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THE EFFECT OF VENTRICULIN ON THE BLOOD SUGAR LEVEL IN PATIENTS WITH PERNICIOUS ANEMIA

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A reduction of the blood sugar content, analogous to that produced by insulin, was noted by Blotner and Murphy (1) after administration of whole liver and certain of the liver fractions ineffective in the treatment of pernicious anemia. Fractions G, an effective liver extract prepared by Cohn and his collaborators (2), appeared to contain little if any blood sugar reducing substances. An observation repeated by Riddle (3) substantiated the evidence that this liver extract contained no specific blood sugar reducing properties. After the introduction by Sturgis and Isaacs of ventriculin as a specific treatment in pernicious anemia (4), it was decided to determine whether or not this preparation possessed blood sugar reducing properties similar to those of whole liver.

The blood sugar level was determined on eleven patients with pernicious anemia at frequent intervals during treatment with ventriculin, liver extract, and on one patient in spontaneous remission. The samples of blood were obtained under fasting conditions at 8 A.M., and the blood sugar values were estimated according to the micro method of Folin and Wu (5). Each patient was given 40 grams of ventriculin daily, and observations were made during the interim of the rise of the reticulated red blood cell count, at intervals of one to two days. Data on the red blood cell counts, hemoglobin and reticulocyte percentage were also recorded.

The fasting blood sugar values obtained during the treatment with ventriculin are listed in Table I. The results for each patient are recorded separately, showing daily variations as well as the general trend. With two exceptions, the initial values were within the range of 84–135 mgm. of sugar per 100 cc. of blood—the majority of the results bordering on the upper limits of normal. Six to ten days after the onset of treatment, the blood sugar values in each case reached their lowest levels, the decrease being gradual. These minimal readings were within the range of 61–97 mgm. The average decline of the blood sugar level was about 45 mgm. per cent, the upper and lower extremes being 30 and 60 mgm. In the series of cases which were studied during the entire period of the rise and fall of the reticulated cell count, the blood sugar levels

TABLE I
Milligrams sugar per 100 cc. of blood

Days of treatment	Ventriculin treated patients											Spontaneous remission
	Patient number											
	1	2	3	4	5	6	7	8	9	10	11	
	mgm.	mgm.	mgm.	mgm.	mgm.	mgm.	mgm.	mgm.	mgm.	mgm.	mgm.	
-2			92		138	109		124	84			
-1	131	107	99	135		115	118	115		94		
0	110	102	85	130	135	137	120	109	90		114	
1	137	107	85	120	120		117	138	78	96	108	
2	110			143	138	105	117	121	85	95		
3			75	125	151	102	103		87	94		133
4	111	98	68		135	97	101	131	81	94	117	
5	103	95	75	106	106	100	105	125		89		91
6	95	104	70	105	95	111	93	121	75	93	100	
7	100	83	61	107	94	83		97	80	85	95	91
8	104	80		93	105	72				95	105	
9	143	78		86	94							101
10	108	75				95				89		
11	97.5	84		102	100	102						103
12		111			117						95	
13	121	109		114		105						
14		148			109							
15	121	118		108	115	125						

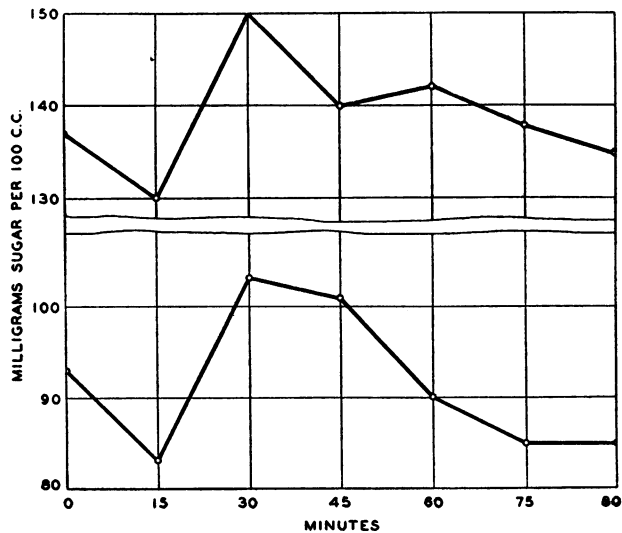


FIG. 1. EFFECT OF INGESTION OF 40 GRAMS OF VENTRICULIN ON BLOOD SUGAR LEVEL OF TWO PATIENTS WITH PERNICIOUS ANEMIA

reached their lowest values at the time of the peak of the reticulated red blood cell percentage rise, subsequently undergoing a gradual upward swing but not quite attaining their initial values in the majority of cases.

In two cases an attempt was made to determine any immediate effect of the ingestion of ventriculin on the blood sugar level. Blood samples were taken before and at intervals of 15 minutes for one and a half hours after the administration of 40 grams of ventriculin. These results are shown in Figure 1. The first specimens showed a slight decrease of 7-10 mgm., followed by an increase which attained its maximum in the one-half hour specimens. The values declined to approximately their original levels within one hour. The immediate effect of the administration of 40 grams of ventriculin was a slight increase in the blood sugar level, similar to that occurring after the ingestion of any other similar food substance.

Following treatment with ventriculin, as with liver extract, a marked increase of appetite was noted in each of the cases. For 2-4 days after the onset of treatment with ventriculin, no change in the appetite was observed; however, with the beginning of the reticulocyte response, a noticeable increase was evident. The usual diet which was more than sufficient during the first few days was supplemented with extra nourishment. Often the patients were given high caloric diets to appease their hunger. Inasmuch as the majority of the patients often lose weight in early remission, due probably to water loss (6), the weight factor could not be used in correlation with the hunger symptoms.

As the symptoms of hunger seem to be associated with both the increase of reticulated red blood cells and the amount of sugar present in the blood, the correlation of these two values is of interest. Determinations of the reticulocyte percentage and blood sugar values of three cases are recorded in Table II. Case 1 was treated with ventriculin, Case 2 with liver extract. Each was selected as representative of a series of ten cases similarly treated. Case 3 is one of pernicious anemia in spontaneous remission. If the blood sugar values are plotted together with the reticulated red blood cell percentage of the same day (Figures 2 and 3), it is noted that the lowest blood sugar level occurs simultaneously with the peak of the reticulocyte percentage rise. Apparently this behavior is physiologic, as it is always present regardless of the type of treatment, or if the remission is spontaneous. It is fair to conclude from this that the reduced sugar level is the result of increased metabolic activity of the bone marrow, as manifested by the increase of young red blood cells in the stream; or, that the reduced sugar values are the result of the increased metabolic activity of the young red cells themselves; or both. Riddle (3) stated that the cause for the lowered fasting blood sugar values during early remission was speculative, and that the evidence pointed to some unknown metabolic process. This process is now thought to be

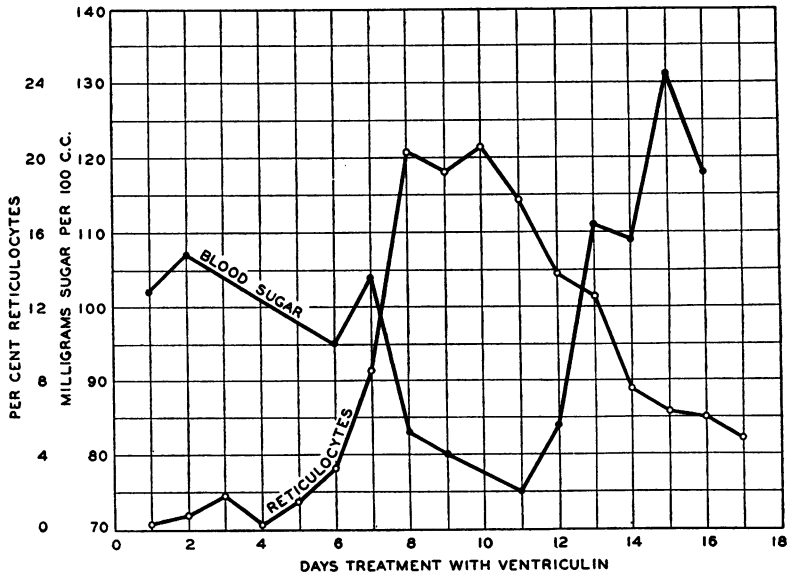


FIG. 2. RELATIONSHIP OF BLOOD SUGAR AND RETICULOCYTES FOLLOWING VENTRICULIN THERAPY

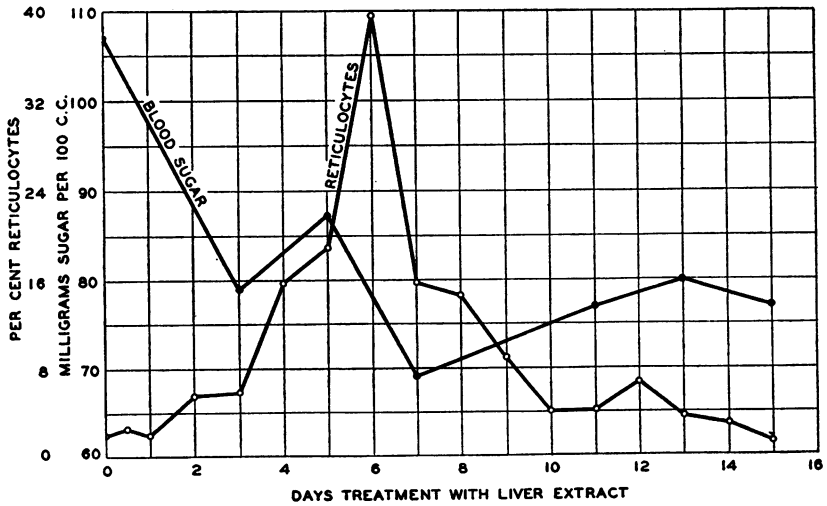


FIG. 3. RELATIONSHIP OF BLOOD SUGAR AND RETICULOCYTES FOLLOWING LIVER EXTRACT THERAPY

TABLE II

Fasting blood sugar values during treatment with ventriculin, liver extract and spontaneous remission

Days of observation	Case 1 *		Case 2 *		Case 3 *	
	Blood sugar	Reticulocytes	Blood sugar	Reticulocytes	Blood sugar	Reticulocytes
	<i>mgm. per 100 cc.</i>	<i>per cent</i>	<i>mgm. per 100 cc.</i>	<i>per cent</i>	<i>mgm. per 100 cc.</i>	<i>per cent</i>
-4			93	2.3		
-3			88	1.4		
-2				2.0		
-1	107	.8	107	2.1		
0	102	.2		2.5		
1	107	.8		2.0		7.5
2		1.9		5.2		10.2
3		.3	79	5.7	133	17.9
4	98	1.5		15.9		18.4
5	95	3.2	87	18.0	91	11.9
6	104	8.5		39.5		9.6
7	83	20.1	69	15.1	91	9.6
8	80	19.2		14.6		7.3
9	78	20.3		9.0	101	8.0
10	75	17.6		4.3		6.8
11	84	13.8	77	4.3		5.5
12	111	12.1		5.8	103	2.2
13	109	7.5	80	3.8		
14	148	6.4	80	3.1		
15	118	6.0	77	2.2		

- * Case 1—40 grams ventriculin daily.
 Case 2—6 vials Lilly's liver extract daily.
 Case 3—Spontaneous remission.

the increased activity of immature red blood cells, of the bone marrow, or a combination of the two.

The results obtained have been made from observations, which disregard the blood volume factor. The influence of the blood volume on the concentration of the blood sugar levels is not known at this time. However, its importance and significance are being studied.

SUMMARY AND CONCLUSIONS

1. In pernicious anemia in relapse, the blood sugar values are usually within the upper limits of normal.
2. The decreased blood sugar values in the beginning of a remission occur at the time of the increase in the percentage of immature red blood cells present in the peripheral circulation.
3. The blood sugar level reaches its lowest value at a time corresponding with the peak of the reticulated red blood cell percentage rise.
4. In early remission the blood sugar level may fall as low as 61 mgm.

per 100 cc.—practically all the values were within the lower limits of normal.

5. The onset of hunger symptoms in early remission may be directly associated with the decrease in the blood sugar level—the result of increased metabolic activity of either the marrow, the immature red blood cells, or both.

6. With general improvement, the blood sugar values increase and maintain themselves at a level not quite as high as their original one.

7. Ventriculin has no specific insulin-like properties when taken by mouth—the immediate effect following ingestion of 40 grams is a slight increase in the blood sugar value for about one-half hour, with a gradual return to its original level.

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