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Special Cerebro-spinal Meningitis Number

THE Indian Medical Journal

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(with which Agra Medical Club Journal is incorporated)

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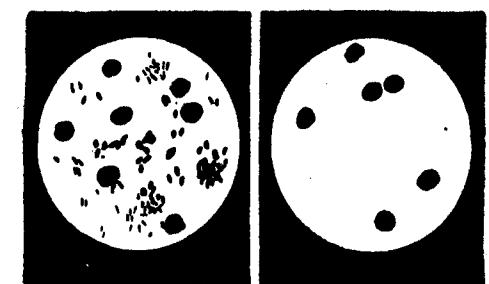
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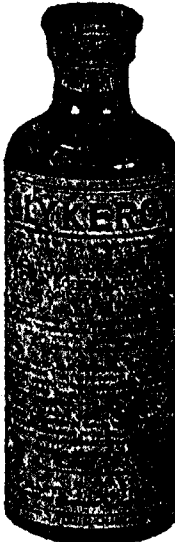
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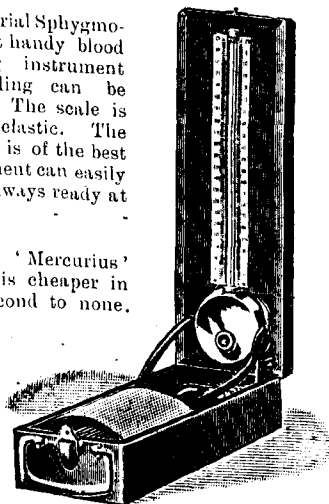
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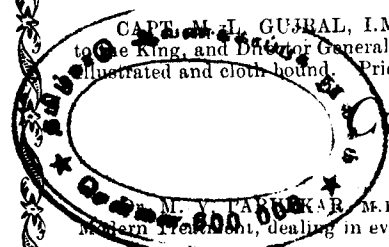
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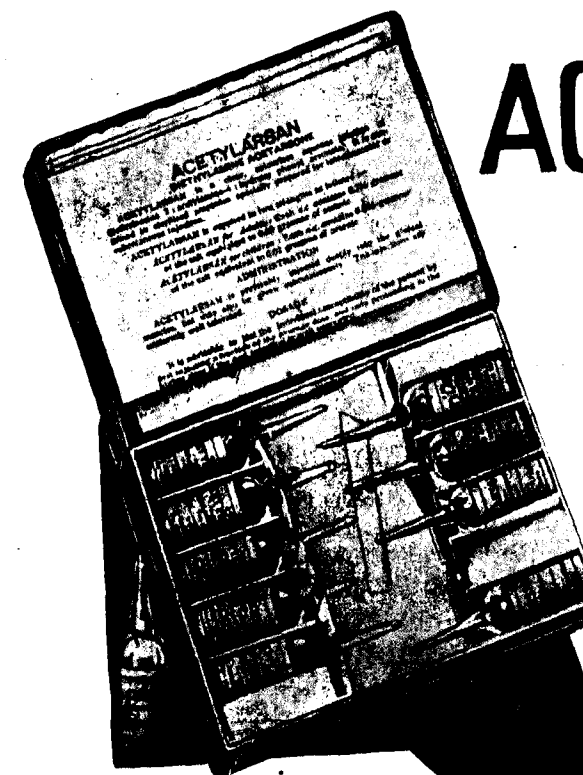
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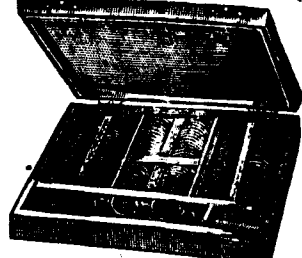
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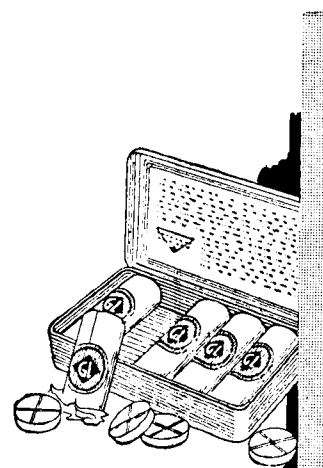
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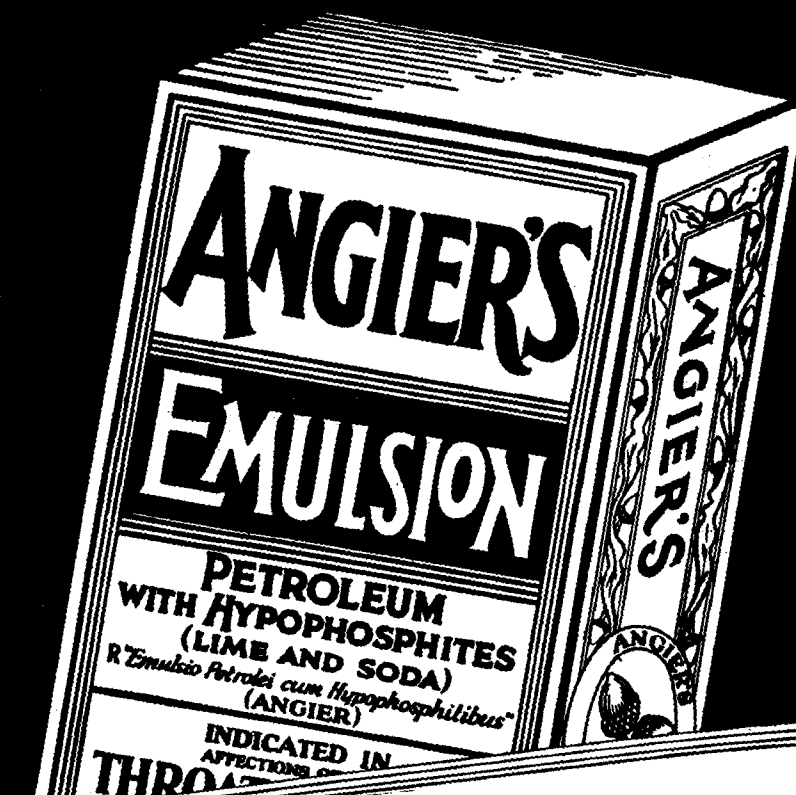
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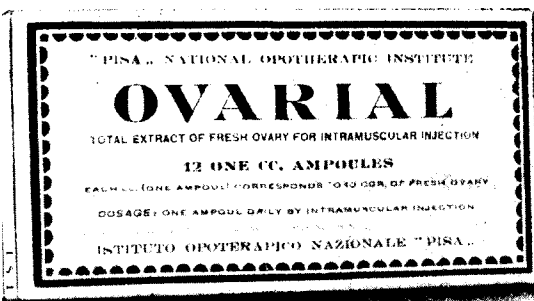
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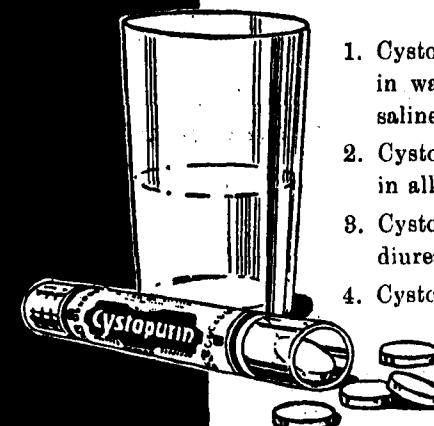
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Cerebro-spinal Meningitis In India¹

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(1)

1927-1931

Enquiries have been made from the individual provinces in order to ascertain as far as possible what the position is in regard to cerebro-spinal meningitis and in this brief memorandum all known facts have been included. The recorded figures refer to the five-year period 1927-31, but figures for 1932 have also been included for certain provinces where these were available.

In India epidemics of cerebro-spinal meningitis have so far been uncommon. Major-General Megaw, I.M.S., in a paper² published in June, 1927, gave the following figures, but did not indicate that the disease ever had appeared in epidemic form.

	N. W. F. Province	Punjab	United Provinces	Bihar and Orissa	Bengal	Assam	Burma	Central Provinces	Bombay	Madras
Seen by the reporting officer.	1	9	7	5	3	4	2	5	3	2
Reported by others	3	6	12	7	11	3	7	5	6	7

¹ Memoranda submitted by the writer to the office International D'Hygiene Publique, Paris. Published in this Journal by permission. Ed. I.M.J.

² "The Geographical Distribution of some of the Diseases of India" published in the "Indian Medical Gazette", Vol. LXII, No. 6, June, 1927.

Two notable epidemics have occurred recently one in the Shikarpur special jail in 1931, and the other in the Borstal Institution, Lahore, in 1932, and details of these have been given under their respective provinces. North Sind in Bombay Presidency and certain areas in Bengal are the only parts of the country which have been called "endemic", but there is considerable doubt as to whether this term has been correctly applied.

The incidence of the disease in the Army in India has been as follows:—

YEAR	ADMISSIONS	DEATHS
1927	... 16	13
1928	... 10	4
1929	... 8	6
1930	... 15	6
1931	... 17	11
1932	... 14*	12*

(a) North-West Frontier Province.—A small epidemic occurred in January and February, 1927, among the Frontier constabulary stationed in Peshawar Cantonment. Nine cases with six deaths were recorded. The original infection could not be traced.

(b) Punjab.—During the last five years no outbreak of any importance occurred, but three cases and two deaths were reported in the Indian barracks at Multan Cantonment during February and March, 1928. Two further cases, one in Rawalpindi and the other in Gujrat, of a doubtful nature, occurred in the same year.

*Up to the end of October, 1932.

The following figures represent total cases treated in hospitals during the last five years :—

District.	
Amritsar	... 17 (5 Sikhs, 8 Muslims and 4 Hindus).
Lahore	... 3
Muzaffargarh	... 69 (all in 1928).
Dera Gazi Khan	... 2 (Hindus).
Mianwali	... 4
Jhang	... 7

During the spring of 1932, an outbreak occurred in the Borstal Institution, Lahore, and 18 cases were reported from the middle of March to the middle of June. Thereafter there were no cases for about 2½ months, but at the end of August a fresh outbreak took place with four seizures up to mid-October.

It may be of interest to give some details regarding the conditions prevailing in this institution prior to the outbreak. Accommodation is designed to provide for 1,705 inmates, primarily adolescent and juvenile offenders. 350 inmates are accommodated in "association barracks" whilst the remainder occupy individual cells. The population at the time of the outbreak was 1,721, but for the preceding four months it had ranged between 1,800 and 2,489. About the middle of November, 1931, owing to the Ahrar movement, a large number of prisoners had been transferred from various camp jails in Kashmir State *e.g.*, Satwari and Udampur. Although no authentic information is available regarding the occurrence of any case of cerebro-spinal fever in the seriously overcrowded camp jails in Kashmir State, some of the transferred prisoners mentioned cases of an illness somewhat similar in nature. It is quite possible that the serious over-crowding prevalent in these camp jails led to an increase in the percentage of carriers in the population confined therein. The epidemic in the Borstal Institution therefore may have been due to a direct increase of carriers.

The first two cases occurred in prisoners working in the kitchen, and at intervals isolated cases were detected in different circles and barracks. It was very difficult to establish any connection between one case and another; one inmate fell a prey to the disease but his close associates entirely escaped. In most instances, the infection seemed to pick out those who were apparently both healthy and well nourished. None of the established carriers (detected by examination of throat swabs) and none of the hospital staff or attendants contracted the disease.

(c) *Delhi Province*.—Only one case is reported to have occurred in Delhi city in 1927.

(d) *United Provinces*.—No outbreaks have occurred among the civil population during the last five years, but two cases with no deaths were recorded in the Thomason Hospital, Agra—one in 1929 and the other in 1930. One suspected case died in the Sadar Hospital, Banda (date of admission not given). Two sporadic cases, one in 1931 and one in 1932, are reported to have been admitted in the Lady Lyall Hospital for Women, Agra. Three fatal cases have occurred in the King George's Hospital, Lucknow, one in 1931 and the other two in 1932. One case occurred in the central jail, Benares, in 1932, and another in the Etah district jail in 1929. The former recovered, whilst the latter died.

(e) *Bihar and Orissa*.—No outbreaks of the disease have been recorded in this province.

(f) *Bengal*.—Cerebro-spinal meningitis is said by some authorities to be endemic in many parts of Bengal, but the disease is neither well recognised nor is it notified. Except for one fatal case in Hooghly district in 1930, all other recorded figures are for the city of Calcutta. These are given in the following table :—

Attacks and deaths from cerebro-spinal meningitis in the city of Calcutta for the years 1927-31

YEAR	ATTACKS	DEATHS
1927	... 9	9
1928	... 17	17
1929	... 19	19
1930	... 13	13
1931	... 13	11

Cases treated in hospitals and dispensaries

Hospitals	1927	1928	1929	1930	1931	1932
Medical College and hospitals, Calcutta	C. D.	C. D.	C. D.	C. D.	C. D.	C. D.
Presidency General Hospital, Calcutta	25	323	1727	1215	55	5...
Campbell Hospital, Calcutta	14	14	1514	1412	74	97...
Sambhu Nath Pandit Hospital, Calcutta	10	...	...	...	...	...
Mitford Hospital, Dacca	...	...	...	...	...	22

(g) *Assam*.—No outbreaks of cerebro-spinal meningitis have been recorded during the last five years.

(h) *Burma*.—Five cases have been admitted in different jail hospitals, one in 1928 in Rangoon jail, one in 1929 and one in 1930 in Toungoo jail, one in 1931 in Rangoon jail, and one in 1932 in Myaungmya jail.

The following cases are reported to have occurred in the civil population :—

YEAR	DEATHS
1927	... 22
1928	... 19
1929	... 19
1930	... 13
1931	... 7

A sharp outbreak with 19 cases and 12 deaths was reported in the Burma Corporation Mines population at Namtu from September, 1929, to February, 1930.

(i) *Central Provinces*.—No outbreak of the disease has been recorded during the last five years. One case was admitted to the jail hospital, Bilaspur, in December, 1927, and died in February, 1928.

(j) *Bombay Presidency*.—The Surgeon-General gives the following details of cases admitted to hospitals for the last six years :—

YEAR	CASES	DEATHS
1927	... 2	2
1928	... 6	3
1929	... 3	...
1930	... 2	2
1931	... 19	16
1932	... 15	8

As regards the prison population, the disease broke out in 1931 in Shikarpur special prison, 13 cases being recorded with 12 deaths. According to the Director of Public Health the number of cases was 15 with 14 deaths.

The Inspector-General of Prisons remarks :—

"The disease appears to have been introduced into the prison from Upper Sind where it is endemic and in spite of all precautions, sporadic cases have occurred in the prison throughout the year beginning in the month of April and continuing till the end of the year."

The Assistant Director of Public Health who investigated this matter has reported that cerebro-spinal meningitis is not endemic in Upper Sind, but that his attention has been drawn to a number of sporadic cases which had been under treatment by a number of practitioners in Upper Sind and Sukkur district. There seems to be some reason to believe that cases have occurred sporadically in Shikarpur town etc., for some considerable time. Otherwise there have been no outbreaks of the disease in the Bombay Presidency jails or among the general population during the quinquennium.

(k) *Madras Presidency*.—Statistics of the incidence of cerebro-spinal meningitis in the general population are not available, but the following figures taken from hospital records indicate a fairly widespread occurrence of spasmodic cases :—

Name of District or Station	Cases treated				
	1927	1928	1929	1930	1931
North Arcot	...	2	...	...	5
Chittoor	...	...	2	...	...
Coimbatore	...	Four (the years in which these cases were treated are not available)			
East Godavari	...	2	...	...	...
Kistna	...	1	...	1	...
Madura	...	...	1	...	1
The Nilgiris	...	...	1	1	4
Ramnad	...	...	...	...	2
Cochin	...	One case during the last 5 years			
Government General Hospital, Madras	1	...	3	...	1
Royapuram Hospital	...	1	...	1	...

No cases have been recorded in the prison populations of the province.

Detailed figures will be found in the appended table.

Statement showing attacks and deaths from cerebro-spinal meningitis during the years 1927-1932

Areas, localities and institutions which reported cases.	Attacks and Deaths from cerebro-spinal meningitis during the years							
	1927	1928	1929	1930	1931	1932		
	Attacks	Deaths	Attacks	Deaths	Attacks	Deaths	Attacks	Deaths
North-West Frontier Province.								
Peshawar cantt. Frontier constabulary	9	6	...	...	...	...	...	...
Punjab								
Multan cantonment (Indian barracks)	...	3	2	...	...	...	...	...
Rawalpindi town	...	1	...	...	...	...	...	...
Gujrat town	...	1	...	...	...	...	...	...

Areas, localities and institutions which reported cases	Attacks and Deaths from cerebro-spinal meningitis during the years					
	1927	1928	1929	1930	1931	1932
	Attacks	Deaths	Attacks	Deaths	Attacks	Deaths
Hospitals and dispensaries.	Quinquennial totals—Amritsar 17 cases; Lahore three; Muzaffargarh 69; Dera Ghazi Khan two; Mianwali four; Jhang seven.					
Lahore Borstal Institution.						22
<i>Delhi Province</i>						
Delhi city	1					
<i>United Provinces</i>						
Thomason hospital, Agra.			1	1		
Banda, sadar hospital	One suspected fatal case—date not known.					
Lady Lyall hospital for women, Agra					1	1
Benares central jail						1
Etah district jail			1	1		
King George's hospital, Lucknow					1	1 2 2
<i>Bengal Presidency</i>						
Hooghly district				1	1	
Calcutta city	8	9 17 17 19 19 13 11 11				
<i>Burma</i>						
Rangoon town	10	7	8	5	2	
Tharrawaddy town	1					
Syriam town	5	1	1			
Prome town	1	2				
Bassein town	1	3				
Yandon town	1					
Pakokku town	1					
Mandalay town	2	1	3			
Akyab town	Not available	Not available	1	Not available	1	
Sandoway town	Not available	1	Not available	Not available	1	
Pegu town	Not available	2	1	3	1	
Maymyo town		1	2	1		
Toungoo town			3		2	
Taungdwingyi town			1			
Pyapon town				1		

Areas or localities where cases were reported	Attacks and Deaths from cerebro-spinal meningitis during the years					
	1927	1928	1929	1930	1931	1932
	Attacks	Deaths	Attacks	Deaths	Attacks	Deaths
Thayetmyo town					1	
Minbu town					1	
Meiktila town					1	
Rangoon jail		1			1	
Toungoo jail			1	1		
Myaungmya jail						1
<i>Central Provinces</i>						
Bilaspur jail		1	1			
<i>Bombay Presidency</i>						
G. T. hospital, St. George's hospital	2	2	4	2	1	1 1 3 3
Civil hospital, Ahmedabad				1	1	2
Civil hospital, Surat						1
Civil hospital, Larkana						4
Civil hospital, Sukkur					13	12 7 6
Civil hospital, Jacobabad						1 1
Civil hospital, Thar Parkar		1	1			
Civil hospital, Poona		1	1		1	1
Total	2	2	6	3	2	19 16 15 8
<i>Madras Presidency</i>						
North Arcot district	2				5	
Chittoor district				2		
Coimbatore district						
East Godavari district						
Kistna district	1					
Madura district	Not available	1	Not available	Not available	1	
The Nilgiris district	Not available	Not available	1	1	4	
Ramnad district	Not available	Not available	Not available	Not available	2	
Cochin						
Govt. general hospital, Madras	1		3		1	
Royapuram hospital		1		1		

*Treated in the special prison, Shikarpur.
†Treated in Kandkot sub-jail.

(2)

1932—1934 (earlier half)

In continuation of the communication submitted to the Office International at its session held in May, 1933, the following paragraphs include all available information as to the incidence of cerebro-spinal meningitis in different parts of India up to the end of June, 1934. They also give some preliminary information as to the types of meningococcus isolated from cases in two epidemic centres, viz., Delhi and Calcutta, and indicate the work which is being done at the Central Research Institute, Kasauli, and at the Hafkine Institute, Bombay, in connection with the preparation of a protective vaccine.

2. Since the preparation of the note in 1932, it has been possible to make some examination of available records; these indicate that cerebro-spinal meningitis is no new disease to India. The first cases were recorded by Vandyck Carter in 1878 in Bombay, whilst Dimmock reported the disease among the convicts of Shikarpur jail during the winter of 1883—84. The jails and army returns since 1881 show that the disease has appeared at intervals and the civil population has probably been similarly infected, although few records exist to substantiate this statement. The Army Medical Directorate has kindly permitted me to include the following table which gives the annual figures for all British troops and their families and for all Indian troops since 1921: the increased incidence during 1933 and 1934 is striking.

Cerebro-spinal fever (cases)

Year	January	February	March	April	May	June	July	August	September	October	November	December	Total
1921	1	1	—	—	1	—	—	—	—	—	—	—	4
1922	—	—	1	1	—	2	—	1	—	—	—	—	6
1923	1	1	1	5	3	—	—	—	—	—	—	—	11
1924	Figures for individual months not available												
1925	—	—	—	—	—	—	—	—	—	—	—	—	8
1926	1	—	—	—	—	—	—	—	—	—	—	—	1
1927	—	—	2	—	—	—	1	1	—	—	—	—	4
1928	1	1	2	2	—	1	—	1	—	—	—	—	10
1929	3	—	2	1	1	2	—	1	1	—	—	—	11
1930	2	2	1	—	2	—	—	—	—	1	5	13	15
1931	3	3	1	3	1	—	—	—	—	1	2	1	15
1932	3	3	1	2	2	1	1	—	—	1	—	3	17
1933	6	6	5	1	1	1	1	—	1	3	3	—	28
1934	9	10	4	1	4	1	2	—	—	—	—	—	81

3. *Epidemiology.*—Since 1932 several outbreaks have occurred, the most notable being those of (a) 1932—33 in the Lahore Borstal Institution, Punjab; (b) 1933—34 in Ahmedabad town in Bombay Presidency; and (c) 1933—34 in Delhi city.

Details of the first of these were given in the previous note presented to the 'Office', but it may be added that, during 1932, 27 cases with 11 deaths were recorded in this Institution. Naso-pharyngeal swabs of 1268 inmates were examined and about 20% showed organisms morphologically indistinguishable from the meningococcus and 66% of the kitchen workers were found to be carriers. Cultural examinations carried out at a later period showed a carrier rate of over 12% amongst the original population, whilst among 1387 new admissions only 9 or 0.65% were found to be carriers.

4. During 1933, 125 cases with 68 deaths were recorded in Delhi city. During the same year, in the neighbouring city of New Delhi, there were 12 cases with 6 deaths; whilst in the Delhi Jail, 4 cases and 3 deaths occurred. Further details of the outbreak in Delhi city will be given in a later paragraph.

During the whole of 1933, the disease continued in the city of Calcutta and no fewer than 387 cases and 348 deaths were reported. A short but sharp epidemic occurred in the Motihari jail in Bihar and Orissa during April, 1933, when 11 cases with 6 deaths were recorded; after a further 4 cases in May the infection disappeared.

In addition to these outbreaks isolated cases were also reported from Chittagong and Baranagar in Bengal and in Lahore city in the Punjab. Reports were also received from Bombay Presidency, from the Central Provinces, from the North-West Frontier Province, from Rajputana and the Central India States and from Burma including the Southern Shan States. These reports indicated that the disease had spread widely during 1933, although it is probable that part of the increased recorded incidence was due to better diagnosis of cases.

5. For 1934, figures have been collected up to the end of June. These indicate that cerebro-spinal meningitis has become still more widespread and it is probable that further outbreaks will be recorded. Cases have been reported from Baluchistan, N. W. F. Province, Kashmir State, Delhi Province, Central Provinces, Bengal, Bombay, Rajputana and Central India States, Hyderabad and Baroda States; whilst a few cases have also occurred in Madras Presidency. Calcutta has experienced another severe epidemic, most of the cases having occurred amongst school boys, students and young adults. The following table gives the monthly figures for cases and deaths in Calcutta during the years 1932, 1933, and 1934. The high mortality rate is probably partly

explained by non-diagnosis and non-recognition of the less severe cases.

	1932		1933		1934	
	C.	D.	C.	D.	C.	D.
January	—	—	13	13	39	38
February	7	7	35	35	87	74
March	16	16	63	63	109	79
April	8	6	28	25	85	66
May	10	10	40	36	90	79
June	13	13	23	16	27	25
July	14	14	29	29		
August	19	19	44	44		
September	7	7	24	19		
October	18	18	26	22		
November	11	11	32	21		
December	22	22	30	25		
Total...	145	143	387	348		

(The figures for 1934 are for Bengal Presidency but these chiefly relate to Calcutta.)

6. The most notable epidemic during 1933 was that in Ahmedabad city in Bombay Presidency. The first five cases in this town occurred early in December, 1933, and from that date the weekly figures gradually increased to a peak during the week ending 10th March 1934, when no less than 115 cases with 36 deaths were recorded. Thereafter the epidemic gradually declined, but up to 30th June the total amounted to 592 cases with 271 deaths.

Bombay city recorded only isolated cases during 1932 and 1933, the totals being 17 in 1932 and 7 in 1933. During the first two quarters of 1934, however, the incidence increased: 23 cases with 17 deaths have been reported during January to March and 35 cases with 29 deaths during April to June.

Delhi city has experienced a further severe outbreak, as the figures from January to June, 1934, indicate.

1934	C.	D.
January	16	16
February	28	21
March	69	42
April	46	35
May	82	62
June	20	16

7. During the first six months of 1934 the recorded figures for cerebro-spinal meningitis for the whole of India amount to 1,991 cases and 1,216 deaths. Although these returns are admittedly still incomplete, it is obvious that cerebro-spinal meningitis has not only spread to nearly every part of India but is causing a considerable mortality. Housing conditions in urban areas being peculiarly favourable for the propagation and spread of infection, it is to be feared that further outbreaks will be experienced.

8. *Periodicity.*—It has not been possible to examine all the figures, but generally speaking it has been noted that the incidence of cerebro-spinal meningitis gradually increases to a peak

at the beginning of the hot weather, *i.e.*, in the months of March, April and May. The figures for Delhi and Ahmedabad both make this quite clear. There is also a definite tendency for epidemics to die out with increasing day temperatures. The fact that many people sleep out of doors as soon as hot weather temperatures prevail may have some influence in causing the decreased incidence.

9. *Age incidence.*—Cerebro-spinal meningitis in India as in other countries takes its heaviest toll from among children and young adolescents. The following table, which gives the figures by age-groups for the 1933 and 1934 epidemics in Delhi, indicates this characteristic.

AGE-GROUPS	CASES	
	1933	1934
Under 1 year	...	...
1-5 years	...	5
5-10 "	16	12
11-15 "	19	11
16-20 "	36	41
21-30 "	34	34
31-40 "	7	16
41-50 "	4	3
51-60 "	1	...
61 and over	2	...
Total	127	122

An examination of the figures for Calcutta and Ahmedabad leads one to the same conclusion.

10. *Sex incidence.*—In this connection, another interesting feature of the outbreak in Delhi city appears. Of the total 68 deaths recorded, 56 occurred among males and only 12 among females. It has not yet been possible to obtain comparative figures for sex incidence from other infected centres but, if these show a similar variation, a possible explanation may be that the lesser incidence among females is due to the fact that the women folk of India are normally less exposed to outside infection than are the men.

11. *Types of meningococcus.*—In order to carry out tests to determine the "types" of the meningococcus isolated from cases of the disease in India, the Central Research Institute, Kasauli, obtained from Dr. Scott of the Ministry of Health cultures of types I, II and III with their homologous sera; sera of the four types were also obtained from Oxford. Strains isolated from cases in Delhi and other places have been typed at the Central Research Institute and, so far, most of these have been found to be type III (Group I), whilst they also react with the Oxford sera to full titre. Sen and his co-workers in Calcutta have published (Journal of Indian Medical Association,

Vol. III, No. 7, March 1934) a preliminary report on the serological typing of the strains isolated during the Calcutta epidemic. Of 35 strains of meningococci typed by agglutination tests only in relation to the four types of Gordon and Murray, 18 were found to agglutinate strongly with type I serum and 17 with type III serum. Their results showed that the epidemic strains of Calcutta during the period from August to November, 1933, were mainly type I, type III or "Type I or III", whilst none belonged to type II, type IV or, "Type II or IV." Further work in this connection is being carried out.

12. *Prophylactic vaccine.*—The Central Research Institute at Kasauli has recently had under preparation an antimeningococcic vaccine manufactured from cultures originally taken from cases in Delhi and this vaccine is now under trial in selected communities, such as jails, schools and other institutions of the kind. Similar efforts have been made by the Director of the Haffkine Institute, Bombay, who has isolated strains from cases at Ahmedabad. The vaccine is now under trial but it is still premature to hazard any opinion regarding its prophylactic value. The difficulty of obtaining statistical evidence as to the value of any preventive vaccine is always great in India and is much greater in the case of cerebro-spinal meningitis. Efforts are, however, being made to collect all reliable data.

13. *Anti-meningococcic serum.*—Anti-meningococcic serum has not hitherto been

manufactured in India, but English supplies have been imported and stocked for the needs of the army and for civil purposes. The preparation of an anti-meningococcic serum in India will depend largely on the results of the tests now under experiment, but it is proposed to make the attempt as soon as the 'type' question has been settled. This seems very desirable especially as the results so far obtained in India with English serum have not been entirely satisfactory.

(3)

1934—1935 (earlier half)

In continuation of my previous note on this subject (presented at the meeting of the Office International in October, 1934), the following paragraphs give a summary of the known facts in regard to C.S.M. in India during 1934 and the first half of 1935. Generally speaking, the disease has continued to spread and provincial reports indicate that outbreaks have occurred in widely separated parts of the country. In support of the thesis that the present epidemic is spreading from West to East, it is to be noted that Burma has now reported several small outbreaks though Assam has not so far recorded its presence.

2. Table I gives figures of reported cases in the provinces and States during 1934 and the first six months of 1935. These figures should be taken as provisional and are liable to revision, but they indicate the extent to which the disease has now spread.

TABLE I

Reported cases during 1934 and 1935

	Jan.	Feb.	Mar.	Apl.	May.	Jun.	Jul.	Aug.	Sep.	Oct.	Nov.	Dec.	Total
N.W.F.P.	—	1	13	17	5	5	7	4	3	1	3	5	64
Punjab	—	—	—	—	—	94*	12	6	2	5	14	11	144
Calcutta	38	87	93	77	75	36	48	76	68	37	70	78	783
Bengal	—	1	15	3	16	5	4	—	—	12	1	—	67
Rajputana	—	1	15	18	14	9	8	2	—	2	2	3	74
C.P.	—	—	2	9	15	6	6	—	1	—	2	2	43
C.I. Agency	—	—	8	10	17	—	—	1	—	—	3	8	47
Bombay Presidency	56	97	377	292	128	36	36	46	34	37	57	39	1,235
Delhi City	17	29	60	67	75	33	27	24	19	20	20	22	413
Baluchistan	—	—	—	—	—	—	—	—	—	—	—	—	4
Burma	—	—	—	—	—	—	—	—	—	—	—	—	6
U.P.	—	—	—	—	—	—	—	—	—	—	—	—	2
Hyderabad State	—	—	—	—	—	—	—	—	—	—	—	—	46
Baroda State	—	—	—	—	—	—	—	—	—	—	—	—	21
Kashmir State	—	—	—	—	—	—	—	—	—	—	—	—	1
Grand Total	2,940												

*From January to June, 1934.

1935

	January	February	March	April	May	June	Total
N. w. F. P. ..	3	11	13	11	4	1	43
Punjab ..	22	80	82	113	65	27	389
Calcutta ..	151	175	173	114	109	92	814
Bengal ..	—	—	—	—	—	—	—
Rajputana ..	2	29	57	106	44	26	264
C. P. ..	1	1	9	38	82	29	160
C. I. Agency ..	—	11	26	21	24	14	96
Bombay Pre- sidency ..	86	80	87	96	93	60	502
Delhi Province	86	180	147	80	62	26	581
Hyderabad State ..	—	—	—	—	—	—	60
Grand Total							2,909

3. With the permission of the Army

TABLE II

		1930			1931			1932			1933			1934		
		A.	D.	Case morta- lity %	A.	D.	Case morta- lity %	A.	D.	Case morta- lity %	A.	D.	Case morta- lity %	A.	D.	Case morta- lity %
British other ranks	...	1	—	—	2	2	100	8	6	75	3	2	66.6	2	1	50
Indian other ranks	...	15	12	80	15	9	60	9	9	100	24	16	66.6	38	15	39.5
Officers, Women and Children	...	—	—	—	—	—	—	—	—	—	1	1	100	—	—	—
Others	...	—	—	—	—	—	—	—	—	—	1	1	100	12	4	33
Total	...	16	12	75	17	11	64.7	17	15	88.2	29	20	69.0	52	20	38.5

4. The Table given in my last note showing cases reported in the British and Indian Armies in India is reproduced with figures added for the latter half of 1934 and first half of 1935. The difference in the totals in Tables II and III are due to incomplete monthly returns. It is obvious that the disease is still giving the military medical authorities some cause for anxiety.

TABLE III

Cerebro-spinal fever cases in the British and Indian Armies in India

Year	January	February	March	April	May	June	July	August	September	October	November	December	Total
1921	1	1	—	—	1	—	—	—	—	—	—	1	4
1922	—	—	1	1	—	2	—	1	—	—	—	1	6
1923	1	1	1	5	3	—	—	—	—	—	—	—	11
1924	—	—	—	—	—	—	—	—	—	—	—	—	8
1925	—	—	—	—	—	—	—	—	—	—	—	—	1
1926	1	—	—	—	1	—	—	—	—	—	—	—	3
1927	—	—	2	—	—	—	1	—	—	—	—	—	4
1928	1	1	2	2	—	1	—	—	—	—	—	—	10
1929	3	—	2	1	1	2	—	1	—	—	—	—	11
1930	2	2	1	—	2	—	—	—	—	—	1	5	13

Medical authorities I have incorporated Table II which gives admissions, deaths and mortality rates in the British and Indian Armies in India during the period 1930-34. The reduced mortality rate in 1934 is partly attributed to the use of a three times concentrated therapeutic serum and its intrathecal administration in daily doses. In those cases which recovered, the average quantity of serum given per case was 119 c.cs intrathecally and 86 c.cs by other routes. In one military hospital, in addition to this routine treatment, iodine was administered intravenously. Only two deaths occurred among 8 cases so treated, of which 3 were classed as very severe, 3 severe and 2 moderately severe. Owing to these satisfactory results, this treatment is being further investigated.

5. In Calcutta, the epidemic conditions of 1933 continued throughout 1934 and 1935 in more intensive fashion. From Table I it will be seen that no less than 783 cases were reported in 1934 whilst during the first six months of 1935, the cases numbered 814.

In contradistinction to Calcutta, the town of Ahmedabad, which experienced a severe outbreak during 1933-34, has reported a lesser incidence during 1934-1935; nevertheless, over 250 cases have occurred in the first half of 1935.

In the Punjab, a considerable increase in the incidence of C. S. Meningitis occurred during 1934. In fact, during January and February, cases were reported from 14 out of

the 29 districts. Four outbreaks occurred in Lahore city alone (a) New Hostel, Government College, (b) Reformatory School Boarding House, Criminal Tribes Settlement, Moghul-pura, (c) Chauburji Gardens Estate, and (d) Montgomery Park. During 1934, cases totalled 144, but in the first half of 1935 as many as 389 cases have been reported.

In the Central Provinces, the disease was recorded for the first time in March, 1934, and, although the cases were few in number, a considerable number of districts were known to be infected.

During 1934, 2,940 cases were recorded in India whilst, in the first half of 1935, the total reached 2,909. *There can be little doubt that these numbers do not indicate with any degree of accuracy the actual incidence of the disease, although the continued increase is obvious.*

6. *Periodicity.*—Further experience has corroborated the statement made in my last note that in India the annual incidence of C.S. Meningitis has its normal peak at the beginning of the hot weather. The monthly figures for Delhi, Calcutta and Ahmedabad, which are given in Table IV, illustrate this point very clearly.

TABLE IV

(a) Delhi City

	1933		1934		1935	
	Cases	Deaths	Cases	Deaths	Cases	Deaths
January	...	1	17	17	75	25
February	...	5	29	22	130	63
March	...	18	7	59	146	51
April	...	20	13	67	40	24
May	...	36	22	75	53	26
June	...	13	5	33	23	9
July	...	6	2	27	16	—
August	...	7	7	24	21	—
September	...	—	—	19	13	—
October	...	8	3	20	16	—
November	...	10	9	20	13	—
December	...	9	9	22	17	—
Total	128	77	413	290	508	198

(b) Calcutta

	1933		1934		1935	
	Cases	Deaths	Cases	Deaths	Cases	Deaths
January	...	13	38	39	151	93
February	...	35	35	74	175	156
March	...	63	63	67	178	114
April	...	28	25	77	58	68
May	...	40	36	75	64	109
June	...	23	16	36	32	92
July	...	29	29	48	40	—
August	...	44	44	76	66	—
September	...	24	19	68	55	—
October	...	26	22	37	31	—
November	...	32	21	70	41	—
December	...	31	25	78	50	—
Total	387	348	783	617	814	539

(c) Ahmedabad

	1934		1935	
	Cases	Deaths	Cases	Deaths
January	...	29	16	43
February	...	79	39	39
March	...	285	109	70
April	...	125	72	47
May	...	51	30	38
June	...	23	11	15
July	...	18	16	—
August	...	32	10	—
September	...	21	13	—
October	...	24	7	—
November	...	18	8	—
December	...	33	13	—
Total	738	344	252	148

7. *Age Incidence.*—Whilst in certain epidemics in European countries, the incidence among children has been greater than among adults, in the urban areas of India where registration is reasonably accurate, records show that the disease is most prevalent among young adults. This is illustrated by Table V which gives the age incidence of recorded cases in Delhi city and Ahmedabad town. The figures for Calcutta show the same general age incidence.

TABLE V

(a) Delhi city

	1933		1934	
	Cases	Deaths	Cases	Deaths
Under 1 year	...	—	—	4
1—5 years	...	8	32	—
6—10 "	...	16	46	—
11—15 "	...	19	51	—
16—20 "	...	36	109	—
21—30 "	...	34	103	—
31—40 "	...	7	48	—
41—50 "	...	4	14	—
51—60 "	...	1	6	—
61 years and over	...	2	—	—
Total	127	413	—	—

(b) Ahmedabad

	1934		January to June 1935	
	Cases	Deaths	Cases	Deaths
Under 1 year	...	6	5	3
1—5 years	...	51	15	9
6—10 "	...	110	42	21
11—15 "	...	118	41	20
16—20 "	...	101	48	36
21—30 "	...	214	107	85
31—40 "	...	95	55	39
41—50 "	...	25	14	10
51—60 "	...	17	16	6
61 years and over	...	1	1	2
Total	738	344	252	148

8. Sex Incidence.—Table VI gives an analysis of the cases recorded in Delhi city from January to June, 1935. The figures also illustrate the higher incidence of the disease among males. It seems that, in Delhi at least, males suffer about three times more frequently than females. Captain Ganguli¹ has noted the same difference in sex incidence in his review of the Calcutta epidemic.

TABLE VI

	Male		Female		Total	
	Cases	Deaths	Cases	Deaths	Cases	Deaths
Under 1 year	2	1	—	—	2	1
1—5 years	30	13	12	4	42	17
6—10 "	43	21	22	10	65	31
11—15 "	58	19	18	9	76	28
16—20 "	64	26	13	7	77	33
21—30 "	123	34	37	18	160	52
31—40 "	35	13	13	6	48	19
41—50 "	18	11	6	2	24	13
51—60 "	8	5	5	2	13	7
61 years and over	2	1	4	3	6	4
Total	383	144	130	61	513	205

9. Carriers.—The figures given below were obtained from an investigation made in the Borstal Institution and the Central Jail, Lahore.

	Nasopharyngeal swabs	Carriers of meningococcus	% Rate Carriers
(1) Borstal Institution	3,950	19	1.0
(2) Central Jail	2,652	21	1.5
Total	6,602	40	—

Cases continued to occur in the former throughout the year, where 34 cases with 10 deaths occurred; of these, 22 cases and 6 deaths were recorded in the first four months of the year. In the latter, there were 6 cases and 4 deaths.

Captain P. Ganguli,² in a comprehensive paper dealing with C. S. Meningitis and its symptomatology, pathology and treatment, records that during the Calcutta epidemic 20-30 % of healthy persons were found to be carrying the meningococcus in their pharynx.

¹ "Current Science", Vol. III, No. 7, January 1935, page 291.
² Ibid

10. Prophylactic Vaccine.—In the Punjab, vaccine was obtained from the Central Research Institute, Kasauli, for controlled experiments among the prisoners of the Lahore jails. The populations of both the Borstal Institution and the Central jail were divided into approximately equal parts,—one being inoculated, the other being used as a control. Both were kept under identical conditions as regards work, general environment, etc.

Vaccine was administered at weekly intervals in 3 doses of 0.5, 1.0 and 2.0 ccs to each prisoner. The numbers are as follows :—

Number of inoculations	Central Jail	Borstal Institution
3	1,000	665
2	2	46
1	0	55
	1,002	766

Inoculations were begun in June and ended in October. Up to February, 1935, no case of C.S. Meningitis had been reported from the Central Jail, except one imported case, while 6 cases occurred in the Borstal Institution among the non-inoculated group and none in the inoculated group. These numbers although suggestive are so small that little significance can be attached to them.

The Director, Central Research Institute, reports that from May to December, 1934, 34,648 c.cs were issued, this amount being sufficient for a full course for nearly 10,000 persons. Reported results are given below :—

(a) District Jail, Delhi.—Daily average population 556 (half population inoculated).

	Cases	Deaths
Among inoculated ...	3	1
Among un-inoculated ...	0	0

(b) Delhi city.—106 persons, including 54 occupants of an orphanage, received 3 doses of the prophylactic vaccine from June to August, 1934. A report in February, 1935, states that one person in this group was attacked at the end of November, 1934, but eventually recovered.

(c) Figures for the Lahore Institutions have already been given.

So far it cannot be said from these reports whether or not the vaccine has been of value. Considering the very low incidence of the disease in any community the number of cases

reported among the inoculated is somewhat disappointing. Further supplies of the vaccine have been issued; large stocks are still in hand; and it is proposed to collect further reports.

EDITOR'S SUMMARY

Lieut.—Col. Russell in his masterly memoranda submitted to The Office International d'Hygiene Publique on different dates records the incidence of cerebro-spinal meningitis in India for the period 1927 to 1935 (earlier half).

It is no new disease to India. The first cases were recorded by Vandyck Carter in 1878 in Bombay, whilst Dimmock reported the disease among the convicts of Shikarpur Jail during the winter of 1883-84. Since 1881, the jail and army returns show the incidence of this disease at intervals and the civil population has probably been similarly infected, although few records exist to substantiate this statement. The increasing incidence among civil population since 1927 is striking although it is probable that it is due to better diagnosis of cases.

Cases are reported from all parts of India and Burma. Lahore, Delhi, Calcutta and Ahmedabad seem to be chief storm centres. The disease continues to spread and the provincial reports indicate that outbreaks have occurred in widely separated parts of the country. It is said that the disease is spreading from west to east, but it is to be noted that Burma has now reported several small out-breaks though Assam has not so far recorded its presence. It is also to be noted that the number of cases, so far recorded in this country, does not indicate with any degree of accuracy the actual incidence of this disease, although the continued increase is obvious.

The periodicity of this disease is striking—it reaches the highest peak during the hot weather, i.e., March, April and May. Its age-incidence seems to show that it is most prevalent among young adults. Males suffer more than the females for obvious reasons.

It is probable that an increased rate of carriers may determine an outbreak of C.S.M.: Eg., the epidemic in the Borstal Institution. Bad housing conditions in urban areas are favourable for propagation and spread of infection.

Prophylactic Vaccine, manufactured from cultures originally taken from cases in Delhi, has been issued for trial by The Central Research Institute, Kasauli; and also by The Bombay Haffkine Institute from Ahmedabad strains. It is, at present, premature to hazard any opinion regarding its prophylactic value.

An effective preparation of Anti-meningococcus serum depends upon the particular Types and strains of meningococci responsible for an epidemic outburst. Much work is being carried out in the Kasauli Institute in this connection and its preparation will depend largely on the results of the tests now under experiment.

Cerebro-spinal Fever in the Punjab

• Dr. Jamiat Singh M.D. (Pb.), F.R.C.P. (Edin.),
D.P.H., King Edward Medical College, Lahore

Cerebro-spinal fever appeared in an epidemic form in the Borstal Institute, Lahore, in March 1932 and has continued since then with varying severity and intervening periods of quiescence. During the same period, Central Jail, Lahore, was also visited by the disease. Circumscribed outbreaks have also been reported from other jails of the Punjab and the disease had its toll from almost every town in the Province.

The disease was imported into the Punjab from Jammu and Kashmir by the Ahrar prisoners, where a similar illness is said to have been prevalent in the jails. The disease is now so well known in the Punjab that the lay public has given it the name of "Gardon Tor Bukhar" or break-neck fever, on account of the presence of fever, severe pain and rigidity of the neck.

Dr. Mohd. Yakub M.B., D.P.H. & D.B. (Lond.) Epidemiologist to the Government of Punjab and his assistants have thoroughly investigated the disease in the Borstal Institute and Central Jail, Lahore. Bacteriological investigation of the nasopharynx of all the inmates of Borstal Institute was done with a view to detect carriers of the disease, who were segregated.

By the energetic efforts of the Punjab Health Department in co-operation with the Jail authorities, the disease has been kept in check, only 27 cases and 11 deaths occurred in 1932 and 1933 in Borstal Institute, Lahore.

As prophylactic measures, the inmates of the Jail were ordered to gargle their throat and douche their nose with 1—5000 solution of Potassium Permanganate in normal saline. A vaccine obtained from Kasauli was also used in doses of 0.5cc, 1.0cc and 1.5cc at weekly intervals as a prophylactic measure, but the results are being awaited with interest. The writer has seen seven cases of the disease. Fever with head retraction, intense headache and Kernig's sign are present.

Rash is very seldom noticed but occasionally it is petechial or hæmorrhagic in type. On lumbar puncture, cerebro-spinal fluid is opalescent in the beginning but becomes definitely turbid

and shows a white deposit later on. Meningococci are difficult to find in the beginning, but a film stained with methylene blue and very carefully examined almost always shows intra and extracellular diplococci and on gram's staining, these are found to be gram negative. Inoculation of cerebro-spinal fluid on blood agar slopes or plates prepared from pigeon's blood (strength 1—10) shows good growth after 48 hours. In severe cases of the disease, sugar is absent and globulin is increased.

In places where laboratory facilities are not available a turbid cerebro-spinal fluid obtained on lumbar puncture during an epidemic is sufficient for diagnostic purposes. No time should be lost in waiting for the bacteriological report in starting serum treatment, which is specific and has greatly reduced the mortality from the disease. Serum should be given intraspinally after removal of cerebro-spinal fluid as early as the disease is diagnosed or suspected and if prompt benefit does not follow the intensive serum treatment, the brand of the serum should be changed and another maker's serum should be tried.

The writer has had excellent results from the use of Bayers antimeningococcal serum.

The amount of serum to be given intraspinally should be at least 5cc less than the amount of cerebro-spinal fluid withdrawn and the injection should be given very slowly. The serum, 5 to 15 cc at ages from 1 to 5 years upto 30cc or more in adults should be given daily for 4-5 days and further repetition should depend upon the condition of the patient and the state of the meningitic exudate. In severe cases, it may be necessary to repeat the injection every 8 to 12 hours for 3 or 4 doses. The ordinary record 20cc syringe may be attached to the lumbar puncture needle for the injection of the serum. A better method of giving the injection is by a rubber tubing about 18 inches long with a glass window, to the upper end of which is attached a glass funnel and to the lower end a tubular metal nozzle which fits into the butt of the lumbar puncture needle. Between the glass tubing and the nozzle is a clip. The apparatus is sterilised by boiling. Sterilised normal saline

is allowed to flow through the apparatus which is then filled with serum warmed to body temperature. Lumbar puncture having been performed and the cerebro-spinal fluid allowed to escape as much as is considered necessary, nozzle is inserted and required dose of serum is allowed to flow slowly. If organisms are demonstrated in blood on blood culture, 50 to 100 c.c. of serum should also be injected intravenously.

Intra-theal serum injections should be continued until the spinal fluid becomes clear, the cell count is reduced to 100 or less, the temperature is normal and the meningitic symptoms have subsided.

If the fluid is very thick or the flow seems to be obstructed or only too little is obtained on lumbar puncture, serum should be injected into the ventricles of the brain or into the cisterna magna, as the serum is bactericidal and only useful, if it comes into contact with organisms—intramuscular injections, if used at all, must be used as a supplement to the intrathecal injections.

Various sequelæ are likely to be left behind. The writer has seen two cases of deafness following the disease. Some preparation of iodine as iodoalbin or iodopin should be given for a long time with the hope of absorbing the exudate and relieving the deafness, but the condition is incurable.

EDITOR'S SUMMARY

The writer says that since the Borstal epidemic in 1932, the disease has been appearing with varying severity and intervening periods of quiescence and had its toll from almost every town in the Province.

The prophylactic measures adopted were: gargling the throat and douching the nose with 1—5000 potassium permanganate solution in normal saline and a prophylactic Vaccine in doses of 0.5cc., 1.0cc. and 1.5cc. at weekly intervals, obtained from Kasauli. The results of the latter are awaited with interest.

Rash is seldom noticed but when present it is petechial or hæmorrhagic in type.

Cerebro-spinal fluid is opalescent at the beginning but soon becomes turbid and shows white deposits later on. In severe cases, sugar is absent but globulin is increased. Meningococci are difficult to find in the beginning but by proper staining and careful examination they can be detected. When laboratory diagnosis is not possible, a turbid cerebro-spinal fluid obtained by lumbar puncture during an epidemic is sufficient for diagnostic purposes.

Treatment by specific serum should be initiated even without waiting for the bacteriological report. The author has had excellent results with Bayer's Anti-meningococcal serum. Intra-theal method is preferred; but if there is block, he suggests injection into the cerebral ventricles or into the cisterna magna, as the serum is bactericidal and only useful if it comes into contact with organisms.

He recommends preparations of iodine for the treatment of complications in the hope of absorbing the exudates.

Cerebro-Spinal Meningitis in Madras

- Y. Suryanarayana Row L.M.P., (Mad) L.T.M., (Cal)., Assistant to the 1st Physician and Assistant to the Lecturer in Medicine, Stanley Medical School, Madras

The occurrence of this disease is so rare in Madras that the report of the following 4 cases which were admitted into the Government Rayapuram Hospital, Madras, is worth publication. All the four cases were admitted within a period of 6 months in 1935.

Case 1

Patient by name B, an anglo-Indian lady of about 21 years, was admitted into the above hospital, on 17-3-1935, with a history of fever and pains all over the body. The fever started with pain in the region of the right ankle. The pain in the lumbar region was very intense. There was no swelling of the right ankle.

Examination.—Bowels were constipated. Throat was congested. The right tonsil was enlarged and tender. There was slight adenitis of the glands of the submaxillary area. The pulse was rapid, but of good volume and tension. The blood showed no malarial parasite, but definite increase in the number of polymorphonuclear leucocytes. Spleen and liver were not enlarged. No tenderness was present anywhere in the abdominal area. Respiratory and urinary systems were normal. Headache was severe and vomiting persistent. There was rigidity of the neck and retraction of the head. The head was in a position of opisthotonos. Kernig's sign was distinctly positive. There was photophobia. The patient lay in bed in a position of complete flexion with the head retracted and almost touching the back. A lumbar puncture was done and the fluid was found to be, not only under pressure but also turbid. The cerebro-spinal fluid did not reduce Fehling's solution as in the normal fluid. On microscopical examination of the centrifuged deposit, gram negative diplococci were found, and meningococci were isolated on culture.

Treatment.—After the withdrawal of about 30cc. of c.s. fluid, 10cc. of Anti-meningococcus serum was put in intrathecally and it was again repeated on 19-3-1935. On the same night, another lumbar puncture was done and after withdrawing 30 to 40cc. of the c. s. fluid, 10cc. of the same serum was given intrathecally.

Since such infectious cases could not be kept any longer in a general hospital like that of ours, the patient was transferred to the Isolation Hospital, Tondiarpet, where, we were informed, she died on 21-3-1935.

During her stay in our hospital, her temperature ranged from 101 to 104°F.

Case 2

Patient P, aged about 24 years, European lady, was admitted into the same Hospital on 14-4-1935 with a history of slight cough, fever, severe vomiting and persistent headache. Duration was only one day.

Examination.—The tongue was coated slightly, both the tonsils were enlarged and the throat was congested. The pulse was rapid, otherwise it was normal. Microscopical examination of the peripheral blood did not show any malarial parasites but it showed definite increase in the polymorphonuclear leucocytes. Occasional rales were present in both the lungs. Liver and spleen were normal. There was persistent vomiting. Kernig's sign was present, but the retraction of the head was not very prominent. Lumbar puncture revealed that the cerebro-spinal fluid was under pressure and turbid. Centrifuged deposit showed the presence of Gram negative Meningococci and plenty of polymorphonuclear leucocytes. Headache was severe. There was also photophobia. The case was diagnosed as one of cerebro-spinal meningitis.

Treatment.—During the first lumbar puncture 40cc of c.s. fluid was withdrawn under pressure and 10 cc of the concentrated antimeningococcic serum was injected very slowly intrathecally. Since the patient was very restless, she was given an intramuscular injection of hyoscine hydrobromide, 1/100 gr. with atropine 1/100 gr. The lumbar puncture was repeated the next day and 20cc of the A. M. serum was put in intrathecally. Her temperature during the stay in the hospital ranged from 99 to 104.

After definite diagnosis, this case also was transferred to the Isolation Hospital, Tondiarpet, on 16-4-1935 for subsequent treatment. She had a

very prolonged course in that hospital, and developed slight partial flaccid paralysis. She eventually recovered and was discharged on 1-6-1935 and was given long leave for recouping her health. During her sickness, she ran a peculiar temperature as shown below.

Case 3

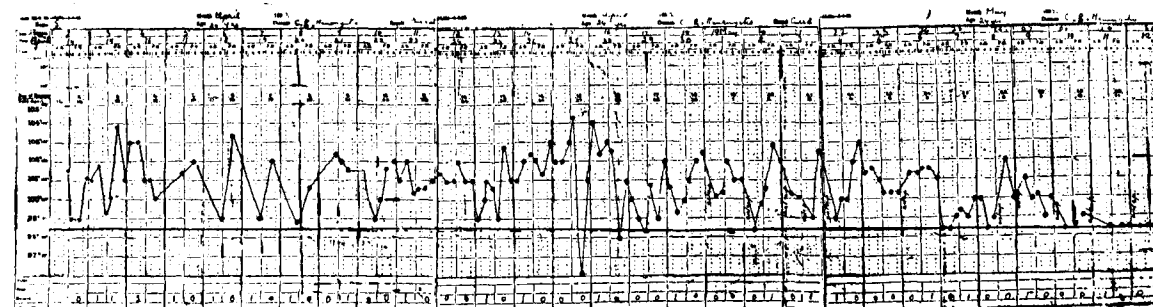
Patient S. Hindu, male, aged about 35 years, was admitted on 29-5-'35 into our hospital. The duration was 2 days. There was a history of fever with convulsions. Two days before, he went on a bicycle ride for about 25 miles in the hot sun. He noticed that he got slight fever soon after his return. There was slight headache. He had also vomiting at home. With the rise of fever, the patient grew unconscious and he was also getting convulsions. The patient was admitted in this state into the hospital.

theally after letting out 30cc of c. s. fluid. Adrenaline, pituitrin, digitalin, and strychnine were given alternately since the general condition of the patient was very bad. The same evening 40cc of the A. M. serum was given intravenously. On the second day, lumbar puncture was repeated and 20 cc of the same serum was put in intrathecally after withdrawing 20cc of the c. s. fluid.

The same day the patient was transferred to the Isolation hospital for further treatment, but it was reported that he died the same day.

Case 4

Patient, K. Hindu, male, aged about 25 years and a resident of Madras, was admitted into our hospital, on 26-8-1935, with a history of fever for three days and also unconsciousness. The fever started with rigor; and on the night previous to admission the patient became unconscious.



Temperature chart of Case 2. Note the protracted course and peculiar temperature

Examination.—The tongue was coated and it was slightly cyanosed. The eyes were half open and deviated to the left. Conjunctivæ were insensitive but the cornea were slightly sensitive. The pupils were equal on both the sides. They reacted to light. There was retraction of the head. Kernig's sign was present. Stiffness of the muscles of the neck was prominent. The patient could not be made to talk. The heart sounds were very weak and rapid. Pulse was 120 and respiration 54 per minute. Peripheral blood showed under the microscope no malarial parasite but increase of polymorphonuclear leucocytes. The breathing was deep and laboured; both inspiration and expiration were harsh. A few crepitations were heard at both the bases. The abdomen was rigid. Enlargement of liver or spleen could not be made out. After lumbar puncture, the cerebro-spinal fluid was found to be under pressure and also turbid. The centrifuged deposit showed Gram negative diplococci (Meningococci).

Treatment.—On the date of admission 20cc of Anti-meningococcus serum was given intra-

Examination.—The tongue was coated, conjunctivæ were dull; the patient was a little emaciated, and was unconscious; the muscles of the neck and lower jaw were rigid; pupils reacted to light; the knee jerk on the right side, the ankle jerk on the left side were absent, while the knee jerk on the left was present. Sensation to pin prick and heat and cold was lost. There was no rigidity of the muscles of the extremities. They were flaccid. Kernig's sign was present. Heart sounds were quick and feeble. Stained blood smear did not show any malarial parasite, but it showed distinct leucocytosis, specially of the polymorphonuclear variety. Respirations were hurried and shallow. Liver and spleen were not palpable. The urinary bladder was distended. The patient lay down in bed in an unconscious state with the eyes closed and did not respond to any questions. There was no paralysis of upper limbs. Lumbar puncture done on the next day after admission revealed the cerebro-spinal fluid to be under pressure and it was also turbid. Microscopical examination of the centrifuged deposit showed plenty of polymorpho leucocytes and Gram negative intra-cellular diplococci (Meningococci).

Treatment.—On the day of admission it was mistaken, before the lumbar puncture, for a case of cerebral malaria and he was given $7\frac{1}{2}$ grs. of acid quinine hydrochloride intra-venously. When the diagnosis of cerebro-spinal meningitis was established after the result of lumbar puncture, 10cc of A.M. Serum was given intrathecally. Later on in the day, the patient was transferred to the Isolation hospital for further treatment, but we were informed that the patient died the next day. During the stay of the patient in our hospital, his temperature was low, ranging between 99 and 101° F only.

Comment

The occurrence of cases of cerebro-spinal meningitis is so rare in Madras that unless one is always on the look out, it is quite possible that he is very likely to miss them. Now and then sporadic cases of the disease occur in our presidency as is reported in the press. It is only the other day that the District Medical Officer, West Godavary Dist., gave a warning to the medical practitioners of the district, while presiding over the East Godavary Medical Association, to be always on the alert for cases of the above disease, as he had one case of cerebro-spinal meningitis recently admitted in the Government Head-quarter Hospital, Coconada, and that they should be prepared to meet with any such emergencies. Though the fever is said to be epidemic in nature, all our above cases occurred in a sporadic form. Since the first two cases occurred in an institution, all the contacts with them were examined for finding out whether any of them were harbouring meningococci in their noses and throats. None of them were found to be the carriers of the disease, nor did any one of them suffer recently or even remotely from it.

Cerebro-spinal meningitis is regarded by Price as a disease of winter and spring. But all the above 4 cases had occurred in the hottest part of the year, viz., from March to August 1935. There is also a doubt expressed by some authors whether the disease is contagious at all. But the evidence that it is contagious far outweighs the one that it is not. The first two cases occurred in a closed community one after the other. It shows that infection has got some part to play in the spread of the disease.

The characteristic symptoms of the disease are sudden onset, fever, headache, and vomiting which were all present in the above cases. Kernig's sign and retraction of the head were also present. In all the cases the throat was congested. No cutaneous rash, described to be

so common in the text books, was present in any of the above cases. Polymorphonuclear leucocytosis was present in all the cases. The last two cases were admitted in a condition of stupor, i.e., in the later stages of the disease.

The disease may terminate in one of the following three ways. 1. Recovery, 2. Death, 3. Becoming chronic with mental defect, deafness, blindness, hemiplegia or monoplegia. The last two cases described above seem to be of the fulminating type.

The common complications of the disease are said to be: 1. hydrocephalus; 2. psychic disturbances as delirium, stupor, mania etc; 3. motor defects as hemiplegia, flaccid paralysis, spastic ataxia, 4. special sensory symptoms as irido-cyclitis, cellulitis of the orbit, keratitis, deafness, etc. 5. swelling and stiffness of the joints. The third and fourth cases showed marked psychic disturbances, as stupor, convulsions, delirium etc. The second case, though developed flaccid paralysis of the lower limbs temporarily, she completely recovered afterwards.

Cerebro-spinal fluid in meningococcal meningitis.—The pressure of this fluid in the above disease is definitely increased. The colour of the fluid is also changed from clear and transparent to various grades of turbidity. The fluid in all the above cases was distinctly turbid.

As regards the chemistry of the fluid, protein is said to be increased to the extent of 2 to 3%. This test was not done in our cases. The cerebro-spinal fluid in this disease shows quantitative increase of lymphocytes in the early stages, and polymorpho increase in the later stages. All our cases showed the latter feature and not the former. In still later stages of the disease, it is said that the lymphocytes will again predominate.

Bacteriology of the fluid.—Films made from the centrifuged deposit in all the above cases showed intra and extra cellular Gram negative diplococci (Meningococci).

Diagnosis.—The chief symptoms for diagnosis are, headache, delirium, vomiting, stiffness of the neck, kernig's sign, and ocular symptoms as papilloedema. All the above symptoms were found in all our cases except the last, for which the patients were not examined.

A rapid method of diagnosing meningococcal meningitis from the spinal fluid was described by Dr. B. G. Macgrath, M. B. as follows for identifying the organism: (1) By using anti-meningococcal serum agar plate. The plate

is swabbed with the deposit of the c. s. Fluid and incubated for 12 to 24 hours and secondly by direct slide agglutination of the organism after it has been grown by the above method, using the stock anti-sera. (2) By the use of precipitin test. This test is done by placing, in Dreyer's tubes, small amounts of cerebro-spinal fluid as antigen, and a suitable anti-meningococcus serum as antibody. Positive reaction is shown by the appearance of a white precipitate ring at the junction of the two fluids. The reaction becomes positive within the first few hours after the onset of the symptoms, and hence affords a valuable aid to early diagnosis. (3) By Complement fixation test with polyvalent A.M. serum, which is done by using spinal fluid in dilutions of 1 in 1; 1 in 8; 1 in 32.

As regards the differential diagnosis of this disease, it has to be diagnosed from influenza, typhoid fever, acute pneumococcus infection, measles, and other forms of meningitis such as pneumococcal, streptococcal, influenzal, typhoid and tubercular.

Prognosis.—This is distinctly grave and unfavourable as is shown in our cases.

Treatment.—Prophylactic. Nasal and pharyngeal passages should be kept clean and they should be lavaged with 1 in 1000, pot. permanganate or hydrogen peroxide, or ordin-

ary saline; anti-meningococcus serum is given in two doses once a week in 1 cc doses.

Curative.—It is vitally important that the anti-meningococcus serum should be administered early and intrathecally after the lumbar puncture was done and some fluid let out. It is less effective if given intravenously and of very little use if given intramuscularly or subcutaneously. The repetition of the subsequent doses should depend on the way in which the patient responds to the previous doses of the serum. It is best judged by the condition of the spinal fluid, whether it is clearing up or not. If the fluid continues to be turbid, the serum should be repeated at frequent intervals.

As regards drugs, urotropine in full doses of 60grs a day is recommended. The rest of the treatment is only symptomatic. For the headache: ice to the head, aspirin; antipyrin, caffein citras, and if violent, morphia have to be given. For delirium: bromides, hyoscine hydrobromide, are useful. For hyperpyrexia: ice to the head, hydrotherapy etc are advocated. Light fluid diet is essential.

My heartfelt thanks and gratitude are due to Rao Saheb Captain P. S. Krishnaswamy, M.B.C.M., M.R.C.P., Superintendent of the Government Rayapuram Hospital, Madras, for having permitted me to make use of the case records of the above cases freely and in permitting them to be published.

EDITOR'S SUMMARY

The writer describes 4 cases of C.S.M. as observed at the Rayapuram Government hospital, Madras, during 1935. Out of these, only one survived. The case that survived had a protracted course and ran a hectic temperature. She developed partial flaccid paralysis from which she eventually recovered.

As against the text-book description that it is a winter-born disease, he notes that all the cases occurred during the hot season of the year. One of the cases was mistaken for cerebral malaria before lumbar puncture was done.

Examination of contacts of the first two cases (which occurred in an institution) did not reveal meningococci on examination of the nasal and throat swabs. Prominent symptoms, as observed in the cases under reference, are noted down. A rapid method of diagnosing this infection is described briefly. He stresses on the early intrathecal administration of A. M. Serum.

Cerebro-spinal Fever within the Municipal Limits of Nadiad

● Ramanik H. Desai L. C. P. S. (Bom)., L. T. M. (Cal).

It is an infection with the meningococcus of Weichselbaum, initially of the upper air passages and secondarily of the blood stream with metastatic involvement, more commonly of the cerebro-spinal meninges and frequently of the other parts of the body. It is also otherwise

called epidemic cerebro-spinal meningitis, spotted fever, posterior basic meningitis, etc.

My observations recorded herein are based on the following 14 cases within the municipal limits of Nadiad during March and April 1934.

Number	Name	Age	Sex	Date	Result	Remarks
1	M. G.	45	Male	17-3-34	Died on 19-3-34	Serum 10 c.c. only intramuscularly given; lumbar puncture was unsuccessful as the patient was not controllable.
2	M. M.	20	"	21-3-34	" 23-3-34	What treatment given, not known.
3	Z. V.	19	"	27-3-34	" 28-3-34	Treated at the Mission Hospital—line of treatment not known.
4	M. H.	19	"	28-3-34	Recovered	Detected early and treatment by serum daily—often lumbar puncture. Total amount of serum upto 80 c.c. given.
5	V. T.	7	Female	30-3-34	Died on 1-4-34	Lumbar puncture as well as serum treatment.
6	B. A.	11	Male	31-3-34	"	No serum treatment given—treated privately.
7	R. M.	14	"	2-4-34	Recovered	Serum treatment and lumbar puncture daily for a week; showed symptoms of recrudescence twice; developed Broncho-Pneumonia—recovered after a prolonged illness of 2 months; 60 c.c. of serum in total used.
8	Rani	1	Female	6-4-34	Died on 6-4-34	The child was being treated for some other disease; specific treatment not given.
9	H. K.	50	"	7-4-34	" 8-4-34	Serum given—often lumbar puncture.
10	H. G.	9	"	9-4-34	Died	Serum treatment instituted, but the patient gradually went down-hill, symptoms of hydrocephalus developed and died after a prolonged illness of 2 months.
11	B. B.	4	Male	10-4-34	Died on 11-4-34	No specific treatment given.
12	M. D.	22	"	12-4-34	Recovered	Serum treatment given.
13	S. P.	3	Female	21-3-34	"	Symptoms mild, resembling "Influenza"—no lumbar puncture was allowed—but the patient recovered. When the fever subsided the patient could not move; gradually locomotion restored and he recovered completely except the deafness which still remains.
14	K. P.	28	Male	15-8-34	Died 14-5-34	Was treated as cerebral malaria by intravenous quinine—2 hours before death lumbar puncture revealed meningococci.

Etiology

This disease seems to be more common during the months of March and April and it is in conformity with the months of greatest prevalence, as recorded in the recent epidemics in Delhi, Calcutta and Ahmedabad. It may be sporadic all the year round and it looks as if these particular months are favourable for its epidemic exacerbation. Further studies on humidity, atmospheric conditions etc., and their relationship to the virulence of the organism are worth undertaking from academic and prophylactic points of view.

The disease is no doubt contagious but my observation is that it is only slightly so. I was not able to prove any case as due to direct infection, except to say in a general manner that most of the cases are from the congested areas of the town.

It is also interesting to note that out of the 14 cases under my personal observation 7 were under 14 years, 5 between 14 and 28 years and only 2 above the middle age. This finding is in conformity with similar age incidence observed in the recent epidemics in other regions of the country.

The incriminating micro-organism is, of course, the meningococcus—*Diplococcus Meningitidis Intracellularis* of Weichselbaum—and can be recovered from the throat and the spinal fluid. Under the microscope it looks smaller than *M. Catarrhalis* and larger than the *Gonococcus*. It is gram negative in its staining reaction. It is an obligatory aerobe. Grows on agar media when added with some animal protein and at temperatures between 36° to 37° C. Its vitality is obviously low as sunlight kills it in less than 12 hours. I have not had the advantage of studying its cultural characteristics in reference to the virulence of the different types of meningococcus. Gardon has differentiated 4 types by the agglutination and absorption tests. It is quite probable from the study of recent epidemic records that the varying intensity of the disease, the varying results of mortality in the different epidemic periods and the varying results of specific serum treatment may all be due to the varying preponderance of the different types of meningococci in the different parts of India and in the different epidemics in the same locality.

Lumbar puncture has to be done for a definite diagnosis. Children and even adults may require local anaesthesia (such as Novocaine or Ethyl chloride) for this purpose; and if the patient cannot be controlled a general anaesthetic may even be necessary. The needle must be strong and provided with a stylet. The

space between the third and the fourth lumbar vertebrae is usually selected. You will find from the flow that the cerebro-spinal fluid is both increased in amount and under pressure. In the early stages of the disease the fluid may be clear but it gradually becomes opalescent and later on frankly purulent. Sugar is absent as shown by Fehling's test. Albumin is present and s. globulin is increased. The cytological changes in the spinal fluid are that the lymphocytes are increased in the early stage and when the meninges are affected the polymorphs are increased. Films made of the fluid show intra and extracellular meningococci.

Symptoms

The symptoms observed in the above series may be classified and described as under:

I. Ordinary or Acute Type.—Incubation period is not definite here. It may be from 4 to 5 days. The disease starts as an ordinary acute fever. Its onset is sudden with fever, headache, malaise and vomiting. Temperature goes up to 102° or 104° F. Headache is intense and is referred to the occipital region. Frequently there is rigor in the adults and convulsions in children. There is invariably catarrh of the naso-pharynx. Vomiting may be intractable. Pain in the neck and limbs is marked. There may even be delirium. After two to four days, symptoms of meningeal invasion are found. Vomiting becomes more persistent, pulse is irregular in rhythm and frequency in comparison to the temperature. Respiration also becomes irregular. *Tache Cerebrale* is present, showing the irritability of the vaso-motor system. The patient lies on his side with the legs drawn up. Pupils are dilated and there is photophobia. Examination of the neck shows stiffness of muscles. Ham-strings are taut and hence *Kernig's Sign* is marked. Abdominal reflexes are absent. There is, of course, restlessness and insomnia. Headache is severe and persistent. In some, a rash may appear in the first week. I have observed *Herpes* to be common. Leucocytosis is marked (20,000 to 40,000).

At the end of the first week the mental condition becomes worse—there is marked stupor. The patient is now in a characteristic huddled posture. Rigidity of the neck muscles increases and with it, the retraction of the neck. Flesh is lost. Polyuria is present. Temperature is high and continuous but sometimes irregular. In later weeks, recovery may occur gradually; but is often interrupted by sudden recrudescences when the temperature shoots up to 103° or 104° F again. If the patient recovers, stupor

passes off, fever subsides, rigidity disappears; but the pulse remains high for some days. In some, the temperature may fall but the general condition does not simultaneously improve and if with this, there is progressive emaciation chronic hydrocephalus may supervene. Sphincters relax and optic neuritis develops. Even after such developments, the patient may recover. But generally such cases die; and even if they recover there may remain mental defects, deafness, blindness, hemiplegia or diplegia. I find that relapses are rare but I have seen recrudescences of the disease more commonly.

II. *Super Acute Type*.—Here, the symptoms are very abrupt, ushered in with severe headache and marked delirium. Temperature is very high (104° to 106°F). Tongue is dry and tremulous. Meningococci may be cultured from the blood and leucocytosis is high (30,000 to 40,000). Within 3 to 4 days he passes from stupor to profound coma. Lumbar puncture does not relieve this condition. Pulse, respiration and temperature are all rising. Pupils are insensitive and corneal reflex is lost. Surface of the body becomes cold and lungs become congested. Such cases do not recover.

III. *Malignant Type*.—This is often seen in older children and adults than in infants and younger children. There is fever, headache and acute delirium which lasts for 12 hours at the end of which the patient becomes comatose. There is rapid development of septicæmia and so, symptoms of septicæmia are more prominent and common than the meningeal symptoms. Such cases also do not recover.

IV. *Mild Type*.—This is more common during the decline of an epidemic. These are the cases which are mistaken for influenza. But a slight rigidity of the neck and Kernig's sign should make us suspect meningitis and the diagnosis must be confirmed by lumbar puncture or by a swab from the naso-pharynx.

V. *Posterior basic Meningitis*.—This is common among infants and younger children. Onset is usually with convulsions and vomiting. There is sudden rise of temperature which is, however, not high. Fever may subside during the end of the week. But the retraction of the head is marked, back becomes arched and there is stiffness of the extremities. Emaciation is also rapid. Pulse and respiration irregular and raised. The infant lies motionless, pupils are dilated, and blindness may supervene in some cases. Lumbar puncture may not show meningococci if the disease has advanced. The cerebrospinal fluid shows increase of lymphocytes

rather than polymorphos. Puncture may be dry due to closure of Foramen of Magendie. Cerebral Ventricles are specially infected. Hydrocephalus may develop. Mortality is very high.

Complications

Pneumonia and enteritis are the frequently observed complications. Deafness, when it occurs, is generally permanent. Hydrocephalus may appear at the onset or develop later on. Pallor, cyanosis, increased pulse rate with low volume and sudden appearance of coma suggest hydrocephalus. Psychic disturbances in the form of temperamental changes may sometimes occur. Hemiplegia or monoplegia are not uncommon. There may be flaccid paralysis of the extremities. Some patients in the convalescent stage have unsteady gait.

Prognosis

Mortality rate differs in different epidemics. In children the death rate is much higher than in adults. There is no doubt that the mortality rate, as judged from the recorded figures, is high. But statistics with regard to this disease in our country are still meagre and do not therefore offer a basis for even an approximately correct conclusion. This much, however, can be said: the earlier the specific serum is given the lesser the rate of mortality.

Prophylaxis

No reliable prophylactic method has yet been evolved. The disproportion between a large number of healthy carriers and the smaller number actually attacked shows that personal contagion is not an important factor in its epidemiology. This much however is obvious that if the rate of incidence of healthy carriers increases, an epidemic of cerebro-spinal meningitis may be anticipated; and this may be truer of closed communities and of those living in insanitary and crowded localities than with others. In Egypt and Soudan prophylactic vaccine is being tried; even in India, I believe, the director of the Central Research Institute, Kasauli, has issued a limited supply of a prophylactic vaccine for trial and study. The final result is awaited. I had not given this vaccine during the epidemics at Nadiad and as such I am not in a position to comment on the same. I adopt the usual prophylactic methods. The patient is isolated—so also the carriers in immediate contact with the patient. Throats of the carriers are irrigated with salt solution or sprayed with the following solution of:

Thymol	5 grs.
Menthol	4 "

Chloretone	... 4 ms.
Liquid paraffin	... 1 oz.

Oral hexamine in 30 gr. dose has been tried.

Treatment

I try to keep the patient as quiet as possible and avoid all causes of external irritation. The hairs are clipped and an ice bag applied to the head. Only liquid diet is given—and water very freely. Bed sores are best avoided by careful nursing. Bowels to be opened by calomel and saline. Urotropine in drachm doses may be tried. Serum therapy is useful, provided it is given early and in sufficient doses—up to 40c.c. It is best given intrathecally. It should be given daily till the symptoms abate and the meningococci disappear from the spinal fluid. A few doses may be given intravenously also or intra-

muscularly to combat bacteræmia. The insignificant success with the present stock serum is obviously due to the strains foreign to the epidemic on hand. If it is possible to make serum locally with the particular Type of meningococci which have caused the particular epidemic, it is quite probable that the results may be better. We have therefore, at present, to fall back on the polyvalent stock sera available in the market. Out of the 14 cases, only six were given serum. Out of these three recovered. It would be rash on my part to draw conclusions from such a small number of cases treated. There is another important factor in dealing with the Indian patients. They are generally afraid of lumbar puncture and so many cases are concealed. This stands materially in the way of our judging its incidence, arriving at a correct diagnosis and instituting specific treatment.

EDITOR'S SUMMARY

The writer records his observations on 14 cases of C.S.M. treated by him during 1934 at Nadiad.

He stresses the need for further study of humidity, atmospheric conditions, and the virulence of the strains of the organism for a clearer understanding of its epidemic spread and occurrence.

According to him, the disease is but slightly contagious and that most of the cases are from the congested areas of the town where insanitation and bad housing are common. He observes that infants and adolescents are more affected.

He describes the symptoms of the different types of the disease and also its common complications and sequelæ.

Mortality rate is very high and among children more than among the adults. It is favourably influenced by a timely administration of serum in good doses.

Lumbar puncture is essential both for purposes of diagnosis and treatment. The changes in the character of the C.S. fluid are briefly described. He mentions the reluctance of the Indian patients to lumbar puncture and states that this stands in the way of proper diagnosis and treatment.

Epidemic Cerebro-spinal Meningitis in Ahmedabad, 1934 & 35

• Dr. Pranalal R. Trivedi, L.C.P.S. (Bom.),
L.T.M. (Bengal)

STATEMENT SHOWING THE CASES OF CEREBRO-SPINAL MENINGITIS EPIDEMIC, 1934—35

	January	February	March	April	May	June	July	August	September	October	November	December	January	February	March	April	May	June	July	August	September	October	Total
No. of cases in the month	22	94	190	77	33	16	14	28	16	19	15	32	33	34	50	35	29	12	8	8	7	6	778
Sex:—																							
Males	20	73	152	65	29	11	11	21	15	18	12	28	27	22	41	28	28	11	6	4	4	6	632
Females	2	21	38	12	4	5	3	7	1	1	3	4	6	12	9	7	1	1	2	4	3	...	146
Age. Incidence:—																							
0—10	5	37	56	16	7	2	2	4	3	1	1	6	3	5	9	8	1	3	3	3	1	0	176
11—20	13	35	59	27	9	8	4	11	6	4	6	16	11	11	16	11	11	3	3	2	5	1	272
21—30	2	14	55	29	9	4	7	9	5	13	2	8	15	13	13	8	14	3	3	1	3	0	236
31—40	2	3	13	3	4	1	1	3	1	1	4	0	4	4	5	5	3	1	0	0	0	1	61
41—50	0	5	6	2	4	1	0	1	1	0	2	2	0	1	1	0	0	2	1	0	0	0	29
51—60	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	3	0	0	0	0	0	0	4
Caste:—																							
Hindus	17	67	155	70	25	12	11	19	13	15	11	23	24	26	44	26	23	8	7	7	4	6	613
Mahomedans	4	24	30	7	7	4	1	5	3	1	4	8	8	8	5	7	6	3	0	0	0	0	138
Ind. Christians	1	2	4	0	1	0	2	4	0	3	0	0	1	0	1	1	0	1	0	0	0	0	21
Parsis	0	1	1	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	5
Sikh	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1
Occupation:—																							
Labourers	4	2	26	17	7	2	4	8	2	8	3	10	11	8	18	7	22	6	1	3	0	3	172
Service	4	14	40	13	8	0	5	4	3	2	4	0	2	3	8	0	0	1	1	1	3	1	119
Students	5	3	3	1	1	0	3	1	0	1	1	3	2	3	2	4	2	0	1	0	2	0	38
Nil	9	75	121	46	17	14	2	15	11	7	9	15	20	21	27	16	5	6	5	4	4	0	449
Localities:—																							
Kalapur	7	25	47	20	11	6	5	3	4	3	1	6	9	8	6	5	6	5	2	0	0	1	180
Khadia	4	21	38	12	5	2	1	3	1	1	1	1	1	1	9	5	2	2	1	1	2	2	116
Jamalpur	5	14	18	12	3	2	1	2	0	4	0	5	6	5	10	2	0	1	0	1	2	1	92
Shahpur	1	3	12	6	5	1	1	1	1	1	1	1	0	5	2	2	4	0	1	1	0	0	49
Dariapur	0	8	12	3	1	1	1	1	1	0	0	1	3	0	1	1	3	0	0	0	0	0	37
Para	6	17	51	20	4	3	3	16	6	6	6	15	12	13	16	15	9	3	3	3	2	2	231
Outside Ahmedabad	1	6	12	4	4	1	2	2	3	4	6	3	2	2	6	5	5	1	1	2	1	0	73
Results:—																							
Cured	16	51	78	25	16	8	3	16	8	14	8	12	12	12	21	10	14	3	3	5	3	4	342
Expired	5	31	83	42	12	5	10	11	8	5	7	18	20	20	28	22	14	9	5	3	4	1	363
*Discharged against Medical Advice	1	12	27	9	4	3	1	1	0	0	0	2	1	2	0	3	1	0	0	0	0	1	68
Error in Diagnosis (Small-Pox)	0	0	2	1	1	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	5

*Amongst the number of patients discharged against medical advice, a large number consisted of patients whose throat swabs were positive, i.e., they showed presence of gram-negative diplococci in their throats.

Short history of the disease in India.—The disease has been first described in India by Dr. V. Carter, who, while working on the relapsing fevers at Bombay, saw some cases of the disease and clinically diagnosed the same in the year 1878. He has also noted some cases at Bombay in the year 1885. Another authentic report was given by Dimmock who saw several cases of this disease in Shikarpur Prison, in Sind, during the years 1883—84. Since this time, there have been sporadic cases almost every year in that prison. Dr. P. T. Patel in his book on *infectious diseases* describes as many as thirty-five cases during the period between 1912 to 1920. In the City of Ahmedabad, Dr. Joseph Benjamin saw some cases of the disease some where in the year 1898—99.

The present epidemic of c. s. meningitis commenced in this city in the beginning of November 1933 and the first few cases were treated at the Civil Hospital, Ahmedabad, and also at the Vadilal Sarabhai Hospital. Subsequently in the month of December 1933, a good number of cases were reported in the city and in consultation with the local authorities a special camp was erected in the premises of Sheth Vadilal Sarabhai Hospital for the treatment of this disease and in all, 778 cases were treated during the period from January 1934 to October 1935. The detailed figures with regard to the incidence is given above.

Seasonal incidence.—As has been described by various authors in the western countries, the epidemic was at its height during winter, parti-

cularly in the months of February, March and April.

Sex.—The proportion of male patients to female patients is about 4.5 to 1, though in other places the number of males is more preponderant.

Age.—As will be seen from the figures, the first three decades of life offered a heavy toll whereas the disease was scarce beyond the age of 45.

Caste.—Highest number of persons affected were Hindus but it is not in any way out of proportion to the total population of the community in the city.

Occupation.—This has not been rightly traced out mainly because most of the patients were admitted in an unconscious state. Most of them were probably from the labour class.

Localities.—The most overcrowded locality gave the largest incidence and figures are also arranged according to the population of the locality concerned.

As for the treatment I shall try to submit the same on some other occasion, but I should mention here my sincere thanks to Drs. G. B. Mohile, M.R.C.P. (Lond), D.T.M. (L'pool) and G. B. Mankad, M.D. (Bom.), M.R.C.P. (Lond.), Hon. Physicians to the Meningitis wards, for their valuable guidance in preparing these figures and also permitting to utilize the same for this Journal. My thanks are also due to my colleagues Drs. I. R. Pathak, P. K. Mody and N. M. Vyās for maintaining very careful records of all cases so as to facilitate my work.

EDITOR'S SUMMARY

The writer analyses the Ahmedabad Epidemic figures for 22 months, commencing from January 1934.

He shows that the months of highest incidence are February, March and April. The first three decades of life offered a heavy toll—scarce beyond the age of 45. The most overcrowded localities of the town seem to have been mainly affected. Most of the cases were probably from the labour class.

A Peep into the Literature of Cerebro-Spinal Meningitis

• T. C. Basu Chowdhary L.S.M.F. (U.P.), Agra

Cerebro-Spinal meningitis means acute inflammation of the meninges of the brain and spinal cord due to the invasion of diplococcus intracellularis meningococcus and is characterized clinically by sudden fever, nasopharyngeal catarrh and extreme nervous shock, attended by painful contractions of muscles, cutaneous eruptions and various grave nervous and other complications.

History

The disease is of comparatively recent history. Viessieux first describes a small outbreak in Geneva in 1805 but the epidemic described by Bascombe as occurring about the close of 1802 in the small Franconian Town of Roettingen, situated on the river Tanber and surrounded by mountains, seems to have been of the nature of cerebro-spinal fever. "After a very hot and dry summer, there were thick fogs and incessant heavy rains during November. Towards the end of this month an extremely fatal disease broke out which was without example in the memory of its oldest inhabitants, it being totally unknown to them previously. The young and strong were suddenly seized with pain and anguish at the heart, with violent palpitations and lacerating pains in the nape of the neck, profuse, sour, ill smelling perspiration broke out over the entire body; and a suffering as though a violent rheumatic fever had seized on the tendinous expansions, in the worst cases a spasmodic trembling ensued, the patient fainted, the limbs became rigid and death closed the scene, frequently within 24 hours from the commencement of the attack." (E. Bascombe M.D. London 1851).

In 1806 it occurred at Boston. According to Drs. L. Danielson and E. Mann it is a singular and very mortal disease which lately made its appearance in Medfield. From 1899 there have been extensive out-breaks in Silesia and in the cities of the United States on the Atlantic Coast. Since then it is occurring very frequently, sometimes in Europe and sometimes in America. It made its headway in India in the early part of the twentieth century; but has not been so wide-spread before as it is now

and hence no authentic records have been kept of its earlier incidence. Some local records have been kept at Bombay and Calcutta. In 1932 it made its appearance at the Borstal Institution, Lahore, where detailed records of all the 22 cases have been kept. This year (1934) also, the disease has visited various towns of India simultaneously. Ahmedabad, Agra, Allahabad, Cawnpore and Delhi were the towns where it did most harm.

Geographical Distribution and Climatic Effect

Every country in the world is liable to be visited by this disease but as its history shows very hot countries have not yet been affected so far and so we may conclude that hot climate is not very favourable for the spread of this disease. The facts we have gathered from the reports of the various epidemics show that it generally occurred either in winter or in spring and we have recently seen in India that it broke out in the month of February and continued upto the month of June '34. In his geographical pathology, Hirsch divides the outbreaks into four periods: from 1805 to 1830, in which the disease was most prevalent throughout the United States, a second period from 1837 to 1850 when the disease prevailed extensively in France and there were a few out-breaks in the United States; and a third period from 1854 to 1874 when there were out-breaks in Europe and several extensive epidemics in America. In Asia it first appeared in 1903 and then gradually it began to extend till recently when we have seen its fatal results in our own country.

Available Statistics

Towns	Year	Total No. of cases	Total No. of deaths
New York	1904-5	6,755	8,455
Glasgow	1907	1,000	595
Belfast	1908	725	518
England and Wales	1915-17	5,800	3,500
"	1929	650	
"	1930	666	about 70%
India	1934	2940	2000
My cases at Agra...	1934	10	4

*Dr. Ramachandrier's Prize Thesis for 1934. Received for publication on 17-6-35. Ed. I.M.J.

Etiology

On this head there is little to say beyond this, that all attempts to explain the origin of the various epidemics, or to bring them within the circle of those laws which apply generally to diseases of the zymotic class have failed. Most of the epidemics have occurred in the cold seasons of the year, but there have been many during the warm months also, especially in France and Sweden. In India too, at Delhi one of my friend's son died in the month of June '34 when the climate was very hot. Still it may be said that the development of the disease is favoured by cold. The inhabitants of high and low districts, of salubrious and insalubrious localities, of ill and well drained towns have suffered alike from the disease. It has generally been remarked that males are more prone to this disease than females, while healthy youths and children have been attacked in greater proportion than those advanced in life. Viessieux in giving the first authentic history of an epidemic of this fever which occurred at Geneva in 1805, says that it attacked people of every rank at once, the poor and the rich, the inhabitants of dirty and crowded rooms in unhealthy districts, as well as the residents in highly sanitary surroundings. The experience in India of recent years has shown that the disease is especially apt to break out in establishments where numbers of people are congregated together as in asylums, barracks, work-houses and prisons. But even here, the disease shows a peculiarity since it attacks soldiers in a larger proportion (as all reports show) than paupers or convicts. There is a great difference of opinion as to whether the disease is communicable by the sick to the healthy. The evidence, especially that derived from the French military experience, is in favour of it being highly infectious, which seems somewhat difficult to combat. The Members of the Massachusetts Medical Society (America) were generally agreed, however, as to its non-infectious character and they reported that out of 268 cases in which the question was asked as to the origin through contagion, the replies were in the negative so far as 252 were concerned. Cerebro-Spinal Fever is a disease of cities. Glover has shown that the dissemination of the meningococcus from person to person (not necessarily the disease) is intimately connected with crowded sleeping quarters. Therefore, the mode of infection is perhaps *Droplet* in character. The greatest incidence of cerebro-spinal fever occurs between the ages of five to ten. T. Mogilnicki states that out of 117 cases of the disease admitted to a children's hospital at Lodz,

Poland, between January 1st 1922 and January 1st 1925, 85 or 72.6% were in the first year of life, 11 were children from 1 to 2 years old and 21 between 2 to 14 years; whereas according to other authorities, specially German, the incidence of this disease among infants is much lower, e.g., 17% (Goppert) and 12 to 17% (Kassowitz). In 1921 Root finds only 6 cases in infants under two years of age. On the other hand Bell and Cook in 1922 reported a case in a sixteen days old child with a fulminating meningococcus infection and extensive petechial rash. J. M. Sturtevant records a case in a female child aged 7 weeks.

Over exertion, long marches in the heat, depressing mental and bodily surroundings seem to be predisposing causes. The disease is not transmitted by clothing or excretions. Cases are recorded of a similar disease in horses, during its epidemic prevalence in man. Extreme fatigue appears to increase the susceptibility. The disease occurs both in limited epidemics and sporadically.

The specific organism which causes the disease is a diplococcus known as meningococcus. Meningococci may be found in the naso-pharynx of perfectly healthy people, who are known as *carriers*. It is possible that the meningococci may remain latent but under favourable circumstances may cause a violent epidemic. It is noteworthy that carriers do not very often themselves contract the disease, but they are likely to disseminate the organisms by sprays of saliva while talking and coughing, and thus the susceptible people may become infected by inhalation and get the disease. It is said that normally about 5% of the population are carriers; but when the number reaches 20 per cent an epidemic may break out. An epidemic does not sweep through the community like influenza; it is only people here and there who contract the disease.

The relation of nasopharyngeal catarrh to the disease has been much discussed. It is maintained that epidemics really consist of epidemic nasopharyngeal catarrh with occasional complicating meningitis. This view is not generally held. The balance of opinion is against the occurrence of a nasopharyngeal type of the disease as distinct from a carrier State. It has been shown that in carriers the organisms may be recovered from the nasopharyngeal catarrh. Fildes has pointed out that those who develop the disease have seldom been carriers before the onset. The route by which the organism reaches the meninges is also a matter of dispute. Three views are held:

(1) that it reaches the base of the brain via the cribriform plate of the ethmoid by lymphatic channels.

(2) that it enters the blood stream through the nasopharyngeal mucosa and ultimately becomes localized upon the basal meninges. This is the most likely route, and the frequent occurrence of meningococcal septicæmia forms an additional argument in favour of this mode of entry (Harries).

(3) That infection passes from the blood to the choroid plexuses and then to the intraventricular fluid. The normal passage of the fluid carries it through the roof of the fourth ventricle out to the subarachnoid space, while there is a special tendency for the inflammatory products to accumulate at the periphery where the fluid is normally absorbed *i.e.*, at the superior longitudinal sinus and in the spinal canal. The evidence for this is (a) that in fulminating case meningococci are found in the ventricle alone, while there is no perceptible inflammation of the meninges, but there is acute inflammation of the choroid plexuses; (b) that in less acute cases the fluid from the ventricular puncture, though it has the same composition as the fluid from lumbar puncture, always contains fewer pus cells, suggesting that these have accumulated at the periphery. In favour of this view it has been shown in dogs that Indian ink when injected into the ventricles, travels from the fourth ventricle upwards in the subarachnoid space along the sulci, resembling the distribution of pus in cases of cerebro-spinal meningitis.

Cases have been recorded of post-traumatic cerebro-spinal fever, which may occur either with or without fracture of the skull. De Wayne Richey and T. R. Helmbold report a case in a boy aged 12 in whom symptoms developed within thirty hours after an injury to the head producing cerebral concussion and probably minute laceration of the brain and rupture of the intracranial capillaries. While it is possible that the occurrence of meningitis after the trauma was only a coincidence, the evidence was in favour of the injury having predisposed to the meningeal localization of the meningococci which have gained an entrance readily to the blood stream through a rent in the nasopharyngeal mucosa and thus been carried to the brain, where *locus minoris resistentiæ* had been created by the trauma. The symptoms rapidly cleared up after intravenous and intraspinal injection of Antimeningococcic Serum and complete recovery took place within sixteen days of the injury.

Bacteriology

In 1877, for the first time, Weichselbaum described the meningococcus—*diplococcus intracellularis meningitidis*. It is a gram negative diplococcus resembling the gonococcus, it dies rapidly outside the body unless kept at blood heat. This is of great practical importance in the collection of specimens for laboratory examination as it dies very rapidly. It is aerobic and can be grown on glycerine agar or blood serum. It is seen not only in the polymorphonuclear leucocytes of the meningeal exudations but also lying free between the cells; it is sometimes found in the blood, in pus from the joints, in pneumonic foci in the lungs, in the mucus of the nasopharynx of the carriers and in the cerebro-spinal fluid of cases of the disease. Four types of meningococci have been distinguished by agglutination reactions and in the vast majority of instances only a single type occurs in any individual case of cerebro-spinal fever (M. Gordon). Types I and II are commonly found in some epidemics as far as in 80 per cent of cases. Meningococci of one or other type are agglutinable by the patient's serum from the fourth day of the disease and onwards. This typing of meningococci is of much importance from the point of view of treatment by specific sera.

Morbid Anatomy

Visseux describes that in malignant cases no characteristic changes are to be found except the extreme congestion of brain and spinal cord. There is intense injection of pia-arachnoid. Fibrino-purulent exudates are to be seen at the base of the brain where the meninges may be greatly thickened and plastered over with it. The cortex is covered with thick, purulent exudate but generally much lymph is seen along the larger fissures and in the sulci. "The cord is always involved with the brain. The exudate is more abundant on the posterior surface, and involves, as a rule, the dorsal and lumbar regions more than the cervical portion." (Osler) "A fluid, resembling pus, is always present between the dura and pia maters." (Danielson & Mann). "In more chronic cases scattered yellow patches are to be seen where the exudate has once been. In acute cases ventricles are dilated and contains a turbid fluid but in chronic cases dilatation is even greater and the brain substance becomes a little softer than normal, and has a pinkish tinge; foci of hæmorrhage and of encephalitis may also be found. The cranial nerves are usually involved, particularly the second, fifth, seventh and the eighth. The spinal nerve roots are also found covered with exudate.

"Microscopically the exudate consists largely of polymorphonuclear leucocytes closely packed in a fibrinous material. In some instances there are foci of infiltration and hæmorrhage. The neuralgia cells are swollen, with large clear and vesicular nuclei. The ganglion cells show less marked changes. Diplococci are found in variable numbers in the exudate, being more numerous in the brain than in the cord" (Osler). Sphenoidal sinuses may sometimes be found full of pus and the surrounding bones inflamed. Meningococci are detected in the nasal secretion during life. Pneumonia, pleurisy and typhoid have been described as complicating the disease. Major P. D. Chopra, I. M. S. and Dr. M. S. Chadha have also given account of cases in which lung complications were present. Councilman reports that in 13 cases there was congestion of lungs with œdema, in 7 broncho-pneumonia, in 2 characteristic croupous pneumonia with pneumococci and in 8 pneumonia due to the presence of *diplococcus intracellularis meningitidis*. The enlargement of spleen varies a good deal. In only three of the Boston fatal cases, spleen was found much enlarged (Osler). Out of 3 cases on which post-mortem was done, in two spleen was much enlarged and acutely congested causing a diffuent condition of the pulp and in the third case the spleen was very much enlarged with trabecular hypertrophy and with diffuent condition owing to decomposition. (Major P. D. Chopra and Dr. M. S. Chadha).

The liver is rarely abnormal (Osler), but Chopra and Chadha have found in two of their cases that liver shows yellow areas of necrosis, surface mottled but smooth, section shows numerous regenerating nodules as seen in toxic cirrhosis. Intestines congested with submucous hæmorrhages at places.

Incubation Period

It is not known but that most usually accepted is from two to five days (Harries).

Varieties

The following is Prof. Dana's classification:—

1. Ordinary Form.
2. Abortive Form.
3. Fulminating Form.
4. Typhoid or Chronic Form.

The Ordinary or acute form begins suddenly like an attack of influenza, with head-ache, fever, vomiting and with convulsions especially in children. The temperature rises to 101° or

102° F., seldom exceeding 104°; occasionally the fatal termination is preceded by a temperature of 108° or 109° F. The pulse is full and strong. The most important and early symptom is the painful stiffness of the muscles of the neck, which may be shown by attempting to bend the head forwards. Often the head is drawn back by the contraction of the deep muscles; the dorsal and lumbar muscles may be similarly affected, so that the back is kept straight (Orthotonos) or even arched with concavity backwards (Opisthotonos) and sometimes the legs and arms are flexed in tonic spasm. Pains frequently extend down into the muscles of the lower extremities and cutaneous hyperæsthesia may also be present. Cases have been described in which rigidity and stiffness was such that the body could be moved like a statue. Paralysis of the trunk muscles is rare, but paralysis of the muscles of the eye and the face is not uncommon. The knee jerks are often active, but may be absent. Kernig's sign, is practically constant, but Brudzinski's sign, often limited to one side, is less often observed. The following symptoms may or may not always be present: ptosis, strabisms, dilatation or inequality of the pupils or contraction of the facial muscles, but trismus is rare; optic neuritis, conjunctivitis, panophthalmia, pain in the ear, tinnitus and defective hearing, suppuration of the labyrinth or of the tympanum. Deficiency of the sense of smell has also been observed. In some cases delirium occurs at the onset, occasionally of a furious and maniacal kind. The patient may display marked erotic symptoms at the beginning. The delirium gives place in a few days to stupor, which, as the effusion increases, deepens to coma. The pulse may be very rapid in children; in adults it is at first full and strong but in some cases it is remarkably slow and may not be more than 50 or 60 per minute. In some cases sighing respirations and cheyne-stoke's breathing are met with. In rare cases bronchitis, pneumonia, pleurisy, endo-carditis and latent peri-carditis do occur. Cutaneous eruptions are very common—rose spots, papular or petechial rashes are the earliest to appear. Herpes facialis, which is usually regarded as the commonest rash, occurs about the fourth day; herpes zoster is much rare. In some instances there have been rose coloured hyperæmic spots like the typhoid rash; urticaria or erythema nodosum, ecthyma, pemphigus and in rare cases gangrene of the skin have been noted.

Sometimes the joints are inflamed, red, hot, painful and swollen due to synovitis; this may

go up to suppuration but generally subsides very soon. Sometimes epididymitis and orchitis are met with. Urine examination shows a little albumin and a trace of sugar. Glycosuria has been noted in some instances and in malignant type hæmaturia. Leucocytosis is an early and constant feature and ranges from 15,000 to 60,000 per c.mm. It persists even in the most protracted cases, it is nearly always polymorphonuclear, only occasionally, in infants and young children, we see lymphocytosis. When lumbar puncture is done and the cerebro-spinal fluid is taken out, in early stages it may be clear but is usually turbid and may be purulent. During the disease the fluid comes out under an increased pressure of from 150 m.m. to 500 or 600 m.m. and its quantity may reach 20 or 30 c.cm. Increased quantity of albumin (Globulin) is found; microscopically meningococci are seen in polymorphonuclear leucocytes; and in chronic cases lymphocytes may sometimes be present in excess. The organisms may also be found free in the cerebro-spinal fluid.

2. *The abortive forms* are of two kinds viz.

(a) Those cases which do not progress further than the septicæmic stage and then get better within 24 or 48 hours before any meningeal symptom arises. This is known as "Intermittent type" and has been observed in many epidemics and is recognised by Von Zeimssen and Stille. It is characterized by daily rise of temperature or it may be remittent or intermittent in character. The pyrexia resembles that of pyæmia rather than that of malaria.

(b) Mild cases with both kinds of symptoms. The attack sets in with great severity but in a day or two the symptoms subside and convalescence is rapid. Strimpell reports a case in which meningeal symptoms set in with the greatest intensity and persisted for four days, the temperature rising to 105.6°F. On the fifth day the patient entered into a rapid and too satisfactory convalescence. Relapses are apt to occur in this form.

(3). *The fulminating type* which is known as "Apoplectic" type begins with maniacal symptoms or the patient may suddenly become unconscious. This generally occurs in epidemics but sporadic cases of this type have also been noted. The onset is sudden usually with

violent chills, headache, somnolence, spasms of the muscles, great depression, moderate elevation of temperature and feeble pulse which may be as low as fifty or sixty per minute. In some cases, even at the onset there may be collapse, vomiting and severe head-ache and sometimes diarrhoea and a purpuric eruption with large hæmorrhagic areas; whereas in certain cases there may be no meningeal symptoms at all, the patient remaining sensible to the end. In other cases coma rapidly comes on. In the epidemic of 1818 in Philadelphia a young girl, apparently quite well, died within twenty hours of this form. Stille reports a case of a young child who died within ten hours of illness; Gordon mentions a case in which the entire duration of the illness was only five hours. Similarly Viessieux reports about two of his cases who died within twenty-four hours. At Agra, in the last epidemic, a young son of an English professor died within six hours of his illness—prior to that he was quite well; a personal case of mine died within 12 hours of the onset of the disease—before that he was healthy and at work.

4. *Chronic Forms* :—(a) purely septicæmic—may not be recognised for days. It may last for weeks with periodic rise of temperature resembling malaria, with joint pains, orchitis and various skin rashes. Sometimes it may show definite meningeal symptoms.

(b) Encysted and loculated meningitis due to the shutting off by adhesions of some of the space containing cerebro-spinal fluid. This kind is generally sporadic and occurs in children. It is known as "Posterior Basic Meningitis". It is differentiated from other adult forms by :—

- (i) the chronicity of the disease,
- (ii) the rarity of skin eruptions,
- (iii) loss of vision quite early in the disease without visible retinal changes or optic neuritis,
- (iv) the rarity of deafness, there is often hyperacuity—the child screaming at the slightest noise,
- (v) the prominence of opisthotonos due to the flexibility of the spine,
- (vi) the bulging of the fontanelle from increased intracranial pressure,
- (vii) Kernig's sign is rather inconstant at first, but it usually occurs late in the disease.

The course of this form is most uncertain. The patient may be in semiconscious state for weeks; at first of course, well nourished but later he begins to waste. Complete recovery may take place, or hydrocephalus, cerebral diplegia, mental deficiency or deaf-mutism may result.

Clinical Stages

There are four recognised stages of this disease.—

1. Prodromal.
2. Irritative.
3. Depressive.
4. Paralytic.

1. *Prodromal Stage*.—The invasion is sudden, there is malaise, head-ache, loss of appetite, intolerable pain in the back of the head and neck extending down the spine, vertigo and purposeless vomiting.

2. *Irritative Stage*.—Noisy delirium and retraction of abdomen are characteristic. Petechial rashes may appear within first three days; herpes labialis is common. There is often intense hyperæsthesia. The head is strongly retracted; the limbs and the trunk are rigid, causing opisthotonos or orthotonos. Tetanoid convulsions may occur.

3. *Depression Stage*.—The temperature is irregular, ranges between 102° to 103° F. The pulse varies similarly and becomes slow. The skin may be either cold or warm. Pupils are contracted and unequal. Optic neuritis is present. Retraction of head is more marked. *Tache cerebrale* present. Respiration becomes irregular, bowels constipated and urine becomes scanty.

4. *Paralytic Stage*.—There may be hemiplegic paralysis of one or more limbs. Exhaustion and emaciation are rapid. Pupils are dilated, the body is covered with perspiration, involuntary micturition and defecation take place and typhoid stage is established; anæsthesia takes the place of hyperæsthesia and the patient becomes stupid, comatosed and then quickly succumbs. If he survives at all the symptoms subside only slowly, and convalescence is long and perilous.

Course and Duration

It is extremely variable. Hirsh rightly states that it may range between few days and

several months. Nearly half or more of the deaths occur within the first five or six days; recovery is heralded by the disappearance of all objective and subjective signs of meningitis. A sudden fall of temperature is a bad omen. Convalescence is extremely tedious and may be hindered by complications which may arise from time to time during the course.

Diagnosis

To make a correct diagnosis in cases of Cerebro-Spinal Fever we have to see many things and have to depend mostly on laboratory findings.

(a) *Clinical Features*.—Fever, persistent headache, delirium, retraction of the neck and severe pain on the nape, tremor and rigidity of the muscles, presence of Kernig's and Brudzinski's signs are the special clinical diagnostic features.

(b) *Laboratory Diagnosis*.—

(1) examination of blood—marked leucocytosis (Polymorphonuclear). 40,000 to 60,000 per c.m.m.

(2) examination of the cerebro-spinal fluid—when the fluid is taken out of the spinal canal it runs, as a rule in normal cases, by drops but in cases of meningitis it gushes out freely under pressure. The pressure is as high as 250–300 m.m. The fluid in such cases is turbid, sometimes purulent, occasionally bloody, and contains a fair amount of albumin. "Meningitis may be present with a clear fluid also" (Osler). In such circumstances, as Flexner wisely advises, we have to examine the nasopharyngeal secretion where the germs are sure to be found. When the fluid is examined microscopically meningococci are found in abundance either free or inside the polymorphonuclear leucocytes. Fluid may also be taken out from the cerebral ventricle directly.

(3) cultural examination :—it is a sure test and should be done either with the cerebro-spinal fluid or with nasopharyngeal discharge. It is done either on agar-agar or in blood-agar.

CHARACTERS OF CEREBRO-SPINAL FLUID

	Normal	Tuberculous Meningitis	Septic Meningitis (Meningococcus)
Colour	Clear and colourless	Clear at first, fine cobweb coagulum on standing	Hazy, turbid or purulent, clot on standing
Protein	About 0.002 per cent.	Increased upto 0.3%	Increased upto 0.3%
Sugar	0.05 to 0.07 p. c.	Diminished	Diminished or absent
Chlorides	0.73 p. c.	Always reduced; may be below 0.6%	Definitely reduced; usually between 0.7—0.6%
Cells	Occasional lymphocytes upto 5 per c.m.m.	Increased 10-400; 75% lymphocytes	Greatly increased; mainly Polymorphonuclear—40,000-60,000 per c.m.m.
Organisms	...	Tubercle bacilli in clot	Organisms can be discovered in dried films, usually meningococci.

Differential Diagnosis:—such diverse conditions as typhoid, pneumonia, Influenza, typhus, relapsing fever, plague, heat-stroke, scarlet fever, small-box, tubercular meningitis and bilateral otitis interna have been confused with this disease. The meningitic form of poliomyelitis may closely resemble meningococcic meningitis. Diagnosis depends on the examination of the spinal fluid which is usually clear or faintly turbid with lymphocytes in predominance in poliomyelitis. Polymorphonuclear leucocytes may at first be increased but promptly diminished.

1. **Typhoid Fever.**—In typhoid fever patient is dull and apathetic, while in meningitis extreme sensitiveness to sound is well marked. In typhoid, sordes are collected in nose or lips while in meningitis the patient is restless and often pricks his nose. In meningitis, hyperalgesia is common while it is absent in enteric. In meningitis, deep reflexes are exaggerated while in typhoid they are not; besides Widal's test and Diazo-reaction of urine clinches the diagnosis.

2. **Tubercular Meningitis.**—It is caused by bacillus tuberculosis; it occurs in childhood and is generally primary; in adults, it is always secondary and affects the base of the brain; prodromata are well marked and take several weeks to develop symptoms. Von Jaksch asserts that albumosuria is present in epidemic cerebro-spinal meningitis and absent in tubercular meningitis, and that it is a positive differential sign of the former disease if no ulceration of the lung is present. Examination of blood and cerebro-spinal fluid will confirm the diagnosis.

3. **Apical Pneumonia:**—It is common in children and is characterised by delirium; but the altered ratio of pulse and respiration and

other physical signs will settle the question. Leichtenstern states that in meningitis following pneumonia, contraction of the muscles of the neck is absent, while in epidemic meningitis it is almost invariably present. Pneumonic meningitis soon leads to delirium and coma, while in epidemic form the sensorium may be normal throughout the entire course. Pneumonic-meningitis is more rapidly fatal than epidemic meningitis.

4. **Influenza:**—In Influenza there is intense head-ache at the very beginning which gradually subsides while in meningitis the headache gradually gets worse. Irregular fever, prostration, vomiting and liability to cardiac failure are to be taken into account.

5. **Bilateral Otitis Interna.**—Pain is very intense but there is no rapid emaciation.

6. **Acute Miliary Tuberculosis.**—The peculiar dyspnoea, the cyanosis, the profuse sweats and the diffuse pulmonary signs render its diagnosis possible.

7. **Malignant form of Small-Pox.**—Fever with persistent vomiting and backache are present in both, but typical eruptions of small-pox coming in course of time settles the diagnosis. In meningitis pulse is comparatively slow whereas in small-pox it is rapid.

Complications and sequelæ

Lungs.—Pleurisy, bronchitis and pneumonia are not very uncommon. Immermann found many cases of cerebro-spinal fever with pneumonia but Chopra and Chadha report that out of 22 cases in Borstal Institution, Lahore, only one developed pneumonia and the patient died within 48 hours. Many authorities are of opinion that pneumonia is due to pneumococci but Councilman suggests that the pneumonia of this disease is not the true croupous form but due to the diplococcus meningitis.

Heart.—Endocarditis and pericarditis may also occur.

Joints.—Arthritis and synovitis have been the most frequent complications in certain epidemics. James Jackson says that one or more joints may be affected simultaneously, and there are swellings over joints, pain and exudation—sometimes serous, sometimes purulent. Out of the 22 cases of Chopra and Chadha only 4 got involvement of the joints. In case of knee-joints with effusion, repeated aspirations and injections of 10 c.c. of Anti-meningococcus Serum into the joints resulted in rapid improvement and disappearance of all joint symptoms.

Eye.—Optic neuritis, purulent conjunctivitis, choroido-iritis, and even keratitis and diplopia are not very uncommon. Randolph found acute papillitis in 6 out of 40 cases. H. Zweig reports two cases of "Metastatic Ophthalmia," which according to Uhtoff, occurs in 4 to 5 per cent of all cases of meningococcic meningitis. A characteristic feature of the condition, which was illustrated in these two cases, is that it occurs in quite mild attacks and therefore may perhaps be regarded as a favourable sign. In one of the cases, iridocyclitis was the only sign of the meningococcic infection. Zweig supports the theory of a hæmatogenous origin of the ophthalmia on the ground that retrolubar signs are absent in cases which come to autopsy. In most cases on record, enucleation of the eye has been performed and on microscopical examination the eye shows the presence of meningococci in extremely large numbers. The case reported by S. Mclean and H. A. Gilmartin in a girl, aged 18 months, in which purulent left iridochoroiditis developed, was remarkable for the fact that there was complete restoration of vision. The favourable result was attributed to meningococcic serum having been given intravenously as well as intrathecally.

Ear.—Otitis media with mastoiditis, parotitis, and deafness which may be due to the inflammation of the labyrinth. Von Zieusseux states that in the Deaf and Dumb Institutions of Baunberg and Nuremberg in 1874 majority of the pupils had become deaf from epidemic cerebro-spinal fever.

Nose.—Coryza is not very infrequent—nasal catarrh always precedes the case of meningitis (Striimpell).

Nervous Complications.—Persistent and severe headache, vomiting, loss of consciousness, convulsions and involuntary discharges of fæces and urine (Von Ziemssen). Paralysis

and peripheral neuritis may also result (Mills).

Testicles.—Orchitis and epididymitis may also occur. Sabrozes de Grailly, and Imbert report a case of a man, aged 40, whose attack, in spite of treatment by polyvalent antimeningococcic serum, was complicated by panophthalmia, suppurative arthritis and double orchi-epididymitis. The last complication did not cause any permanent impairment of testicular function, as when the patient's semen was examined six years later, it was found to be quite normal in every respect, which is in contrast to what occurs after double orchitis due to syphilis, gonorrhoea, tuberculosis or mumps.

Few interesting cases

In the cases reported by Achard, Bloch and Marchal in a girl of 8, the insidious and protracted onset suggested tuberculous meningitis; but repeated examinations of the cerebro-spinal fluid for tubercle bacilli were negative, whereas the abundance of polymorphonuclear leucocytes in spite of the scarcity of meningococci in the fluid apparently justified the diagnosis of cerebro-spinal fever. As there was no improvement in the general condition after three days of serum treatment, and as the severity of the symptoms were in contrast with the scantiness of the meningococci, intraventricular injection of anti-meningococcic serum was employed. The ventricular fluid differed from the spinal fluid in containing more meningococci, but showed only a few leucocytes. Death occurred a few hours after intraventricular injection, and the autopsy showed, in addition to a serous exudation, granulations in the meninges in which tubercle bacilli were found, and also miliary tubercles in the lungs.

Ernst reports a case of the association of cerebro-spinal fever and typhoid fever in a boy, aged 13, who was admitted to hospital with well-marked signs of cerebro-spinal fever, the diagnosis being confirmed by the presence of meningococci in the cerebro-spinal fluid. The suspicion of typhoid fever was at first dismissed owing to a negative "Widal Reaction" but on the admission of the patient's brother a few days later with undoubted typhoid fever, a blood culture was made which showed typhoid bacilli, although the "Widal Reaction" was again negative. The autopsy confirmed the diagnosis of concurrent cerebro-spinal fever and typhoid fever, several typical ulcers being found in the lower end of the ileum and cæcum. The negative Widal Reaction in spite of the intestinal ulcers having

nearly reached the stage of cicatrization is perhaps to be attributed to the cerebro-spinal fever interfering with this agglutination. The blood picture, however, showed well-marked lymphocytosis, absence of eosinophils, and a total leucocyte count of 9800 only which was in favour of typhoid fever.

The association of meningococcic and the tuberculous meningitis has recently been recorded by Vialard, and by Achard, Bloch and Marchal. Vialard's case occurred in a soldier in whom the meningeal symptoms had a sudden onset. No improvement followed intrathecal injection of serum, vaccine treatment or fixation abscess. The cerebro-spinal fluid remained clear and contained polymorphonuclears and lymphocytes in almost equal proportion as well as meningococci, but no tubercle bacilli were discovered during life. On post-mortem examination, miliary granulations were found in the cerebral meninges containing both tubercle bacilli and meningococci. There was also a tuberculous cavity in the left lung.

Prognosis

In children the death rate is higher than in adults. Hirsch states that the mortality varies from 20 to 75%. The earlier the Serum is given the better the out-look but the mortality is very high at the very beginning of the epidemics. It nearly always leaves some permanent defects in the patients. According to S. Mclean and J. P. Caffey, before the introduction of anti-meningococcus serum, the mortality of the disease in the 1st year of life approached 100 percent whereas approximately 50 percent of the children of this age treated by them with serum at the Babies' Hospital, New York, recovered; and among the children between the ages 1 and 5 years the recovery rate was 85%. Forty four cases which had been treated by serum were followed up for a period ranging from one to ten years. In 9 cases the following serious sequelæ were observed: deaf-mutism in 4, hydrocephalus in 2, visual impairment in 2 and mental deficiency in 1; 5 patients died during the period of observation while 30 were alive and normal in every respect.

Appelbaum reports a case of concurrent meningococcus and paratyphoid B infection in a male infant aged 7 months who was taken suddenly ill, with high fever, followed by convulsions and attacks of projectile vomiting.

Zoeller records a case of relapsing cerebro-spinal fever in a young sailor in whom the disease ran its course in three stages.

Jonsset and Delalande report a case of meningococcal infection accompanied by renal and meningeal hæmorrhage.

Prophylaxis

Prevention is better than cure and so we must devise means and ways by which we can protect ourselves from such fatal diseases. As the infection is droplet in character and therefore, for infections of this kind, a close contact is generally necessary. The meningococci are organisms of very low resisting power and die outside the body in an amazingly short time; so generally the infection is carried either by carriers or by the patients suffering from mild abortive type who are going about unnoticed in the community for days together. The following preventive measures are usually adopted.

1. *Isolation of the sick*.—the patient should always be sent to the Infectious Hospital and if that is impossible, he should be kept separate in an airy room under strict hygienic conditions. Isolation should be maintained for at least 3 weeks after the cure.

2. *Contacts and carriers should always be segregated*.—Students who have been in contact with patients of this disease should be excluded from the school for at least three weeks.

3. During the epidemics, every one should be advised to have much *fresh air and exercise*. Nose and throat should be sprayed twice daily with some antiseptic lotion such as potassium permanganate, 1 in 1,000 or E.C. 1 in 500 or a solution of iodine and glycerine or 1% solution of peroxide and if nothing is available, salt solution is quite sufficient. Carriers are effectually disinfected by the use of chloramine-T. 2% solution of this is sprayed into a small chamber or inhalatorium and then the carrier is placed in this room for a period of not exceeding twenty minutes. He is then quite free from organisms. Spraying with dichoramine-T in oily solutions is also very profitable.

4. *Protective inoculations* with stock serum should always be taken during epidemics. The quantity depends on age and health of the subject but generally 5 to 20 c.c. is quite enough. In view of the fact that prophylactic injections of Anti-meningococcic vaccine have seldom been employed on a large scale, special interest attaches to a paper by Calbairæ, although the results are not absolutely conclusive, owing to the slight contagiousness of the disease. After an epidemic of cerebro-spinal fever (which in a few days killed 13

out of 18 cases) Calbairæ carried out a series of injections on 1850 men. Two injections were given, the first consisting of 1 c.c. of vaccine and the second of 2 c.c., five to six days later. When all the vaccinations were complete, no further cases of cerebro-spinal fever developed.

5. *Avoidance of over-crowding*.—during epidemic, all the over-crowded areas should be vacated under supervision. School and college classes should be held in open air or in verandahs. Workers should also be allowed to remain at a sufficient distance from each other so that they can avoid infection through sneezing, coughing, etc. Cinemas, theatre halls and other places of public amusements should be closed during epidemics. These things should be brought into action strictly in prisons, asylums, convents, hostels and such places.

6. Drains, latrines, dust-bins, streets and lanes should be cleaned twice daily. Phenyle or calcium hydroxide (lime) should be sprinkled over them.

7. Lectures should be delivered by the Health Authorities and public men regarding the utility of prophylactic measures. Leaflets should also be distributed showing the dangers of haphazard spitting, sneezing and coughing in the presence of others.

8. In hospitals, visitors should be reduced to a minimum and those who come at all should be advised thoroughly.

9. The clothing etc., of the patients should be washed with chlorine lotion and then dried in the sun and if possible, all the cotton clothes should be boiled before they are to be used.

10. The utensils especially drinking vessels, etc., should be cleaned thoroughly with boiling water. Common drinking vessels which are very common among Muhammadans should strictly be prohibited.

11. Phenyle cups should be provided in institutions at various places and the inmates should be requested to spit into them only and not out-side here and there.

Treatment

As soon as the case is diagnosed as cerebro-spinal meningitis the patient should be isolated at once and should be kept as quiet as possible, handled gently and all sources of external irritation removed. Special care of the skin should be taken so that bed sores may not develop. Ice bags should always be applied to the head to avoid cerebral irritation and to bring down temperature if it is high. The bowels are to be opened by calomel and saline

purges and laxative or enemata used later, if necessary. Morphia injection is the best for severe head-ache, general pains or vomiting. In olden days, leeches to the nape and blisters on the spine were applied. Now, of course, it is not very widely practised. Sixty grains of hexamethylenamine per day, may be given as a routine. Chloral or bromides may be useful for the pains and convulsions.

The strength of the patients should be kept up as much as possible by judicious feeding. The diet should be given at short intervals. If swallowing is difficult, the patient can be fed through a tube. Water should be given freely. Fresh fruit juice is very beneficial.

Serum Therapy

As soon as the case is suspected to be one of cerebro-spinal meningitis, 20 to 30 c.c. of anti-meningococcic serum (polyvalent) should be injected intramuscularly; but some authorities are of opinion that intravenous injection should be given. Without losing any time, lumbar puncture should be done and about 10 to 20 c.c. of cerebro-spinal fluid withdrawn, and then examined bacteriologically. If the result is positive, intrathecal injection of the serum should be given. 20 to 30 c.c. of serum is administered intrathecally but before giving injections take out equivalent or a little more amount of cerebro-spinal fluid than the quantity of serum to be injected. Intrathecal injections should be repeated every 24 hours until the patient's condition shows improvement and the cerebro-spinal fluid is found to be free from meningococci. If it is found possible to find out the predominating type of the meningococci, one can as well try to give monovalent serum, or anto-vaccine but if that cannot be done one should not hesitate to use stock serum. Average amount of serum required per head is about 100 to 250 c.c. but there are cases in which we may have to use up to 600 c.c. in all.

In some cases serum reaction has been noted; judicious precautionary measures should therefore always be taken to avoid any untoward results. Injections are continued until the spinal fluid becomes and remains sterile. Turbidity of the fluid may result from meningeal irritation by the serum; this does not necessarily indicate continued infection. Where doubt exists, it is far better to give too much than too little serum. The needle should not be removed for several minutes after serum administration to facilitate the withdrawal of serum in the event of alarming respiratory failure which occasionally follows the procedure. This generally does not happen

if sufficient amount of cerebro-spinal fluid is taken out before serum administration. Cases have been noted in which about 90 c. c. of the fluid is taken out in one sitting.

Sometimes, a dry lumbar tap is met with indicating spinal blockage which necessitates introduction of the serum directly into the cisterna-magna. This cisternal injection may prevent the formation of fibrous adhesions in the fourth ventricle; irrigation of the theca with normal saline or 3.8 per cent sod. citrate has been of value in preventing adhesions. When adhesions have already been formed and the intracranial contents are shut off, the lateral ventricles may be tapped and serum injected. In children this can easily be done through the anterior fontanelle. Cases of cerebro-spinal fever cured by intraventricular injection of anti-meningococcic serum after trephining the frontal region so as to reach the anterior base of the lateral ventricle have been recently recorded by Sicard and Achard, Marchal and Laquiere.

Intravenous administration should never be omitted when signs of septicæmia are present. It is frequently advantageous to combine the two methods, intrathecal and intravenous. Serum should always be introduced at blood heat and slowly. Failure of serum therapy to bring about clinical improvement may be due to three factors:—

1. Serum not potent,
2. Serum used may not correspond to the type of the prevalent organism.
3. Fibrinous loculation of meningeal infection mechanically prohibiting serum activity.

In posterior basic meningitis, intrathecal injections of serum are also given in suitable doses. L. Merle records a case of meningococcal septicæmia in which, though serum treatment had a good effect on meningitis, yet the septicæmia was not affected thereby. Rapid recovery, however, took place after injection of an auto-vaccine. On the other hand, in a case of pure meningococcus septicæmia reported by L. Birdin, no benefit was derived either from serum or vaccine therapy, but rapid recovery followed treatment by a "Fixation abscess" produced by an injection of 1.5 c.c. of Turpentine. O. Buss records three cases in children (12, 13 and 14 years old respectively) in whom no improvement occurred in spite of daily intrathecal, intravenous and intraventricular injections of anti-meningococcic serum for three weeks, but rapid recovery took place after four intrathecal injections of "Dispargen" (Colloidal

Silver). Intravenous and intrathecal injections of mercurochrome and acriflavine have also been successfully tried in some cases. But nothing definite can be said at present about the use of these drugs owing to the paucity of published records. It has been reported that in Moscow the Soviet Doctors have prepared a specific vaccine for the treatment of this diseases; but we do not know any details about it.

Technique of Lumbar Puncture

The method is a very simple one. A stout antitoxin or exploring needle is selected and sterilized by boiling and the skin, in the region of the third and fourth lumbar inter-spaces (the spinous process of the fourth vertebra is on a line joining the iliac crests), is to be carefully purified. The patient sits or lies with the body well flexed. The needle is then inserted in the fourth interspace, either in the middle line or a third of an inch from it; it must be pointed forwards, with a very slight inclination upwards. In most cases the needle will go straight into spinal canal below the termination of the cord, and the fluid will begin to escape. If bone is encountered, it is advisable to withdraw the needle and re-insert it at a slightly different angle. In cases of repeated failure the third interspace may be tried. Under ordinary circumstance the fluid escapes quietly drop by drop, but in cases of increased tension it may gush out freely.

Normal cerebro-spinal fluid is slightly alkaline and as clear as water, with a specific gravity of 1006 to 1008, it contains a trace of globulin (not more than .025 per cent) and of a copper reducing substance, and perhaps a few lymphocytes. In normal adult persons about 100 to 130 c.c. of the cerebro-spinal fluid is present.

Technique of Sub-occipital Puncture

This method of withdrawal of cerebro-spinal fluid is through the occipito-atlantal ligament which stretches from the posterior rim of the foramen magnum to the corresponding part of the lamina of Atlas vertebra. In this way we withdraw fluid directly from the cisterna-magna. As can be readily understood, owing to the close proximity of the fourth ventricle which lies in the floor of the cistern, we do not adopt this route rashly or as a routine method of obtaining cerebro-spinal fluid. It should be done under the following conditions, viz:—

- (a) in compressive lesions of the spinal cord, where a comparison is to be made between the composition and pressure of the fluids above and below the level of compression.

- (b) For the purpose of introducing lipiodol to see whether it falls to the bottom of the sac in the sacral region or whether it is held up at a higher level owing to mechanical obstruction between the theca and the spinal cord.
- (c) For therapeutic purposes where curative sera into the cerebral arachnoid space is to be introduced as in certain varieties of meningitis.

First, the position is located after thoroughly sterilizing the part and then the needle is inserted with great care. If it is obstructed by any portion of the bone it should at once be taken out and again tried at a different angle.

Ventricular Puncture

Like cisternal puncture, this procedure requires considerable technical dexterity and

should be reserved for exceptional cases. Sometimes it is of the utmost value both for the purpose of diagnosis and of treatment—thus for example, inflammatory affections, acute or chronic, of the nervous system, as in meningococcal, tuberculous, or syphilitic meningitis. It is a painless operation, only local freezing of the scalp is all that is required as an anaesthetic, even in the case of children. The mark on the scalp and cranium made by Purves-Stewart's Drill is only about the diameter of a large pinhole. As a matter of fact, within a few days after such a puncture it is impossible to detect any mark whatever, whether by the eye or by palpation of the patient's head. If a subsequent puncture is to be done, it is necessary to make a fresh drill hole.

EDITOR'S SUMMARY

The writer gives an exhaustive and comprehensive survey of the existing literature on the disease.

He traces its history briefly and points out its increasing incidence in our country during recent times.

Symptoms and differential diagnosis are also described. Prophylaxis consists of isolation of the sick, treatment of the carriers by gargles, sprays and vaccine inoculation. The results of the last are still undetermined.

Apart from symptomatic treatment, the specific treatment consists of the administration of autogenous sera or vaccine, if possible, or stock polyvalent sera in any case. He lays stress on the fact that the serum should be given in sufficient daily doses till the spinal fluid is free from the incriminating organism. It must be given early and by intrathecal route; and intravenously also if there is septicæmia. He also stresses on the fact that the quantity of c. s. fluid withdrawn should at least be equal to the quantity of serum to be given. He describes briefly the technique of spinal, cisternal and ventricular punctures, the latter being reserved for cases where there is spinal blockage.

Cerebro-spinal Fever— A Synopsis

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Synonyms.—Epidemic cerebro-spinal meningitis, spotted fever, malignant purpuric fever, petechial fever etc.

Definition.—It is an acute infectious disease occurring in epidemics as well as sporadically caused by the meningococcus, and is characterised by the inflammation of cerebro-spinal meninges locally and followed by general meningococcaemia.

History.—The disease made its first appearance in 1805 in Geneva in small epidemic form. In the period from 1805 to 1830, there were isolated epidemics in Europe and America. Between 1837 to 1850 there were severe epidemics in both the places. During the period 1854 to 1875 it spread to some parts of Asia and Africa. A few outbreaks of this epidemic occurred upto 1907 in British Isles and other places. During the period of late war some epidemics occurred in England, France, America and India. Since then, epidemics have been noted in all parts of the world, but the disease is more prevalent in temperate zones. Countries more affected in the East are Asia Minor and India. Cerebro spinal fever has been first noticed in India in 1878; about 4 cases occurred in Bombay. Some sporadic cases occurred in 1885. In 1881, during cold season, in Shikarpur Jail, few cases occurred in Sind. In 1881 cases were reported all over India in various jails, army barracks, etc. In Bombay proper,

some cases were first admitted into the City Isolation Hospital in 1912. Upto 1920 about 32 cases have been reported. These cases were diagnosed first from clinical signs but there-after by lumbar puncture and examination of the cerebro-spinal fluid for presence of meningococci. The disease commonly occurs in jails, army barracks, overcrowded localities, and in

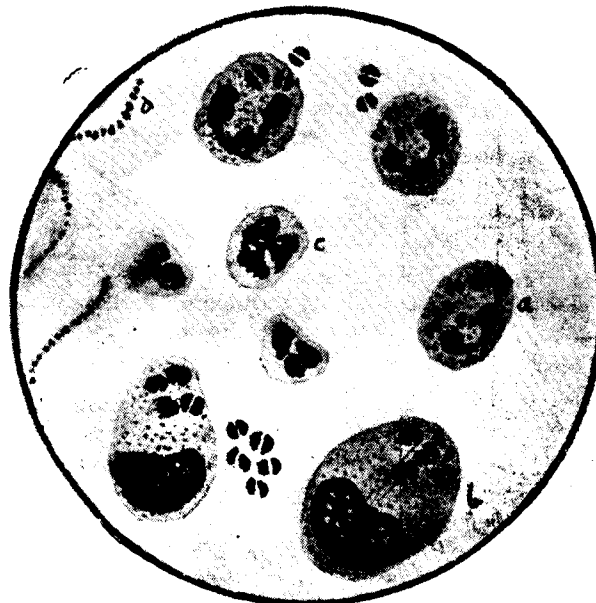
such places where people congregate in large numbers.

Etiology.—It is a winter-born disease. Most cases have been seen occurring during winter and spring. Sudden variations of temperature appear to be a predisposing factor. Over-crowding, exposure to cold, starvation, catarrhal conditions of the upper respiratory passages, poverty and over-exertion are the predisposing factors.

Age.—In epidemics, no ages are exempt. Children and young adults were the common sufferers. Females too contract the disease, though their number may be small in comparison to children and young adults. Old people also suffer from the disease.

Epidemics are of common occurrence more in big cities than in villages, as large slums and overcrowding exist under urban conditions. The cases occurring in sporadic form amongst children are known as post basal meningitis.

Occupation.—All classes are affected. Mostly poor people, mendicants, bhaiyas,



DIPLOCOCCUS INTRACELLULARIS MENINGITIS

Cocci about 1 micron in diameter, arranged in pairs, apposed surfaces are flattened.

- a. Polymorphonuclear Leucocyte.
- b. Mononuclear Leucocyte.
- c. Pus Cell.
- d. Streptococci

pathans, labourers, and such others who expose themselves to the cold weather conditions during their work may contract this disease. Medical attendants, nurses and others who come in contact with the patient or with the infected material may also contract this disease.

Bacteriology.—The responsible organism is a meningococcus, first found in 1887 by Weichselbaum.

Synonyms.—(a) Micrococcus meningitis.

(b) " intracellularis meningitidis.

(c) Diplococcus intracellularis meningitidis.

Morphology and cultural characters.—**Size.**—It is a small coccus about 1 micromillimeter in diameter. It occurs in pairs with flattened sides apposed and is found either free or within polymorphonuclear leucocytes in the fluid or exudation. It is a non-motile, non-spore forming gram negative organism. It requires an optimum temperature of 37°C for growth. It does not grow well on ordinary media; it requires blood serum or ascitic fluid for its proper growth. Its optimum reaction is neutral to phenolphthalein. Colonies appear as moist grey circular discs about 2 m.m. in diameter; later, its centre becomes opaque and periphery remains transparent. There are four main types of meningococci recognised, according to their agglutination and absorption reactions. It is difficult to identify the different strains as their reaction depends upon the type of serum available for the test. The type of organisms in cerebrospinal fluid and in mucous membrane of the naso-pharynx are generally the same. Organisms have been found in blood in septicæmic cases. Organisms are most commonly found in cerebro-spinal fluid, in naso-pharynx and meninges, and rarely found in conjunctivæ and in secretions from broncho-pneumonia. Meningococcus has been found in the naso-pharynx of certain contacts and healthy carriers. Intraventricular or intrathecal injections of the organism may produce in monkeys the same condition as occurring in man. Mice, guinea pigs, rabbits and even dogs when injected intravenously or intraperitoneally suffer from this fatal disease.

Path of infection.—It is said that the infection primarily starts from the naso-pharyngeal mucous membrane and reaches the meninges through the sphenoidal sinus. It is also said that the infection may be conveyed to the meninges, via, blood or lymph; but this has not yet been proved.

Morbid appearances.—Brain and spinal cord are extremely congested, pia mater and arachnoid are intensely injected and thickened. Fibropurulent exudate found at the base of the brain. Lymph deposits along the largest fissures of the cortex and purulent exudation present in the sulci. Cord is always involved with the brain. In dorsal and lumbar region, exudate is more in abundance. The cerebral ventricles are dilated and contain turbid pus and at times pure pus. Brain substance is softened, and hæmorrhagic areas are noticed. Cranial nerves and the roots of spinal nerves are involved and are embedded in the exudations. The exudate shows numerous diplococci and an increase of polymorphonuclear leucocytes. Nasal secretion may reveal presence of diplococci. Sphenoidal air sinuses may contain pus. Spleen enlarged, kidneys congested and acute nephritis present.

Meningococcal Carriers.—These carriers, perhaps, play an important part in spreading the disease, especially when the incidence of carriers is high.

(a) Temporary carriers.

(b) Chronic carriers.—these harbour organisms for long time, for weeks or months. The carriers themselves may develop the disease.

Onset.—The onset is usually abrupt.

Incubation Period.—not certain but it varies from 24 hours to 7 days. It may even be some months.

Premonitory symptoms.—Headache, pain in the back, stiffness of the neck, photophobia, loss of appetite; vomiting may or may not be present. At times vomiting is persistent. Temperature rises to 101° to 102°F. or more. Pulse: full and strong. Patient is greatly sensitive to noises. Children become irritable and restless. There is opisthotonos or orthotonos, retraction of the head is marked. Pain is present in the back and limbs. Spasmodic contractions of the muscles of the leg and arms occur. Stiffness and rigidity of the neck muscles is present and head is drawn to such an extent that occiput rests between shoulder blades.

Strabismus or squint is of common occurrence. Ptosis is also present. Paralysis of the muscles of the eye and face may occur. Hyperæsthesia or increased sensitiveness over the spinal area may be detected. Headache is persistent from the onset and is of the occipital type. Delirium occurs from onset; low muttering type to furious maniacal type. It ends in stupor and if effusion increases, the patient becomes comatose.

Temperature.—Is irregular. Remissions are frequent. In some cases fever is absent. At times temperature goes very high. Pulse: full and rapid or slow about 50 to 60 per minute. In some cases it is imperceptible.

Respirations.—Are sighing. In fatal cases cheyne-stroke breathing develops. If any lung complications are present, respirations are increased in frequency.

Cutaneous symptoms.—Herpes occur on the angle of lips as in case of other infectious fevers. Petechial rash is seen in some cases, hence it is termed as spotted fever. Dusky mottling is seen on the skin, over arms and fore-arms, abdomen, faces, etc. It is roseolar or bronze-coloured in some cases. Urticaria is occasionally present. Gangrene of the skin may occur.

Digestive system.—Vomiting frequent at the onset; but it gradually subsides. In some cases it persists. Bowels usually constipated. Diarrhoea is present in bad toxic cases. This is not good from prognostic point of view, if it persists in spite of treatment.

Urinary system.—Quantity of urine may be increased or diminished. It may contain albumin in some cases. Glycosuria present in some cases. Haematuria in malignant cases.

Duration of the disease.—This varies from few hours to some days or months. In bad cases, death occurs within four to five days. In favourable cases improvement is noticed, temperature returns to normal, and other symptoms are relieved. Sudden crisis or fall of temperature is a bad omen. Convalescence is prolonged and tedious.

Types of the disease :—

1. Abortive type.
2. Intermittent type.
3. Chronic type.
4. Septicæmic or malignant or fulminating type.

1. **Abortive type.**—Onset is sudden with severe symptoms for a day or two. Symptoms subside after first lumbar puncture and convalescence is rapid.

2. **Intermittent type.**—The temperature rises every second or third day along with other symptoms and it is more characteristic of pyrexia of pyæmia.

3. **Chronic type.**—The disease lasts for several months and passes into a chronic stage. The blocking of the foramen of magendie occurs and a condition of hydrocephalus develops. Other symptoms persist in spite of treatment;

abscess of brain may form; ventricles are dilated and contain fibro-purulent exudation. Meninges are thickened and adhesions may occur. Cerebral walls get thinner as a result of internal tension. In such cases, prognosis is always grave.

4. **Septicæmic or fulminant or malignant type.**—Onset is sudden with violent symptoms followed by unconsciousness. Fever may be high or moderate with low feeble pulse. Delirium may be present in early stage, from violent to maniacal type. If patient is not regaining any consciousness, he dies within 24 hours. In this type rash is more marked. It occurs as purpuric form of eruptions. There is generalised blood infection known as meningocococæmia. Rash appears within few hours of onset and is scattered over the body. It is more abundant on hips and extends over surfaces of the limbs; hence the disease is termed as spotted fever. Cardiac and lung complications are more frequent in this type of the disease.

Diagnosis

Points for diagnosis.—

1. Sudden onset.
2. Occipital type of headache.
3. Persistent vomiting.
4. Irregular rise of temperature with chills.
5. Pain in the region of the neck down the spine. (There is increased sensitiveness in the spinal area.)
6. Rigidity and stiffness of the cervical muscles.
7. Retraction of the head.
8. Kernig's sign.
9. Brudzinski's sign.
10. Lumbar puncture and subsequent examination of the fluid for the presence of the meningococci. This is a valuable and reliable diagnostic method. It can be done with or without general anaesthesia or under local anaesthetic.

Characters of the Cerebro-spinal Fluid

In case of meningitis it rushes under pressure; quantity may be increased from 250 to 300 millimeters or high up. Normal amount of cerebro-spinal fluid is 120 m.m. in health. As a rule it is clear under normal conditions. In case of meningitis it is usually turbid; it may be opalescent or purulent or in some cases blood stained. Meningitis may also occur with clear spinal fluid. Polymorphonuclear leucocytes are abundant. In tuberculous forms of meningitis lymphocytes are in excess. Diagnosis can be established by inoculation experiments, agglutination tests and by stained preparations under the microscope.

Prognosis

This is extremely difficult. Patients with hopeless condition may recover at times, while

mild cases may die within a few days. It depends upon the extent of meningeal involvement. Generally fulminant cases die soon. Ambulatory or mild and chronic cases recover. Earlier the treatment is commenced the better are the chances for recovery. Death rate is higher in children than in adults. Yellow, thick, purulent cerebro-spinal fluid is a sign of grave prognosis. Diminution of its amount or a dry tap is also bad. Blood pressure under 100 h. g. in early stage is of grave importance. It suggests intense infection. High blood pressure and nystagmus are grave signs. Intense rash, restlessness, hyperpyrexia and extremely low blood pressure and presence of complications as pneumonia and pericarditis and cheyne-stoke's breathing are all grave features. By early diagnosis and timely commencement of serum treatment, we have been able to reduce the mortality rate to some extent.

Sequelæ

1. Permanent mental or physical disability may occur.
2. Occasional paralysis.
3. Deafness.
4. Aphasia.
5. Blindness.

Treatment

1. Preventive.
2. General Management.
3. Medicinal treatment.
4. Serum.

1. Preventive treatment.—

- (a) Prevent overcrowding. Free ventilation and sufficient cubic space for each individual is necessary as a general prophylaxis in case of any contagious disease.
- (b) As far as possible or practicable, patient should be isolated in a hospital in special part of the hospital and not in a general ward, as chances of infection are frequent.
- (c) Identification of carriers and their isolation and treatment till their nasopharynx are free from meningococci—rather impracticable.
- (d) Treatment of carriers by gargles and nasal spray.
- (e) **Inhalatorium treatment.**—This is tried in America. A room is charged by chloramine T. vapour and persons are exposed to this vapour to inhale for 2 to 5 minutes in this chamber, and afterwards discharged to other rooms. This method of sterilisation by inhalation of Chloramine T. vapour is adopted for general masses as prophylaxis.

General management.—1. Fresh air and careful nursing. 2. **Diet.**—strictly liquid in the

beginning. Milk is allowed in acute stage. Later on, semi-solid diet may be allowed. Nourishment should be maintained throughout the course of the disease. In comatose patients feeding through rectum or nose has to be resorted to. Fruits as sweet lemons may be allowed. Coffee, weak tea, glucose water and such other drinks may be allowed.

3. Turn the unconscious patients frequently from side to side to avoid hypostatic pneumonia and to prevent bed sores.

Medicinal treatment.—Application of leeches or antiphlogistine to the neck relieves pain. If temperature is high ice bag should be applied over the head. Bland liquids and water should be given freely. Hot water bottles should be applied to the loins to relieve congestion of the kidneys. If bowels are constipated in the beginning, calomel and soda bicarb powder followed by a dose of saline purge should be given. If obstinate constipation is present, glycerine or soap water enema may be given. Analgesics and hypnotics such as veramon tablets, luminal, pyramidon, etc. may be given for restless patients. Morphia ($\frac{1}{4}$ to $\frac{1}{2}$ gr.) may be given hypodermically in badly restless patients. *It should never be administered in case of children.* Urotropin in 30 to 60 grains doses three times a day will be useful. Doses may be regulated according to the age of the patient. Salicylates are given internally in case of joint complications as arthritis, etc. Iodides given for the absorption of the exudate at the base of the brain. Mercury in the form of liquor hydrargyri perchloride in small doses acts as antiseptic in early stage of the disease. Treatment of various complications should be given according to their nature. Strength should be supported by suitable tonics. Cardiac tonics as digitalis may be administered to support the heart. If respirations are bad, injections such as of digitalis, strychnine; camphor in oil; musk in ether; cardiazol; ephedrin adrenaline hydrochloride (1 in 1000 solution) may be given. Nasopharynx should be sprayed daily by any suitable antiseptic solution in order to render it free from meningococci and to prevent relapse.

Complications

1. Pleurisy, pericarditis, parotitis.
2. Pneumonia, may be lobar or lobular with oedema of the lungs.
3. Arthritis.
4. Synovitis.—swelling, pain serous or purulent exudation in joints.
5. Epididymitis, common.
6. Chronic hydrocephalus.
7. Aphasia.
8. Peripheral neuritis due to the involvement of the

roots of the cranial nerves. 9. Hiccough (a bad sign). 10. Eye complication: e.g. optic neuritis due to oedema of the optic disc as a result of exudation at the base of the brain. Purulent choroiditis and perforating keratitis as a result of inflammation of the fifth nerve. Purulent conjunctivitis also occurs. 11. Ear complications.—deafness due to inflammation of labyrinth. Otitis media and mastoiditis from direct extension. Deafmutism may occur in children. 12. Nose.—coryza may occur and persons may harbour organisms for some weeks or upto 3 months.

Serum Therapy

It has been observed that earlier the treatment by serum is commenced, the better is the outlook and that high mortality can be prevented. Polyvalent serum should be preferred when specific type serum is not available. It can be injected after lumbar puncture intrathecally. Other methods of administering serum are by intravenous injections or intramuscular injections.

The object of lumbar puncture is to drain the subarachnoid space of its purulent exudation. In the beginning, daily lumbar puncture should be done till clear cerebro-spinal fluid comes out. In fulminating type, the serum treatment has been of no avail.

Dosage.—This is regulated according to the age of the individual. To test anaphylaxis, about 2 to 5 c.c. of serum is at first injected

subcutaneously. To adults, about 30 to 40 c.c. of polyvalent antimeningococcal serum at a time can be administered after lumbar puncture without any ill effects. Serum should be given as a rule in little less quantity than the cerebro-spinal fluid removed. Serum should be injected gently. In children the dose varies from 10 c.c. to 30 c.c. The dose of serum depends not only upon the age but also on the nature of the fluid and quantity drained. In the beginning, for 3 or 4 days, these injections are repeated; if the meningococci are still present in the fluid the injections may be continued. If recovery is to occur, after 4 to 8 punctures the patient recovers. In ambulatory type, after 1 or 2 punctures patient comes round and other symptoms abate. Maximum dose of serum that can be administered is 80 to 100 c.c. intrathecally according to indications and intravenously about 200 c.c. If the serum is administered intramuscularly (in 20 to 30 c.c. doses) the area of buttock is selected, Collargol injections are tried, injection of sterile cerebro-spinal fluid have also been tried, but, it has not given any satisfactory results. Serum anaphylaxis can be treated by adrenalin injection and calcium lactate (20 to 30 grains) twice a day by mouth. The specific serum is usually and best given intrathecally. In cases, however, where there is spinal block, cisternal or ventricular puncture may have to be done for the introduction of the serum. But they are serious procedures. The general practitioners must not dabble in such methods.

EDITOR'S SUMMARY

The writer gives a synoptic review of the disease under reference. He mentions that, while usually the cerebro-spinal fluid is turbid or purulent in this disease, it may at times be clear in some cases. Prognosis is difficult, as he finds that apparently bad cases recover while the one thought to be mild dies. It is, as a rule, bad in fulminant cases, in children, in those who have extremes of blood pressure and whose cerebro-spinal fluid is either scanty or thick, yellow and purulent and in cases which are complicated by pneumonia or pericarditis. Serum treatment is ineffective in fulminant cases. Better results are obtained when it is given early.

VIII

The Pathological and The Bacteriological Aspects of Cerebro-spinal Meningitis

• Dr. Samuel Ram Singh M. S. M. F. (Pb)., D.T.M. (Cal)., Assistant Pathologist, Amritsar Medical School

The term cerebro-spinal Meningitis is rather comprehensive and suggests, perhaps, a number of causes for one disease. The plan of nature is *unity in variety* and this is no where more true than in the case of cerebro-spinal meningitis. In a very strict sense, however, it may be said that when we speak of cerebro-spinal meningitis, the causative organism that is uppermost in our mind is the *Neisseria Meningitidis*—a gram negative diplococcus first described by Weichselbaum in 1887. In this paper we shall confine ourselves mainly to the pathological and the bacteriological aspects of the meningococcic meningitis and incidentally mention the other types for differential purposes.

The chief and the main pathology concerns the localisation of the disease around the brain and the cord. There are two types of reaction, just as in the case of the pneumococcal and hæmolytic streptococcal meningitis. Firstly, there is intense congestion of the arachnoid and secondly there is infiltration of polymorphonuclear cells around the blood vessels. Thus there may be pus formation. This purulent reaction brings about the collection of the fibrin and pus which cause obstruction to the ventricles and secondary abscesses in the brain. So, conditions such as pyocephalus or hydrocephalus are initiated. These prolong the clinical course of the disease and produce the well-known sequelæ pertaining to the central nervous system.

Really, however, the pathology extends far beyond the meninges—especially in cases of severe meningococcalæmia, the pathological changes spread all over the tissues of the body or at least over a larger portion of them. There are hæmorrhages in the skin and the serous surfaces. The skin shows maculo-papular or purpuric rashes. Herpes of lips occur. The spleen and the lymphatic glands are soft and swollen, especially the glands of the intestines.

Blood shows the characteristic changes due to an acute infection. There is a definite increase of polymorphonuclear leucocytes and may range between 20,000 to 30,000; some times it is even higher.

No nephritis usually occurs, but there is albuminuria without the presence of tubular casts.

The central nervous system is involved most markedly. The obstructive collections of fibrin and pus cloud the sensorium and produce severe headache, stuporous delirium and loss of sphincter control. The depth of delirium in the meningococcal meningitis is more pronounced than in tubercular meningitis but less than in the pneumococcal. The muscles of the body are rigid. The rigidity of the neck muscles gives a useful clinical sign, *the Kernig's*; ankle and patellar clonus are also elicited due to the condition of rigidity of the muscles. Strabismus, nystagmus, focal or general paralysis are some of the complications following the involvement of the central nervous system. *Tache Cerebrale*, an useful sign, indicates vaso-motor instability. The extreme wasting that is noticed after recovery of the patient is a result of the poisoned and starved nerves.

Any description of pathology of C.S.M. will be incomplete without the presentation of the causative organism and the laboratory examination of the cerebro-spinal fluid, the findings of which are so important in explaining the morbidity of the disease, its differentiation from meningitis caused by several other organisms and for accounting the various nerve and cerebral complications. The organism *N. Meningitidis* is mostly found lying within the pus cells which are, in this disease, abundant in the cerebro-spinal fluid. It is gram negative, arranged in pairs with the flat surfaces apposing, unlike its cousin the *Neisseria gonorrhoea* the apposing surfaces of which are concave. Its biological tests are also helpful in distinguishing it from allied

organisms. The bionomics of the animal and vegetable organisms which are harmful to human beings is one of the most interesting natural phenomena and it is a sigh of relief for us to know that *N. Meningitidis* has the constant habit of committing suicide. Place it outside the tissue environment at a lower temperature than that of the body, it dies at once. Even at the body temperature it does not live very long, unless transferred to a suitable medium. Even in the selection of the medium, it is very fastidious. The pigeon blood agar (10%) is the best medium. Other media such as ascitis-agar, 10%, serum agar or tryparagar are also used. In case of emergency where special media are not available, we can use ordinary agar smeared with fresh blood from the tip of a finger.

It is important that the practitioner who seeks the aid of the pathologist should be quick in transferring the puncture fluid very early to the laboratory and to make arrangements to keep it warm while in transit.

The pathologist conducts the following examinations of the cerebro-spinal fluid :

- (1) Physical
- (2) Chemical
- (3) Bacteriological.

General Physical Examination: Colour.—The normal fluid is absolutely colourless. It may be yellow due to altered hæmoglobin, jaundice, or due to administration of drugs like acriflavine. It may be red due to blood or hæmoglobin. *In Meningitis it is greenish or greyish.*

Transparency.—The normal fluid is perfectly clear and transparent. A single drop of blood in 5 cc. may make it opalescent. The transparency is classified as follows :

Perfectly clear
Faintly opalescent
Distinctly opalescent
Faintly turbid
Markedly turbid
Purulent

Coagulum-Sediments.—The normal fluid does not coagulate. In acute or chronic meningitis, fibrin is present and it therefore coagulates. The character of the coagulum has some significance. It is numerous and small in paresis; cob-web or pine-tree coagulum is present in tubercular meningitis; in acute suppurative meningitis the coagulum and the sediment are heavy and sink to the bottom of the tube.

Specific gravity.—Normal is 1006-1008. Take it as in the case of urine.

Reaction.—Normal is slightly alkaline.

Cell Count.—This is important and should be done as soon as the fluid is received, while the cells are in suspension and before coagulum occurs. In cases where much fibrin is not present and coagulation does not occur, it may be done later on even on the next day. There will not be any harm if the fluid is well shaken to obtain an even suspension of the cells.

Total Count.—The leucocyte count has a great value in syphilis, acute anterior poliomyelitis and encephalitis lethargica where the increase is very small and needs, therefore, a great precision in the cell count. But in cases of acute suppurative and tubercular meningitis where the leucocytosis is considerable, slight errors in count do not make much difference. The counts have the following significance :—

0—8	in diluted fluid is normal,
10—12	„ „ „ a border line increase.
15—30	„ „ „ a slight increase.
30—100	„ „ „ a moderate increase.
100—1000	„ „ „ a great increase.

Differential significance

1. A few lymphocytes and occasional endothelial cell may be found in normal fluid.
2. Polymorphos predominate in acute suppurative meningitis due to meningococcus, pneumococcus and streptococcus.
3. Small lymphocytes are found in tubercular meningitis.
4. In acute poliomyelitis, polymorphos in the earlier stage and small lymphocytes in the later stage are usual.
5. In syphilis, pareses etc., small lymphocytes are in excess.
6. In meningismus or acute meningeal congestion, endothelial cells predominate.

Chemical tests

Chemical tests are conducted mainly for protein, sugar and chlorides. These tests have great value and recently a very useful and informative test, known as *Tryphanene Test* (described in the *Medical Annual* 1934) has been introduced for the detection of tubercular meningitis.

Bacteriological

Proteins.—This is largely in the form of serum globulin. Its quantitative test is more helpful but long and tedious. 15-40 milligrams per 100 c.c. is normal. Any increase above this level is pathological. This test is reliable only in fluid which does not contain any appreciable amount of blood. Heavy bacterial content of the fluid also yields false positive reaction. It is only the qualitative tests that are ordinarily done. The tests for protein have their own limitations.

Sugar.—To be helpful it must be a quantitative test. It is better to draw the fluid after fasting the patient over-night. The spinal fluid sugar varies according to the blood-sugar. The ventricular fluid has a higher content of sugar than the spinal fluid. Sugar is absent in acute suppurative meningitis. It is very much reduced in chronic conditions like tubercular meningitis and syphilis of meninges.

Chlorides.—They are in the form of sodium chloride and when considered in relation to sugar content are of great diagnostic value. 720-750 milligrams of sodium chloride, per 100 c.c. of cerebro-spinal fluid is a normal amount. Cisternal, ventricular and spinal contents are usually the same. In tubercular meningitis the amount frequently goes below 600 mgs. per 100 c.c. In acute suppurative meningitis, as meningococcal, it varies between 630-680 mgs per 100 c.c. Note that whenever there is blood present (as can be noted by the naked eye) this test has no value. Colloidal tests are not done as a routine.

EDITOR'S SUMMARY

(1) The writer reviews briefly, yet simply and succinctly, the pathology and bacteriology in connection with cerebro-spinal meningitis.

(2) *N. Meningitidis*, in the picturesque language of the author, has got the habit of committing suicide and is fastidious in its selection of environment and media. It is thus self-arresting to an extent.

(3) The main pathological features are due to the localisation of the disease-process around the brain and the cord. Most of the well-known symptoms, complications and sequelæ are the result of fibrinous and purulent infiltration in the brain and the spinal cord.

(4) When the meningococci invade the blood stream, symptoms of septicæmia occur with hæmorrhages, herpes, rashes and lymphatic enlargements.

(5) According to him, the depth of delirium in the meningococcal meningitis is more pronounced than that of the tubercular meningitis but less than that of the pneumococcal.

(6) Changes in the cerebro-spinal fluid have been mentioned from the point of view of differential diagnosis. Physical, chemical and bacteriological tests have been briefly indicated. He stresses that, since *N. Meningitidis* quickly autolyses, the fluid has to be examined fresh and in warm condition for its successful detection and that, if there is a pronounced leucocytosis of the polymorphos, the case can be taken as one of meningococcal infection even in the absence of the incriminating organism.

Laboratory diagnosis of Meningococcic Meningitis

● Dr. Md. K. Rohman, L.M.P., Assistant Pathologist and Demonstrator, Berry-White Medical School, Dibrugarh.

Meningococcus of Weichselbaum (1887) bears a striking similarity to the gonococcus in its morphology. The former is coccoid, about one micron in diameter and usually arranged in pairs. The flattened surfaces are in apposition to each other. Usually found in the polymorphonuclear leucocytes, it may also be found to lie outside the cells. It is non-motile, possesses no flagella, no spore and no capsule. Involution forms are common in old cultures. The size of the cocci often varies in the same smear and this variation, I consider, is of some diagnostic importance.

Much has been written about the different serological Types and Strains of meningococci. Until 1909, it was believed that the meningococcus group was homogeneous and that no essential difference existed between the individual members of the group. In the same year Dopter isolated some meningococci from Paris strains and distinguished them by specific agglutination reaction from the ordinary or normal Type. He called them, Para-meningococci. After him Gordon examined a large number of meningococcus from cases occurring among the British and Canadian troops and found that all the organisms studied by him could be divided into four types by agglutination reaction and by controlling them with absorption tests. Tulloch,* following up Gordon's work found that out of 356 cocci investigated 234 gave specific results with Gordon's Types Sera and that, with remarkably few exceptions, the organisms responsible for out-breaks among British troops were found to fall within the classified types of Gordon. He also found that the meningococci as derived from the naso-pharynx did not react with any of the Type Sera, though closely resembling the usual pathogenic Type. He had some suspicion whether they were virulent at all. But the organisms obtained by Gordon from carriers belonged to one or other of his four types known to exist in actual cases of meningitis.

The correspondence of the different types as named in various countries may be summarised as follows:

- (a) Gordon Type I = Para meningococcus.
 " " II = Normal "
 " " III & IV = Intermediate or irregular Strains, of which there are considerable number of different ones shading into each other serologically.
- (b) Rockefeller Institute recognises two types: The normal and the Para-Strains and also irregular Types.
- (c) The English recognises 4 types: Type I corresponding to Flexner's Para strains and Type II to his normal one. Type III & IV are irregular.
- (d) Holm and Davison state that Gordon Types I & II correspond to Rockefeller Para Strains and to Pasteur Types A: Gordon's II and IV correspond to Rockefeller Normal strains and to Pasteur Type B. Pasteur Types C and D are rare.

N.B.—(1) Gordon notes that there is somewhat close affinity between his Types I and III and between II and IV. He also states that chronic carriers tend to carry the same Type organism. As to frequency of Types in cases in England he has found the following:

Type I	10%	Type II	45%
Type III	10%	Type IV	5%

(2) In India, it is said that the organisms in epidemic meningitis belong to Type I and those in sporadic cases belong to Type II.

The Meningococcus

Staining reaction.—It stains readily with ordinary aniline dyes, such as Romanowsky's, Leishman's or Giemsa's. Gram negative.

Pathogenicity.—It causes epidemic and sporadic cerebro-spinal fever. Its pathogenic properties probably depends much on the relative virulence of the strains of the organisms. No definite conclusions have yet been arrived at on this subject.

Cultural reaction.—It grows well in Agar and Broth. The best media are Hormone Agar and Hormone Broth, Tryp Agar on Trypsized Broth. The cultivation is most satisfactory in sub-cultures. The colonies are moist, grey, oval or circular and translucent with irregular margins.

Fermentation in Sugar.—It ferments glucose and maltose with production of acid; but does not ferment lactose, levulose and galactose.

Inoculation reaction.—Inoculated intraspinally, monkeys get typical meningitis. Intraperitoneally guinea pig and mice are susceptible but not when injected subcutaneously.

Differentiation.—It has to be distinguished from micrococcus catarrhalis and gonococcus. Meningococcus ferments dextrose and maltose; not so micrococcus catarrhalis. The Gonococcus does not grow in ordinary media, is not suitable for cultivation and ferments glucose only. Whereas the meningococcus grows well in ordinary media, especially in sub-cultures, abundantly in serum-broth and ferments glucose and maltose.

Where found?—It is mainly found within the polymorphonuclear leucocytes of the exudates, fluids which pathologically collect in the serous cavities. But it is also occasionally found in bronchial secretions in pneumonia, in the pus of complicating joint affections and in the pericardial effusions. From septicæmic cases it can also be recovered from the blood of the infected patients. It is also interesting to note that meningitis is usually preceded by an infective rhinitis due to the meningococci and this is said to play an important role in spreading disease by such carriers.

Mode of transmission.—This question is at present unsettled. Considering, however, the primary naso-pharyngeal infection, it looks probable that the disease may be conveyed through the secretions of the upper air passages. The existence of healthy carriers is a problem yet to be solved.

Pathology.—In rapidly fatal cases there is intense congestion of the para-arachnoid. In cases of longer duration, the exudation first appears as slight accumulation of lymph between the pia-arachnoid, subsequently changing into fibrinous, sero-fibrinous and ultimately into whitish or yellowish fibro-purulent matter. The exudation is most marked at the base of the brain. The spinal meninges is chiefly affected and more on the dorso-lumbar region. There is an increased amount of cerebro-spinal fluid which remains under pressure. It is invariably turbid, unlike in tubercular or

pneumococcic meningitis. The membranes are much thickened, the cerebral ventricles are dilated by pus and turbid fluid. The veins of Galen may be thrombosed causing hydrocephalus.

Laboratory Diagnosis

Laboratory diagnosis of cerebro-spinal meningitis falls under one or other of the following heads:

1. Physical, chemical, cytological, bacteriological, serological examination of the cerebro-spinal fluid obtained from lumbar punctures.
2. Culture of blood for meningococcus.
3. Examination of blood for leucocytosis and differential count.
4. Examination of blood films to exclude malaria. (It is reported that a few cases of C. S. M. have been mistaken for cerebral malaria in the first Calcutta epidemic of this disease).
5. Examination of swab (smear and culture) from the naso-pharynx.

Examination of Cerebro-spinal fluid

Normally it is clear, colourless with a specific gravity of about 1007—1009 in adults. It is formed by the choroid plexuses in the cerebral ventricles by a process of dialysis. It differs from plasma chiefly by the absence of concentration of dextrose. Starting from the lateral ventricles, it reaches the third ventricle through the foramen of Munro, thence through the aqueduct of Sylvius to the fourth ventricle from where it escapes through the foramina of Luschka and Magendie to the sub-arachnoid space over the surface of the brain and the cord. It is a waste product of the nervous system and is reabsorbed through the Pacchionian granules and by the capillaries of the pia-arachnoid. The fluid is always under a certain pressure which may be roughly said to correspond to the flow of a drop per second through the lumbar puncture needle. The normal pressure of flow is 7—9 mm. of Hg. or 95—120 mm. of water in adults and 5—7 mm. of Hg in children. *This pressure is increased markedly in meningitis* and also in other diseases such as hæmorrhages, cerebral tumour etc. It is normally free from any cell, except a few lymphocytes which rarely exceed 5% per cu. mm.; these are supposed to be derived from meningeal vessels.

Chemical constituents.—These are the same as found in blood plasma and exist in the following proportion:

*Journal of Royal Medical College, Feb. 1918 P. 9.

Constituents	Percentage	Value per 100 c.c.
Chlorides ...	0.74 %	720—750 Mg
Glucose ...	0.09 „	50—100 „
Urea Nitrogen ...	small Quantity	3—13 „
Creatinin ...	„	0.4—2.2 „
Serum albumin and globulin...	0.025 „	S. globulin 20—38 Mg S. albumin 4— „
Water ...	about 99 „	

N. B.—In meningitis albumin is increased—chiefly serum globulin. Glucose is usually absent.

Functions.—The cerebro-spinal fluid protects the central nervous system from external injury and lessens the effects of such a trauma. It maintains an uniform pressure on the brain and the cord. It also acts as a channel for carrying away waste products from the nervous system. It is also supposed to possess some nutritive value and said to act as a buffer substance.

Indications for lumbar puncture.—In all suspected cases of cerebro-spinal fever where there is even a slight stiffness of the neck, especially during the period of epidemic, the first step must be lumbar puncture. Not only for diagnostic purposes, but also as an useful method of therapeusis in meningeal infections, the spinal fluid can be drained by puncture to relieve the effects of intracerebral tension and to drain, to some extent, the toxins contained therein. The technique is simple enough and quite safe with ordinary precaution.

Changes in the cerebro-spinal fluid.—The first indication of a pathological mischief is the change of colour. In cerebro-spinal meningitis it is usually turbid, often purulent and clots are easily formed on standing. In intraspinal or intracerebral hæmorrhages it is usually red; but the absence of red colour, it must be stressed, does not negate bleeding. In jaundice, it is yellow; usually clear and colourless in tubercular and pneumococcal meningitis. Fine grades of spontaneous coagulation often indicate disease. A fine pellicle of coagulum is observed in tubercular meningitis. A somewhat heavier coagulum is noted in purulent type of meningitis. A massive coagulum occurs in most cases of complete spinal block (Froin's syndrome). S. globulin is usually increased in cerebro-spinal meningitis (also in poliomyelitis); but this test is useless if the c.s. fluid contains blood. Other chemical constituents are not materially reduced or increased in C.S. Meningitis.

Serological Tests

Lange's Test.—(Colloidal gold precipitation test): This is a very delicate test and it is based upon the colour changes produced by precipitation of colloidal gold in different dilutions of

the spinal fluid. In meningitis, the colour changes at higher dilution, 1 in 320 to 1 in 2560.

Wassermann's or Khan's Test.—This is not usually done in cases of C.S. Meningitis.

Precipitin Test.—Vincent recommends this test for epidemic cerebro-spinal meningitis. It is simple. It is performed by adding a drop or two of antimeningococcus serum to a tube containing a small quantity of fresh cerebro-spinal fluid, which has been cleared by centrifugalisation for 10 to 15 minutes. The tube is then placed in an incubator at 37°C for 2 to 5 hrs together with a control tube. The formation of a precipitate (or a turbidity) shows a positive test.

Diagnostic agglutination.—It may be done against Type sera or against polyvalent sera, the organism being emulsified in isotonic sodium chloride solution. Half c.c. of this bacterial emulsion is mixed with .5 c.c. of polyvalent serum. A control should be made with similar amount of emulsion in 50 c.c. of sodium chloride solution. It is always well to run a tube with a known type and strain of meningococcus. Usually, meningococcus shows a certain amount of resistance to agglutination.

Microscopical Examination: cytology.—As has been mentioned earlier, ordinary aniline dyes stain the meningococci well. Meningococcus, tubercle bacilli, pneumococcus, strepto and styaphylococcus may be found in the smear in respective infections. The first two are more commonly found than the rest. The detection of meningococci will, of course, settle the diagnosis of C. S. Meningitis. It has also been said by us earliar that the c.s. fluid is ordinarily free from cells except a few lymphocytes. In acute meningitis due to meningococcus there is marked P. N. leucocytosis—it may go over 1000 per cu. m.m. while lymphocytosis is more in favour of chronic tubercular meningitis. This P. M. leucocytosis is characteristic of all acute infections of the meninges, not to say of meningococcus alone.

Cultivation of meningococcus

It can be cultivated from cerebro-spinal fluid, blood and throat smears. It is no good to rely upon media to which no animal protein in the form of blood serum or ascitic fluid has been added. Agar to which whole rabbit's serum is added forms an excellent medium both for cultivation and keeping the organism alive. It is advisable, when cultivating directly from cerebro-spinal fluid, to plant rather large quantities of it (1 to 2 cc.),

since many of the cocci in the exudate will fail to develop colonies (possibly because of their prolonged exposure either to the body fluid or to their own products in a closed space). Upon broth, growth is slow and takes place chiefly upon the surface. Glucose added to agar and to broth renders the medium more favourable for rapid growth; but there is this disadvantage, namely, that it forms acid and thereby causes more rapid death of the cultures. Growth is definitely stimulated by replacing about 10% of air by carbon-di-oxide. While slight alkalinity or acidity does not inhibit, the most favourable reaction of media is a Ph. of 7.4 to 7.6. Oxygen is necessary for development. It is an important aid to the recognition of meningococcus that it never grows at ordinary room temperature. Growth may take place at 25° to 42°C, but the optimum is 37.5°C. It is extremely sensitive to heat and cold, to disinfectants even of a high dilution and to even short exposures. It grows well in sub-cultures and it is strange to note that after prolonged artificial cultivation some strains of meningococci refuse to develop when freshly transplanted.

Animal pathogenicity.—Animals seem to be not very susceptible to this infection. Subcutaneous inoculation is rarely followed by more than a local reaction, unless large quantities are used. White mice is more susceptible than other animals. Intraperitoneal and intravenous inoculation of sufficient quantities usually results in the death of mice, rabbit, guineapig and dog.

Exclude Malaria

I may be pardoned if I end this cursory article, written at the request of the Editor, with the usual but not an unimportant slogan: exclude malaria before attempting to diagnose cerebro-spinal meningitis. This is specially relevant to this country where cerebral malaria, being common, is likely to be mistaken for cerebro-spinal meningitis. I therefore stress on the examination of blood film for malarial parasite before arriving at the diagnosis of meningococcic meningitis. This does not involve much time and certainly does not prejudice an early treatment for meningitis, so necessary for its successful termination.

EDITOR'S SUMMARY

Dr. Rohman suggests that the variability in the size of meningococci in one and the same smear is of some diagnostic importance.

He tabulates the correspondence of the different types of meningococci in various countries by different workers.

He discusses briefly many laboratory diagnostic tests, of which the microscopical examination of a throat swab and spinal fluid smear, cytological study of the c.s. fluid and its cultural examinations are the most important and handy. He utilises the fact of the meningococci not growing at ordinary room temperature to suggest that it is an important aid to their recognition.

He warns that cerebral malaria should always be excluded by blood examination for M.P.

Preparation of Anti-meningococcus Serum

- Dr. A. K. Hazra, M.B., B.S., D.T.M. In-charge, Serum and Vaccine Section, Biological Laboratory (B.C.P.W)., Calcutta

Anti-meningo serum was first introduced in the treatment of cerebro-spinal meningitis due to meningococcal infection by Jochmann some 30 years ago. He prepared a polyvalent serum by injecting horses first with dead and then with living cultures. His sera contained agglutinins, bactericidins and bacteriotropins.

Subsequently, antisera were produced with varying claims of their efficacy, by immunizing horses, goats, etc., with various antigens—viz., living cultures, broth filtrates, autolysed cultures, endotoxins, etc. In view of the somewhat confusing records by different observers the significance is by no means easy to assess, so far as selection of antigen for immunization of horses is concerned.

It was not till Flexner¹ in 1913 published his observation on the subject, that we owe our present knowledge of the value of serum treatment.

Of late, the most striking results were published by Wadsworth in 1932, when sera prepared under Wadsworth's direction in the laboratories of the New York State dept. of Health were used and the mortality rate was 18.4 per cent., among 742 patients.

In order to be able to utilise an antigen potent for the production of therapeutically valuable sera, it is important to have some acquaintance with the mode of 'action' of meningococcus.

The course following an animal inoculation with meningococci is not the normal course in acute infection as observed by Flexner² after intraperitoneal injections of living cocci in guineapigs. He was led to conclude that animals died of poison liberated from the bodies of the cocci. Albrecht and Ghon failed to kill mice with filtered broth culture injections, but were able to show that 24 hours' culture killed by heat could produce fatal effect on mice when injected intraperitoneally and the post-mortem appearances resembled those of animals dying after an injection of live cultures. Without discussing in detail the available evidences regarding the mode of action but considering the above results

coupled with the failures to isolate cocci from blood and viscera on every occasion from animals dying of injections of living cocci, it would appear that the main cause of death is a toxæmia. In early or severe cases, however, cocci are frequently found in blood where bacteriemia is marked or when in later cases septicæmic picture may develop. Elser, working on the subject, reported 10 out of 40 blood cultures being positive in early cases of meningococcal infections.

Hence, summarising, it may be said that death in the main is due to toxin, with occurrence of bacteriemia, even septicæmia being not improbable.

In order that a serum may be of real therapeutic value, it is essential that it should be both antibacterial as well as antitoxic.

Technical details that influence efficacy of produced Sera.—Selection of strains and their types.

Regarding typing of the meningococci the main issue between different workers is not whether meningococci can be classified serologically, but whether they are to be classified in two or four groups.

Gordon and Murray³ by using absorption test found that isolated strains fell sharply into 4 groups differing completely from Dopter's parameningococcus.

In view of the later work it has become increasingly clear that the principle of classifying the races of meningococci in four types is no longer satisfactory. The differences observed by different workers, in the serological behaviour of the meningococcus may be due to the complexity of the antigenic structure. In typing the prevalent type in India, we observed that Type I and III represent two antigens which may be found separate or together in almost any proportion. It was also observed that on isolation a strain that belonged to Type III with a little of I was on repeated subcultures found to be I with some of III. Moreover strains vary during different epidemics. As observed in some epidemics in

U.S.A., first types II and IV were the prevalent types, later in subsequent epidemics types I and III were found to replace Types II and IV. Thus sera prepared with standard strains or sera once prepared and stored during one epidemic may not be of any use during subsequent epidemics.

Friedemann discussing the causes of variable results with different anti-meningococcus sera attributed them to the presence or absence in the sera of antibodies which are effective against the local epidemic strains, otherwise typical, and isolated from cerebro-spinal fluid have been found to show no agglutination with either group sera and have hence been classed as X.

It is therefore important to arrange for the determination of the prevalent types and to include fresh representative types in the antigen to be used in the preparation of the serum. This point has been given special stress by the Public Health Commissioner with the Government of India in his report for the year 1933. It is pointed out in the report that local strains alone can yield therapeutically useful sera as it suggests the desirability of "type question" (meaning the prevalent types) to be "settled" before proposing to produce antisera. It is also pointed out in the report that "the results which have so far been obtained in India with English Serum have not been entirely satisfactory."

There is ample evidence pointing to the necessity of inclusion of local prevalent types in the preparation of antisera. Thus, for instance, an American stock of serum of established therapeutic value in America failed in the treatment of the disease among soldiers in Great Britain during the war, whereas "good results were obtained by the substitution of sera prepared in England from the epidemic strains". Similar observations are reported from South Africa, Belgian Congo and some other quarters too. Even sera possessing agglutinins for prevalent strains may not be of high therapeutic value as shown in recent outbreaks in America by Norton⁴, Smithburn⁵ and others.

Another important factor to consider in selection of strains for production of therapeutic sera is their broad antigenic quality.

It is interesting to note that Wadsworth's serum mentioned above is made by the use of six representative strains, which have been on laboratory media for over 10 years.

In our laboratory we started preparation of anti-meningococcus sera in 1933 on a large

scale. Having the above facts in view it was thought desirable to include local representative strains for which, strains were collected from all over India by Dr. Sen, the Director of our laboratories, and typed. These results have been published before⁷.

These strains of known antigenic value and other foreign 'standard' strains which were found antigenically broad were utilised for immunization of horses.

A point of interest and of no less importance in production of antimeningo sera has recently been established by the work of Ferry, Norton and Steele⁸. Prior to their work the consensus of opinion was that no soluble exotoxin has ever been conclusively isolated from the meningococcus, and the accounts of so-called toxin given by a number of investigators have been of autolytic extracts consequent of cultures kept long in broth, thus enabling a certain amount of extraction or autolysis to occur. "Poisonous substances" obtained referred specifically to products endoplasmic in character and not to those commonly classified as soluble toxins.

Ferry and his collaborators have obtained bouillon filtrates from young cultures containing extracellular toxins "specific to the four types as well as a toxin common to all types". They have also been able to obtain skin reactions in very high dilutions and have further shown that the filtrates can produce specific protective antibodies. This work was also carried out in our laboratories and we obtained almost identical results as reported by Ferry and others.

It was also found that individual animals injected with the 'toxins' develop anti-toxins specific to homologous toxins as well as anti-toxins which will neutralise the heterologous toxins. Also a polyvalent sera containing specific antibodies for individual toxins can be produced by utilising toxins of all different types.

We prepared serum with strains of known antigenic value and utilised living cultures as well as endo and exotoxins for the purpose of immunization of horses. Thus a serum was obtained which was both antibacterial as well as antitoxic. The sera produced are tested for agglutinins and by complement fixation test and other animal protection tests.

For a serum to be of real therapeutic value it must possess bacteriolytic power and should be able to neutralise endo and exotoxins and in addition must needs be able to promote phagocytosis of virulent cocci in the presence of complement.

The sera produced in our laboratory were widely distributed and some very encouraging results have been reported. Dr. P. T. Patel, in-charge of Arthur Road Hospital, Bombay, who has contributed valuable information on the subject of meningococcus infection in India in his book on *Infectious Diseases and other Fevers in India* tried our locally made sera in the treatment of his cases, and wrote in favour of the sera thus prepared.

In conclusion, it will not be out of place to suggest that a systematic study of cases be made to establish the value of specific serotherapy in epidemic cerebro-spinal meningitis in India. So far as is known, the serum treatment has not been adopted under conditions which from a statistician's point of view could be considered satisfactory.

As regards laboratory standardization and concentration of sera it is proposed to discuss them in a separate paper. As seen above, preparations of sera varies with different workers in different countries and so do the methods for their standardization. Also the value of serum treatment of meningococcal infection is yet to be established but the facts that the earlier the serum is given the better are the

results obtained and that some batches are more efficacious than others and, finally that a combined intrathecal and intravenous method gives a lower mortality than intrathecal method alone seems to point in favour of the use of serum as therapeutic agent.

I wish to thank Dr. A. K. Sen, Director of our Laboratories without whose zeal and suggestions it would not have been possible to produce anti-meningococcus sera, so early in our country.

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EDITOR'S SUMMARY

The writer summarises the work so far done in the research laboratories of the B.C.P.W., Calcutta, regarding the preparation of a potent anti-meningo serum for therapeutic purposes.

In view of Dopler's work, it has become increasingly clear that the principle underlying the race classification of the meningococci in four types is no longer satisfactory. The author suggests that the differences in their serological behaviour may be due to the complexity of the antigenic structure.

The variable results with different A.M. Sera are attributed by Friedemann to the presence or absence in the sera of antibodies which are effective against the local epidemic strains. Selection of strains for an effective therapeutic sera should be based on their broad antigenic quality. The Bengal Chemical laboratories have obtained almost identical results as those of Ferry and his collaborators regarding the specificity of extracellular toxins (contained in bouillon filtrates from young cultures) to the toxins of individual types as well as to the toxin common to all types.

All this knowledge has been utilised in the Bengal Chemical laboratory: local representative strains from all the epidemic centres in India have been pooled, typed, and studied. Serum is prepared with strains of known antigenic value; living cultures as well as endo and exo. toxins have been utilised for immunising horses; the serum, so obtained, is both anti-bacterial and anti-toxic, as a therapeutic sera should be.

Yet, the writer points out that a systematic study of cases should be made to establish the value of specific serotherapy in epidemic meningitis and notes that the information so far obtained is not satisfactory from the statistician's point of view. He further suggests that a combined intrathecal and intravenous injections of serum will give a lower mortality than by intrathecal method alone.

Treatment of Cerebro-Spinal Meningitis

• Dr. U. D. Gopal Rao, L.M.P., Madras

Cerebro-spinal meningitis has been engaging the serious attention of medical men in this country during the last 5 or 6 years. Northern India particularly has seen, during this period, many severe epidemics which claimed a heavy toll of mortality, while South India, barring a few sporadic cases, has up till now escaped an epidemic invasion of this fell disease.

Modern progress in scientific medicine and some of the most successful measures that are being adopted in continental countries where the disease had been occurring either in endemic or epidemic form ever since its first appearance (or recognition) in the year 1806 are mainly responsible for combating this disease early and preventing its spread in those areas.

It is not unnatural that the medical practitioner should concentrate on the treatment of the specific cause. While none can cavil at this attitude, one should not forget, that, after all, bad ventilation, insanitation, unhygienic habits and overcrowding pave the way for the growth, development and activity of disease germs. Most of us are painfully aware of the existence of such conditions in our country; and as in other infectious diseases, so in this, these afford a fertile soil for diplococcus intracellularis meningitidis of Weichselbaum to play its mischief either in an endemic or epidemic form. In this respect, we have much to learn from the western nations who, by concerted action and sanitary discipline, never allow a disease to grow to epidemic proportions.

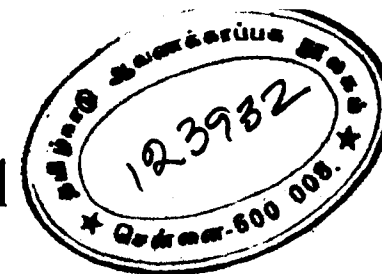
Hence we have to concentrate on the two important principles of treatment, viz., prevention first and cure next.

The primary difficulty in the successful prophylaxis and treatment lies, the disease being unfamiliar to many, in its recognition and timely diagnosis. This difficulty is materially enhanced by the fact that some of the varieties of this disease appear suddenly and end fatally. Cases are frequently reported in medical journals of a few fulminating types and other forms where the delay in diagnosis and early treatment resulted in permanent injuries like deafness. One of the most common, almost every day fever that a medical practi-

tioner has to treat in India is malaria, the cerebral type of which closely simulate cerebro-spinal fever. Now that this latter disease is getting to be more common than before, the writer would stress on the necessity of careful diagnosis and corresponding treatment. It is well known now that the best results of treatment of cerebro-spinal meningitis are obtained only when it is treated early.

Treatment of cerebro-spinal meningitis depends on several conditions and the presence or absence of special symptoms. The cases can be classified as mild, abortive, severe, fulminating, etc., on the basis of clinical manifestation and on the variations in the virulence of the meningococci. It is not within the purview of this paper to discuss separately the signs and symptoms of each type. Suffice if I were to point out that our aims in treatment should be to relieve the serious nervous phenomena due to excessive intracranial pressure brought about by excessive cerebro-spinal exudates, to drain the pathogenic bacteria and the exudates and to antagonise the specific organism by injecting sufficient quantity of anti-meningococcus serum (polyvalent) which, though not dramatic in its effects, has to some extent reduced the mortality, specially of the mild and abortive forms. The only way to do these three things at one stroke is by lumbar puncture. Other methods, such as application of leeches to the mastoid portion of the temporal bone or the nasal region, ice compresses or massage with iodine ointments to the nape of the neck or by electricity, should or may be done as adjuncts but never in preference to lumbar puncture.

Lumbar puncture in cerebro-spinal meningitis would thus fulfil several of our objects. In the first place, the high intracranial pressure which is the central feature of this disease and the chief cause of morbidity and alarming symptoms would be relieved. This is followed by the abatement, in some cases cessation, of the alarming cerebral symptoms such as opisthotonos, delirium, unconsciousness, hyperpyrexia and vasomotor disturbances. Secondly the meningococci, their toxins and other consequent exudatory products would be drained



to an extent, at least sufficient enough to prevent further complications and unfavourable progress of the disease; while at the same time it will allow the simultaneous introduction of the specific serum into the intra-spinal space which obviously seem to be the favourite site for this specific organism. Intrathecal administration of the serum is the method of choice and gives by far better results, so far observed, than intravenous or subcutaneous methods; and is the only means, known at present, by which deafness, blindness, paralysis and mental defects, not uncommon sequelæ of this disease, can be prevented with any measure of success. Intravenous or subcutaneous serum may be given as a secondary measure in cases where a larger dose of the serum is desired or where there are severe symptoms of septicæmia. Lastly, but pre-eminently an important, inevitable and necessary procedure, the lumbar puncture is of unquestioned value in correct diagnosis. It would indicate, if roughly, the amount of pressure of the c. s. fluid; it would reveal the nature of the pathological processes involved by enabling us to observe with our naked eye whether the fluid is transparent, turbid, or purulent; it would, above all, help us to submit the drained product for microscopic and cultural detection of the meningococci or other organisms.

The technique of lumbar puncture is well-known and need not be repeated. I would, however, like to lay emphasis on certain points of procedure. The lumbar puncture needle should have a sufficiently large calibre to allow a free flow of the cerebro-spinal fluid and the exudatory products contained there-in. If the fluid does not flow it must be due to one or other of the following causes: (1) blockage within the lumen of the needle, (2) the needle has not entered the intra-spinal space, (3) having entered there may be no fluid to drain owing to a block above due to adhesions at the base of the brain preventing the passage of the fluid from the ventricles to the sub-arachnoid space, or to the presence of heavy fibrinous clots. The first one can be settled by the use of stilette. The second is due to wrong technique and the needle has to be inserted at the right place with the patient in the correct position needed for this operation. The first needle need not be withdrawn at all, as you are only clearing your doubt whether the needle has entered the intra-spinal space by introducing a second one. If still the puncture is dry, in spite of the right technique, it is then that you have to decide whether your needle has entered the space or not. To settle this doubt, I would recommend to run a

small quantity of sterile water through the needle *in situ*. The facility with which the water enters will indicate that you have reached the spinal canal, that it is patent, but that there is very little or no fluid owing to the inflammatory block high above, as mentioned earlier.

It is in this last contingency that the question of cisternal and ventricular punctures arise. The writer, however, has to confess that he has not seen a case so tapped and that therefore he is not in a position to assess their value and importance in the diagnosis and treatment of this disease under reference.

The writer has seen in a few cases that anti-meningococcus polyvalent serum gives fairly good results in early cases, especially in children. The route of serum administration may well be left to the experience and discretion of the attending physician. The intrathecal dose is usually slightly less than the quantity of the c. s. fluid removed. In a case of average severity 20 to 25 cc. of the spinal fluid is withdrawn and about 5 to 10 cc. of the serum injected. More can be given with perfect safety, if the severity of the case demands it. As a rule one injection per day will suffice but it can be more frequently given, if necessary. Some advocate withdrawal of 50 cc. of the spinal fluid and injection of 40 or 45 cc. of the serum. No hard and fast rule seems necessary; it is better to err on the right side than be timid about dosage. The good effects of serum therapy will be evident, usually within 3 or 4 days and less often within 24 to 30 hours, by the disappearance of delirium, of septicæmic symptoms, and other characteristic syndrome complex of this disease. A careful watch over the effects of serum therapy should be maintained from the point of view of prognosis and a further increase in dosage. If possible, autogenous vaccine by intravenous route will usefully supplement serotherapy. One should not forget the possibility of serum anaphylaxis in some susceptible cases; usually serum shock and illness are but transitory and can be checked by adrenaline injection.

Serum therapy is of course the specific treatment; but the symptoms of the disease should be relieved by what is commonly known as symptomatic treatment. Hydrotherapy, in the form of ice bag to the head and the nape of the neck, sponging, tub-baths, etc. will check hyperpyrexia and mitigate the severity of cerebral symptoms, such as restlessness, insomnia, delirium etc. Eliminative treatment such as cleansing the gastro-intestinal tract either by calomel (4 to 6 grs.) and saline purgative or by high enema will

also be a valuable method in the alleviation of the urgent symptoms. Treatment by means of drugs is usually of little value in very severe cases. In early cases, where there is consciousness and the patient is suffering from incessant vomiting, menthol in 1 gr. doses or Tr. of Iodine in minim doses or iced water may be tried with occasional relief. Hyoscine hydrobromide, 1/6000 to 1/3000 gr. given every few hours would relieve muscular spasm and twitching. Or sodium bromide in 5 to 30 gr. doses or codeine 1/10 grain will do much to soothe the irritated nervous system. Suitable diet is essential to maintain the body resistance. Peptonised milk, eggs, broth may be generously given; and if there is vomiting, plenty of diluted fruit juice with glucose—D may be all that is necessary. Rectal feeding may be ordered if the patient is unconscious or vomiting intractable. A full course of restorative treatment should be adopted during the period of convalescence. Preparations of cod liver oil with vitamins, of hæmoglobin with liver and stomach extract, iron and arsenic may be given according to the particular indications of the case. A course of sodium iodide or colloidal iodine injections will be particularly useful in aiding the absorption of the exudatory residues in the central nervous system.

Prophylaxis is always a ticklish problem. Especially it is so in this disease where a definite and conclusive knowledge about the various types and strains of meningococci is not yet available and whose source and spread cannot yet be satisfactorily explained. The fact of the existence of healthy carriers of meningococci should not lull us into a false sense of security and be the foolish explanation for neglecting essential sanitary and quarantine measures. General overcrowding and insanitation are now the acute public-health problems in our country and I would not expatiate on them lest I may be accused of platitudes. The fact that the initial symptoms invariably pertain to naso-pharyngeal catarrh makes it quite probable that the infec-

tion may be conveyed by means of what in medical parlance called *the droplet infection*, through sneezing, coughing and even loud speaking. The first step in the prophylaxis is therefore the free use of antiseptic gargles and washes of mouth and nose, at least during the period of epidemics; and the suspected carriers, whenever detected, should be coaxed to systematically observe this procedure. Injection of anti-meningococcus serum, 1 to 5 c.c. 3 times a week is said to confer immunity which will last for 2 to 3 weeks. This may be tried with advantage, at least among close contacts and known carriers. Oral administration of pure hexamine 2 or 3 times a day in 10 gr. doses is also strongly recommended. Clean habits, clean food and clean clothes—in a word, attention to personal hygiene, epidemic or no epidemic—will always protect the individual against catching infectious diseases and confer on him the powers of resistance to overcome the disease easily if unfortunately he is infected.

There seems to be some connection between body lice and meningitis. This has been noted in some epidemics in the continent. This may be kept in view in our attempts at general prophylaxis.

Closing of schools and colleges, cinemas and places of public resort may be attempted during an epidemic.

House to house inspection by health workers (or officers) will probably reveal more cases of cerebro-spinal fever and this opportunity may be utilized for instructing the people in general and personal hygiene and in advising them to keep their mouth and nose clean by means of antiseptic gargles and washes—as is usually advised during the periods of influenza epidemic.

Such a regime of preventive measures may not be possible of wide-scale application under Indian conditions. But India is fast changing and there is no reason to believe that she will not fall in line with the more advanced public-health spirit of the western countries.

EDITOR'S SUMMARY

The writer discusses briefly the curative and preventive treatment of C. S. Meningitis.

He lays stress on the treatment with specific polyvalent serum and maintains that best results are obtained if it is given early in the disease and intrathecally.

He emphasizes the importance of lumbar puncture for diagnostic and treatment purposes and explains lucidly the circumstances and causes of a "dry puncture". Prophylaxis recommended by the writer consists of segregation of the known carriers and their treatment by gargles and washes of mouth and nose. A small immunising dose of the serum, 1 to 5 c.c. 3 times a week is suggested. Attention to personal hygiene, important at all times, is more important during epidemics.

He utters a note of warning: the fact of the existence of healthy carriers of meningococci should not lull us into a false sense of security and be the foolish explanation for neglecting the essential sanitary and quarantine measures.

General Pathology and Principles of Treatment of Cerebro-Spinal Meningitis

• Dr. Priyo Gopal Mukherjee, L.M.F. (Cal), Saranga, Burdwan

Pathology

Cerebro-Spinal Meningitis may be caused by organisms other than meningococcus (Thomas Horder). But in most of the cases it is caused by the meningococcus (*Diplococcus meningitidis intracellularis* of Weichselbaum). The infection is conveyed by means, perhaps, of "carriers" through the secretions of naso-pharynx and carried to the meninges through the lymphatics or blood. The initial congestion of naso-pharynx and posterior nares lends colour to this view.

The pathology of different types of this disease varies:

1. In the ordinary or acute type there is a great congestion of the meninges with profuse fibro-purulent exudate chiefly seen at the base of the brain. The ventricles of the brain contain a turbid fluid and are dilated. Much lymph is poured into the larger fissures and in some cases the whole cortex is covered with pus. The meninges in this region are generally thickened. The spinal cord is also similarly involved. Hæmorrhagic areas are seen on section of the brain and the spinal cord.

2. In the fulminating type there may not be found any change except the congestion of the meninges as the patient dies within 24 hours before the actual appearance of symptoms.

3. In chronic type there is generalised thickening of the membranes and dilatation of cerebral ventricles. Optic, trigeminal, facial and acoustic nerves may be involved in the course of the disease. The brain substance becomes softer, looks much more reddish and injected. Hæmorrhages are seen here and there over it.

4. In post-basic meningitis of infants the pathology is the same as in acute and chronic types except that there is an early infection of the pia-arachnoid with a special tendency to involve the cerebral ventricles by ependymitis.

Cerebro-Spinal Fluid

The amount and pressure of the cerebro-spinal fluid are increased. Its transparency is lost, it becomes turbid. The albumin of the fluid is increased. In the early stage of the disease the lymphocytes are increased. In the

acute inflammatory stage the polymorpho-nuclear-leucocytes are in large numbers (70% to 80%). In the chronic stage, again, the lymphocytes are seen in greater numbers. In the post-basic type of the disease there is a relative increase of lymphocytes.

Intra or extra cellular meningococci may be seen in the films made directly from cerebro-spinal fluid, or better still from its centrifuged deposits. Gordon has differentiated four types of meningococci occurring in the cerebro-spinal fluid of actual cases by agglutination test. Specific gravity (normal 1007 to 1009) is also increased.

Other changes

There is also considerable leucocytosis (P. M.). Blood: R. B. Cs. decreased. (20,000 to 40,000). The lungs, the kidneys and the liver may be seen congested. The heart may be dilated. Spleen may be enlarged. Muscles of the body especially the neck muscles, abdominal muscles and the ham-string muscles are contracted.

Treatment

The treatment of cerebro-spinal meningitis falls under the following:—

1. *Prophylactic*.—As it is an infectious disease, it is better to isolate the patient as well as the 'carriers' as early as possible. The healthy 'carrier' is perhaps more responsible for the spread of the disease than the patient himself. All contacts who are found to be carriers should be placed under quarantine and should be kept there until the naso-pharynx is free from meningococci. As a gargle, a weak solution of izal may used, or hydrogen peroxide, or a 1 in 1000 solution of permanganate of potash, adding 1.5% of sodium sulphate to assist penetration (Gordon). For spraying the nose and fauces, a 1% solution of iodine with a 2% of menthol in paroline may be used. Osler recommends direct application to the mucous membrane of a solution containing chloramine 1% and zinc sulphate 2%.

2. *Curative*.—Since the time of Fowler's introduction of specific serum treatment in this disease, it has been largely employed with varying success. After correct diagnosis, the first dose of the serum should be given as early

as possible. If the result of using one brand of serum in a particular case proves unsatisfactory then different brands should be tried. The serum may be given sub-cutaneously, intravenously and/or intrathecally. But in urgent cases the serum should be given by the intra-spinal route. In mild cases it may be given sub-cutaneously or intravenously. Its therapeutic value is greater when given by the intra-spinal route. It is preferably given in the lumbar region. Lumbar puncture is performed for both diagnostic and therapeutic purposes. Therapeutically it is done to relieve intracranial tension, to drain away toxins and meningococci and to introduce anti-meningococcal serum. The indications for lumbar puncture in this disease are:

1. High temperature,
2. Rigidity of neck,
3. Kernig's sign,
4. Extreme headache,
5. Vomiting,
6. Delirium,
7. Coma.

Its technique is simple. The patient lies on the left side with drawn-up knees and flexed head and shoulders. The puncture is made in the 4th lumbar inter-space as identified by the line connecting the summits of the iliac crests which crosses this region. No anaesthesia is necessary in the majority of cases. In some patients with hyperæsthesia of the skin, a local anaesthesia is useful. In delirious patients a general anaesthesia has to be given. After thorough sterilization of the part and the needle, insert the needle in 4th lumbar inter-space in the middle line. It must be pointed forwards with a slight inclination upwards. In children about $\frac{1}{2}$ " to 1" and in well-built adults about 3" to 4" penetration of the needle is necessary to find the fluid. Remove the stylette if there is much tension, check the flow by keeping the stylette on; otherwise it may be dangerous. When the fluid is coming at the speed of one drop per 3 to 4 seconds, introduce the specific serum by means of serum syringe. The injection should be made very slowly and with uniform pressure. Rapid injection is harmful and may even lead to fatal results. (Rate of giving injection: 2 c.c. in 1 minute.) Pulse and respiration should be watched at the time of injection. We must be on the alert for symptoms of serum reaction such as respiratory and cardiac failure, anaphylaxis and shock. If there is evidence of respiratory failure, injection should be stopped then and there. Artificial respiration should be given or some serum injected should be drawn out. Adrenaline injection usually relieves this condition.

The following are the usual doses of the serum:—

1. *In infants*.—Single injection, 5 to 10 c.c., not more than 15 c.c. in exceptional cases.

2. *In adults*.—(over 18 years of age) the average dose of each injection should be 30 c.c. to 40 c.c. In severe cases, the serum should be repeated every three hours. In mild cases, the serum should be administered once a day, then every other day provided that the progress of the disease is satisfactory. Injections are continued if the cerebro-spinal fluid is turbid, if meningococcus is still present, and if there is no abatement of symptoms. Generally polyvalent anti-meningococcal serum is given. Sub-cutaneous injections are of no value in severe cases. But when septicæmia is present, intravenous injections are to be preferred.

3. *General Management*.—The patient should be strictly confined to bed, the diet restricted to fluids—diluted milk, lemon juice, barley water, freshly prepared meat essences, should be given in small quantities at regular intervals. Citrated or peptonised milk are also very useful. If the patient cannot swallow, nasal or rectal feeding should be undertaken. Water must be given freely. Raw egg mixed with milk and a little brandy may be given if the heart is weak. If there is intractable vomiting, peptonised milk and albumin water should be used; or no food should be given per mouth for 24 to 48 hours except water or diluted fruit juice. Rectal saline with glucose may be given with advantage. Constipation is relieved by saline purgative or enema. In cases of distension of the bladder use catheter. If cystitis is present, irrigation of the bladder with weak antiseptic lotion may be done.

4. *Drugs*.—Practically drugs are not useful in this disease.

1. Some recommend urotropin about a dram daily, but Foster and Gaskell are of opinion that it is of no value in this disease.
2. Mercurochrome solution.—1% given in doses of 5 c.c. to 10 c.c. intravenously once in a day in acute stage of the disease.
3. Pot. Iodide is given in big doses.
4. Arsenical preparations are given by injections:—
 - (i) Soamin 1 gr. intramuscularly on alternate days.
 - (ii) Myo-Salvarsan is given by some with success.

The usefulness of these drugs are doubtful.

(5) *Treatment of certain symptoms and complications*:—

- (a) For headache: Shave the scalp, apply ice-bag over the head. In severe cases, antipyrine, aspirin and caffeine may be tried. Morphine $\frac{1}{2}$ gr. given in very severe cases.

- (b) For high fever: sponging the body with cold water and application of ice-bag to the head are necessary.
- (c) For pains all over the body: these may be relieved by sponging with warm water.
- (d) For insomnia, restlessness and delirium prescribe chloral hydrate and bromide. If delirium is exhausting and there are maniacal symptoms, give chloroform inhalations or better, give morphin with atropin.
- (e) For arthritis: fixation of the joint and application of hot stupes or ichthiol-belladonna are useful. If there is effusion in the joint, aspiration should be done and 5 to 10 c.c. of serum injected into the joint cavity.

- (f) For hydrocephalus: tapping of the lateral ventricles and instillation of of the specific serum. In infants tapping should be done through anterior fontanelle. In adults, decompression is necessary; lateral ventricles are punctured, some amount of fluid is withdrawn and serum introduced into the ventricles.
- (g) For eye and ear complications consult the specialist. But the treatment of deafness and optic neuritis is invariably unsuccessful.

Let me state that cisternal and ventricular punctures require considerable skill and special knowledge. Excellent results are said to have been obtained by these punctures.

EDITOR'S SUMMARY

Brief mention is made of morbid changes in the different types of C.S.M. Isolation of the patient, quarantine for the contacts, antiseptic gargles and sprays for carriers form the chief prophylactic measures. There are no specific drugs for the disease except serum administration. Complications and special symptoms are to be relieved, if unsuccessfully at times, by the usual routine methods.

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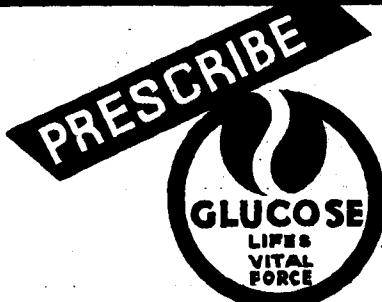
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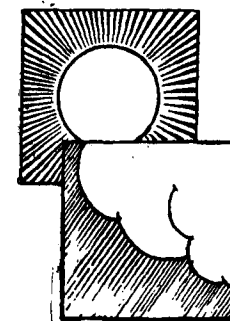
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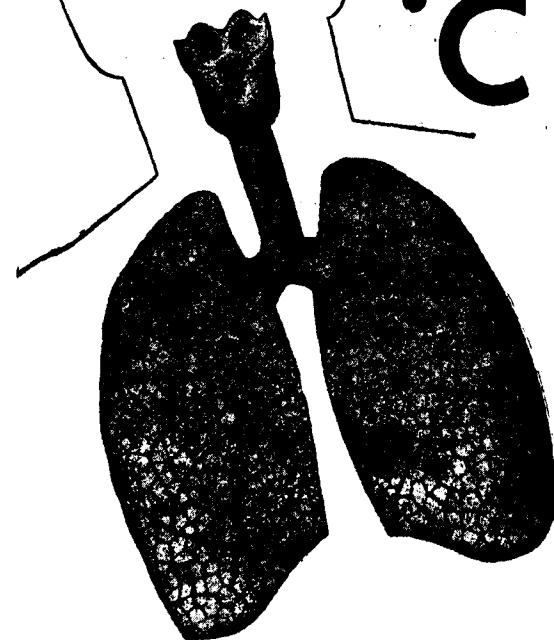
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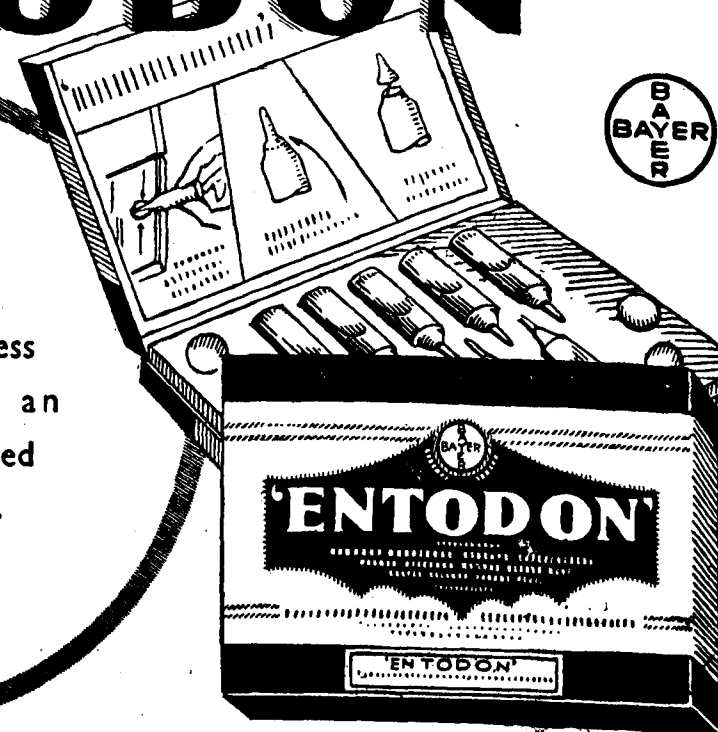
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JANUARY 1936

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and well-wishers in India and abroad, whom we strive
to serve, we extend our best wishes for a bright
and busy new year

CEREBRO-SPINAL MENINGITIS

Known also as Meningococcic Meningitis or Cerebro-Spinal Fever, this disease, from all accounts, is no new one to our country, at least it has been heard of and described since the year 1878. Its first clinical recognition dates back to 1805 when Vieusseux described an epidemic that occurred in the South of France and in Switzerland. And from this year onwards we find records of this epidemic in the different parts of Europe and America, epidemics of varying severity but always localised and of short duration, claiming however a heavy toll among the affected. Since such epidemics have only been subsequently described in eastern countries notably in Egypt, Sudan, and India, it has been said that the disease is spreading from West to East. There is nothing, however, to substantiate this statement except the sequence of time. As Lt. Col. Russell points out elsewhere in this issue, if this statement is wholly true it is inexplicable how Burma is affected while there are no reports of this epidemic from Assam. It looks to us as if the *time-test* should not be the only criterion to describe it as spreading from West to East. This disease does not follow the known laws of infection (*vide infra*). Its path and mode of spread is still undetermined. It would therefore be premature to say that it is spreading in an easterly direction. We have gone through the available records of

this epidemic carefully and we find that its recognition was directly proportional to the progress of medical knowledge in the different parts of the world and the extent of its detection went *pari passu* with the development of the art of scientific observation and with the increasing facilities for a scientific diagnosis which, one can say without fear of contradiction, have been striding from West to East, at least since the last 200 years.

This, after all, is an academical question which we can safely leave at the hands of the future medical historian. The fact, however, remains that since 1878 cerebro-spinal meningitis has been progressively increasing in its incidence in our country. Its epidemic waxing and waning in the widely separated parts of the country is one of its striking features. If it has not increased by leaps and bounds and spread like a whirlwind as influenza, small-pox and cholera, it is due to the peculiar nature of this infection which seems to follow a law of its own as yet undetermined and which does not stand on all fours with the known laws of infectious spread. A close study of the recent epidemics in India reveal many peculiarities. In almost all epidemics the source of infection cannot be traced with any degree of accuracy or authenticity. It is said that North Sind and certain areas in Bengal are endemic areas but Col. Russell doubts whether this term has been correctly applied. Another peculiarity is that the epidemics are localised, and confined to communities and occur in widely separated parts of the country. Lahore in the North, Ahmedabad in the West. Calcutta in the East and Madras in the South with varying atmospheric temperature and humidity have all been visited by the epidemic while the intervening areas have escaped or have been only slightly affected. Since it does not show any slight indication that it travels along the routes of human communication or that the infecting organism is carried along the paths of monsoonic winds—as in the case of influenza—it would be premature, at present, to draw any conclusion regarding its epidemic dissemination. Still another peculiarity is that it does not seem to be highly infectious, even though the disease is often explosive in character and 80% fatal in its termination. Rarely two persons in the same family are attacked though living under the same set of circumstances. It makes no fetish between the occupant of a hovel in a slum and that of one living under ideal conditions. There are perhaps more number of healthy carriers of this disease than those of other infectious diseases, carriers not after the attack of the disease, as in typhoid or dysentery, but before the actual

attack. And yet they seem to escape victimisation by the swarming meningococci in their throats. All these are inexplicable at present and await solution.

Two facts stand prominent in the recent history of this epidemic in this country. The one is that the same locality is often erratically subject to the epidemic at varying intervals of time and with varying degrees of severity. The other is that, apart from these epidemic seasons or prevalences, the disease, as General Megaw observed, occurs sporadically almost throughout the year in at least the urban areas of India. These indicate that, once the infection is introduced in a locality, the meningococci remain in lingering persistence, though dormant, and await a suitable soil and environment for their re-activation. This hypothesis, perhaps, explains the sporadic occurrence and the recurrence of the epidemic in one and the same locality.

Dr. Samuel Ram Singh mentions elsewhere in an expressive language that *the meningococci have got the constant habit of committing suicide*. This may be true *in Vitro* but certainly not *in Vivo*. The circumscribed nature of the epidemic, the relative rarity of direct infection and the promiscuity of healthy carriers without themselves being affected or affecting those coming in contact with them in any large measure are to be explained by other characteristics of the organism than its alleged suicidal habit. The explanation probably lies in the fact that there are different types and various strains of these types with differing cultural, bio-chemical and pathogenic properties, and *these differences* obviously influence the degree of infectivity and virulence, the mode of spread and dissemination, the selection of suitable soil and environment, the epidemicity and sporadicity of the disease.

With such uncertain and insufficient knowledge, prophylaxis is bound to be unsatisfactory and indeterminate. The only possible and feasible method, at present, is the segregation of the affected person and early and proper treatment. The rest of the methods are problematical and have but to be classed as next best. The segregation of the carriers is impossible and their treatment by gargles, sprays and inhalation are easier described than done. They cannot be applied in mass scale, except in institutions like jails or asylums; and their application, though not questionable, does not seem to substantially affect the incidence or spread of this disease. Protective vaccine made from Delhi and Ahmedabad strains has been issued by the Central Research and

Hafkin Institutes, Kasauli and Bombay respectively, for purposes of trial and the results are awaited. It is just possible that this vaccine would be effective, as the bouillon filtrates of the cultures of the four Gordon types of meningococci contain soluble, extracellular toxins which seem to be specific not only to the individual type but also to all types. It has also been found that the experimental animals receiving an injection of this filtrate containing the soluble toxins develop anti-toxins specific to their homologous toxins and an anti-toxin common to all types. As a rule, soluble toxins, when injected, give rise to the development of anti-toxins as well as confer immunity against the organism. It is yet to be determined whether the latter holds true also of the soluble toxins of the meningococci.

The mortality in cerebro-spinal meningitis at present is as high as 80%, though this is truer of epidemic cases than the sporadic. With the introduction of specific serum treatment, it has been somewhat reduced; but on the whole it has been a failure for obvious reasons. The types and strains of the meningococci as common to Indian epidemics have only been recently pooled for study and classification. The available serum with which the disease has been treated up till now may not have been derived from proper strains. Besides, insufficient dosage and late administration will naturally give disappointing results. It is hoped that these difficulties will soon be overcome and a trust-worthy serum will be made available.

The route of administration of serum is of considerable importance. As Dr. Jamiat Singh writes, it should be given intrathecally since the serum is only bactericidal. This is undoubtedly true and it would be utterly unsafe if this route is avoided in preference to the intramuscular or the intravenous. The latter can be used to supplement a further dose of the serum or in toxæmic cases; but the main dose should be introduced into the intra-spinal space. Mention has been made by some of our contributors about cisternal and ventricular punctures in case of the failure of lumbar puncture and in what we fancy to be rather uncommon cases of spinal block. We would, however, earnestly plead against cisternal or ventricular punctures. Cisternal puncture is at all times unsafe in the best of hands. As regards ventricular puncture our experience has been that if the lumbar puncture has been unsuccessful, the ventricular puncture is likely to give the same result. We would, therefore, recommend that ventricular puncture be reserved to cases occurring in very young infants

in whom the ventricles can be safely approached through the unclosed fontanelle and that also, only when there is a necessity for the same.

When to stop the serum treatment? Serum has to be continued so long as the spinal fluid is not free from meningococci; and *continued not more than a day or two after their disappearance*. Intrathecal administration of the serum after the disappearance of meningococci is decidedly dangerous as, by itself, it may set up a meningitis. This has to be borne in mind.

If only the serum is powerfully anti-toxic, besides being bactericidal as it is at present,

intravenous injection would suffice. It may not be very long that such a serum will be made available and the fact that the soluble extra-cellular toxins of the meningococci are capable of being specific to the toxins of the homologous type as well as to those of all types, lends hope to the possibility of preparing a potent anti-toxic meningococcus serum. Recent researches also indicate that it is possible, as in the case of diphtheria, to evolve a toxin-antitoxin sera (or vaccine) for the purpose of conferring more or less permanent immunity against this infection. These are the hopes that lie ahead of us in the effective prevention and treatment of this mortal disease.

SELECTIONS

ACUTE IMMUNIZATION WITH MENINGOCOCCUS TOXIN

N. S. Ferry, M.D., and A. H. Steele, M.D.

(Reproduced from *The Journal of the American Medical Association*, March 22, 1935, P. 933)

In 1931 it was shown that bouillon filtrates of young cultures of the four recognized Gordon types of the meningococcus contain soluble or extracellular toxins specific to the individual types, as well as a toxin common to all types, and that animals injected with these toxins develop antitoxins specific to their homologous toxins and an antitoxin more or less common to all types.

It was also shown that a certain proportion (about 50 per cent) of children are susceptible to one or more of these toxins, following intracutaneous injections of the diluted toxins, the test being carried out in a manner similar to the Schick and Dick tests for susceptibility to diphtheria and scarlet fever respectively.

It was later demonstrated that this soluble toxin has a specific action on the central nervous system of laboratory animals, especially the monkey, and that when injected intracisternally it produces symptoms similar in nature and approaching in severity those resulting from intraspinal inoculations of live meningococci. It was discovered at that time that recovery from previous intracisternal injections of the toxin induced a state of active immunity in those animals against an intraspinal inoculation of a fatal dose of live organisms, similar to that immunity following recovery from the disease, shown previously in one of these studies.

The meningococcus, therefore, produces a true soluble toxin that will stimulate an active immunity in laboratory animals against the live organism as well as its toxin.

The present work was carried out to determine whether active immunity against the toxin, or at least the skin test dose of toxin, could be induced in man by a series of subcutaneous injections of the undiluted toxin. Accordingly, a large number of children, ranging from 12 to 18 years of age, were skin tested and those showing positive reactions to one skin test dose of the toxin were injected subcutaneously with the undiluted material.

The method of procedure was as follows: A toxin was prepared from type I-III culture of the meningococcus and diluted according to a standard toxin, so that 0.1 c.c. contained a skin test dose. This dose was previously determined to be that amount of toxin which, when injected intracutaneously in a dose

Results

Number tested	...	605	
.. positive	...	285	47.1%
.. injected	...	282	
<i>Three Dose Group</i> —Number in Group 149			
Negative reactors on retest	...	98	62.4 "
Reactions smaller than original...	...	89	25.5 "
.. same size as ..	...	11	7.8 "
.. larger than ..	...	7	4.7 "
<i>Four Dose Group</i> —Number in Group 88			
Negative reactors on retest	...	62	74.3 "
Reactions smaller than original...	...	7	8.4 "
.. same size as ..	...	7	8.4 "
.. larger than ..	...	5	6.0 "
.. very large ..	...	2	2.3 "

of 0.1 c.c. into an individual susceptible to the toxin, will produce a local skin reaction at least 10 m. m. in diameter. The diagnostic test toxin used in this work contained 5,000 skin test doses per cubic centimeter. All individuals were injected intracutaneously with 0.1 c.c. of this test toxin. Those showing a skin reaction of 10 m.m. or over in diameter were considered susceptible and were later injected with the immunizing toxin. Since it was believed that skin tests with one toxin should be sufficient to demonstrate the point in question, the children were not subjected to tests with toxins of all four types. The immunizing toxin, on the other hand, was composed of an equal mixture of toxins of the four types and contained, in all, 5,000 skin test doses per cubic centimeter, approximately 1,250 skin test doses in each of the four toxins. The susceptible children to be immunized were divided into two groups. One group was given three injections of the following doses of the mixed toxin one week apart: 0.1 c.c., 0.5 c.c., and 1 c.c. equivalent to 8,000 skin test doses in all. The other group was given four injections, also one week apart, the doses being 0.1 c.c., 0.5 c.c., and 1.5 c.c., equivalent to 13,500 skin test doses. As the immunizing toxin contained approximately an equal amount of each individual toxin, it is

evident that the toxin homologous to the test material represented but from one fourth to one third of the whole, depending on the amount of toxin common to all types present in the mixture. In other words, the children injected with the four doses did not receive more than the equivalent of 4,000 skin test doses of any one of the type toxins.

At the end of eight weeks all the children were retested with a skin test dose of toxin to determine the number of those who had become immune to the toxin.

Three types of reaction to the injection of undiluted toxin were observed. First, local reactions: about 50% of the children showed local reactions mostly of a mild character which caused the child to complain only of slight soreness or stiffness of the arm. Second, general or systemic reactions: approximately 10% of the group exhibited mild systemic reactions following the second or third injection, the symptoms of which were headache, dizziness, gastro-intestinal

upsets and a slight elevation of temperature. These reactions invariably disappeared within eighteen hours. Third, allergic reactions: in four instances immediate reaction after the second injection, consisting of generalized urticaria and, in one case, abdominal cramps accompanied by mild prostration. These symptoms were promptly controlled by an adequate dose of epinephrine. Further injections were discontinued in these cases as a precautionary measure.

Out of the 285 positive reactors fifty-three, for one reason or another, did not receive full treatment and were not retested.

Of the 232 who were given the full number of injections and were retested, including both groups, 155, or 66.8% gave negative reactions on retesting. Had the amount of toxin been increased, or had only the homologous toxin been given, the percentage of negative reactors would undoubtedly have been higher.

Comment

This work has demonstrated two facts: first, that certain individuals who are susceptible to the skin test dose of meningococcus toxin can be made immune to this dose of toxin by at least three subcutaneous injection of the undiluted toxin in graduated doses, and, second, that this immunity can be pro-

duced against the toxin of one type by injections of a mixture of toxins of all types.

While the results of these tests indicate certain facts in regard to the stimulation of active immunity in man against meningococcus toxin, they do not necessarily signify that an immunity against the organism can be produced at the same time, although such a condition is true of some soluble toxins and it is not unreasonable to expect the same of this toxin. The method of immunization, however, does suggest a possible means of active protection against the disease itself and is worthy of consideration and further study, especially since it was shown in a previous paper in this series that active immunity against injection with the virulent meningococcus can be stimulated in laboratory animals following prophylactic injections of this toxin. The answer to this question, while of great importance, must of necessity be deferred until such a time as more conclusive clinical data are available.

Only ethical advertisements are accepted. Our readers may, therefore, confidently prescribe what is advertised in The Indian Medical Journal

MENINGOCOCCIC MENINGITIS—
A NEW FORM OF THERAPY

Archibald L. Hoyne, M.D., Chicago

(Reproduced from The Journal of the American Medical Association, March 23, 1935, p. 980)

Weischelbaum, although not credited with priority in observing the meningococcus, isolated and cultured it in 1887; thus he laid the foundation for the present etiologic conception of the disease. Jochmann initiated the clinical intrathecal use of an antiserum evaluated earlier by animal experimentation by Kolle and Wassermann.

Flexner in 1907-1908 reviewed the entire subject of meningococcic meningitis and as the result of extensive laboratory and clinical investigations demonstrated the value of an antimeningitis serum in the treatment of the disease. He attributed the benefits of the serum clinically to its antibacterial qualities.

This work has stood unquestioned, and very little change has been made in methods of preparation of sera, largely because the ability of the meningococcus to elaborate a toxin was not recognized. None of the more important articles on the subject, including the comprehensive reviews of Gordon in 1920 and Murray in 1929, admit the possibilities of the production of a soluble toxin but do agree to the elaboration of endo-toxin. Murray states that no one has yet succeeded in demonstrating a soluble toxin in meningococcus cultures and all are ready to admit that such a toxin is not produced.

Efforts to associate any one type of meningococcus or any particular strain with various epidemics have not been successful. Clinicians generally agree that the present polyvalent antibacterial sera and methods of standardization are not wholly satisfactory, and this was well demonstrated in 1929 by Wright who showed in an outbreak observed by him that "a serum uniformly of the highest titer was not effective clinically". I have made somewhat similar observations in the contagious disease department of the Cook County Hospital.

Table 1. Reasons for discarding cases from report

Reason	No. of cases
Received both antitoxin and antiserum...	16
Questionable diagnosis	17
No serum given	7

Reason	No. of cases
Incorrect diagnosis reported	11
Miscellaneous	20
Records absent from file	5
Total	76

In an attempt to clarify the perplexities of the situation in regard to antimeningococcus serum, Ferry recently succeeded in demonstrating soluble exotoxins in bouillon filtrates of the four recognised Gordon types of meningococcus. These toxins, when injected individually into animals, developed specific antitoxins. Convalescent sera were shown to possess neutralizing properties towards homologous soluble toxins. Less extensive, but corroborative, work on the toxin and antitoxin has been recorded.

Ferry concludes from his observations that the symptoms of meningococcic meningitis in laboratory animals (guinea-pig, monkey and rabbit) result from a selective action of the toxin towards the cerebro-spinal nervous system. He found that the animals receiving lethal doses of toxin intracisternally or lethal doses of viable culture intraspinaly could be protected by intraperitoneal injections of antitoxin but not by standard antimeningococcus serum, and that animals immunized by sublethal intracisternal doses of toxin were resistant to lethal doses of live culture. Ferry reports elsewhere in this issue that susceptible human beings can be immunized against meningococcus toxin as revealed by subsequent skin test.

The experimental antitoxin used in the present clinical study was of the same lots reported on by Ferry. This antitoxin was prepared by injecting horses subcutaneously with increasing doses of individual soluble toxins of the four types of meningococci. The antitoxin property of the serum was determined by its ability to neutralize toxin, as shown by intradermal injection in susceptible human beings and by its ability to protect laboratory animals from lethal doses of toxin and culture. Concentrated antitoxin was used in a few of the cases in my series. This was prepared by standard concentration methods.

Three hundred and seventy-two patients were discharged from the Cook County Hospital, Contagious Disease Department, from November 1932 to June 1934, with the diagnosis "epidemic meningitis". Of these, the records of 296 have been included in this report, the remaining being discarded for various reasons (table 1).

The 296 patients have been separated into a series of eighty-five receiving meningococcus antitoxin and a series of 211 receiving two well known standard brands of antimeningococcus serum. The clinical diagnosis of all but forty cases was verified by smear or cultural identification of the specific micro-organism in the spinal fluid.

Approximately every fifth to seventh patient received the experimental antitoxin during the early studies and every third patient during the latter half of the period. Patients to receive the antitoxin were selected only by reason of their not having had previous antimeningococcus serum therapy. It was the general impression among the hospital personnel that the patients treated with antitoxin were as a group severely ill and had less hopeful prognosis on admission than those treated with the standard sera. This was undoubtedly true during the latter half of the period as the efficacy of the antitoxin became more apparent. The resident staff was specifically instructed not to withhold

Table 2. Comparison of Fatality Rates of Cases of Meningococcic Meningitis in which Meningococcus Antitoxin and Standard Antimeningococcus Serum were given

Therapy	No. of Cases	All Deaths	Excluding Cases Fatal Within		
			24 hours	96 hours	48 hours
Antitoxin ...	85	23.5%	17.5%	10.9%	9.6%
Antiserum ...	211	45.9.	40.9.	35.9.	29.6.
All cases ...	296	39.5.	34.2.	28.6.	22.6.

antitoxin when an untreated case presented itself, regardless of the prognosis. All fatalities have been analysed on the basis of their relation to the date and hour of admission without reference to complications or instances of delayed treatment. All antitoxin deaths that occurred are classed as therapeutic failures and any factor that might show a lower and more favourable death rate for the antitoxin series has been studiously avoided. The patients in many instances were police patrol pick-ups without family or friends; on several occasions, identification could not be established prior to death or convalescence. Very frequently adequate history could not be elicited and therefore statistical figures for cases entering this hospital cannot be compared with other institutions in the city.

The fatality rate for the combined series is 39.5 per cent, with 53 per cent of the deaths occurring within forty-eight hours after hospital admission.

The efficacy of the antitoxin over antimeningococcus serum is apparent by comparison of the respective

Table 3. Cases and deaths by Ten-Year Age Groups

Age Group	Cases	Deaths	Fatality rate
1 to 10	89	18	20.2 %
11 to 20	69	23	33.3 "
21 to 30	51	15	29.4 "
31 to 40	34	18	52.9 "
41 to 50	22	16	72.7 "
51 to 60	14	12	85.7 "
61 to 70	4	4	100.0 "
71 to 80	4	4	100.0 "
Unknown	9	7	77.7 "

fatality rates of treated cases occurring at the same time, in the same hospital and under the same supervision. Consequently seasonal variations that might influence virulence of the meningococci are eliminated from the contrasted figures of table 1. Twenty deaths occurred in the series of eight-five patients treated with meningococcus antitoxin, 117 deaths were recorded in the group of 211 patients treated with antimeningococcus serum. The percentage death rate was 23.5 for the antitoxin and 45.9 for the antiserum.

The age of patients included in the entire series ranged from 3 months to 80 years, averaging 22.7 years. The cases treated with antitoxin averaged 18.1 years and the antiserum-treated group 24.7 years. From a study of table 3, arranged in ten-year age groups and respective fatality rates, it appears that the antitoxin was given to the most favourable subjects.

Seventy-three antitoxin-treated patients and 188 antiserum-treated patients were 80 years of age or younger. These cases are arranged in ten-year age groups in table 4 and show that, regardless of age, the antitoxin resulted in a lower fatality rate. Above the age of 80 the ratio is more favourable, but the number of antitoxin treated cases is not sufficient to warrant comparison.

Table 4. Influence of Age on Antitoxin and Antiserum Therapy

Age	Cases		Deaths		Fatality Rates	
	Anti-toxin	Anti-serum	Anti-toxin	Anti-serum	Anti-toxin	Anti-serum
1 to 10	88	56	4	15	12.5 %	26.7 %
11 to 20	22	48	6	17	27.2 "	35.4 "
21 to 30	19	34	2	18	10.5 "	52.9 "
Totals	73	188	12	45	16.4 "	23.9 "

The period of hospitalization for all recovered patients averaged 17.3 days. It is notable that those receiving antitoxin averaged 16.2 days as compared to the antiserum-treated group which averaged 18.0 days per case. The average hospitalization time for 398 cases at the Cook County Hospital recently reported by Borovsky was twenty-three days.

Table 5 shows the cases discharged from Cook County Hospital diagnosed "epidemic meningitis," 1915-1933 inclusive, with respective fatality rates. An improvement in the fatality rate during 1933 over other comparable years is seen. During 1933 in approximately 20% of the cases reported the patients received antitoxin, and its effect on the death rate for that year is significant.

The average total amounts of experimental antitoxin and standard serum given to a patient who had recovered was approximately 161.7 c.c. and 128.5 c.c. respectively. The largest amount of antitoxin and standard serum administered in recovered patients was 360 c.c. for the former and 245 c.c. for the latter, and the smallest amount 75 and 40 c.c. respectively. Allergic manifestations occurred in 17.7 % of the antitoxin treated cases as compared to 28.9% of those in which standard serum was given. In no instance did an ocular or auditory complication develop after the institution of antitoxin therapy; nevertheless, large doses of antitoxin were sometimes given in unsuccessful efforts to overcome such conditions when present at the time of the patient's admission.

Of eighty-five patients receiving the antitoxin, cisternal puncture was resorted to on only five occasions on many patients. In only three

Table 5. Epidemic Meningitis: Annual Reports of Librarian, Cook County Hospital, Chicago

Year	Cases	Deaths	Fatality Rates
1915	24	16	66.6 %
1916	21	14	66.6 "
1917	178	92	51.7 "
1918	145	69	47.5 "
1919	49	20	40.8 "
1920	21	19	90.4 "
1921	20	10	50.0 "
1922	9	6	66.6 "
1923	20	7	35.0 "
1924	44	36	81.7 "
1925	5	0	0.0 "
1926	18	9	50.0 "
1927	88	48	54.5 "
1928	187	85	45.4 "
1929	285	186	65.3 "

Year	Cases	Deaths	Fatality Rates
1930	134	73	54.4 "
1931	224	112	50.0 "
1932	116	56	48.2 "
1933	267	111	41.6 "
Total	1,815	919	50.6 "

instances and on the same number of patients were spinal drainage and treatment done twice during the same calendar day. The average number of lumbar punctures per case was not materially reduced except in a group of patients receiving antitoxin intravenously and intramuscularly.

In twenty-eight extremely severe but uncomplicated cases, 20 c.c. or more of meningococcus antitoxin was given intravenously or intramuscularly; of these patients eight died, with a fatality rate of 28.6%. The twenty patients who recovered received an average of 178.6 c.c. of antitoxin per patient, of which an average of 58.5 c.c. was given intravenously and/or intramuscularly and 115.1 c.c. per patient intraspinally. The period of hospitalization for this group averaged 18.6 days per case as compared to 17.5 days for the combined series.

Summary

My experiences during the past one and half years seem to justify certain conclusions regarding the treatment of meningococcic meningitis. Meningococcus antitoxin has reduced by approximately 50% the deaths from meningococcic meningitis at Cook County Hospital.

For many years it has been customary in the Contagious Disease Department of the Cook County Hospital to administer antimeningococcus serum intrathecally not oftener than once in twenty-four hours. This plan was adhered to when meningococcus antitoxin was given. Lumbar punctures when made every twelve hours or at eight hour intervals, as sometimes recommended, are extremely disturbing to many patients and seem to be of no added value in lowering the fatality rate.

Although cisternal punctures are much more easily performed by one with experience than lumbar punctures and are often preferred by the patient, this procedure should not be encouraged in a public hospital in which interns and residents are frequently changed. I do not believe that cisternal puncture is necessary in the treatment of meningococcic meningitis in order to secure the most efficient results. It is not essential to adopt this route for

the purpose either of drainage or of administration of serum except in case of block in the spinal canal. In no instance among the entire series of 372 patients was an intraventricular puncture required.

In the brief report of a meningococcal meningitis patient treated at Cook County Hospital in 1918, the value of giving antimeningococcus serum intravenously was emphasized. Since that time it has been customary to resort to intravenous serum therapy for all adult meningococcal meningitis patients admitted to my service. The value of this procedure is still more apparent when antitoxin instead of antimeningococcus serum is the remedy. As our experience with the antitoxin increased, larger and larger amounts of meningococcus antitoxin were given intravenously. The dose ranged from 22 c. c. among the earlier cases up to 100 c. c. and more during recent months. These large amounts of antitoxin intravenously explain chiefly the greater average dose of antitoxin as compared with antimeningococcus serum. On the other hand, the greater the quantity of antitoxin given intravenously, the smaller the average amount required for intrathecal injection. The most outstanding feature of intravenous and intramuscular antitoxin treatment is the prompt response of the infection and a more than 20 per cent reduction in the period of hospitalization. In fact, it is my impression that eventually it may be regarded as entirely unnecessary to administer any serum intrathecally if sufficient antitoxin is injected intravenously. Under such circumstances lumbar puncture would be done only for the purpose of diagnosis and for drainage.

A problem is now under way to compare the efficacy of intravenous and intramuscular methods of administration supplementing intrathecal antitoxin. One young woman with a fulminating type of meningococcal meningitis whose child died of meningococcal meningitis was treated only by large doses of antitoxin intravenously. Meningeal infection did not progress and she was discharged completely recovered on the seventh hospital day.

For the treatment of meningococcal meningitis with meningococcus antitoxin the following plan may be followed:

1. Intravenously from 60 to 100 c. c. of the antitoxin is administered in from 120 to 200 c. c. or more, respectively of physiologic solution of sodium chloride or 10 per cent dextrose solution. The smaller amount may suffice for a child, the larger quantity for an adult. This form of treatment may be repeated daily if the condition of the patient seems to require it. As a rule, one large dose intravenously

when therapy is started will prove sufficient by this route.

2. Intraspinally the amount of antitoxin, undiluted, and given by the gravity method, will be governed by the volume of spinal fluid withdrawn. Usually the quantity of antitoxin administered should be less than the amount of spinal fluid released. The initial dose of antitoxin intraspinally will usually vary from 20 to 40 c. c. Daily punctures should be made until the fluid is clear and free from organisms. At such a time the cell count of the spinal fluid will generally be less than 100.

3. Intramuscular administration of serum in an initial dose of from 30 to 60 c. c. is of value, but because of the serious nature of the disease the intravenous route is to be preferred.

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THE TREATMENT OF CEREBRO-SPINAL FEVER

By Joseph Morrow Kennedy, M.D., D.P.H.

Senior Medical Officer,
Lodge Moor Hospital, Sheffield

(Reproduced from the British Medical Journal,
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Historical Survey of the Malady

Cerebro-spinal fever was first differentiated by Vieusseux, in Geneva, in 1805. Danielson and Mason recorded an outbreak in Massachusetts in 1806, since when various manifestations of the disease have been recorded at intervals. In 1887 Weichselbaum gave a full description of the diplococci found in the direct smear of meningeal exudate observed post mortem in people who succumbed to meningitis. In 1896 Heubner was the first to demonstrate meningococci in cerebro-spinal fluid obtained from a living person. The most beneficial contribution was probably the discovery of antimeningococcus serum by Jachmann in Germany and by Flexner in America, and the introduction of the intraspinal injection of the serum by Flexner in 1904.

Outbreaks of the disease were being recorded from nearly all parts of the world, with the result that towards the end of the nineteenth century cerebro-spinal fever had become—or at least was generally recognized as—a cosmopolitan disease. Except for two or three small epidemics recorded in London and Rochester, this country was comparatively free until the early part of the present century. The first serious outbreak in the British Isles occurred in Glasgow in 1907-8: there were 1,238 cases, with 838 deaths. About the same time the disease was prevalent in Belfast, where there were 725 cases.

The disease was made notifiable in 1912, and the following table shows the incidence since that year.

Year	Notified Cases	Registered Death
1912	104	142
1913	305	163
1914	315	194
1915	2,566	1,974
1916	1,806	1,214
1917	1,465	1,531
1918	798	812
1919	848	573
1920	588	412
1921	411	416
1922	344	360
1923	301	284
1924	397	301
1925	402	354
1926	385	365
1927	470	430
1928	412	438
1929	650	588
1930	664	638
1931	2,157	1,440
1932	2,095	1,199

The increased prevalence of the disease amongst the civilian population during the war-year was a striking feature, and coincided with the outbreaks in the Army, where there were 4,238 cases, with 1928 deaths, in the Home Commands from 1914 to 1918.

Epidemic Position

Thirty years ago it might fairly be said that cerebro-spinal fever was almost unknown in Great Britain, until in 1907-8 the malady appeared in epidemic form in Glasgow, Belfast, and Edinburgh.

The spread of infection of this disease cannot be explained on the basis of most other infectious diseases, as it differs considerably in several ways.

- The disease tends to remain localized in one particular district, and does not spread to the surrounding areas.
- The source of origin of the epidemic cannot be traced, as the disease starts suddenly in some area when the remainder of the country is free, and after about two years, more or less, suddenly stops and does not reappear again in that district.
- The disease is not highly infectious, as it is seldom that a second case appears in the same house.

Of 500 cases admitted into Lodge Moor Hospital there were only four instances where a second case had occurred in the same house: also, none of those in attendance in the hospital developed the malady. Again, Dickson records an outbreak of thirty cases of cerebro-spinal fever, with twenty-two deaths, at Ojuela, a compactly built and greatly overcrowded mining town of 5000 inhabitants in Durango, Mexico, between March and July, 1929. The patients' ages ranged between 2 months and 40 years, and the disease was equally prevalent at all ages up to 25. In no instance did two cases occur in the same house or family, although isolation was impossible.

- The cases cannot be traced to have any relation to each other, as one case appears for the first time in one thickly crowded street or area, and the subsequent case from the other end of the district, in perhaps ideal surroundings, no common source or means of infection being traceable between the cases.
- For each case that was diagnosed in Sheffield, in the epidemic under review, the other members of the house were sent to the university laboratory, where a posterior nasal swab was taken, and any carriers found were isolated until free. It is interesting to note that none of these carriers developed the disease themselves, and in no instance could they be traced to be a source of infection to other cases.

Diagnosis

The disease presents no difficulty in those cases which show the classical signs of meningitis, such as head-ache, neck rigidity, and Kernig's sign, but it is in respect of those cases where the above signs are wanting that I wish to make a few remarks. I have found that, in most infants of about 1 year and under, a correct diagnosis can only be made after lumbar puncture. These cases merely showed the following features.

- (a) A remittent type of temperature of about 102°F., for which no definite cause could be found.
- (b) Irritability and resentfulness, which became more marked in routine examination.
- (c) Complete absence of neck rigidity, head retraction, and Kernig's sign.
- (d) Several cases showed a very heavy and dull appearance of the eyes, with slow gyrate movement of the eyeball, to which latter sign I attached some importance.

Speaking of the symptomatology of cerebro-spinal fever, Mogilinski states:

"The onset in infants differs considerably from that in adults, in whom it is sudden and accompanied by shivering, vomiting, high fever from the first, headache, rigidity of the neck and limbs, and in most cases (60 to 70 per cent.) herpes labialis. In infants, on the other hand, it is rare to find an onset accompanied by convulsions, high fever, and vomiting, but the disease usually begins insidiously, without meningeal symptoms or herpes. In some cases there may be signs of respiratory disease, followed later by meningeal symptoms."

The fever seems to bear little or no relation to the severity of symptoms, except immediately before death, when the temperature may reach hyperpyretic degrees—107°F. or over. The pulse appears to be as variable as the temperature when the patient is seen in the early days of the disease: it is usually soft, full, and slow. Often one sees a patient with a temperature of 102°F and a pulse rate of 60. When the patient is restless and suffering much pain the pulse is usually small and rapid.

As regards the special symptoms—vomiting, headache, and rashes—about 98 per cent of patients give a history of vomiting in the first day or so of the disease, but it is not seen much in hospital when they are under treatment. Most of my patients complained of severe frontal headache during the early days of their illness. The large purpuric type of rash resembles that seen in an acute pyæmic infection, and appears rapidly. The prognosis is very grave. The other type of hæmorrhagic rash—the petechial variety—is not so likely to be fatal, and resembles the "rose spot" of typhoid fever of fresh flea-bites. Herpes usually appears around the mouth, but may occur in any part of the body, such as the hands, feet, legs, around the vulva, and the anus. The most characteristic point about the herpes is that it appears with unfailing regularity on the fourth day of disease, and also that the contents of the vesicle contain the meningococcus.

Lumbar Puncture as an Aid to Diagnosis

Too much stress cannot be laid on the value of lumbar puncture. I consider that it is a simple and harmless operation, and should be performed more often—especially during epidemics of cerebro-spinal fever—in those patients where the slightest suspicion arises. I have carried out over 1,500 lumbar punctures, and never have I seen any fatal results follow the operation.

Lumbar puncture is one of the most valuable aids and means at our disposal for arriving at a correct diagnosis. The microscopic appearance of the cerebro-spinal fluid usually gives a fair idea of the type of meningitis. Should it be the least turbid, anti-meningococcal serum should be given forthwith, without waiting for a bacteriological report. On the other hand, a clear fluid does not eliminate cerebro-spinal fever, as the following case illustrates.

A female child, aged 3 years, was in a normal state of health, and quite playful. One Saturday afternoon, at 9 p.m. she was taken ill very suddenly, with vomiting, restlessness, and irritability with mild delirium. The following morning she became unconscious, and numerous purpuric hæmorrhages appeared on the skin. She was admitted into Lodge Moor Hospital about 3 p.m. on Sunday, and died at 8-30 p.m., death having taken place in less than twenty-four hours from the onset. Lumbar puncture was performed. The cerebro-spinal fluid was perfectly clear, and the pressure appeared normal. Only one polymorphonuclear cell was seen. Protein was 0.02% and direct examination of a film showed no organisms. A broth culture was examined after fifteen hours' growth, and was also negative, but after thirty-six hours' incubation at 37°C was found positive, and a meningococcus, Group I, Type I was isolated. At necropsy, dilatation and congestion of the blood vessels over the surface of the brain were present, and on sectioning the cerebral hemispheres numerous small pin-point striated hæmorrhages were seen throughout the grey and white matter. The ventricles did not appear dilated, but the choroid plexuses were swollen and hyperæmic.

This type of case bears out the statement made by Herrik, that *no other infection so quickly slays*.

Present Lines of Treatment

In the treatment of cerebro-spinal fever I think it is generally agreed that the best results have followed the introduction of anti-meningococcal serum. When Flexner read his paper on the treatment of cerebro-spinal fever by the use of anti-meningococcal serum he gave the mortality rates in epidemics before serum was introduced or applied as follows: New York, 79%; Edinburgh, 80%; Glasgow, 74%; Belfast, 70%; France, 75%; Belgium, 77%; Palestine, 80%.

He then showed a mortality of 30.9% on 1,294 cases treated with anti-meningococcal serum.

Robb produced the following figures:—

	Cases	Deaths	Mortality %
Cases treated without serum in Belfast Fever Hospitals, January to August, 1907	275	199	72.3
Cases treated at home without serum September to December, 1907	34	29	85.2
Cases treated with serum in Belfast Fever Hospitals, September to December, 1907	30	8	16.6

Ker also reduced his death rate in Edinburgh, by the use of serum, from 80 to 37 per cent.

When Flexner introduced his serum he advised the following method in the treatment.

A daily lumbar puncture and intrathecal injection of 30 c.cm. of serum for at least three or four days, in adults, with a proportionately smaller injection, if thought advisable, in infants. In more severe cases he considered that larger doses of serum should be given at even shorter intervals, say, every twelve hours, and that this treatment should be continued for as many days as were necessary to clear the cerebro-spinal fluid and alleviate the symptoms of meningitis.

Since the introduction of serum many observers have differed as to the best route for its administration.

Herrik, believing that the disease originates as a generalized meningococcus sepsis, endeavours to sterilize the blood stream by massive doses of anti-meningococcal serum given intravenously. Banks states that it has been his practice to give large doses of multivalent serum—for example, an initial dose of 100 to 200 c.cm. intravenously—and to do repeated lumbar punctures at twenty-four-hour or forty-eight-hour intervals, with or without an initial intrathecal administration of serum.

Peters and Gunn reported the results of 134 cases which occurred in Glasgow between January and the end of June, 1929, which were 112 deaths with only twenty-two recoveries, producing a death rate of 83.6 per cent. These cases were all treated in hospital with the use of serum, and Peters and Gunn pointed out that the mortality rate among cases in this outbreak (1929) was rather higher than that of the epidemics of 1906-8 by about 10 per cent. This seems to point to the absence of any degree of success attributed to improved methods of preparing and administering the specific antiserum. Experience in Glasgow does not confirm that of Flexner and others in America, where the case mortality is said to be halved by the use of serum.

Underwood reports an outbreak of the malady in Rotherham between January and December, 1931, when sixty-nine cases were notified. Sixty of these were admitted to hospital, and in thirty-seven the diagnosis of cerebro-spinal fever was confirmed, and the death rate of these cases was 89 per cent.

Goldman and Bower compare the results of forty-eight cases of cerebro-spinal fever treated by lumbar puncture plus the injection of serum intracisternally, intravenously, and intramuscularly. The forty-eight cases treated by the lumbar puncture method gave a mortality rate of 58.3 per cent. The average number of lumbar punctures performed in each case was 8.4. The average amount of serum given intrathecally was 200 c.cm., and 95 c.cm. either intravenously or intramuscularly. The total average amount was 295 c.cm. The fifty cases treated by the cisternal puncture produced a mortality rate of 86 per cent. The average number of serum given intracisternally 135 c.cm., and 128 c.cm. either intravenously or intramuscularly, the total amount being 263 c.cm.

Ford, Shera, and Purves-Stewart report a case of fulminating meningitis with recovery following systematic cisternal punctures and polyvalent serum. In this case five lumbar punctures and five cisternal punctures were performed, 90 c.cm. of serum given intrathecally, and 28 c.cm. of serum intravenously—total amount of serum, 172 c.cm.

Josephine B. Neal states, on the result of treatment of over 1,000 cases, that the Research Laboratory of the New York City Health Department advises the following method: "Intraspinal administration of serum is continued about every twenty-four hours, until at least two successive specimens of the fluid show no organisms by smear or culture. The dose of serum is usually 20 c.cm., if as much or more fluid has been obtained.

J. Cantacuzene has published perhaps the best results ever known, and he has reduced his mortality rate as low as 4.8 per cent. In brief, serotherapy is administered as follows:

(a) Intraspinal inoculation as early as possible. (b) Daily inoculation of 25 to 35 c.cm., the operation being always preceded by microscopical examination of the cerebro-spinal fluid, which should serve as a guide. (c) Stop the inoculations as soon as the meningococci have disappeared and the purulent character of the fluid is changed, otherwise there is a danger of serous meningitis. (d) Inoculate the serum as closely as possible to the infected site, and in young children perform intraventricular injections through the fontanelle. (e) The intraspinal injections should be accompanied by intramuscular inoculations.

Personal Experience

During the years 1931-2-3, 369 cases of cerebro-spinal fever were admitted into Lodge Moor Hospital Sheffield, of which 132 were fatal, giving a mortality rate of 35.76 per cent. Of these 132 deaths, fifty-two occurred within forty-eight hours of coming under treatment, which, when deducted, gives a mortality rate of 25.26 per cent. In 1931 there were eighty-five cases, with thirty-six deaths (42.35 per cent). In 1932 there were 100 cases, with forty-nine deaths (49.00 per cent). In 1933 there were 124 cases, with forty-seven deaths (37.9 per cent).

The following table shows the age incidence and death rate amongst the 369 cases during the three years.

Age	Cases	Deaths	Death Rate per cent.
Under 1 year	25	15	60
1 year and under 5 years	76	25	32.8
5 years " 30 years	218	67	30.7
30 years and over	50	25	50
Total	369	132	35.76

During the year 1931 serum produced in Great Britain, France, and the United States of America was used, in the hope that we should find an efficient or active remedy, but it gave rather unsatisfactory and disappointing results. Towards the end of 1931 we were advised by Dr. E. L. Sturdee, of the Ministry of Health, to try a serum produced in London. We used this serum exclusively for the

treatment of our cases during the years 1931-2-3. By the results obtained during 1932-3 this serum would seem to have been very effective.

Of the 188 cases which recovered during 1932-3 by the use of this serum I found that meningococci disappeared completely from the cerebro-spinal fluid after one intrathecal injection in ninety-eight cases, or 52.1 per cent and that the meningococci disappeared in 148 cases, or 78.7 per cent after having three consecutive intrathecal injections of serum. I believe that the presence or absence of the organism in the cerebro-spinal fluid is the only criterion by which we can form an opinion as to the value of the serum. I am inclined to agree with Dr. Cantacuzene that once the cerebro-spinal fluid has become sterile further intrathecal injections are dangerous, but it has been my practice to continue until the cerebro-spinal fluid has been found to be sterile on three consecutive days.

Out of the total of 192 deaths, the fifty-two occurring within forty-eight hours of admission to hospital were regarded as fulminating types of the disease. Of the remaining eighty deaths, it was found that in sixty-five instances (81.25 per cent), the cerebro-spinal fluid remained persistently positive in spite of daily intrathecal injections of serum.

It is my opinion that the intrathecal method is the best, and gives the most satisfactory results. I used this method in all cases, and in those cases which showed signs of a septicaemia (by the appearance of purpuric or petechial hæmorrhages) intravenous and intramuscular injections were used in addition.

We are informed that the cerebro-spinal fluid contains no complement, and thus no direct bactericidal action is likely to occur. The action of the serum is probably that of an increased phagocytosis. Physiologically, the lining membrane of the choroid plexus and the subarachnoid space is impermeable to substances passing from the blood to the cerebro-spinal fluid, except in the case of a few drugs. Serum injected intravenously may not reach the subarachnoid space, and, even if it does, must be in only very small and diluted quantities, and nothing like the amount which is brought into immediate and direct action by the intrathecal method.

I think that one can afford to neglect the clinical signs and symptoms that appear in the treatment of cerebro-spinal fever, and to attach the greatest importance to the condition of the fluid, as to whether meningococci are present or absent. Rigidity and irritability are increased by the intrathecal injection of serum, the following case being one of the many examples.

Case 175.—This boy was admitted on the second day of his illness. He was moderately conscious, and complained of severe headache. Neck rigidity, and Kernig's sign were present. He was lumbar-punctured, and serum was given intrathecally. The following day the cerebro-spinal fluid was sterile, yet his clinical condition was apparently worse, as the rigidity was increasing with head retraction, and towards the same evening he had great difficulty in swallowing fluids. The following day he was so rigid and retracted that opisthotonos was present and he was unable to swallow anything.

He was fed by an œsophageal tube. This condition became more marked each day, until lumbar puncture was stopped, and on the first day, that this was omitted he was able to swallow a little fluid the same evening. The following day he enjoyed his full meals.

Some authorities advise cisternal puncture in the treatment of cerebro-spinal fever, but this method does not appear to me to have any advantage over the more simple lumbar puncture. It entails more risks, and should only be attempted by one skilled in the operation. By doing lumbar puncture one is able to drain the cerebro-spinal fluid very well and inject serum without any danger; the field of operation is quite safe, whereas in cisternal puncture the field of operation is exceedingly dangerous, and the injection of serum has to be done very cautiously. If one does not obtain cerebro-spinal fluid by lumbar puncture in patients suffering from cerebro-spinal fever it is my experience that it will not be obtained by cisternal puncture, as the blockage usually occurs at the foramina of Luschka and Magendie, and has produced an internal hydrocephalus, so that the only thing that is of any value is ventricular puncture, which can be done quite easily in infants if the fontanelle is still patent.

The following table shows the average amount of serum used by the different routes, and the average number of lumbar and/or cisternal punctures performed by various authorities. The figures from Lodge Moor Hospital are included.

Herrick:—				
Average number of lumbar punctures	7			
„ amount of serum given intravenously	400-600	c.cm.		
„ amount of serum given intrathecally	100	„		
„ total amount of serum given	650	„		
Banks:—				
Average number of lumbar punctures	5			
„ amount of serum given intravenously	255	c.cm.		
„ amount of serum given intrathecally	45	„		
„ total amount of serum given	300	„		
Goldman and Bower:—				
Average number of lumbar punctures	8.4			
„ amount of serum given intravenously	95	c.cm.		
„ amount of serum given intrathecally	200	„		
„ total amount of serum given	295	„		
„ number of cisternal punctures	6.4	„		
„ amount of serum given intracisternally	135	c.cm.		
„ amount of serum given intravenously	128	„		
„ total amount of serum given	263	„		
Ford, Shera, and Purves-Stewart:—				
Average number of lumbar punctures 5, with average number of cisternal punctures 5	10			
„ amount of serum given intrathecally	90	c.cm.		
„ amount of serum given intravenously	82	„		
„ total amount of serum given	172	„		
Lodge Moor Hospital: (1932-33):—				
Average number of lumbar punctures	5.2			
„ amount of serum given intrathecally	76.2	c.cm.		
„ amount of serum given intravenously and intramuscularly	11.8	„		
„ total amount of serum given	88	„		

Choice of anæsthetic

I prefer to do all lumbar punctures under a local anæsthetic, avoiding a general anæsthetic in all cases except those where a widely delirious patient necessitates its use. In doing punctures under a local anæsthetic I give either morphine 1/3 grain or heroin 1/6 grain, according to the age of the patient, about a quarter of an hour beforehand, followed by 1 or 2 c.cm. of a 2 per cent solution of novocain. With a general anæsthetic, when the patient is coming round he is exceedingly irritable, noisy and very restless, and even the subsequent administration of morphine or heroin has very little effect.

Death occurring during the acute stage of cerebro-spinal fever is usually brought about by respiratory failure. I have seen numerous cases in which this condition occurred, and artificial respiration was carried out for several hours while the heart continued to beat regularly and forcibly. Under general anæsthesia respiratory failure is more liable to occur, and this is another reason in favour of a local anæsthetic. Another point of interest may be mentioned here. The meningococcus is not so delicate an organism as is generally believed. As a routine, about 5 c.cm. of cerebro-spinal fluid was collected from the patient by punctures and run into a similar quantity of glucose broth. This was incubated overnight, and the following morning a tube was forwarded to Dr. Scott (of the Ministry of Health) by ordinary post, in most instances arriving quite safely. From a broth culture I inoculated a blood agar slope, which gave me a good growth. This was washed off with normal saline containing 0.5 per cent phenol, and an emulsion obtained, which I put up against the four standard sera and the type of organism identified. The typing of the meningococcus during an epidemic is exceedingly valuable, as the particular type is always kept in view, and any change that may occur in the types is recognized and, if necessary, the serum altered.

Conclusion

During an epidemic of cerebro-spinal fever, when a patient complains of headache, and has some pain or tenderness on flexing the head—not necessarily neck rigidity—the examination of the cerebro-spinal fluid should be carried out without any further delay. One cannot stress too much the great importance of lumbar puncture in infants where there are no definite signs or symptoms of meningeal irritation other than pyrexia, with fretfulness or irritability. I am convinced that a number of infants die during an epidemic when the disease is not even suspected.

During an epidemic, serum should be prepared at once from the type of organism causing the disease, and freshly isolated strains of the infecting organism should be sent at regular and frequent intervals to the manufacturers of the serum. Once the disease is diagnosed, or when a turbid cerebro-spinal fluid is obtained, some anti-meningococcal serum should immediately be given intrathecally, without awaiting a bacteriological report on the fluid.

In treating the disease the condition of the cerebro-spinal fluid is very important, and as soon as it

becomes sterile further punctures and injections of serum must be carefully considered. It has been my practice to obtain three consecutive fluids before stopping the injections, though after I have obtained the first sterile fluid I reduce the quantity of serum. I believe that we do more harm than good by continued drainage of the cerebro-spinal fluid and intrathecal injection of serum. The examination of a direct smear is not sufficient evidence of persistent infection; the fluid must be cultured before it can be said to be sterile. Frequently the rigidity is increased by the intrathecal injection of serum, and no great importance need be attached to this, provided that, the cerebro-spinal fluid is sterile on culturing.

In conclusion, I do not claim that my results are any better than those of other workers, but I think I can safely state that the quantity of serum used and the number of lumbar punctures performed are much less, and that the number of days the patient is under active treatment has been reduced.

I am deeply indebted to the late Dr. Egerton Williams, Medical Superintendent, Lodge Moor Hospital, to Dr. Sturdee and Dr. Scott (Ministry of Health) for valuable suggestions; and also to my friends and colleagues Dr. Mackenzie and Dr. Wilburn, for their assistance in carrying out the treatment.

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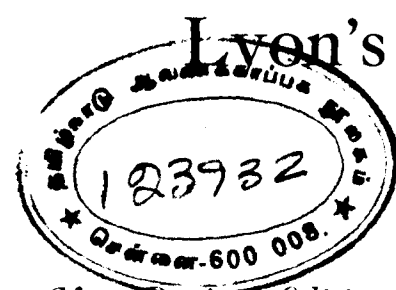
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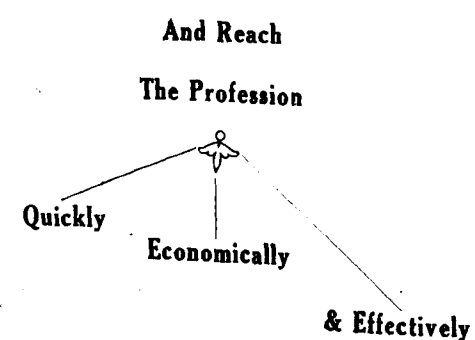
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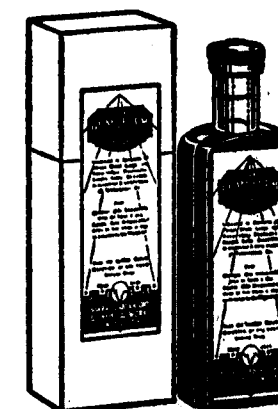
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