STUDIES ON THE ANEMIA OF PELLAGRA

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Extensive studies limited to the anemia of endemic pellagra were made in 1923 by Huck (1) and in 1933 by Turner (2). These investigators observed that anemia did not occur frequently in this type of pellagra, but, if present, was usually of a mild degree with a low color index and microcytosis; macrocytosis was not noted.

The pellagra occurring in the northern part of the United States has been termed "pseudopellagra," "alcoholic pellagra" or "pseudo-alcoholic pellagra" (3, 4, 5, 6) in contrast to the endemic type found in the southern part of the United States. Spies and DeWolf (7), however, showed that alcoholic and endemic pellagra are similar. The essential difference between the two types is that in "alcoholic pellagra" the patient loses the desire for food and lives almost exclusively from the calories in the ingested alcohol. In endemic pellagra, on the other hand, the patient receives a diet which is more complete but still deficient in some necessary nutritional constituents. They recognized, moreover, that "alcoholic pellagra" is in general more acute and more often fatal; this may be due to the fact that it follows almost complete abstinence from food.

Since so few determinations of blood values had been made on individuals who developed pellagra secondary to alcoholism, it seemed worth while to make the following hematological studies.

METHODS

Red and white blood cell counts, hemoglobin determinations, and estimations of mean corpuscular volume were performed twice a week or oftener, if indicated, on each of 30 consecutive cases of severe pellagra admitted to the Lakeside Hospital for treatment. While from 10 to 46 hematological studies were made by the authors on each of the 30 pellagrins, the blood values in the table were obtained by averaging the first two determinations. Pipettes certified for accuracy by the U. S. Bureau of Standards were used; the cells were counted by the usual technique. The hemoglobin determinations were made by the Sahli acid hematin method, using standards which were checked by the Van Slyke and Neill method (8) for determination of oxygen capacity. The mean corpuscular volume was calculated by the hematocrit method of Van Allen (9). These procedures were further standardized by repeated observations on 10 adults in good health. The pipettes, calibrated tubes, hemoglobinometers, and hemocytometers were the same as those used for the pellagrins. The only difference in the two studies was that the observations on the individuals with pellagra were continued for a longer period of time. After the completion of all blood determinations on the 30 patients and the 10 individuals serving as controls, the color index, volume index, mean corpuscular hemoglobin in micromicrograms, mean corpuscular volume in cubic microns, and the saturation index were calculated. In all instances 15.5 grams hemoglobin were regarded as 100 per cent, and all persons with a hemoglobin value below 80 per cent and a red blood cell count of 4 million or less were arbitrarily considered as having anemia.

Repeated gastric analyses were done on only 27 of the 30 pellagrins; the remaining 3 were considered too ill. Breakfast was withheld the morning of the test, a small Rehfuss tube was passed, and the fasting contents of the stomach were withdrawn. Immediately after this procedure, 0.0005 gram ergamine acid phosphate was injected subcutaneously. Twenty minutes later and again 40 minutes later the contents of the stomach were once more withdrawn. Free and total acidity were determined in the usual way, N/10 sodium hydroxide being used for titration and Topfer's reagent and phenolphthalein as indicators. A quantitative estimate of pepsinogen was made by the Mett tube method, and the presence of rennin was determined by incubation of a mixture of 5 drops of gastric juice and 5 cc. of milk for 30 minutes at 37° C.

TABLE I

Blood values of thirty cases of alcoholic pellagra

Date	Number	Name	Hospital number	Age	Sex	Race	Free gastric acidity after histamine	R.B.C.	Hemoglobin	Hemoglobin	Hematocrit	Color index	Mean corpuscular hemoglobin	Volume index	Mean corpuscular volume	Saturation index
				years			*cc. N/10 per 100*	*millions*	*per cent*	*grams per cent*	*per cent*		*micro-micro-grams*		*cubic microns*	
June 8, 1933	1.	C. F.	133089	49	M.	W.	0	3.79	82	13.0	45	1.09	35.1	1.33	121	.83
June 11, 1933	2.	W. M.	152770	70	M.	W.	0	4.47	74	11.4		.87	26.1			
June 27, 1933	3.	J. C.	152763	42	M.	W.	0	3.85	85	13.7	44	1.10	36.2	1.25	116	.80
June 30, 1933	4.	H. D.	122436	43	M.	W.		2.93	60	9.69	29	1.04	33.1	1.09	100	.95
July 3, 1933	5.	R. H.	152893	42	M.	W.	39	3.73	78	12.9	38	1.06	35.1	1.12	103	.94
July 3, 1933	6.	A. S.	135696	26	F.	C.	5	3.46	78	12.1	43	1.13	34.8	1.35	123	.84
July 3, 1933	7.	R. R.	153011	36	F.	C.	0	3.35	68	10.3	34	1.01	31.9	1.10	103	.92
July 6, 1933	8.	C. A.	152207	43	M.	W.	0	3.71	71	10.6	37	.96	28.5	1.08	100	.88
July 6, 1933	9.	W. C.	153208	31	F.	C.	0	3.77	68	11.0		.92	29.9			
July 7, 1933	10.	A. M.	153224	44	M.	W.	0	3.71	78	12.1	44	1.05	32.7	1.28	119	.82
July 11, 1933	11.	M. C.	153286	44	M.	C.	0	3.56	80	12.8	42	1.13	36.6	1.31	120	.80
July 17, 1933	12.	A. C.	144625	36	F.	C.	0	3.46	83	12.9	43	1.20	37.1	1.35	123	.74
July 27, 1933	13.	R. S.	153568	32	M.	C.	0	4.21	82	13.0		1.00	30.9			
August 1, 1933	14.	C. L.	153454	51	M.	C.	20	3.19	72	10.9	35	1.14	34.0	1.20	113	.94
August 1, 1933	15.	J. T.	153620	48	M.	W.	18	3.65	82	12.4	42	1.12	33.5	1.22	114	.90
August 16, 1933	16.	W. R.	137902	48	M.	C.	40	4.18	73	11.0	42	.88	25.7	1.08	100	.80
August 18, 1933	17.	M. W.	153944	36	F.	W.	58	3.68	78	12.4	42	1.07	33.5	1.25	114	.85
August 18, 1933	18.	C. W.	143320	26	F.	C.	12	3.03	75	11.6	41	1.25	38.7	1.50	136	.80
August 24, 1933	19.	B. M.	152573	30	F.	W.	5	4.71	90	14.2	44	.97	30.0	1.02	94	.94
September 11, 1933	20.	O. Q.	154338	38	F.	C.		4.48	80	12.4		.91	28.2			
September 23, 1933	21.	G. P.	154544	44	M.	W.	0	3.13	71	11.2	42	1.13	36.1	1.46	136	.80
November 18, 1933	22.	S. L.	155469	15	M.	W.	23	4.75	84	13.0		.90	27.7			
November 20, 1933	23.	G. W.	155481	29	M.	C.	0	3.94	73	10.2		.93	26.2			
November 22, 1933	24.	A. Y.	153313	31	F.	C.	0	3.15	70	10.0	38	1.09	32.2	1.28	123	.85
December 1, 1933	25.	E. H.	155669	38	F.	C.	21	3.84	60	9.9		.79	26.1			
December 8, 1933	26.	W. T.	149182	28	M.	C.	0	4.71	85	12.1	44	.90	25.7	1.02	94	.90
January 16, 1934	27.	G. E.	156351	47	M.	C.		5.47	89	14.3		.85	26.5			
January 23, 1934	28.	E. S.	153688	29	F.	C.	0	4.28	79	13.2		.93	31.3			
February 10, 1934	29.	A. L.	149424	41	M.	C.	0	4.82	94	15.6	46	.98	32.5	1.04	96	.94
February 10, 1934	30.	F. C.	156057	51	M.	C.	0	4.99	97	13.7	45	.99	27.9	1.00	95	.99

OBSERVATIONS

Nineteen of the 30 patients, 63.3 per cent, had an anemia with an average red cell count of 3.5 million and an average hemoglobin value of 74 per cent (see Table I). Of these 19, 15 had a color index averaging 1.11 (see Figure 1) and a volume index above 1. Identical determinations made on the individuals used as controls gave an average color index of 0.98 and an average volume index of 1.04 (consistent with the normal values of Haden (10) and Osgood (11)).

Seventeen of the 30 pellagrins had achylia gastrica as evidenced by the absence of free HCl, pepsinogen, and rennin following the administration of ergamine acid phosphate. Five of the remaining 10 pellagrins on whom gastric analyses were performed during the acute stages of the disease had definite hypoacidity and decreased values of pepsinogen and rennin. The gastric juice in nearly all instances was markedly reduced in volume, nearly always being less than 20 cc. Oftentimes it appeared to be entirely mucus, but occasionally it was free-flowing and limpid. The volume of gastric secretion increased following the

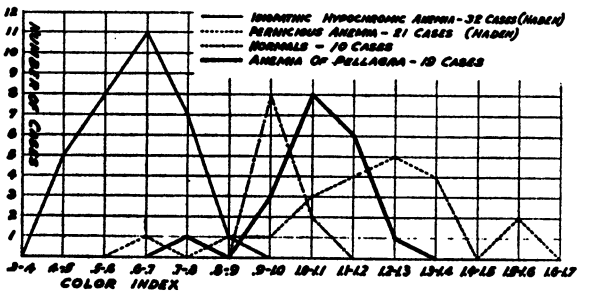

FIG. 1. SHOWING HOW A CURVE REPRESENTING THE COLOR INDEX VALUES OF THE ANEMIA OF ALCOHOLIC PELLAGRA LIES NEAR THE NORMAL AND BETWEEN SIMILAR CURVES REPRESENTING THOSE OF IDIOPATHIC HYPOCHROMIC ANEMIA AND PERNICIOUS ANEMIA.

injection of ergamine acid phosphate but even with the increase, the majority of cases did not have so much as 20 cc. gastric juice which could be withdrawn from the stomach. In this small series of cases the degree of anemia did not seem to be significantly related to the degree of hypochlorhydria or achlorhydria.

DISCUSSION

It has been shown in the course of this investigation that 63.3 per cent of the severely ill pellagrins had an anemia, which can be classified into the following 2 types: (1) about 75 per cent of the patients with anemia had definite increase in the volume of the red blood cells and a color index of 1 or above; (2) the other 25 per cent had an anemia characterized by a decrease in the red blood cell volume and color index. Since all of these patients with pellagra are known to have eaten only small amounts of food for a long period of time, it seems likely that they suffered from the lack of many necessary food substances, including iron and the antianemic substance found in liver.

It is theoretically conceivable that the anemia associated with pellagra may be caused by one of the following factors or by some combination of these factors:

1. Dysfunction of the stomach.
2. Failure of adequate ingestion of iron or other nutritional substances important in erythropoiesis.
3. Possible hepatic changes interfering with storage of the antianemic factor.

Any attempt, however, to correlate the presence of anemia in pellagrins with the above factors gives rise to various difficulties. In the first place, it is important to realize that all pellagrins do not develop anemia. This is true regardless of whether they give a history of small food intake or heavy drinking over a period of many years, or whether they have achylia gastrica. Since this is the case, it is possible that some quantitative relationship may exist between some of the aforementioned factors and the development of anemia. In the second place, the administration of any one specific therapeutic agent such as yeast, liver extract, or iron did not invariably bring about a uniform hematological response in those patients who did develop anemia. Further studies must be made before this latter mechanism can be understood, but at the present it has been shown that the pellagrins who developed anemia eventually attained normal blood values when given antipellagric therapy over a long period of time. The relationship of achylia gastrica to the development of anemia in pellagrins may be of some quantitative importance, but the studies of Spies and Payne (12) showed that the gastric juice from 2 pellagrins activated beef in such a manner as to cause a remission of pernicious anemia, thus demonstrating that the unknown constituent of the gastric juice which is lacking in the pernicious anemia patient, was present in the stomach contents of the pellagrins. The possible relationship between hepatic changes and hemopoiesis in these cases is at present only a theoretical concept. It may be of some importance, however, that postmortem examination of the livers from the patients who have died in this clinic frequently showed fatty infiltration (13).

CONCLUSIONS

1. It has been shown in this study that the peripheral blood findings of an anemia, usually characterized by increased red blood cell volume, occur in 63.3 per cent of 30 severely diseased "alcoholic" pellagrins.

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