

Serum Analyses Compared with Widal after Inoculation with Typhus-Paratyphus

(Clinical Laboratory Investigations of Male Chronic Alcoholics)

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Zusammenfassung

20 Patienten typische chronische Alkoholiker ohne Cirrhosis hepatis – wurden mit hitzegetöteten Typhus-Paratyphus Bacilli geimpft. Die Impfung rief keine Veränderung im Inhalt von Zucker, Transaminasen (GOT, GPT) oder Rest-N des Serums hervor. Die Serumproteine, die durch Papierelektrophorese geprüft wurden, zeigten vermehrte Globuline und verminderte Albumine nach der Impfung.

Alkoholiker bilden Antistoffe ebenso gut wie Nicht-Alkoholiker.

Résumé

20 malades – des alcooliques typiquement chroniques sans cirrhosis hepatis – furent vaccinés avec des bacilli de typhus-paratyphus, tués par la chaleur. La vaccination ne provoqua pas de changement du contenu de sucre, de transaminases (GOT, GPT) ou de N-résidu du sérum. Les protéines de sérum, qui furent examinées par l'électrophorèse de papier montrèrent une augmentation des globulines et une décroissance des albumines après la vaccination.

Les alcooliques produisent des anticorps aussi bien que les non-alcooliques.

Paper electrophoreses and immuno-electrophoreses have shown that the serum proteins are subject to a considerable change in chronic alcoholics without cirrhosis hepatis. The main part of the globulin group shows a tendency to decrease in concentration, while, on the other hand, a few fractions show an increase. The last mentioned reaction is mainly true for the macroglobulins. An inoculation of these patients with heat-destroyed typhus-paratyphus bacilli gave a certain knowledge about the amount of the circulating anti-substances. More than 700 chronic alcoholics have been inoculated and investigated in different ways. The investigation showed that the function of the liver cells was of no importance to the development of the anti-substances, which, anyway, was not to be expected in theory. The quantity of N-residue did not affect the quantity of circulating antisubstances. On the other hand, if the glucose was 130 mg% or more, a decrease of the antisubstances was found. With an increase of negative Widal tests there was a decrease of the hemoglobin percentages as an indication of a decreased amount of circulating anti-substances.

It proves that the amount of anti-substances in the serum against O-antigens is dependent on the amount of the concentration of the γ -globulins.

A decrease of the concentration of the γ -globulins corresponded with a decrease of the anti-substances. On the contrary, the H-globulins show a clear connection with the α - β -globulins, and many circumstances support the theory that the β_{2M} -globulins are the carriers of the anti-substances against the H-antigen (7, 8). Infections with typhus, paratyphus, and other salmonella bacteria show an increase of the globulins contrary to the circumstances at dysentery, and here particularly of the β -globulins (6).

The Experimental Material and the Procedure of the Investigation

The alcoholics used for this work did not differ from the material I have discussed in other works dealing with about 600 alcoholics (1, 2, and 3).

All of them had been hard drinkers for several years. They had a typical anamnesis, exterior signs of a large consumption, and they also showed changes in a series of laboratory investigations.

The patients were inoculated with heat-killed typhus-paratyphus bacilli. In 1 ml of vaccine there were about 2 000 million germs, distributed in the proportion: 50% s.typhi, 25% s.paratyphi A, 12.5% s.paratyphi B, and 12.5% s.Newport. Before the inoculation and ten days after the inoculation the Widal was checked at the same time as a series of laboratory tests were made. 5 of these are included in this work.

The Result

Widal was negative in all 20 patients before the inoculation. It so happened that they were all positive after the inoculation, which was not normally to be expected. It will be seen from the table that s.typhi and s.paratyphi B most often resulted in agglutinations, and here again in particular against the H-antigen. 31 of the reactions were positive at the dilutions 1/40–1/80 and 1/160, while 23 gave positive results at higher dilutions.

The glucose was changed a little after the inoculation. The younger alcoholics as a whole have a tendency to low fasting glucose values in the period of abstinence, while the older alcoholics rather often show a tendency towards high fasting values in this period. After a treatment lasting 4 to 6 weeks these slightly pathological changes are normalized. Such was also the case in this work.

The N-residue values were within the limits of what could be considered as acceptable, with the exception of one patient, who, when discharged from hospital, showed an increase, the cause of which was not found. High N-residue values were rather unusual, while the function of the kidneys of the alcoholics often deviates from the normal, probably because of hormonal disturbances. The older the patients are – which, for these patients, means: the longer they have been hard drinkers – the greater is the tendency to isostenuria. Completely normal concentrations of water were found in only about 10%, and then most often in patients under the age of 50. The clearly diphasic curve after a charge of water is very strongly flattened out in these

patients. It is possible to observe one sort of isostenuria, where the specific gravity keeps about 1.020, and another form where the specific gravity remains about 1.010. They all seem to end in an isostenuria with a specific gravity about 1.004.

Table 1: 20 Alcoholics on whom an analysis of the blood was carried out before and after the inoculation with salmonella. The ages varied between 27 and 53 years.

A) *Glucose, N-residue, Transaminases* (before and after inoculation)

	before the inoculation				after the inoculation			
	Glucose	N-residue	GO-T	GP-T	Glucose	N-residue	GO-T	GP-T
Minimum	70	21	24	24	14	17	29	80
Maximum	126	49	108	165	108	64	87	112
Average	99	35,1	49,7	58,8	37,5	46,3	41,1	95

The transaminases normally show an increase in the chronic alcoholics. When some of the patients had normal values for GO-T and GP-T, the reason was in most cases that they had been treated 1 or 2 weeks before they came to my department. The transaminases were usually normalized in 4 to 6 weeks, although it was a longer time in 21%. This is the reason why the mean values in these patients are somewhat high (37.5 and 46.3).

B) *Serum Proteins* (before and after inoculation)

	before the inoculation						
	Total Proteins	γ -	β -	α_2 -	α_1 -	Albumines	Albumins Globulins
Minimum	6,00	0,30	0,30	0,10	0,10	4,90	
Maximum	7,70	1,10	0,60	0,40	0,20	6,00	
Average	6,94	0,73	0,41	0,22	0,12	5,46	3,6/1,0

	after the inoculation						
	Total Proteins	γ -	β -	α_2 -	α_1 -	Albumins	Albumins Globulins
Minimum	6,50	0,60	0,30	0,20	0,10	4,30	
Maximum	7,60	1,70	0,90	0,50	0,20	6,10	
Average	7,08	0,88	0,55	0,34	0,15	5,16	2,7/1,0

The serum proteins – investigated by means of paper electrophoresis – did not show the very strong deviations in these 20 patients which are often found in alcoholics. It will, however, be seen from the table, that the globulins show rather low values, particularly for the γ -globulins. The changes in the ratio albumin/globulin, which was 3.6 in this material, are very clear. An index of

5.0 – 8.0 is not unusual. This peculiar circumstance makes a clear distinction between these alcoholics and the alcoholics who have developed a cirrhosis hepatitis. In the latter group the alb./glob.-index may be changed to about 1.0 and less. In the whole of my large material I have met only 4 patients with so serious changes of the liver.

C) *The result of the inoculation*

	S. Typhi			S. Paratyphi A			S. Paratyphi B			S. Newport		
	unsp.			unsp.			unsp.			unsp.		
	H	H	O	H	H	O	H	H	O	H	H	O
Total Result:												
No. of positive Titres	18	0	4	4	0	0	10	0	2	2	14	0
No. of negative Titres	2	20	16	16	20	20	10	20	18	18	6	20
Distribution of positive Titres:												
Dilution 1/40	1	0	0	0	0	0	2	0	1	0	2	0
Dilution 1/80	4	0	2	0	0	0	3	0	1	1	2	0
Dilution 1/160	4	0	2	1	0	0	1	0	0	0	4	0
Dilution 1/320	3	0	0	3	0	0	2	0	0	0	2	0
Dilution 1/640	2	0	0	0	0	0	2	0	0	0	2	0
Dilution 1/1280	2	0	0	0	0	0	0	0	0	0	1	0
Dilution 1/2560	1	0	0	0	0	0	0	0	0	0	1	0
Dilution 1/5120	1	0	0	0	0	0	0	0	0	1	0	0

After a treatment from 4 to 6 weeks the serum proteins change in the direction of the normal with a decrease of the albumins and an increase of the globulins. This normalization will also be seen from this work. It is not probable that the typhus-paratyphus inoculations have contributed very much to this change in the protein fractions. Investigations, which are being carried out at present, and in which the changes in the proteins are being followed in alcoholics who have not been inoculated, show changes that are almost identical with those shown in this table. The immuno-electrophoreses, however, show differences in the lines of precipitation in the β -globulin group when the patient has been inoculated. These changes do not seem to have been caused by abstinence and sufficient food.

Discussion

Chronic alcoholism shows a series of characteristic changes both at the objective examination and at the laboratory investigations. Inoculation with a mixed typhus-paratyphus vaccine shows that these patients have quite a good reaction measured by the Widal reaction. This was not to be expected, because these patients often had a very pronounced reduction of the concentration of the globulins in the serum.

There is a certain bias in an investigation of this kind, in that patients with sufficient diet and an extra dose of vitamins are treated at the same time. Were it possible to inoculate a group of alcoholics who went on with their hard drinking without receiving any special treatment, the results obtained might be slightly different from those which, among other things, this work describes. This, however, is not certain, because the curious fact observed in all investigations of inoculations was that the alcoholics gave positive Widal reactions more often than a normal group.

On the whole this investigation gave results similar to those which resulted from an examination of 600 alcoholics.

Synopsis

Glucose, N-residue, transaminases and paper electrophoreses are examined in 20 alcoholics without cirrhosis hepatitis, before and after a typhus-paratyphus inoculation.

Literature

- [1] *Dahl Sven: Sv. Läkart.* (1963) Water-metabolisms
- [2] *Dahl Sven: Sv. Läkart.* (1963) Blood-investigation
- [3] *Dahl Sven:* Ugeskrift for Läger (1963) – Sugar-metabolism
- [4] *Dahl Sven:* To Gastroenterology U.S. – Transaminas
- [5] *Dahl Sven:* To Quart. J. Alcohol. U.S. – Protein-metabolism
- [6] *Dittmer A.:* «Papierelektrophorese.» Jena 1961 (G. Fischer Verlag)
- [7] *Grabar P.:* Director, MD at the Pasteur Institute. Personal information about works which had not been published by October 1962
- [8] *Dahl Sven:* Z. Präventivmed. 8, (1963), 311–318

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