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Historical background and epidemiology of cerebrospinal meningitis (CSM)

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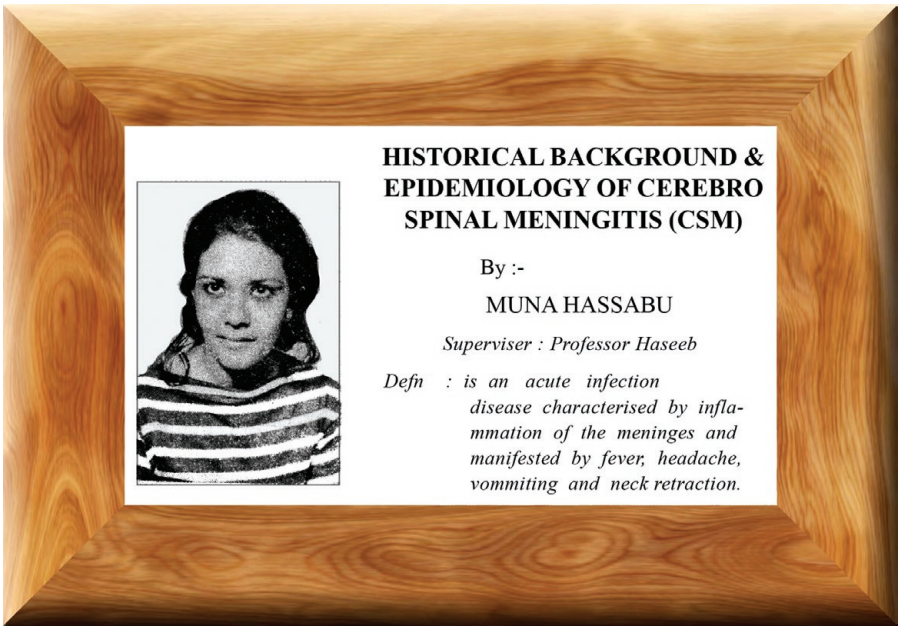


HISTORICAL NOTE

Cerebrospinal meningitis (CSM) was known to exist as far back as man could remember but the first knowledge about this disease is due to Vieusseux who in 1805 described an outbreak of CSM in Geneva. Since then this disease has shown a gradual increase both in its geographical range and in the number of persons it has attacked. From 1805 to 1874 the disease was prevalent in Europe and America and from 1875 it became prevalent in Asia, Africa and Australia. In the Sudan, the disease has been known for a long time under the name of "Abu Farrar" and it was rife in the years before the Anglo-Egyptian reoccupation (1898) but it was confused with typhus fever. During the days of the Mahdiya it was the cause of 800 to 900 deaths/ years amongst the population of Omdurman and El Mahdy is said to have died from this disease in 1885. However, in the 1st outbreak on record occurred in 1898 in Omdurman with 40 reported deaths. Most cases were among the Soldiers of the Khalifa, the town at that time being subjected to overcrowding and food shortage. The invading Egyptian troops had suffered outbreaks of CSM before. This epidemic followed by the return of the Khalifa's soldiers to their homes and the Anglo-Egyptian forces moving to conquer more places should be considered as a land-mark in the wide disseminations of the disease

for years to come. Since that time the disease has prevailed as an endemo-epidemic disease with a total of 100 deaths/year and from time to time it assumed the character of small localized outbreaks varying in severity and magnitude. In 1918 the South was connected to the North by steamers and hence the disease was introduced to the South and Equatoria, suffered an outbreak. From 1926 it was possible to see some uniformity of the epidemic pattern and a number of big epidemic cycles have been described:

1) A 5 years cycle (1926-1930) in Southern Sudan when famine conditions prevailed. The Blue Nile Province also suffered an outbreak when Sinnar Dam was open in 1928.
2) A 3 years cycle (1934-1936) when CSM prevailed in the far South of the Country, reached the south of the Kordofan and from the Nuba Mountains came towards the Blue Nile Province and then Darfour was affected. It covered all Sudan except the Northern Province and reached its climax in 1936. It was the first big epidemic cycle before the introduction of sulpha drugs and the fatality rate was 65%.
3) A 9 years cycle (1938-1948) with the 2nd world war started in Aweel and Tong and spread in the three Southern Provinces with an average fatality rate of 20% as sulfonamides were introduced in 1939. The hardest year was 1945, most of the deaths being in the Wau District with an outbreak in the Upper Nile Province.
4) A 5 years cycle (1948-1952) in the Western and Central Sudan.
5) A 6 years cycle which witnessed a reactivation of CSM in Bahr El Ghazal and Upper Nile Provinces.
6) A 2 years cycle emerged in 1961 and affected Western and Southern Sudan. Equatoria suffered a severe outbreak in 1962. In the same year CSM flared up in Darfur.

From this cyclic pattern we can observe that:-

a) There is a clear alternation of epidemics between the three Southern Provinces and the six Northern Provinces; the whole of the Sudan is practically never affected by CSM at one time.
b) The duration of the epidemic outbreaks is different in the Northern and Southern Provinces (three years in the North and 3 - 9 in the South).
c) There is no constant rule for the duration of the interepidemic cycles (7 - 14 years).

Until the introduction of sulfonamides in 1939 no measures adopted in the Sudan can be said to have modified the disease, although evacuation of village to temporary shelters sufficiently numerous to provide a separate shelter for each person has been thought to have limited the spread in infected communities. Prophylactic vaccination was adopted but found ineffective. Attempts have been made to relate the seasonal incidence of CSM to dietary insufficiency due to lack of carotene in the dry weather for millet producing areas and to the effect of ultra-V light on persons suffering from Vitamin A shortage. So Corkill (1936) the diets to improve nutrition, but the results were conclusive. Specific anti-sera have proved of little use in treatment in Sudan and were discovered after trial in 1934.

The mortality rate:

The treated in the hospital was the same as that in untreated cases, as there was nothing to offer except repeated lumbar punctures (which were believed by the people to have hastened the end of many patients).

This depressing picture was suddenly altered with the introduction of the sulfonamides and the demonstration of their efficacy under field conditions in the. Sudan.

They were first used in Bahr El Ghazal by Bryant and Fairman and later by Somers. The drug was called M & B 693 (Sulfapyridine) since then people started to have more confidence in modern medicine because of the high cure rate and the reduced incidence of complications.

The agent:

It is a gram negative diplococcus called Nisseria Meningitides. Keebs (1875) was the first to see the cocci in CSF and to consider them as being the cause of CSM. In 1887 Weichselbaum of Vienna published his classical paper on the findings of a gram-ve diplococcus which he called the Diplococcus Intracellularis meningitis. The first mentioned to the isolation of the organisms and their identification. The Sudan reported by Balfour (1904) Riding and Corkill (1932), during a study of a trial of a vaccine in Khartoum Province carried out grouping of some of the strains they have isolated and found that they all belong to group B. Further work was done by Kirk and Co-workers in the all state labs, where they carried out grouping of 25 strains isolated from cases in Khartoum Province in 1950 and all fall in group B. However, Dr. Erwa in 1968 could demonstrate that the strain responsible for epidemic is group A., where he grouped 10 strains isolated by him. Kirk and his co-workers (1950) performed virulence experiments on white mice and could describe the diplococci. Moreover, they did immunity tests in mice using a vaccine they prepared but the results were inclusive.

EPIDEMIOLOGY

Incidence and Morbidity:

The disease exists in the Sudan in a state of endemicity with seasonal exacerbations which might develop into epidemics of varying magnitude. Most authors agree that there is definite preponderance of the disease in rural areas.

CSM Trend in the Sudan for a period of 10 years

Year	Attack rate/ 100,000	Province	Attack rate/100,000
1958 - 59	4	Khartoum	248
1959 - 60	59	Bahr El Ghazal	45
1960 - 61	43	Blue Nile	32
1961 - 62	13	Kurdufan	21
1963 - 64	23	Equatoria	17
1964 - 65	16	Upper Nile	9
1965 - 66	100	Northern	8
1966 - 67	21	Kassala	7
1967 - 68	22	-----	----

The data reveals an attack rate ranging from 4 to 23/100,000 increasing to over 50 and up to 100 during epidemics.

Attack rate/100,000 in the Province between 1968 - 1972:

Province	68/69	69/70	70/71	71/72
Bahr El Ghazal	62	42	43	237
Blue Nile	8	14	18	42
Dar Fur	71	11	9	20
Equatoria	18	5	3	2
Kassala	14	6	7	6
Khartoum	685	26	294	225
Kurdufan	31	7	8	12
Northern	24	45	66	19
Upper Nile	11	1	11	5

Mortality: The mortality rate is almost l00% below one year, but it decreases to 50% at the age of 25 and again rises to 90% at 55 years or more. The mortality rate in the whole Country in the years 1930-1937 was 70 - 80%. It dropped to 53°/o after the partial use of the sulfonamides in 1939 and since then the mortality rate has been between 11 and 37%, the higher rates being associated with sporadic ·cases in the interepidemic years and may have been due to delay in diagnosis and establishment of treatment.

Fatality: The fatality rate of the disease is high and the main factor affecting it is the period of time that elapses between the onset of symptoms and the start of the treatment.

Geographical Distribution: The Sudan lies in the African Meningitis Belt which extends between the desert and the forest and is limited by Isohyte 300 mm north and 1100 mm South. Large epidemics seem to occur at about the same time in many countries of the Belt and they take lateral (from East to West) rather than a vertical spread.

No part of Sudan is altogether free from the infection. Even Port Sudan area which seems to be the only part of the Country where the disease is not known to have caused any severe outbreak, sporadic cases do appear. By far, the most affected province is Khartoum which although it has less population than others, it is the most crowded of all, the bulk of the population being in the three towns of the Province. It also suffers from a great migration of people from rural areas seeking work and settlement in the Capital. In addition, during the summer Khartoum suffers very high temperature and the people are subjected to excessive exhaustion in work and transport.

On the other hand, Kassala, Northern and Upper Nile Provinces) seem to be the least affected parts of the Country.

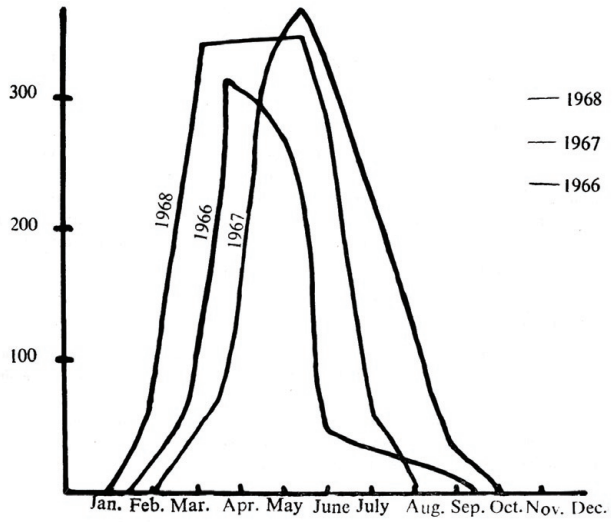
Seasonal Distribution: In the African meningitis belt epidemics occur in the hot dry summer month. In the temperate zones epidemics occur during the winter. However, this seasonal difference is not absolute, for example, in the Sudan the first cases of CSM, which may develop into a general outbreak, appear during the harvest and cotton-picking which start during the cool month.

The pattern of monthly incidence of CSM in the Sudan is well defined, epidemics taking place during the hot dry summer months. Northern and Southern Sudan behave as epidemiologically different areas.

The transmission persists in the South in spite of the rains and stops when the raining season starts in the North.

Cases start to appear during the winter months. With little variation the epidemic peak is reached in April or May and the fall of rains in June is followed by a rapid decrease of the outbreak. During years of light incidence cases are rarely reported in the Autumn, but after heavy outbreak cases may continue to occur throughout the year. In the Wetter Southern Provinces there is a greater tendency for cases to occur in all months of the year.

Fig (1) incidence of CSM in Khartoum Province in 1966 - 68



HOW DO EPIDEMICS ARISE?

1. When an unusually aggressive variant arises and is propagated.
2. A high nasopharyngeal carrier rate of this variant.
3. Many people simultaneously become susceptible.

Hence, I am going to discuss the factors affecting the agent, the host and the environment.

AGENT FACTORS

Reservoir: It is strict human pathogen that inhabit the nasopharynx of carriers.

Survival: It is a delicate organism readily destroyed by unfavorable environmental conditions such as extreme heat, dryness, exposure to direct sunlight and easily killed by comparatively weak antiseptics. It can however with-stand relatively low temperatures.

Antigenic structure and Virulence:

There are 4 antigenic strains A, B, C, & D each variant has a different virulence although this virulence could not be tested experimentally as the meningococcus loses its virulence rapidly in culture. The virulence is increased by repeated rapid passage of the organism from one person to another. It was found that group A is prevalent during epidemic and group B is responsible for sporadic cases.

Spread: CSM is an airborne infection and spread is direct from person to person through droplet nuclei spread from the nasopharynx or far less commonly through contaminated objects such as bed sheets, blankets, towels, handkerchiefs, etc..... .

Spread is enhanced by catarrhal conditions of the nasopharynx which induce coughing and sneezing and is propagated by overcrowding. Although the meningococcus is of importance as the cause of CSM, its capacity to produce this disease in susceptible individuals is more and unfortunate accident which plays no part in furthering its own survival in this world, the red life being passed as a harmless inhabitant of the throats of carriers.

Incubation period:

Two to five clays.

Infectivity:

It is believed to be low and it is very rare to spread directly from one case to another case and hence it is rare among hospital staff.

HOST FACTORS

The prevalence of CSM is closely associated with variation affecting the host making him susceptible.

Race: There is no racial selection.

Age: The disease affects particularly children, adolescents and young adults. The most susceptible age is 0 to 5 year although it is rare below three months of life (Most cases being due to organisms other than the meningococci). The susceptibility is slightly less from 5 to 15 years and for the remainder of life it remains fairly low. This is clear because children who did not encounter the disease before are none-immune and hence at a higher risk. This age susceptibility is true for sporadic cases which appear during the interepidemic period. During an outbreak ·all ages are susceptible when precipitating factors prevail. The greatest incidence is in the age group 10 to 25. Age groups over 30 were less affected in all the territories.

Distribution by age group (1950-1951)

Locality	Age-Group	% of Total Cases
(i) Fung District	0 - 5	14
	6 - 10	17
	11 - 20	22
	21 - 30	26
	31 - 40	10
	41 - 60	8
	over 60	3
(ii) Nuba Areas	0 - 5	25
	6 - 10	28
	11 - 15	20
	16 - 25	11
	26 - 40	12
	41 - 60	3
	over 60	1
(iii) Darfur	0 - 4	23
	5 - 9	31
	10 - 19	23
	20 - 40	16
	over 60	7

Sex:

It is commonest amongst males, but this appears to be related more to increased opportunity for infection than to any special sex predisposition. In rural areas women face an equal risk.

Nutrition:

Some outbreaks occurred during famines, hence it is postulated that bad nutrition predisposes to the disease.

General condition of the Host:

Dehydration and fatigue exert a powerful influence, hence the disease IS prevalent in prisons, military camps and the working class where the element of overcrowding can be added.

Diseases:

Upper respiratory tract infections decrease the resistance of the host and in addition enhances the spread of the disease.

Unhygienic Habits:

People usually do not use handkerchiefs while sneezing or coughing and hence facilitate spread of the disease.

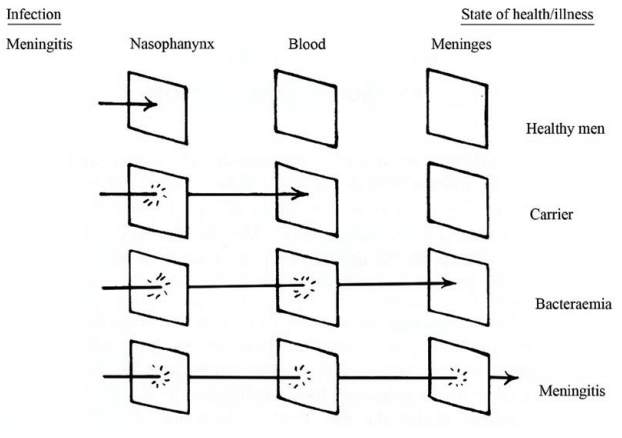
Immunity:

Once the meningococci harbor in the nasopharynx, there will be antibody formation against them and this will provide immunity against the clinical disease. It increases by age and exposure to the infection. It is longer lasting than herd immunity but it is relative and not absolute, in other words it may break at any time if a virulent organism is encountered. There are reported cases of C.S.M. in people who had a previous attack, the interval between the 2 attacks being variable.

Carriers:

C.S.M. is regarded as a disease of carriers although the disease does not commonly arise in carriers. The incubation period being short. The organisms which reach the nasopharynx may set up a rhinopharyngitis, but more usually appear to give rise to no troubles. In some cases they gain access to the meninges giving rise to the clinical disease.

Fig. (2) Barriers to Infection (Physiological and Immunological)



The organisms are found in the nasopharynx of cases, contacts and non contacts. Organisms are found in 5 to 10% of healthy people and during outbreaks this figure rises up to 90%. It is clear therefore that the meningococcus is able to vegetate in the nasopharynx frequently without giving rise to meningitis and hence it is accurate to speak of the infection as a "carrier's state". Preceeding an epidemic there is a "warning rise" in the carriers rate (20% or more), but some authorities have found that the carriers rate may rise without causing an epidemic or it may fall preceeding an epidemic. Hence the role of the carrier rate is "Debatable" and the prevalence of C.S.M cannot be regarded as a simple function of the carrier rate, other factors such as the virulence of the organism and the susceptibility of the host being very important.

Types of Carriers :

Primary Carrier is the one who harbors the organism

for the first time.

Secondary Carrier is the Convalescent case.

If the carrier harbors the organism for 3 to 4 weeks only, he is a temporary carrier and if he harbors them for more than 4 weeks he is a chronic carrier. The chronic carrier (10% of carriers) is the most important type because as symptomless carrier he maintains the organisms from one epidemic to another; during epidemics, while the case is too sick to spread the disease, the carrier is free to do so.

Since the main factor in the occurrence of epidemics is the meningococcal strain, type A carriage is of great significance in this respect.

ENVIRONMENTAL FACTORS

Climate:

Although outbreaks occur during the summer, the carrier rate starts to increase from the winter months. This is clear since people tend to sleep in-doors in the winter under conditions of overcrowding and poor ventilation which promote droplet transmission of the meningococci. Moreover, in the tropics during winter people are very susceptible to upper respiratory tract infections and as these induce coughing and sneezing they facilitate transmission.

During the hot dry summer months there is a very high temperature, a fall in atmospheric humidity and in addition there are dry dusty winds. As a result the rhino pharyngeal mucosa becomes desiccated, crusted and prone to bleed and therefore losses its capacity for defending itself against any local infection, meningococcal or other. Moreover, during the dry weather, the factors of dehydration, exhaustion and malnutrition are more prevalent and hence precipitate the disease. It sounds paradoxical that an epidemic tightens its grip in a dry hot climate when the organisms are supposed to be least viable.

The first shower of rain in the North coincides with rapid treatment of epidemics. This is due to cessation of air-borne infections during the rainy season and the fact that humidity increases the temperature and hence prevents overcrowding. However, the accomplished epidemiologist, Lapeyssonie, claims that the onset of the rains happens to coincide with the establishment the herd-immunity which is the factor responsible for ending the epidemic. Hence, he thinks, the simultaneous onset of rains and end of epidemics is just a casual coincidence. He may be supported by the fact that, in the Southern Sudan, epidemics persist inspite of the rains. Corkill (1936) mentioned that epidemics were abated when the 1st clouds appeared and hence he claimed that U.V. radiation plays an important role in the causation of C.S.M.

Overcrowding:

Overcrowding seems to be the axis of epidemiology of C.S.M., there being a direct relationship between increases in the carrier's rate and overcrowding.

As the spraying capacity of a person has a distance of 3 feet if the distance between people is 3 feet or less, the chance of transmission are very high. Conditions of overcrowding are found in school barracks, buses, markets and social gatherings in funerals, marriages and tribal dances. Migrations from rural areas increases the density of the population in a town and live under conditions of overcrowding slums.

Mass population movement induced by agricultural and religious necessities also help in spreading the disease. Pilgrimage to Macca across the Sudan particularly from Nigeria and Chad and back carries the danger of spread of infection either way.

The movements from the west to the Gezira for cotton picking and back provide and effective means for the spread of infectious diseases, including C.S.M., between West Africa and the Sudan. After opening of the Managil Extension the number of laborers

was doubled. The non-immune laborers are brought together to live under conditions of overcrowding in temporary huts and a state of mere subsistence and hence they are prone to get C.S.M. Eritreans flood from across the Ethiopian borders to Khashm El Girba for agricultural engagement and the mechanical crop production, and the Gadarif area is attracting many new comers from inside the Sudan and from across its eastern and western borders. The situation is further aggravated by the operation of the Rahad Scheme. Lapeyssonie, however, does not believe that overcrowding plays an important role in the transmission of C.S.M. and he supports this by the fact that some African tribes live under condition where overcrowding never exists (they sleep on top of the trees) but still suffer from very severe outbreaks of C.S.M.

Socio-economic factors:

Visitations of C.S.M. will always be anticipated as long as poverty, ignorance and slums exist, as non-immune persons are particularly susceptible to the infection under poor conditions of living in which overcrowding prevails. That is why the disease is seen more in rural areas with bad housing conditions, bad health conditions, improper sanitation, lack of personal hygiene and poor health education.

Herd Immunity:

The idea of "Sentialzone" i.e. areas of severe outbreaks escaping the following waves indicates that an immunity of short duration prevailed after severe attacks. Dr. Richards made this observation from the epidemics that occurred in the Nuba mountains, Darfur and the Blue Nile Province during the period (1934 to 1952). He noted that: Successive years epidemics reappeared at the periphery of districts that had been mainly attacked. The previous years and districts hearity infected during one season tended to escape relatively lightly in subsequent seasons.

Herd immunity does not last very long, particularly as regards carriage. After the passage of the epidemic of rhinopharyngeal meningococcal transmission, leaving behind it residual immunity, the susceptibility of the community gradually becomes re-established. Furthermore, the appearance of completely susceptible persons (new born babies and young children and the rushing rural migraters to new centers) finally brings back the number of susceptible persons above a certain threshold which permits transmission to become active again. Hence, three factors act as constant depressing factors for herd immunity factors.

The meningitis belt may be on the eve of the replacement of a periodic epidemic cycle by a continuous endemic sporadic situation as a result of the establishment of the under lying basis of herd immunity similar to that which exists in the countries of the temperate zone and which would thus hinder any undispread epidemic outbreak.

Conclusion:

The tragedy of epidemics in Africa is that maximum interest coincides with maximum emergency, which is not very propitious for research, and then the governments and the public lose interest during the calm periods, the very fine when some basic work could be done. With the use of sulfonamides a permanent solution for the problem was expected and efforts were directed towards areas with unjustifiable reluctance in preventive measures. With such a queer epidemiology, no wonder treatment alone failed to eradicate the disease for although the mortality has remarkably sunk the incidence remained the same. Hence, the conclusion is summarized in two words:-

Epidemiological reason:

The question of rhinopharyngeal carriers, the role of overcrowding, the effect of the rain, the study of individual and herd immunity and the methods of carrying out special prophylaxis are all fields where research is needed.