SUMMARY

Horse gastric mucin differentially pseudoagglutinates human erythrocyte suspensions. Suggestions of a selective trend toward pseudoagglutination of Hr positive samples is noticed.

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Addendum: The non-specific role of mucins in erythrocytic pseudoagglutination has been demonstrated by the recent elicitation of this phenomenon with an artificial mucinoid, sodium carboxymethyl cellulose.

FIFTEEN YEARS' STUDY OF OCCULT LYMPHOCYTOSIS IN 280 HYPERCHOLESTEROLEMIA PATIENTS

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TREATMENT and study over a fifteen year period of 280 hypercholesterolemia patients has disclosed a symptom triad including the following:

1. A relative lymphocytosis
2. Hypercholesterolemia
3. Hypothyroidism.

Various experimental investigations agree in establishing an inverse relation between the thyroid sluggishness and the blood levels of cholesterol.

For example, Artom (1), (2), reported the increase in blood cholesterol levels of thyroidectomized dogs. Perlzweig (3), observed a decrease in the total blood lipids of hyperthyroid cases. Knauer (4), reported a decrease in the blood lipids in hyperthyroidism and an increase in hypothyroidism.

Westra and Kunde (5), showed that the high blood cholesterol levels in certain rabbits could be reduced by feeding thyroid. Mason, Hunt and Hurxthal (6), found a decrease in blood cholesterol levels in hyperthyroidism which was generally lowest in proportion as acute toxemia prevailed. Gilligan and associates (7), demonstrated that blood cholesterol levels are related to the basal metabolic rate. Not all drugs that stimulate basal metabolism lower blood cholesterol levels. For example, Cutting, Rytand and Tainter (8), raised the basal metabolic rate by administering dinitrophenol. It lowers the respiratory quotient, which implies a selective oxidation of fat rather than an enhanced oxidation of all foodstuffs, but it does not lower blood cholesterol. Tuttle (9), reported that most of the patients having diabetes mellitus for a number of years showed disturbances of the vascular system to a varied degree, depending upon the length and control of the disease. Out of 88 cases, sixty-five or 73.8 per cent, showed hypercholesterolemia in this study of "Diabetes Mellitus. Factors Influencing Cause, Course, and Complications. Analysis of 88 Cases."

Joslin, Eliot (10), makes a similar prognosis, and strongly favors the belief that the usual increase in the cholesterol in the diabetic blood is responsible for the vascular change.

Tuttle (11), found hypercholesterolemia in almost all of 500 obesity patients treated. The rationale of treatment was based on the need for proteins to maintain cellular integrity. With weight loss, there was a progressive reduction in blood cholesterol.

Thyroid extract (1) raises the metabolic rate, (2) contributes to fat oxidation including (3) the lowering of blood cholesterol, and in addition, (4) it influences the maturation and differentiation of cellular elements.

OCCULT LYMPHOCYTOSIS

Differential white cell counts were made according to the method suggested by Arneth as described by Wintrobe (12).

The basis of the classification was the number of lobes of which the nucleus was composed. The lymphocytes were classed into large and small, the difference being, not so much one of actual diameter, but rather the relative proportion of cytoplasm to nucleus. Small lymphocytes appear as if their nucleus almost completely usurps the cell, there being a barely perceptible cytoplastic margin; whereas large lymphocytes show a wide margin of cytoplasm surrounding the nucleus. In size, the large lymphocytes are nearly always of much wider diameter than the small lmphocytes.

Typically illustrative of the findings are the counts, made as described in the following cases (Table 1).

Two conspicuous characteristics are notable. Of the multilobed white cells, the more "mature" forms tend to be increased. This would be a "shift to the right" by the Arneth or Schilling interpretation. It suggests an emphasis of the more matured forms of neutrophilic cells. The preponderance of mononucleated forms is even more characteristic. Frequently, the number of lymphocytes is in excess over the number of neutrophiles. In all cases, there is a relative lymphocytosis; and in some cases, there is an actual lymphocytosis despite the nearly normal total white cell count. For example, the average total normal white cell count is 7,000 cells per cubic millimeter of blood. Of this number, about 2,100 are normally lymphocytes (from 27% to 33% of the total white cells). When the lympho-

TABLE I

CASE HISTORY NUMBER		ARNETH CLASSIFICATION OF POLYS					MONONUCLEAR CELLS				LYMPHOCYTIC
		1	2	3	4	5	POLYS	SMALL	LARGE	TOTAL	INDEX
11	C-1	9	26	43	19	3	50%	30	20	50	1.66
23	C-2	2	18	42	36	2	48	48	3	51	1.67
39	C-3	15	32	36	14	3	45	52	3	55	1.83
52	C-4	5	33	46	16	0	51	40	9	49	1.63
68	C-5	2	4	34	40	22	40	40	20	60	2.00
82	C-6	2	8	28	41	21	54	31	15	46	1.53
93	C-7	2	12	58	28	0	37	46	17	63	2.10
106	C-8	10	14	38	26	12	41	24	35	59	1.96
120	C-9	1	14	36	40	9	55	12	33	45	1.50
131	C-10	1	5	30	39	25	53	10	37	47	1.56
140	C-11	4	14	48	28	6	49	40	11	51	1.70
156	C-12	6	14	30	40	10	50	32	18	50	1.66
167	C-13	7	19	36	30	8	53	23	24	47	1.51
182	C-14	4	8	44	32	12	39	25	36	61	2.03
193	C-15	6	15	49	25	4	48	29	23	52	1.73
201	C-16	5	20	45	26	4	47	29	24	53	1.77
215	C-17	2	20	50	20	8	50	25	25	50	1.66
235	C-18	6	12	38	34	10	30	52	18	70	2.33
240	C-19	1	24	40	32	3	24	11	65	76	2.53
272	C-20	7	19	51	20	3	39	38	23	61	2.00
278	C-21	2	3	39	46	10	43	15	42	57	1.90

(For easy recognition of the degree of occult lymphocytosis, a "lymphocytic index" has been used in this study. It is obtained by dividing 30 (representing the average normal percent of lymphocytes) into the actual percent of lymphocytes found. For example, Case 39 shows 55% lymphocytes; therefore, 55/30 gives a lymphocytic index of 1.83).

cytes amount to over 50% of the total white cells, as is seen in many of the cases, the actual total lymphocytes per cm. of blood can be considerably higher than the normal 2,100 and may range from 2,500 to 5,000 or more.

We are dealing with an occult lmphocytosis. Hidden in the approximately normal total white cell count of the blood of the hypercholesterolemic patient with hypothyroidism is a real lymphocytosis. This is manifested as a relative lymphocytosis on differential count and expresses an increase above normal of lymphocytic cellular output.

All blood cells are derived from the mesenchyme. The parent hemoblast is actually a huge lymphocyte, from which both red and white cells are subsequently differentiated. This is related to bio-oxidation. Sabin (13), for example, has developed experimental evidence to show that leucocytic differentiation is related to oxygen tension.

Occult lymphocytosis in hypercholesterolemia with hypothyroidism indicates inadequate cellular differentiation. Therapeutic measures are directed to 1) diet, 2) thyroid stimulation, 3) weight control, 4) psychotherapy, 5) bio-oxidation, 6) lipotropic agents and 7) supportive measures.

TREATMENT

1) Diet. Diet has little effect on the hypercholesterolemia of hypothyroidism. It is restricted as an important aid in its control. Sources of visible fat must be restricted, except the vegetable oils which contain phytosterol, because it is not utilized in the human economy. Special care must be given to meats whose content of invisible fat is high, as much of this fat is cholesterol. Glandular meats are completely eliminated from the diet. Egg yolks are restricted. Egg white is permitted. Whole milk is replaced with skim milk. All cheese avoided except cottage and pot cheese.

2) Thyroid stimulation. Deficient thyroid activity is stimulated to normal by use of thyroid gland prescribed to tolerance, guided by basal metabolic rate, blood cholesterol and differential white cell count. The highest tolerated thyroid dose may be continued indefinitely.

3) Weight control. Overweight is the rule in this syndrome. The dietary program, in such cases, is similar to that followed in the treatment of obesity: High protein, low caloric, low cholesterol.

4) Psychotherapy. Considerable psychotherapy is needed in many of these patients. When atonia of the sympathetic nervous system is found, treatment is directed toward its correction. As thyroid function is restored and emotional instability is dispelled, the patient-physician relationship is gainfully achieved.

5) Bio-oxidation. As the study progressed, it became increasingly apparent that the underlying biochemical dysfunction was a matter of lowered bio-oxidation. Greater emphasis was then given to stimulating intermediary metabolism. This included the fostering of increased aerobic and anaerobic bio-oxidation. The drugs of choice for this objective include the enzymatic functioning B vitamins given in proper proportion as suggested by Cayer (14). These are combined with supplementary amino acids now known to be necessary for building the B vitamins into appropriate enzymes and conjugated further with catalytic metals. Intensive treatment with such prescriptions gave prompt results.

6) Lipotropic agents. Suitable lipotropic agents are necessary aids in affecting the reduction of blood cholesterol levels. Choline, inositol and methionine were made part of the B complex formulation. A new lipotropic agent is without conspicuous effect on the total lipids of the blood, but is selective in lowering blood cholesterol. It is an unsaturated fatty acid split away from lecithin derived from sunflower seed oil. ("Povon" 9, 12-octadecadienoic acid*)

7) Supportive measures. Liver extract and iron are given when indicated. Vitamins supplant restrictions in diet.

*John Peck Laboratories, Inc., New York, N. Y.

BRIEF ABSTRACTS OF CASE HISTORIES

Randomly selected case histories from the series of patients disclose the symptom triad mentioned,—Hypothyroidism, hypercholesterolemia and occult lymphocytosis on their initial visit as follows:—

Case 11: M. Age 58, excessive fatigability. Obese. BMR—29%. Blood cholesterol, 331 mgs. Lymphocytic index, 1.66.

Case 23: F. Age 32, headache, insomnia, joint pain, constipation, obese. BMR—15%. Blood cholesterol 292 mgs. Lymphocytic index, 1.83.

Case 39: F. Age 54, precordial pain, dyspnoea, exhaustion, insomnia. BMR—16%. Blood cholesterol, 328 mgs. Lymphocytic index, 1.83.

Case 52: F. Age 45, emotional instability, headache. BMR—20%. Blood cholesterol, 387 mgs. Lymphocytic index, 1.63.

Case 68: M. Age 37, tinnitus, vertigo, progressive deafness. BMR—25%. Blood cholesterol, 282 mgs. Lymphocytic index, 2.00

Case 82: F. Age 45, exhaustion, headache, incipient osteoarthritis. BMR—14%. Blood cholesterol, 244 mgs. Lymphocytic index, 1.53.

Case 93: M. Age 46, rapid gain in weight, painful joints. BMR—23%. Blood cholesterol, 294 mgs. Lymphocytic index, 2.10.

Case 106: M. Age 60, history of very low blood pressure. Hypertensive past five years. Dyspnoea, myocardial changes, paroxysmal tachycardia. BMR—30%. Blood cholesterol, 294 mgs. Lymphocytic index, 1.96.

Case 120: F. Age 49, painful joints, fatigue, constipation, headache. BMR—15%. Blood cholesterol, 282 mgs. Lymphocytic index, 1.50.

Case 131: F. Age 53, gall bladder disease, headache, osteoarthritis. BMR—19%. Blood cholesterol, 308 mgs. Lymphocytic index, 1.56.

Case 140: F. Age 16, frequent sore throat, fatigue, constipation, painful joints. BMR—25%. Blood cholesterol, 257 mgs. Lymphocytic index, 1.70.

Case 156: F. Age 54, exhaustion, headache, constipation, indigestion, marked hypotension. BMR—22%. Blood cholesterol, 284 mgs. Lymphocytic index, 1.23.

Case 167: F. Age 22, indigestion, constipation, obese, hypotensive. Blood cholesterol, 286 mgs. BMR—20%. Lymphocytic index, 1.51.

Case 182: M. Age 56, precordial pain, headache, myocardial damage, obese. BMR—18%. Blood cholesterol, 282 mgs. Lymphocytic index, 2.03.

Case 193: M. Age 42, insomnia, osteo-arthritis, obese. BMR—19%. Blood cholesterol, 393 mgs. Lymphocytic index, 1.73.

Case 201: F. Age 54, arthritis 15 years, headache, indigestion, hypotensive, osteo-arthritis. BMR—20%. Blood cholesterol, 276 mgs. Lymphocytic index, 1.77.

Case 215: F. Age 52, Headache, constipation, osteo-arthritis, hypotension. BMR—13%. Blood cholesterol, 214 mgs. Lymphocytic index, 1.66.

Case 235: F. Age 23, exhaustion, headache, indigestion, hypotensive, underweight. BMR—15%. Blood cholesterol, 254 mgs. Lymphocytic index, 2.33.

Case 240: F. Age 70, precordial pain, fatigue, vertigo, osteoarthritis, obese. BHR—25%. Blood cholesterol, 273 mgs. Lymphocytic index, 2.53.

Case 272: F. Age 39, headache, obese, constipation, hypotensive. BMR—19%. Blood cholesterol, 275 mgs. Lymphocytic index, 2.00.

Case 278: F. Age 44, Obese, fatigue. BMR—20% Blood cholesterol, 366 mgs. Lymphocytic index, 1.90.

SUMMARY

Degenerative diseases are primarily those in which mesodermal structures are at fault; and lymphocytes are primarily mesodermal structures.

A poverty of leucocytes is a prominent consistent finding in the hypercholesterolemia of hypothyroidism. This depletion of leucocytes deprives the body of an important defense against disease. It has also been demonstrated that the lymphocytes are a factor in the production of antibodies.

In 280 hypercholesterolemia patients with hypothyroidism, a pattern of common clinical symptoms presented, 1) Undue exhaustibility. 2) Nervous tension. 3) Increased reaction to the histamine test. Dermatographia was generally demonstrable. Some manifestation of gastro-intestinal dysfunction was present in practically all cases, and constipation was a common complaint.

An impressionable number of cases were, at one time, treated for sinusitis and/or migraine. Rarely did an x-ray examination confirm sinus disease. Post nasal drip was an almost universal finding, generally accompanied by a perennial sub-acute rhino-pharyngitis.

From the consistency of these complaints, it is apparent that lymphocytosis is associated with histamine hypersensitivity, reduced resistance to infection and lowered recuperative powers. It may therefore be concluded that:

1. An occult lymphocytosis develops in cases of hypercholesterolemia with hypothyroidism.

2. A common pattern of symptoms is presented.

3. Thyroid activity is reflected in cellular differentiation expressed by selective increase in mesodermally derived lymphocytes.

4. Corrective therapeutic measures gave gratifying results with a more normal re-equilibration of the white cells, a drop in the blood cholesterol (The mean blood cholesterol level in this study is 300 mgs. of total cholesterol), and a correction of the basal metabolic rate to the normal levels.

5. A newer cholesterotropic drug, derived from the lecithin of sunflower seed oil, "Povon", is helpful in specifically lowering blood cholesterol which fails to respond to the more usual lipotropic factors,—choline, methionine and inositol.

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