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The Relationship of the circulating leukocytes to the spinal fluid in acute poliomyelitis

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THE RELATIONSHIP OF THE CIRCULATING LEUKOCYTES TO THE SPINAL FLUID IN ACUTE POLIOMYELITIS

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Introduction:

In April, 1950, Ford (1) published an article reporting the results of a serial study of the spinal fluid protein and cytology in cases of acute poliomyelitis. Ford suggested that such a study would be of value in justifying the diagnosis of subclinical disease. This paper would, in part, attempt to verify the results of Ford's studies.

In addition, it was felt by the author of this paper that there may be a correlation between the spinal fluid and the total white count and differential of the peripheral blood. As Ford pointed out, there were consistently higher concentrations of spinal fluid protein in the paralytic cases than in the non-paralytic cases, and that in the spinal fluid there was an earlier decrease in total cells in the paralytic cases than in the non-paralytic. The principal purpose of this investigation is an attempt to find a similiar correlation in the peripheral blood which would be useful in evaluating the progress of the disease and which would be a simpler procedure than repeated spinal punctures.

Materials and Methods:

In this study a statistical method was used instead of a serial method, although the latter would be more accurate. It was felt that the statistical method would be sufficient to denote a trend in the disease if a large enough number of determinations

were used and an arithmetical mean determined for each day which would be compared with the average course of events in the disease. The records of poliomyelitis at Childrens' Memorial Hospital, Omaha, Nebraska, were surveyed from June, 1948, through November, 1950, a total of 350 cases.

From each case history, the three chief symptoms (headache, fever, malaise, stiff neck, stiff back, gastro-intestinal disturbances, weakness, sore throat, nervousness, muscle pain, or diplopea) and their duration were recorded. In the same manner, the three chief signs (stiff neck, stiff back or hamstrings, flushed face, weakness, bulbar signs, masophargyngitis, lethargy, disorientation, nodes, tremor, fever, and paralysis) and their duration were tabulated. From the three chief symptoms and signs the onset of the preparalytic stage was determined.

The spinal fluid cell count, the differential, and the total protein for each case was tabulated according to the days duration of the disease from the onset of the preparalytic stage. A similiar procedure was used for the peripheral blood total white count and differential. The average range for the spinal fluid cell count used as a comparison was taken from Kolmer (2) and was 0 to 10 cells per c.mm. The method for the protein determination was that of Young, Bennett, Christlub, and Myers (3); the average value was also derived from Kolmer (2) and was 30 mgm per cent with a range of 15 to 45 mgm per cent. The average values of the peripheral blood

total white count and differential used for comparison in this age group were taken from the Handbook of Hematology (4), the average total white count being 7,300 with 53% polymorphonuclear and 45% mononuclear cells.

After the determinations were grouped according to the number of days duration of the disease, for each group of findings the arithmetical mean for each day was calculated. Because there seemed to be no significant difference between consecutive days, the span of thirteen days was divided into five periods: period one, covering days one and two of the disease from the onset of the pre-paralytic stage; period two, days three and four; period three, days five and six; period four, days seven and eight; and period five, days nine, ten, eleven, twelve, and thirteen.

Table I contains the results of the peripheral blood determinations in the non-paralytic cases; Table II contains the results of the peripheral blood determinations in the paralytic cases; Table III contains spinal fluid results in the non-paralytic cases; and Table IV has the results of the spinal fluid determinations in the paralytic cases.

Of the total number of cases surveyed 190 were used in the final statistical analysis. The rest of the cases were discarded as unsuitable because the date of onset of the illness could not be determined; the illness was complicated by some other disease process; the patients were beyond the established age range of

2 to 15 years; or because an insufficient amount of laboratory data was available to warrant their inclusion in the final statistical analysis.

The age of the patients used in the final analysis ranged from 2 to 15 years, the average being 7.4 years. There were 151 cell counts and protein determinations each in the non-paralytic spinal fluid; there were 61 each of the paralytic spinal fluid determinations. There were 159 non-paralytic peripheral blood determinations, and 66 paralytic blood determinations each of the total and differential counts.

Results:

Unfortunately, a large enough series of paralytic patients could not be obtained to make an accurate statistical comparison between the paralytic and the non-paralytic determinations for the entire five periods, but a tendency for variation between the two could be observed. The analysis was not carried beyond the thirteenth day because of insufficient data, consequently the peak protein values could not be established.

In Tables III and IV, it can be seen that the spinal fluid ppotein did not show any significant variation as the disease progressed in either the paralytic or non-paralytic cases. However, the total average protein value for the non-paralytic cases was 39 mgm percent and the total average for the paralytic series was

51 mgm per cent. As is noted, the ranges overlap for the two series, especially in the high values where they are nearly identical. The variation appeared in the minimum values. A minimum was not found below 18 mgm per cent in the paralytic series and that only in the first period, and was above 20 mgm per cent in the others; in the non-paralytic series the minimum values were below 15 mgm per cent in all except one period, the lowest being 9 mgm per cent in the third period.

In both the paralytic and the non-paralytic series, there was a wide variation in the total spinal fluid cell counts (Tables III and IV). In the non-paralytic series, it was found that 7% of the examinations were negative despite the fact that a clinical diagnosis of poliomyelitis could be made; in the paralytic series 5% of the examinations were negative. In view of this, and the fact that the high and low ranges in both series overlapped, no significant difference could be found in the magnitude of the cell count between the paralytic and the non-paralytic series. In the non-paralytic group, there was a gradual decrease in the total count until the end of the fourth period, or after the eighth day, when a significant drop occurred. In the fourth period of the non-paralytic series there was a rise over the preceeding three periods but this was felt to be due to two particularly high counts of 1,186, and 1,040 cells per c.mm. In the paralytic group there was also a gradual decrease in the total white count until the end of the

third period, or after the sixth day, when a significant change occurred.

At the onset of symptoms in both series, there were about equal distribution of the polymorphonuclear and the mononuclear cells. This gradually shifted towards a predominance of the latter. However, the predominance becomes more apparent in the paralytic series after the third period. Until this time the ranges for the paralytic and the non-paralytic cases were the same, but following the third period in the paralytic series, the polymorphonuclear cells did not exceed 25% while in the non-paralytic group they reached 55% until the end of the fifth period.

The peripheral blood determinations are tabulated in Tables I and II. A consistent finding was a slight to severe leukocytosis with a moderate shift to the left in the differential. In the non-paralytic and paralytic series the mean total white count remained elevated to the end of the fifth period with the greatest drop occurring after the first period. There was no significant difference in the degree of leukocytosis between the paralytic and the non-paralytic series, the mean being 10,900, and 10,500, respectively. In the first two periods the minimum value for the non-paralytic series was 5,100, and in the paralytic series the minimum was 8,100.

The differential in the non-paralytic series returned to the average levels for this age group during the third period, while in the paralytic series it did not do so until the fourth period.

Some degree of granulocytic predominance remained until these times.

In all five periods for each series, there was a wide range for the total white count and the differential indicating that some of the cases even as late as the fifth period had a leukocytosis with a shift to the left in the differential; conversely, as early as the end of the first period some of the cases had a normal blood picture.

No correlation could be found between the total spinal fluid cell count and the total white count of the peripheral blood. Apparently, the significant drop in the spinal fluid count after the third and the fourth periods in the paralytic and the non-paralytic series respectively does not have a counterpart in the peripheral blood.

In the differential of the spinal fluid it was pointed out that after the second period the predominance of the mononuclear cells became more pronounced in the paralytic series than in the non-paralytic series. However, in the peripheral blood the opposite was true. The predominance of polymorphonuclear cells lasted until the fourth period, while in the non-paralytic series the leukocytosis was present until only the third period. It would seem that an inverse relationship existed between the differentials of the spinal fluid and the peripheral blood.

There was no significant trend in the spinal fluid protein in either series over the limited period in which the determinations

were made. However, the arithmetical mean of the protein was higher in the paralytic cases than in the non-paralytic. In the peripheral blood of the two series, little can be found to account for the difference; the total white counts in the two series are essentially the same. The only significant difference was the granulocytic leukocytosis lasting two days longer in the paralytic cases.

Comment:

McQuarrie (5) divides the course of poliomyelitis into three stages, the prodromal, the preparalytic and the paralytic. The first consists of a nonspecific acute febrile illness, followed by the preparalytic stage, or stage of invasion, which lasts three to six days. If the disease continues to progress, the paralytic stage is entered about the third or fourth day following the onset of the preparalytic stage. However, it may begin anywhere from the first to the seventh day.

Bodian (6) presents evidence that the onset of pathologic changes in the spinal cord appear early in the stage of invasion. The first evidence is cytoplasmic chromatolysis which is followed shortly by a moderate amount of inflammatory exudate with polymorphonuclear cells predominating first and shifting gradually to mononuclear predominance. If the process is arrested at this point the cells will go to eventual recovery. Apparently this point is reached by the third or fourth day and extension of the disease stops in non-paralytic cases.

Bodian (6) further found that as early as the first day of the paralytic stage the virus was widely disseminated among the motor

cells of the spinal cord which were either quickly destroyed during the first few days or eventually recovered. Therefore, one would conclude that in the paralytic cases the process is still active several days beyond the average three or four days duration of the non-paralytic cases.

If extension of the disease stops after an average of three or four days in the non-paralytic case, the systemic reaction of leukocytosis should begin to diminish shortly after this time. In a paralytic case, in which progression is continuing, the systemic reaction should last for several days longer. The results of this analysis seems to confirm this. On the average, the white count and the differential return to normal in the non-paralytic patients during the third period. The white count and differential did not return to normal until the fourth period in the paralytic cases, or two days later than in the non-paralytic cases.

As noted by McQuarrie and Bodian, there was considerable individual variation in the time element for each individual. This is indicated by the marked variation in the ranges of the determinations seen in the tables. Some patients maintained a leukocytosis and shift until the end of the fifth period while others apparently had returned to a normal count by the end of the first period. Any given patient might maintain a systemic reaction until extension of the disease terminated; in such a case, peripheral blood counts would be of value in determining whether extension of the disease was continuing or had stopped.

The following case histories are presented to illustrate the foregoing supposition:

Case 3195: This was a seven year old white male child admitted to the hospital on 9-28-49. He had suffered severe frontal headaches with nausea and vomiting for three days prior to admission. Two days prior to admission he began to have stiffness of the back, neck and hamstrings. A blood count on 9-29-49 revealed a total white count of 10,900 with a differential of 69% mature polymorphonuclear cells, 10% immature polymorphonuclear cells, 25% lymphocytes, and 1% monocytes.

His condition slowly progressed with increasing spasm of the involved muscles and some weakness developed in the muscles of the lower extremities. A repeat blood count on 10-5-49 revealed a total white count of 9,200 with a differential consisting of 54% mature polymorphonuclear cells, 18% immature polymorphonuclear cells, 24% lymphocytes, and 1% monocytes.

He progressively demonstrated more extensive muscle weakness, and continued to run a low grade fever until 10-8-49. On that day he clinically began to improve. A repeat blood count was done on 10-10-49 showing a total white count of 9,300 with a differential of 45% mature polymorphonuclear cells, 7% immature polymorphonuclear cells, 39% lymphocytes, and 9% monocytes.

Case 893: This was a five year old white male child who entered the hospital on 9-22-48 complaining of muscle pain and malaise of two days with nervousness for one day; stiffness of the neck, back

and hamstrings had been present for two days and on the day of admission he had begun to have a nasal twang to his voice. A blood count on 9-24-48 showed a total white count of 7,500 with a differential of 54% mature polymorphonuclear cells, 11% immature polymorphonuclear cells, 30% lymphocytes, and 5% monocytes.

On 9-25-48, he was having more difficulty with his speech and was unable to swallow. A repeat count at this time showed a total white count of 8,400 with a differential of 38% mature polymorphonuclear cells, 10% immature polymorphonuclear cells, 30% lymphocytes and 2% monocytes.

On 9-28-48, the patien'ts condition began to improve and on 10-1-48, a blood count revealed a total white count of 6,400 with a differential of 28% polymorphonuclear cells, 3% immature polymorphonuclear cells, 60% lymphocytes and 3% monocytes.

Case 877: This was a nine year old white female child who entered the hospital on 9-20-48 complaining of diplopea, stiff back and neck for one day with a fever for two days. A blood count on 9-21-48 showed a total white count of 10,600 with a differential of 50% mature polymorphonuclear cells, 13% immature polymorphonculear cells, 36% lymphocytes, and 1% monocytes.

On 9-23-48, the muscles stiffness had involved the hamstrings as well; the patient also showed some weakness of the facial muscles. A blood count at this time showed a total count of 6,800 with a differential of 54% mature polymorphonuclear cells, 1% immature polymorphonuclear cells, 42% lymphocytes, and 1% monocytes.

This study was able to confirm the results of Ford in part. As previously mentioned, this study could not be carried out beyond the thirteenth day, hence it was not possible to determine the peak for the protein values. However, it was possible to demonstrate that the protein concentrations were definitely higher in the paralytic cases than in the non-paralytic ones. Ford reported that the average protein value in his non-paralytic series was 46 mgm per cent, and 68 mgm per cent in the paralytic. The results of this paper were not as striking, being 39 mgm per cent for the non-paralytic and 51 mgm per cent for the paralytic.

The minimum values reported by Ford were 25 mgm per cent for the paralytic series and 15 mgm per cent for the non-paralytic series. This analysis reported 20 mgm percent and 9 mgm per cent respectively for the minimum values. It appears that a spinal protein concentration of less than 20 mgm per cent is unlikely to be a paralytic case. However, any concentration over that figure loses any value for prognostication because the range of maximum values was nearly identical.

In the non-paralytic cases, Ford reported a significant decrease in the total cells of the spinal fluid after the fifth to the eighth day. In this series, this also appeared true, with the significant drop appearing in the fifth period. In the paralytic cases Ford reported that the decrease occurred after the first to the fourth day. In this series, it occurred after the third period or after the sixth day. As was the case with the protein concentrations,

there is considerable overlapping of the two ranges, although extremely low counts are less apt to be paralytic. Since the ranges for the two series are nearly identical, there seems to be no significant difference between the two series.

Summary:

The spinal fluid cytology, spinal fluid protein, peripheral blood total white count, and the differential from 190 patients with acute poliomyelitis were analyized in an attempt to find a correlation between the course of the disease, the peripheral blood and the spinal fluid.

1. This study was able to verify the results of Ford, et.al., in finding that the protein concentrations in spinal fluid were consistently higher in paralytic than in non-paralytic cases.

2. A significant decrease in total cells in the spinal fluid occurred after the fourth period in the non-paralytic cases, and after the third period in the paralytic series.

3. In 7% of the non-paralytic patients and in 5% of the paralytic patients, spinal fluid examination was negative despite the fact that a clincal diagnosis of poliomyelitis could be made.

4. Early in the course of the disease there is about equal distribution between polymorphonuclear cells and mononuclear cells in the spinal fluid. There is a gradual shift in cell predominance toward the mononuclear cells. This predominance becomes greater in the paralytic group of patients. In the paralytic peripheral blood

the leukocytosis remains longer than in the non-paralytic cases. Hence, there is an inverse relationship between the differential of the spinal fluid and the blood.

5. In the peripheral blood, a consistent finding is a leukocytosis of a moderate degree which persisted until the end of the fifth period in both the paralytic and the non-paralytic series.

6. The differential became normal in the non-paralytic series after the second period, and after the third period in the paralytic series.

7. The three case histories presented and the prolonged granulocytic leukocytosis in the paralytic series suggests that the peripheral blood total white count and differential may be useful in determining if the disease is progressing or has become arrested.

TABLE I

Results of Blood Determinations in the Non-paralytic Patients
* Per cent of immature forms

Period	No. of Determinations	Total WBC		Per cent Granulocytes		Percent of Mononuclocyte	
		Average	Range	Average	Range	Average	Range
1	28	12,750	22,200 to 5,100	70 (14)	86 to 42	30	51 to 13
2	37	10,050	26,000 to 5,500	60 (8)	89 to 34	39	57 to 10
3	29	9,350	15,400 to 5,900	54 (8)	82 to 32	45	62 to 25
4	22	9,650	15,000 to 4,600	58 (8)	75 to 31	40	65 to 24
5	25	10,400	24,800 to 6,700	54 (5)	74 to 39	44	58 to 25

TABLE II

Results of Blood Determinations in Paralytic Patients
* Per cent of immature forms

Period	No. of Determinations	Total WBC		Per cent Granulocytes		Percent of Mononucleocyte	
		Average	Range	Average	Range	Average	Range
1	3	16,200	21,900 to 11,000	78 (9)	80 to 73	22	27 to 19
2	13	11,000	15,600 to 8,100	63 (10)	79 to 35	35	64 to 22
3	17	11,500	18,000 to 5,600	60 (7)	81 to 34	39	66 to 26
4	8	9,800	14,400 to 5,900	54 (9)	73 to 36	43	62 to 35
5	9	11,100	14,000 to 5,500	59 (8)	77 to 42	38	53 to 25

TABLE III

Results of the Spinal Fluid Determinations in the Non-paralytic Patients

Period	No. of Determ-inations	Total WBC		Percent Granulocyte		Percent Monocytes		Protein mgm %	
		Average	Range	Average	Range	Average	Range	Average	Range
1	41	200	1440 to 17	48	96 to 5	52	95 to 4	37	95 to 15
2	31	150	1300 to 9	29	92 to 2	71	98 to 8	42	80 to 15
3	27	109	444 to 17	25	93 to 0	75	100 to 7	36	75 to 9
4	20	210	1186 to 21	22	56 to 0	78	100 to 42	43	81 to 25
5	13	21	64 to 5	14	55 to 0	86	100 to 45	31	90 to 10

TABLE IV

Results of Spinal Fluid Determinations in the Paralytic Patients

Period	No. of Determinations	Total WBC		Percent Granulocyte		Percent Monocytes		Protein mgm %	
		Average	Range	Average	Range	Average	Range	Average	Range
1	8	185	237 to 86	46	71 to 16	55	84 to 29	50	80 to 18
2	17	200	1040 to 27	29	90 to 2	71	98 to 10	48	75 to 25
3	11	175	528 to 14	15	45 to 0	85	100 to 55	48	98 to 20
4	8	80	180 to 16	15	25 to 0	85	100 to 74	39	90 to 21
5	3	18	26 to 11	6	11 to 5	94	100 to 89	115	130 to 105

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