of each equation with respect to each variable in the model above. Using $\left|A^* - \lambda^* I\right| = 0$ Where

$J_0 = A^*$ ie $\left|A^* - \lambda^* I\right| = 0$ (22)

becomes

$$\Rightarrow \begin{pmatrix} -\mu-\lambda_1 & 0 & 0 & \theta \\ 0 & -(\mu+\kappa)-\lambda_2 & 0 & 0 \\ 0 & \kappa & -(\mu+\delta+\sigma+\tau)-\lambda_3 & 0 \\ 0 & 0 & (\sigma+\tau) & -(\mu+\theta)-\lambda_4 \end{pmatrix} = 0 \tag{23}$$

which give

$$\lambda_1^* = -\mu, \quad \lambda_2^* = -(\mu+\kappa) \qquad \lambda_3^* = -(\mu+\delta+\sigma+\tau) \ and \ \lambda_4^* = -(\mu+\theta)$$

Since all the parameters are positive, it shows that $\lambda_1^*, \lambda_2^*, \lambda_3^* \ and \ \lambda_4^*$ are all negative real and distinct root, as a result of that, the model is stable.

E. Sensitivity Analysis

Sensitivity analysis allows us to measure the relative change in state variable when a parameter changes. The normalized forward sensitivity index of a variable to a parameter is the ratio of the relative change in the variable to the change in the parameter, when the variable is differentiable function of the parameter, the sensitivity index may be alternatively defined using partial derivatives [5]

$$\xi_\beta^{R_0} = \frac{\partial R_0}{\partial \beta} \times \frac{\beta}{R_0} \tag{24}$$

Table C Meningitis parameters with their respective sensitivity values

PARAMETERS	SENSITIVITY VALUES	INITIAL VALUE OF PARAMETERS	SOURCE OF INITAL VALUES
β	1.0000	0.1	WHO 2010
τ	-0.6357	0.7	Estimated
δ	-0.0009	0.001	Estimated
μ	0.00071	0.00004	*Ibrahim & Salma (2017)*
σ	-0.7459	0.4	Estimated
κ	0.2530	0.2	Estimated

F. Numerical simulation result

A numerical simulation of the model was performed for better understanding of impact of effective contact rate on transmission dynamic of meningococcal meningitis in a population. The numerical simulation was conducted using Maple 18 software with different scenarios of effective contact rate on Susceptible, Carrier, Infected and Recovered.

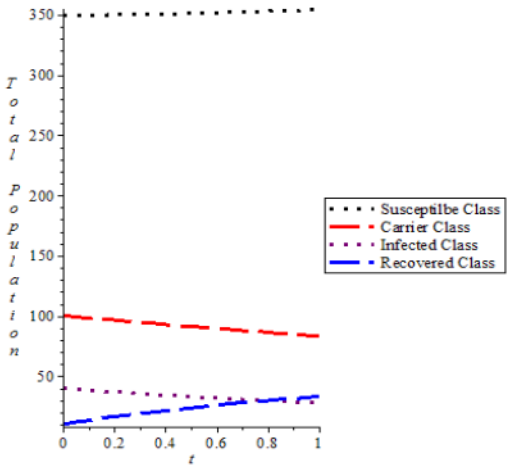

Figure 1: Graph of the total population against time (t)

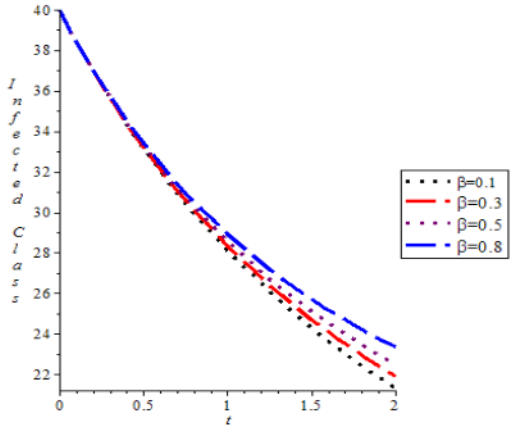

Figure 2: Graph of infected population against time (t) for various values of β

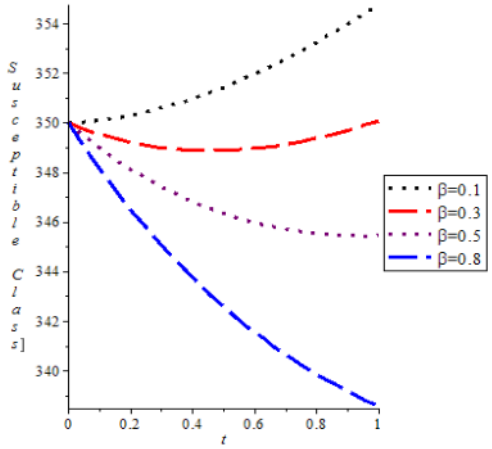

Figure 3: Graph of Susceptible population against time (t) for various values of β

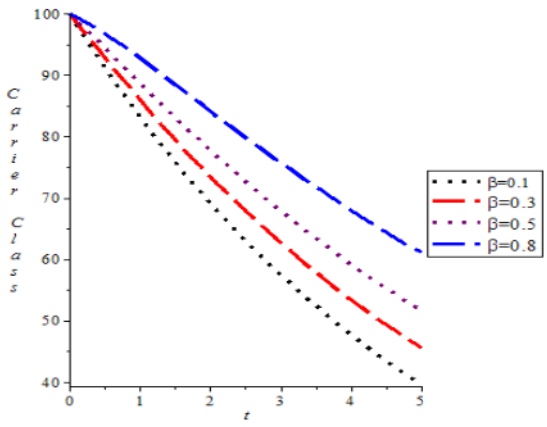

Figure 4: Graph of Carrier population against time (t) for various values of β

III. DISCUSSION OF RESULTS

Figure 1 shows the graph of total population. Figure 2 and 3 show the growth and fall of effective contact rate β on susceptible and infected classes. When the values of β were 0.1 and 0.3, the susceptible population increases unlike when the value was increased to 0.8 which in turn decreases the population. Carrier population also reduces faster when the values of β were 0.1 and 0.3 than when the values of β were 0.5 and 0.8. The figures confirmed that the higher the value of effective contact rate β, the higher the reproduction number R_0 and difficult it becomes to have disease free environment. Figure 5 shows the impact of treatment rate τ on infected class.

CONCLUSION

The DFE of the model equation (6), is locally stable if $R_0<1$ and unstable if $R_0 > 1$. The threshold quantity R_0 is the basic reproduction number for the model. Epidemiologically, if $R_0<1$, the disease will die out in the community and if $R_0>1$, the disease spreads in the population. In this paper we have developed a mathematical model that shown the impact of effective contact rate on the transmission dynamics of meningococcal meningitis disease. Analysis shows that effective contact rate increases the basic reproduction number R_0. The increment in basic reproduction number makes it more difficult to have disease free environment.

REFERENCES

[1] A. A. Bartfield. "Bacterial Meningitis." *International Journal of Infectious Diseases7*: N0.2 49-54 ,2000.

[2] K. A. Cartwright. Introduction and Historical Aspects in Meningococcal Disease. Eds. 1st Baffins Lane, Chichester, John Wiley & Sons Ltd. P p.1-19, 1995.

[3] Centre for Disease Control and Prevention (CDC) /Mr. Gust. Hhttp://phil.cdc.gov/phil/home.asp. Accessed 12/10/19

[4] P. G. Coen, K. Cartwright, & J. Stuart. Mathematical modeling of infection and disease due to Neisseria meningitidis and Neisseria lactamica. *Int. J. Epid.* 29 (2000) 180-188, (2000).

[5] N. Chitnis, J. M. Hyman & J. M. Cushing. Determining Important Parameters in the spread of malaria Through the Sensitivity Analysis of a Model, *Bulletin of Mathematics Biology* (2008) Dot 10 1007/s1538 008 9299 0, 2008.

[6] L.H. Harrison. Prospects for vaccine prevention of meningitis infection. *Infectious Diseases Epideiology Research Unit*, University of Pittsburgh School of Medicine, 7ittsburgh Pennsylvania, 2000.

[7] M. E. Ibrahim & O. A. Salma. A Mathematical Model for Meningitis Disease. *Red Sea University Journal of basic and Applied Science.* Vol (2) Special Issue (2) Apri-2017

[8] T.J. Irving, K. B. Blyuss, C. Colijin &C.L. Trotter. Modeling meningococcal meningitis in the African meningitis belt. *Journal of Epidemiology Infection.* (2012), 140, 897-905.doi:10.10.1017/S0950268811001385

[9] Kalimh Vereen. An SCIR Model of Meningococcal Meningitis. *Graduate School at VCU Scholars' Compass.* Http://schoolrascompass.vcu.edu/etd/710, 2008

[10] Kloss Deborah. Caring for the Patient with Meningococcal Meningitis. *The American Journal of Nursing* 96: N0.4 (1996): 16F-16L.

[11] M. J. Martinez, E. G. Merino, J. E. G. Sanchez, A. M. Del Rey & G. R. Sanchez. A Mathematical model to study the meningococcal meningitis. *International Conference on Computational Science* doi:10.1016/j. Procs.2013.05.426, 2013.

[12] M. Martcheva & G. Crispino-O'Connell. The transmission of meningococcal infection: a mathematical study. *Journal Math. Anal. Appl*. 283 Pp.251-275, 2003.

[13] D. P Van Dn. & J. Watmough. Reproduction Numbers and Sub-Threshold Endemic equilibra for compartmental models of disease transmission, *Mathematical Biosciences*. 180, pp (29-48), 2002.

[14] Word Health Organization "Technical Basis for the WHO Recommendations on the Who.2013.http//www.who.int/gho/epidemicdiseases/meningitis/en/index-html (visited 17.09.2019), 2010.

[15] WHO. Control of epidemic meningococcal disease. WHO practical guidelines http://www.who.int/csr/resources/publications/ meningitis/whoemcbac983.pdf. Accessed 15 September, 2019 Woodburne, R. T.& Burkel, W.E. (1988). Essentials of Human anatomy. 8th New York, Oxford University Press, Inc.