Influenzal Meningitis

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I. ABSTRACT

HISTORY OF MENINGITIS DUE TO BACILLUS OF PFEIFFER (Hemophilus Influenzae)

1892, Pfuhl[1] reported gram negative bacilli present in meningitis.

1899, Slamyk[2] reported first authentic case in which Pfeiffer supervised the bacteriologic studies.

Except for case reports, no further studies were made until 1911 when Wollstein[3] reported eight cases with careful analyses of the spinal fluids and virulence tests because as she states, "It remains, however, for the present, an undecided question whether influenza bacilli may not occur in the cerebrospinal fluid without setting up inflammation, just as pneumococci and some other organisms have been known to do." She produced fatal meningitis in monkeys with her human strains.

1921, Neal[4], New York Department of Health, reported thirty-two cases with one recovery.

1922, Rivers[5] reported twenty-three cases with one recovery together with a complete review of the literature and a careful study of factors tending to support his belief that the disease is a primary one produced by meningitic strains of influenzal bacilli closely allied to each other and differing from ordinary respiratory strains.

Incidence

In Neal's recent report of 111 cases, influenza bacillus ranks fourth among the types of the purulent meningitis.

Table 1. Distribution of Most Common Forms of Meningitis (all ages)

Meningococcic meningitis	1216
Tuberculous "	961
Pneumococcic "	209
Streptococcic "	203
Influenza bacillus "	111
Staphylococcic "	27

The disease occurs chiefly in infancy and early childhood. Although there are no figures obtainable in the literature to determine its position as a cause of meningitis in the early years, some idea can be gained by Rivers' and Neal's tabulation of its age incidence.

Table 2. Relation of Age to Incidence of Influenzal Meningitis

Age	Rivers No. Cases	Rivers Per-Cent	Neal No. Cases	Neal Per-Cent
Under 2 years	152	79	62	54
Over 2 years	41		49	
Under 5 years				84

At Children's Hospital, Boston, from 1926 to 1931, there were 56 cases of meningococcus meningitis and 25 cases of influenzal meningitis in children under 2 years of age. The high incidence is in distinct contrast to the infrequency with which the diagnosis of influenzal meningitis occurs in the records of local hospitals. At this (Minnesota General) hospital, since 1928, only one case, a child of twenty-three months (today's case report), is to be found. At the Minneapolis General Hospital, 1932 to 1935, three cases, 2 aged 2 years and 1 aged 6 months, all in 1934. At Ancker Hospital, St. Paul, influenzal meningitis has been diagnosed three times in the last 4 years.

Although the explanation for the seemingly low incidence is not known, Rivers suggests that, "While the bacilli are easily demonstrated in direct smears or in cultures by one accustomed to working with them, they may be overlooked by one less experienced. Consequently, some cases of influenzal meningitis may be treated as meningococcus infections in which no organisms were seen or grown and tabulated as deaths from epidemic cerebrospinal meningitis." In addition, there is the strong possibility that, because of the bizarre appearance of the long curved filamentous forms frequently present, contamination is suspected and the fluid discarded. A third reason is that only peptone, in which they do not grow, rather than blood agar, is some-

times used for spinal fluid cultures.

Spinal Fluid Examination

The spinal fluid does not differ in appearance from other forms of purulent meningitis. It is cloudy to purulent in appearance, shows marked pleocytosis with a predominance of polymorphonuclears, increased protein and low sugar content. The number of bacilli present is usually large and differs from the type originally described by Pfeiffer (i.e. short rod with rounded ends; so short as to be almost coccal) in that there is frequently a large number of long, thin, wavy or curved, threadlike forms sometimes lying together in tangled masses and resembling the leptothrix group in morphology. Wollstein noted that this pleomorphism increased with age of the culture.

If gram negative bacilli are seen on direct smear or if no organisms are found, an indol test should be done. B. influenzae and B. coli are the only two organisms which form indol in spinal fluids. Some strains of B. influenzae do not produce indol. B. influenzae grow best on rabbit's blood agar, appear as minute dewdroplike colonies and are likely to be overlooked.

Etiology

A great deal of discussion has arisen as to whether influenzae bacillus meningitis is a primary or secondary disease, many older writers considering it a complication of a respiratory infection. The largest number of cases occur in the last half of the year coinciding with the peak of the curve of pneumonia incidence. In New York City, there was no increase in the number of cases during the influenza epidemic in 1918 and 1919. Rivers states that 74 per cent of the cases studied by him were probably primary infections. He found that 15 meningitic strains could be divided into 4 groups by absorption tests and that one of 18 respiratory strains was identical with these groups. Povitzky[6] finds that over 50 per cent of the strains of influenzal meningitis fall into one group by agglutinin absorption tests in contrast to the multiplicity of respiratory strains. Pittman[7] by means of cross precipitation and direct agglutination reactions found that all but 4 of 41 meningeal strains fell into one group, all are smooth (S) strains, contain capsules and produce a specific soluble substance.

Clinical Picture

This differs in no way from that of meningococcic meningitis, a hemorrhagic rash may even be present which is supposed to be characteristic of the latter disease. The earliest signs are usually irregular fever, irritability and gastro-intestinal disturbance. The diagnosis is frequently difficult because so large a percentage of cases occur in the age (infancy) when symptoms are not referable to the nervous system. It is most often mistaken for pneumonia because of the unexplained fever associated with rapid, difficult, embarrassed respiration. The leucocyte count is increased - 11 to 76,000 cells with an increase in percentage of polymorphonuclear cells (70-80%) which is in striking contrast to epidemic influenza.

Blood cultures are positive in a large percentage (7 out of 8 in Neal's series). Joint involvement with recovery of organisms in the fluid is further evidence of a generalized infection (rather frequent).

Pathology

The picture is usually one of massive purulent meningitis as described in the present case report. In protracted cases, diffuse involvement of the cerebral parenchyma may occur with hemorrhages and abscesses. Organization of the pus at the base of the brain with formation of fibrous strands in the meninges also characterizes the cases of longer duration.

Course of the Disease and Mortality

Although a short fulminating course is occasionally observed, the disease is usually protracted. In Neal's series, the duration of the greatest number was between 10 and 20 days. In Rivers' 22 cases, the average length of life was

20 days. Thirteen of Neal's 111 cases lived 30 to 60 days or longer but only 4 recovered - a mortality of 96 per cent. In Rivers' collection of 220 cases only 17 recovered - a death rate of 92 per cent. Thirty-five was the total number of reported recoveries up to 1934 and two more have been added this year.

Treatment

The first serum for the treatment of influenzal meningitis was developed by Wollstein[9] who immunized goats and was able to prevent death in two monkeys given influenzal bacilli intrathecally. The same serum was used in two recoveries reported by Torrey[10] and in five cases by Neal with no recoveries. The Department of Health research laboratories, New York City, has prepared anti-influenza serum since 1920 by immunizing horses with strains of the influenza bacillus found by Povitsky to predominate their cases of influenzal meningitis.

In 1932, Ward and Wright found that complement was absent in the spinal fluid of influenzal meningitis patients and recommended the addition of normal serum to anti-influenzal serum before injection. They found that this produced a temporary disappearance of organisms from the spinal fluid in eight cases all but one of which, however, died and at autopsy showed abscesses (walled off) from the general subarachnoid space.

Pittman in 1933 developed a type-specific H. influenza antiserum using a predominating strain with which 37 out of 40 strains agreed. She found, experimentally, that the dosage of the culture could not be too large or the serum would not completely protect no matter how large the amount given. Employing the serum in a series of 18 patients with influenzal meningitis, recovery occurred in one. In two others, although the patients ultimately died, the spinal fluid cultures became sterile and remained so for from 7 to 14 days. Among 5 patients in whom septicemia was present before treatment, in 4 the blood cultures, after treatment with serum, became sterile. An effort to produce a more potent specific serum is suggested by this work.

Some patients at autopsy show the meningitis to be practically subsided but severe toxic changes in many of the viscera indicate the advisability of intravenous as well as intraspinal administration of serum.

Ingraham and Fothergill[8] are attempting to find a better method of introducing the antiserum than by simple lumbar or ventricular injection in order to prevent basal abscess formation. Kubie[11] has discussed the method and underlying principles of forced drainage of the cerebrospinal fluid in influenzal meningitis and Neal has reported apparent benefit from its use.

SUMMARY

1. Influenzal meningitis, occurring chiefly in infancy and early childhood, is produced by strains of influenzal bacilli closely allied to each other and differing from respiratory strains, culturally and serologically.

2. Its low incidence in this region compared with its frequency in other areas suggests that it occurs much oftener than it is diagnosed.

3. The diagnosis is often overlooked because of:

(a) Bizarre pleomorphism of the bacilli.
(b) Using inadequate media for growth.
(c) Failure to utilize corroborative tests.

4. It is most frequently a primary disease.

5. A positive blood culture is often found.

6. Massive purulent meningitis, a protracted course and a high mortality are the chief feature of the clinical picture.

7. A serum with higher antitoxic and antibacterial properties is needed.

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II. CASE REPORT

INFLUENZAL MENINGITIS

Case is white female, 23½ months of age, born at University of Minnesota Hospitals 8-18-33 and discharged 8-28-33 (10 days); readmitted 7-10-35 and expired 8-3-35 (24 days). Total stay- 34 days.

Upper Respiratory Infection

7-9-35 - Appeared irritable in morning. Face flushed and temperature 102.6 in afternoon. Vomiting in evening. Physician called. Throat reddened and left ear slightly injected. Given sponge baths and throat irrigations. During night, breathing became more difficult.

Severe Toxicity

7-10-35 - 8 A.M. - Temperature 100.6. During morning, played about in bed but vomited. 8 P.M. - Child stuporous and pale. 8:30 P.M. - Admitted. Physical Examination shows generalized inflammation of throat without membrane. Breath sounds replaced by laryngeal stridor; no rales. Ears, abdomen and extremities - negative. Laboratory: Blood - white blood cells 3,500, polymorphonuclears 92%. Chest plate - no areas of density. Laryngoscopic examination - some exudate over arytenoids and glottis but no obstruction.

Transfusion

7-11-35 - Given 150 cc. citrated blood, 500 cc. saline, and glucose. Temperature 103.6. Respirations 70. Pulse 160. Laryngeal stridor still present. Some diminution of breath sounds suggesting atelectasis of lungs. Paraoral fluids given. White blood count shows rise to 12,000 with 90% polymorphonuclears.

Pulmonary Signs

7-12-35 - Difficulty in breathing. Signs of consolidation in right upper lobe. Urine - 1 to 2+ albumin, occasional white blood cells.

Meningeal Signs

7-13-35 - Drowsy. Elevated temperature continues. Kernig sign negative. Pupils moderately contracted. Lumbar puncture done: cell count 840, 74% polymorphonuclears; smear shows no organisms; cultures taken remain sterile. 11 P.M. - Still stuporous. Neck rigidity 2+. Temperature 101.8. Spinal puncture repeated - cell count 180 per cmm; smears and cultures negative.

Improved: Pyelitis

7-14-35 - Temperature 102. Meningeal signs decreased. Chest clear. Urine (centrifuged) - large numbers of white blood cells. Fever still persists in latter part of day. 7-16-35 - Temperature 103. Urine culture - coli and streptococci, sediment loaded with pus.

Improving

7-17-35 - Neck rigidity present but less marked. More alert. Spinal puncture - pressure 240 mm., smears and cultures negative. Urine - large numbers

of white blood cells and bacteria.

7-18-35 - Temperature 103. Chest clear. Knee jerks negative.

7-19-35 - Temperature same. Urine improved.

7-22-35 - Temperature same. Urine - pus and bacteria present.

Cystoscopy

7-24-35 - Negative cystogram. Cystoscopy - enlarged kidney pelves and ureters; no other change.

7-26-35 - Temperature rising somewhat higher, reaching 104.

7-27-35 - Urine - less white blood cells.

Relapse; H. Influenzi in Spinal Fluid

7-30-35 - Increased neck rigidity. Pressure - 100 mm. mercury; fluid cloudy; cell count 350; direct smear - loaded with gram negative pleomorphic organisms of coccoid and long filamentous forms as well as small rods. Appearance is characteristic of hemophilus influenzi. Spinal puncture repeated in afternoon, on two occasions: increased pressure; cell count 750; smear shows same organisms. Cultures on chocolate agar and on Levanthal's media remain sterile. Serum obtained from Massachusett's General Hospital.

Serum

7-31-35 - Serum administered. No change in patient's condition. Cell count rises. Organisms much less in number than on previous dates.

No Improvement

8-1-35 - No improvement in condition. Serum still administered.

Death

8-3-35 - No improvement. Child expired.

Autopsy

Body is well developed, well nourished, white female, 23½ months of age, measuring about 89 cm. in length and weighing approximately 15.4 kilograms. Rigor present. Hypostasis purplish and posterior. No cyanosis, jaundice or edema. Pupils round and equal, each 5 mm. in diameter. No special marks.

Peritoneal Cavity is smooth and glistening; no excess fluid. Appendix hangs free.

Purulent Fluid

Right Pleural Cavity contains about 75 cc. slightly purulent fluid; left negative.

Pericardial Sac shows no change.

Heart weighs 85 grams. Musculature is firm. Valves show no evidence of recent or old endocarditis. Root of aorta and coronaries are negative.

Atelectasis

Lungs each weigh about 110 grams. Patchy lobular type of atelectasis about margin of left lung and along righ lower lobe.

Spleen shows no change.

Toxicity

Liver weighs 550 grams and is mottled throughout with yellow markings of fatty change.

Gall-Bladder shows no change.

Gastro-Intestinal Tract shows no ulcerations, inflammatory reaction or diverticulae.

Pancreas is soft. No tumors or cysts.

Adrenals are well formed.

Pyelitis

Each Kidney weighs 80 grams. Capsules strip easily. Kidney substance somewhat pale. Enlarged pelves. Mucosa edematous, reddened and thickened. Ureters dilated and mucosa likewise shows inflamed tissue. Ureters more injected than pelves of kidney proper.

Genital Organs - negative.

Meningitis, Localizing Abscesses

Head: Scalp and calvarium show no change. Meninges reddened throughout. Fluid very turbid. Over entire surface of brain, both vertex and base, there are localized collections of thick yellow pus. These patches are irregularly distributed. Largest collection is over occipital poles of cerebellum and adjacent medulla. Other large collections over tips of both temporal lobes on ventral surface about 3 or 4 similar collections over convolutions of cerebellum. Base of brain is bathed in pus but there does not appear to be a localized collection such as is present in other areas. These collections of pus average about 4 x 3 cm. Pus seems to be held in position by adhesion of pia against brain tissue. Over posterior poles of cerebellum when collection of pus is punctured and pus evacuated, there is a depression in the surface of the brain marking out the position of the collection. Over the pituitary, there is a nodule of firm organized pulp having a consistence suggesting old pus infiltrated with fibroblasts. The middle ears and mastoids are opened on both sides. There is stringy mucus but no pus. The interior of the brain shows no change. There is congestion and dilation of the blood vessels. No abscesses within brain substance itself. Ventricles filled with turbid fluid and choroid is markedly congested.

Smears are made at postmortem of various viscera. The following results are noted:

Fluid from right pleural cavity shows mixture of organisms in which streptococci predominate.

Spleen and lungs show no organisms.

Kidney pelves again show heavy mixture among which very large gram negative rods, having morphology of proteus, predominate.

Smears of collections of pus from over surface of brain show very scant number of same type of pleomorphic gram negative rods seen in spinal fluid.

Diagnosis

1. Influenzal meningitis.
2. Pulmonary atelectasis.
3. Pleurisy.
4. Bilateral Pyelitis.
5. Ureteritis.

III. LABORATORIES

The following is reprinted from the Bulletin of April 4, 1935, Volume VI, number 23 for the benefit of the new interns and fellows:

"1. Requests dealing with individual research projects cannot be accepted by the hospital laboratories for the time being.

"2. The number of chemical procedures per day is limited. Some of these (glucose-tolerance tests) must be scheduled ahead. Not infrequently the work is so heavy that the schedule is filled for days ahead.

"3. All chemistries must be in the laboratory by 9 o'clock. All subsequent chemistries requested must be emergencies and arrangements must be made with Miss Zschiesche.

Special tubes are provided for each chemistry:

Large oxalated test tubes 1/3 full of blood, well mixed (to prevent clotting) are used for:	Uric acid N.P.N. Cholesterol Creatinine
Oxalated centrifuge tubes 3/4 full of blood for:	CO_2 combining power Plasma chlorides
Small oxalated tubes 1/4 full of blood for	Sugar
Plain centrifuge tubes are used for:	Icterus index Van den Bergh Calcium Phosphorus

Blood for sugar, calcium, phosphorus, CO_2 combining power, chlorides must be sent to the laboratory immediately. Results are not otherwise accurate.

"4. Basal metabolism rates and electrocardiograms are scheduled ahead. The schedule for the subsequent day is closed by 4 P.M.

"5. The various divisions of services are given a certain allotment of BMR's. The excess cannot be taken care of and it becomes essential for the physicians to request examinations on only those cases in which the tests are of most value.

"6. To reduce the amount of time devoted to charting and eliminate the reduplication of work, the laboratory sheets are sent to the laboratory directly from "admissions." They reach the ward only after the admission laboratory work has been completed. During this interval, the laboratory sheet cannot be expected on the chart.

"7. Follow-up laboratory studies are done by the clerks or interns. These reports on the chart do not have the signature of the laboratory. The laboratory cannot at present handle these follow-up studies. When, however, circumstances arise in which a check upon the clerk's findings is indicated, the laboratory will do such tests providing they are notified.

Example: "John Jones
Catheterized urine

Dr. A."

A specimen with such a request shall be placed in the student laboratory.

"John Jones
Catheterized urine
To Main laboratory.

Dr. A."

Such a specimen will be examined in the main laboratory.

"8. Keep the laboratory available for those tests which are actually important. Do not burden it with matters of casual interest -- for instance, cell count on thick, yellow pus; examination of pus for leukemic cells; differential cell counts on urine, etc.

"9. The laboratory closes at 4:30 P.M. The night laboratory service is for emergencies. In order to keep it available for emergencies, routine work must wait until the following day. Please remember that emergency laboratory work is trying and difficult - be human. Remember that your emergency probably is no more important than the one with which the technician is occupied at the time.

"10. Finally, and above all, bring your suggestions, troubles, criticisms and the errors which you observe or suspect to the laboratory. Through such cooperation, we can give better service."

IV. RAYMOND MICHAEL AMBERG

Halbert Louis Dunn, Director of the University of Minnesota Hospitals, left for Washington, D. C., July 1st, 1935, to head the Statistical Division of the Department of Vital Statistics. His place has been taken by Assistant Director Amberg. Raymond Michael, fortish (St. Paul, August 24, 1895), plump, greying, Irish-German, for years has had easy sailing because of his Scandinavian name and appearance. Spent his early days in Hastings, later moving to Grand Rapids where he graduated from the local high school in 1914.

He received his degree of Ph. C. from the University of Minnesota in 1920, following which he spent 2½ years in the School of Business Administration. He followed professional pharmacy at intervals until 1922 when he associated himself with the Students' Health Service in Pillsbury Hall. In the formative days of the Health Service, he proved himself invaluable in a variety of ways and in 1924 was made Business Manager. His official connection with the hospital

started in 1929 when he helped plan and organize the Out-Patient Department. In 1932, he was made Assistant Director of the Hospital and in 1935, Acting Director.

He is a member of the Minnesota State Hospital Association, American Hospital Association, Minnesota Pharmaceutical Association and a few years ago received the honor of being designated a Fellow of the American College of Hospital Administrators. In all these organizations, he has played an active part in various capacities. It is said of him that very few young men in the hospital field have received such instant recognition for administrative planning and execution. His military service extended from 1917 to 1919 as a member of the Air Corps of the United States Army, entering service before war was declared by the United States.

It is not difficult to predict continued success for Mr. Amberg. He enjoys the confidence of the staff and the administration of the University. Builder, developer and diplomat, he has that rare gift of being able to plan something and then see it through. He has perfect knowledge of the needs of the various departments and the ability to get whatever he goes out for with apparent ease. It has already been said of him that he combines in his personality practically all of the good points of the men who have helped build and administer our Hospital. It looks like smooth sailing ahead with "Skipper Amberg" at the helm, and we are most grateful to the administration for giving him to us.

V. MOVIE

Title: The Land of the Eagle

Released by: RKO.

VI. LAST WEEK'S MEETING

Date: October 3, 1935.

Place: Recreation Room, Nurses' Hall.

Time: 12:15 to 1:21

Program: Movie (Marine Mysteries)
Angiomatosis
Chorionepithelioma
Remarks (Dean Harold Diehl)

Present: 85

Discussion: Rudolph Koucky
Leo G. Rigler
William T. Peyton
Charles Rea
W. K. Stenstrom
Richard Johnson
J. C. Litzenberg

Errata: Internes 1935-1936, not 1934-1935.

Gertrude Gunn,
Record Librarian

VII. ANNOUNCEMENT

FRANCES R. VANZANT, M.D.
Announces the opening of an Office for Practice of Internal Medicine

1109 Medical Arts Building
Houston, Texas

Preston 2522 Hadley 1630