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Blood - Changes in Dementia Praecox

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Blood-Changes in Dementia Præcox

And Artificial Leukocytosis in Its Treatment

By HALVAR LUNDVALL, M. D., Lund, Sweden

EDITORIAL NOTE.—We owe this paper to the kindness of Dr. Bayard Holmes, of Chicago, to whom it was sent with a view to its publication in America. This paper should be read in association with the one by Doctor Holmes, which follows.

MANY tracks have been beaten by those endeavoring to make out the nature of dementia præcox. I am not entering upon everything written on the importance of heredity. The vast amount of industry and intellectual power spent upon this matter can scarcely be said to have contributed to a better understanding of the disease in question. Nor can it be said that Freud's theories about this disease have been of any considerable service to us.

The histologic examination of the brain has given no results worth noticing; at least, the changes mentioned are not constant and may well be secondary.

The experiments with cultivation of bacteria from the blood and other fluids of the body of patients suffering from dementia præcox, and the experiments of agglutination of the same made by Bruce, may also prove to be a failure when critically examined.

Clinical science, which has enabled us to distinguish different forms within the large group of diseases styled dementia præcox, has also called our attention to the obvious relation that this disease has to the genital glands. The trials with the Abderhalden reaction which Fauser, Wegener, and others have already made also point to the supposition that a dysfunction of the genital glands is a fairly constant symptom in dementia præcox.

However, if one has spoken of a relationship subsisting between dementia præcox and the genital glands, as proven both by clinical investigation and the Abderhalden reaction, it would, for all that, be a hasty inference to think that this dysfunction of the genital glands is the cause of the disordered mentality.

Still less is one likely to feel tempted, by virtue of these experiments, to enter upon some kind of specific therapy against dementia præcox.

Another way, still, has been tried, in order to get at the nature of this disease. I am thinking of the morphologic examination of the blood. Investigations of this kind have been published ever since the middle of the preceding century. Considerations of space prevent my giving a somewhat close account of all these investigations. I shall content myself with pointing out that, what strikes one most strongly, perhaps, when examining their results, is the discrepancies encountered, not alone between different authors, but even between different cases of the same author. Even if these poor results may in part be accounted for by the somewhat unreliable methods of blood examinations resorted to by many investigators as also by the long-prevailing uncertainty of the psychiatric diagnoses, I am of opinion that the chief reason lies in another direction.

Variability of Blood Composition—Striking New Observations

The fact is, that all these authors, almost without exception, obtained their results by making but one single test of the blood of their patients, and then thought they thus had obtained an adequate picture of its composition. But this is a fallacy. As a matter of fact, in the few instances in which the blood of the same patient has been examined on more than one occasion, and during different mental states, distinct changes in the blood-picture have been evidenced. A few examples may illustrate this fact.

In five cases of manic depressive insanity, Fisher has shown that there is an increase in the cellular element of the blood during the maniacal stage. The increase in the white blood-corpuscles is represented chiefly by a polynucleosis. I myself have examined, during a considerable period, the composition of the blood in two cases of the same disease, and I made the same observation. Klippel has pointed out the same relationship in a case of transitory delirium (*delire transitoire*), in which he had examined the blood twice—in the excited and in the quiescent period.

In "acute mania," Bruce has found, at the beginning of the seizure, a decrease in the number of the leukocytes. Later there appears a leukocytosis, chiefly as a polynucleosis. If the latter is pronounced, it is a good prognostic. As to katatony, Bruce tries to prove that the disease begins acutely with fever and a polynucleosis, which later passes into a mononucleosis. If health ensues, a temporary eosinophilia will be found. These

Mononucleosis is a sign of the deficient reaction of the organism against a toxi-infection of long standing.

Eosinophilia is a "critical" sign.

In 1907, I found that in dementia præcox there occurred, under ordinary circumstances, no decrease in the red nor an increase in the white blood-corpuscles, but I demonstrated periodical "blood-crises" appearing in the form of anemia and an increase in the white corpuscles. These states might appear days or weeks before the agitated periods, but otherwise they coincided with them. I took the cause to be a toxemia.

Kuhn, Purdum and Wells, and Heilemann find a decrease of the polynuclear and an increase of the mononuclear and eosinophile leukocytes.

Some of the Results Tabulated

Leaving aside my results of the year 1907, it is held that the blood of patients suffering from dementia præcox exhibits: a decrease

TABLE I

		RED CORPUSCLES	WHITE CORPUSCLES	NEUTROPHILE LEUKOCYTES PERCENT	EOSINOPHILE LEUKOCYTES PERCENT
Males.....	Quiet.....	6,820,000 to 4,480,000	10,550 to 5,200	67.8 to 42.1	2.6 to 0.1
	Agitated.....	5,220,000 to 3,450,000	17,300 to 7,800	79.1 to 58.6	10.3 to 1.6
Females.....	Quiet.....	6,100,000 to 4,000,000	10,500 to 5,600	61.2 to 40.9	4.1 to 0.1
	Agitated.....	4,960,000 to 2,600,000	19,300 to 8,900	77.7 to 58.4	11.2 to 0.9

interesting investigations were not carried out, however, with the minuteness necessary for scientific blood examinations. Later English authors, however, confirm this increase in the leukocytes. Whether and to what extent this is due exclusively to disturbances in the concentration of the blood (these are not at all rare with the insane), it is impossible to decide. And Bruce and his successors have rendered the possibility of control in this respect impossible by not stating at the same time the number of the red corpuscles present.

Rougean finds in lunatics oligocythemia and an increase in the polynuclear leukocytes, and from this he infers that the psychoses rest upon a toxi-infectious basis. (Such a conclusion as regards the mental diseases seems altogether too bold, though!)

Dide finds anemia, which should be a sign of intoxication or infection. A rise of the red blood-corpuscles depends on a molecular condensation of the blood. It is found, therefore, together with a rise of the leukocytes, during states of excitement, when the excretions are increased.

in the number of red corpuscles, an increase in the number of white corpuscles, with a decreased percentage of the neutrophile elements, and an increased percentage of the lymphocytar, mononuclear, and eosinophile elements. I am going to show that this view is onesided and misleading.

Apart from the serial examinations which I shall present further on, I have also made single blood examinations in the case of a number of patients and in this way, in 150 cases of dementia præcox, I found the following values:

I arrived at these figures by taking 2 specimens from a patient at the same time, then took the mean proportional of the numbers for the two specimens. It goes without saying that I avoided the leukocytosis of digestion.

In Table II, I have put together the results of blood calculations on 14 other patients. The different specimens were taken at intervals of a week. The results were the same. These figures show, however, that the composition of the blood of the same patient is different during different phases of the disease.

In order to gain a still clearer view of the changes developing during different mental states, I have examined the blood of 15 other patients daily, or every other day, over a long period of time, up to more than three months. I arrived at the following results:

The Phenomenon of Blood-Crises

During the periods when the patients are free from phenomena of psychical irritation, one finds, as a rule, no changes other than leukopenia with a relative mononucleo-

tions during the course of the day, it also exhibits profound recessions, often going down to normal values. Frequently one can distinguish an initial and a terminal leukocytosis. The latter occasionally remains for some time after the number of red corpuscles has again gone back to the values they showed before the crisis.

The leukocytosis is chiefly a polynucleosis. This increase often is preceded by a considerable but rapidly passing decrease in the polynuclear cells.

TABLE II

CASE		QUIET	QUIET	AGITATED	AGITATED	AGITATED	QUIET	QUIET
1.	Red corpuscles.....		5,530,000	4,855,000				
	White corpuscles.....		10,600	15,000				
2.	Red corpuscles.....		5,605,000	4,755,000				
	White corpuscles.....		10,300	12,950				
3.	Red corpuscles.....		5,280,000	4,875,000	4,565,000			
	White corpuscles.....		6,300	8,200	13,500			
4.	Red corpuscles.....		6,200,000	5,300,000				
	White corpuscles.....		8,000	12,000				
5.	Red corpuscles.....		5,860,000	5,140,000				
	White corpuscles.....		9,000	16,500				
6.	Red corpuscles.....					3,125,000	4,270,000	
	White corpuscles.....					17,300	8,100	
7.	Red corpuscles.....					4,755,000	5,095,000	
	White corpuscles.....					12,200	7,800	
8.	Red corpuscles.....				4,710,000	4,725,000	4,960,000	
	White corpuscles.....				12,500	11,600	7,500	
9.	Red corpuscles.....					3,650,000	3,980,000	4,750,000
	White corpuscles.....					11,000	17,000	8,000
10.	Red corpuscles.....					4,270,000	5,050,000	
	White corpuscles.....					8,800	10,100	
11.	Red corpuscles.....				4,060,000	5,340,000	5,540,000	
	White corpuscles.....				15,100	16,300	12,300	
12.	Red corpuscles.....	5,250,000	4,900,000	4,650,000				
	White corpuscles.....	6,700	11,200	10,500				
13.	Red corpuscles.....			3,960,000	3,940,000	4,250,000	4,500,000	
	White corpuscles.....			13,200	10,300	16,500	8,000	
14.	Red corpuscles.....		4,230,000	4,150,000	4,350,000		5,150,000	
	White corpuscles.....		13,000	11,000	16,000		7,000	

sis, decrease of the neutrophile and the eosinophile leukocytes, and a seeming polycythemia. The polycythemia certainly depends upon vasomotoric disturbances, and changes of concentration connected therewith, in the peripheral vessels.

In the case of patients presenting periodical states of excitement, on the other hand, one finds quite typical changes recurring at intervals and to these I have given the name "blood-crises." These occur in every degree, from hardly perceptible changes to the most radical alterations, and consist in a decrease of the number of red corpuscles and in an increase of the white ones.

The leukocytosis does not occur as a smooth wave. Besides the physiological oscilla-

The eosinophile leukocytes show, at the beginning of the crisis, a further reduction from their already low values, and then they rise, sometimes considerably. The eosinophilia often remains for a long time after the blood-crisis.

The "mast-cells" usually appear in a somewhat increased number at the time of the critical, but especially of the post-critical, eosinophilia.

During the blood-crises, the vasomotoric disturbances and the changes in the blood concentration connected therewith may also be of some significance. They cannot be supposed, however, to be the chief cause of the blood-crisis; the motley changing of the blood-picture hardly is consistent with such

a supposition*. Here we must assume a new growth, namely, a pumping into the blood system of leukocytes from the bone-marrow; this view being favored by the almost constant appearance of neutrophile myelocytes, especially near the close of the blood-crisis. A real hemolysis also is to be assumed—an interesting parallel to the periodical increases in the "N-ausscheidung," (nitrogen elimination) occurring in lunatics.

These blood-crises I have found in the case of patients who had been suffering for more than twenty years, and I have observed them also in fairly recent cases. It seems justifiable, therefore, to consider them a constant phenomenon.

These blood-crises often pass without perceptible symptoms. Only if they are sufficiently intense or have lasted for a sufficiently long time, they are attended by phenomena of physical irritation. Consequently these crises which may partly appear without perceptible mental disturbances, partly precede (often by days and weeks) the physical disturbances, the state of excitement, cannot be considered as the result of increased muscle work or of physical excitement.

An Explanation Suggested

The most natural explanation seems to me to be the assumption of a toxemia, of whatever kind that may be†. And as we do not now hesitate, in the case of many infectious diseases, to see in a strong leukocytosis a sign of the protecting processes going on in the body, whereas we assign to leukopenia a bad prognostic significance, because we see in it a sign of the diminished fighting-power of the body, it does not seem to be presumptuous to apply the same point of view to the case in question.

Thus, then, the leukocytosis we meet with in the blood-crises is a sign of the activity of the organism, the struggle of the organism against the cause of the disease.

Sodium Nucleate: A Promising Remedy

He who is really convinced that dementia præcox depends upon material causes must also feel it his duty to find a remedy. He cannot possibly feel satisfied with the expect-

tative treatment we now give our patients. Moreover, the idea of trying to find a somatic treatment for dementia præcox, as well as for other diseases, is by no means an unfamiliar one. On the other hand, many signs go to show that the disease is accessible to psychical therapy.

We have long known that certain intercurrent diseases often influence dementia præcox in a striking way. Abdominal typhus no doubt is most known in this respect. In another publication I have pointed out that the important thing in this case is the hyperleukocytosis which regularly develops after typhus. The idea suggests itself then, to call forth by deliberate infections or by other, less dangerous means, an increase of the leukocytes; and in paralysis such an artificial hyperleukocytosis has been resorted to. Occasionally some case of dementia præcox may also have come under treatment. Thus, in 1910, Pilz administered tuberculin, with good results, in katatonia.

I have paid attention to dementia præcox exclusively. After trying a great many other substances, I eventually fixed my choice on sodium nucleate, or, as we say here, natrium nucleicum.

However, I thought I observed that the patients became accustomed to the remedy too quickly when the treatment was long continued, responding less even to increased doses. For this reason, I have, for some time, combined the nuclein with other remedies likely to increase the leukocytes, namely, hetol and arsenous acid. Now I use exclusively the following combination.

Formula for Lundvall's Nuclein Mixture

R̄ Quassinisicci depurati (Merck)	Gm. 40.0
Sodii nucleatis.....	Gm. 200.0
Acidi arsenosi.....	Gm. 0.1
Aquæ destillatæ, q. s. ad.....	Cc. 1000

The ordinary doctor can very well prepare this solution himself; but inasmuch as it is somewhat difficult to obtain a clear and tenable preparation, it will be better to have it prepared by an apothecary. (The chemist's-shop "Hjorten" at Lund keeps it on hand, sealed in sterilized ampules holding 5 and 10 Cc., respectively.)

Mode of Administering the Nuclein Mixture

Of this solution a dose of from 2 to 15 Cc. is injected hypodermically twice a day. It may be mentioned here that at the site of the injection there appears a more or less painful infiltrate, although often this is inconsiderable. In order to lessen the pains

*Compare the circumstances in manic-depressive insanity!

†The results obtained with the Abderhalden reaction seem, perhaps, to suggest that there circulates in the blood the abnormally decomposed albumin from the genital glands. The primary cause, perhaps, lies deeper still, so that the dysfunction of the genital glands, i. e., the toxemia, the morphologic changes in the blood, and the psychical disturbances are merely symptoms of the same pathologic state. We do not know which of these three symptoms appears first; but everything goes to show that the psychical disturbances appear later than the morphologic changes in the blood.

and accelerate the resorption, I apply, during the first day, a cold compress, while the second day I begin with a cautiously applied massage, which is continued until the infiltrate has disappeared.

Some hours after the injection, a strong rise of the temperature and the number of leukocytes ensues, combined, occasionally, with spells of shivering and a feeling of illness. However, the elevated temperature generally recedes rapidly and usually is on its downward grade after twenty-four hours; still, now and then slight increases of the evening temperature will appear for some days afterward. The leukocytosis runs tolerably parallel with the course of the temperature, although usually it sets in some hours earlier, and persists for a day or more after the temperature is at normal again. Still, this parallelism is not pronounced, and leukocytosis not infrequently is found without there being an increase of temperature. Nor is the time for each new injection to be determined by the curve of temperature, but, instead, by the number of the leukocytes.

Since the purpose of the treatment is not, to throw a certain quantity of the remedy as quickly as possible into the patient's body, but, on the contrary, to sustain by the smallest possible doses a leukocytosis for as long a period as possible, there is no fixed rule for the dosage, and, so, one has to feel his way in each individual case.

Above all, it is useless, a labor thrown away, to content oneself with only a few injections. If the patient has acquired immunity to the remedy, so that no effect is produced even by large doses, it is best, temporarily, to interrupt the treatment and, after a while, resume again.

During the course of this treatment, the patients should be kept on a highly nutritious diet, and preparations of lecithin may, perhaps, be of a certain value.

In the presence of cardiac diseases and of phthisis, the treatment is contraindicated, or, at least, great caution must be exercised.

The injections nearly always are followed by improvement, lasting several days, in the patient's psychic state. When evaluating the results of the treatment, however, I have not taken this factor into consideration.

Before passing on to the account of my own cases, I will mention certain experiments conducted by others at the same time as mine, or later.

Lepine found, out of 12 cases of dementia præcox treated with sodium nucleate solely, a slight improvement in 3 of the patients.

He gives no information, however, of the total doses he used, whence it is impossible to decide whether the treatment was carried out with all the energy required.

Itten has treated 9 serious cases, and in 3 of them observed a temporary improvement. One must say, though, that 4 of his cases, at least, had insufficient treatment. For, 2 patients received only 3 injections each, with a total dosage, respectively of 3.8 and 3.0 grams of sodium nucleate; 2 other patients received only 1 injection each, containing 0.8 gram. On an average, his patients received 5.8 grams of the nucleate. I have emphasized already that, if the treatment is to demonstrate anything, it is indispensable that one try to keep up the increase in the leukocytes for as long a time as possible.

Out of Donath's 14 patients, 3 were cured, 5 were improved (2 of these able to work), 3 showed signs of improvement at first but then deteriorated again, and 3 remained uncured.

Hauber has treated 20 patients, 12 of whom were diseased a long time and already considerably demented. In 2 cases, the treatment was not finished at the date of publication; in 1 case, the treatment had to be interrupted on account of a recrudescence of phthisis. Seven of them could be discharged, subject to more or less severe remissions.

I myself have treated, in the manner above described, 25 patients, many of whom were old and their cases hopeless. Out of these, 11 could be discharged as clinically cured; 2 could be discharged not quite cured but able to work; 5 showed signs of improvement, but only temporary or else not considerable enough to permit of their leaving the institution; 7 remained uncured.

If, now, we take into consideration only those cases in which the treatment was finished, the results are these:

Of Hauber's cases, 37 percent could be discharged; and that in spite of the fact that 70 percent of his cases were old dement cases, i. e., with irreparable cerebral changes already developed. Of Donath's cases, mostly rather recent, the cured and improved aggregate 57 percent. Of my own patients, many of whom, however, were old and helpless, 52 percent could be discharged, while 20 percent showed signs of recovery, although temporary only or too slight to allow of discharging them.

However skeptical one may feel about this form of therapy, the results thus far obtained are quite too obvious to be neglected or to be passed over as spontaneous recoveries. More-

over, since the treatment is so simple as to be applicable by any ordinary practitioner, it certainly seems to be our duty to give it a trial, for so long at least as we are in want of a specific therapy.

References

- L. Bruce: *Journal of Mental Sciences*, 1903, 1908.
M. Dide: "Etude cytologique, bactériologique et expérimentale du sang chez les aliénés." XVI. Congr. des Méd. Alien. et Neurolog., Lille, 1906.
J. Donath: *Zeitschrift d. gesammten Neurologie u. Psychiatrie*, 1914, Bd. XXIV, Heft. 4.
Fauser: *Deutsche medizinische Wochenschrift*, 1912, No. 52; 1913, No. 7.
J. W. Fisher: *American Journal of Insanity*, 1913.
F. Hauber: *Zeitschrift f. gesammte Neurologie u. Psychiatrie*, Bd. XXIV, Heft. 1, 1914.
W. Itten: *Idem*, 7. (Orig.)
Klippel: "L'Encéphale," 1906.
W. Kuhn: *Journal of the American Medical Association*, 50, No. 15.
J. Lépine: *Presse Médicale*, 1910, No. 9.
H. Lundvall: *Hygiea*, 1907.
H. Lundvall: *Nord. Tidskr. f. Retsmed. o. Psych.*, 1911.
Purdum and Wells: *Journal of the American Medical Association*, 51, No. 1.
R. Rougean: "Contribution à l'étude du sang chez les aliénés." (Thèse.) Toulouse, 1906.
Wegener: *Menchener Medizinische Wochenschrift*, 1913, No. 22.

