Lipoproteins in Cancer Patients

Marion Barclay, Ph.D.
Vladimir P. Skipski, Ph.D.
Olga Terebus-Kekish
Edward M. Greene
Richard J. Kaufman, M.D.
C. Chester Stock, Ph.D.

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Dr. Barclay is Associate Member, Division of Experimental Chemotherapy, Sloan-Kettering Institute for Cancer Research, Walker Laboratory, Rye, New York.

Dr. Skipski is Associate Member, Division of Experimental Chemotherapy, Sloan-Kettering Institute for Cancer Research, Walker Laboratory.

Miss Terebus-Kekish is Research Assistant, Division of Experimental Chemotherapy, Sloan-Kettering Institute for Cancer Research, Walker Laboratory.

Mr. Greene is a volunteer, Sloan-Kettering Institute for Cancer Research, Walker Laboratory.

Dr. Kaufman is Associate Attending Physician, Department of Medicine, Memorial Hospital for Cancer and Allied Diseases, New York, New York.

Dr. Stock is Vice President and Acting Deputy Director, Walker Laboratory.

ABBREVIATIONS

VLDL: Very-low-density lipoproteins with density less than 1.006 g/ml.

LDL: Low-density lipoproteins with density less than 1.063 g/ml.

HDL: High-density lipoproteins.

HDL₂: A component of the LDL, designated as S₁ 3-0.

Components of the fraction with densities less than 1.125 g/ml are HDL₂: [(S₁ 4-0) the main component, S₁ 12-4 and 20-12 are the less dense components in this fraction]; HDL₃: High-density lipoproteins with density less than 1.21 g/ml.
For some years, we have been studying the pattern of lipoproteins in serum and have found what may be a consistent difference in this pattern between normal people and those with cancer.

Because all lipids in serum are in some form of lipoproteins, all changes in lipid transport and, often, lipid metabolism appear in the serum as changes in the levels of lipoproteins and/or their chemical constituents.

Some years ago, tests for the amounts of lipoproteins in the plasma of breast cancer patients showed that levels of a particular type of lipoprotein, HDL, were somewhat lower in these women than in normal controls. The levels of HDL were, in fact, influenced by the stage of cancer, so that the lowest, most abnormal levels occurred in women with the most serious disease.1

The suggested abnormality of lipoprotein metabolism in cancer was subsequently confirmed by several investigators using different techniques for measuring them in serum.2,3

In this study we found that the serum of men, women and children with cancer have unusually low values for one of the HDLs, HDL2. The normal subjects in this study who had abnormally low levels of HDL2 in their serum also had a pronounced incidence of cancer in their blood relatives and a possibly greater risk of developing cancer than the controls with normal levels of HDL2.

SUBJECTS

Normal Subjects

The normal subjects, except for the children, were employees or volunteers of Memorial Sloan-Kettering Cancer Center. There were 38 women, 10 men and 3 children. All the normal adults were placed in one of four groups:

| M-CF — Men | with cancer in their immediate families |
| W-CF — Women | |
| M-NO — Men | with little or no family history of cancer |
| W-NO — Women | |

It was possible to follow 13 of the normal women (7 in group W-CF and 6 in group W-NO) and the 10 normal men (6 in group M-CF and 4 in group M-NO) for 10 years. Initially, at 0 year and again at 5 years, these subjects completed, in the presence of qualified physicians, an extensive questionnaire designed to elucidate conditions which would influence levels of lipoproteins in serum; in addition, they were given complete physical examinations to detect any disease. At the 10-year period, only the questionnaires were given. Since
the subjects were a well integrated group in terms of living conditions, diets and activities, the information obtained can be considered reliable. The women’s ages ranged from 25 to 44, and the men’s from 30 to 55.

Subjects with Cancer

All the patients were at Memorial Hospital. There were 23 women, 9 men and 7 children. These subjects, especially the women, were chosen after screening to eliminate patients with hormonal imbalances, diabetes and/or thyroid disorders. The patients studied did not have liver or biliary involvement which might affect the levels of serum lipoproteins.

RESULTS

Certain lipoproteins (VLDL, HDL1, HDL3 and HDL2) showed significantly different average quantities in the sera of several categories of patients than in the sera of people in groups W-NO and M-NO or normal children. (Table 1.) Emphasis is placed on the significant differences in the values of HDL2.

Normal Women and Women with Cancer

In the two groups of normal women only the HDL2 component differed. Women in the W-NO group had significantly higher levels of HDL2 in their serum than women in the W-CF group (66 percent of the W-NO women showed values for HDL2 of over 100mg./100 ml. of serum as compared with only 6 percent of the W-CF women).

At the beginning of the study (0 year) five subjects with very low values for HDL2 reported positive family histories of cancer (group W-CF). Two other normal subjects, who had marginal or low values for HDL2, did not have a family history of cancer at 0 year; subsequently, however, both of these women reported the appearance of cancer in close relatives, and they were also placed in group W-CF. (Table 2.)

Two women in the W-CF group developed skin cancer shortly after the five-year survey was made and, although none of the women in the W-NO group did, the number of individuals participating was not adequate to draw any definite conclusions about the difference in the incidence of cancer between the two groups.

Seventeen of the patients studied had breast cancer, three with primary operable disease and fourteen with advanced inoperable disease.

The three women with operable cancer averaged high values for VLDL and one of these patients showed a normal level of HDL2. The average value of HDL2 for these three women, however, was still significantly lower than the average for group W-NO. (Table 1A.)

Of the 14 women with advanced breast cancer, all but one had substantially higher levels of VLDL than the normal women in both groups. The values for HDL2, in all but two of the advanced breast cancer patients, were well below the average of the women with primary, operable tumors and all were below the average for the women in group W-NO, but practically identical to the average of group W-CF.

Four women with advanced breast cancer had bilateral oophorectomies. They were studied preoperatively and at periods ranging from three months to four years postoperatively. Two of these patients responded well to surgery and their postoperative levels of HDL2 increased while the two patients who did not respond to oophorectomy showed no increase in their levels of HDL2.

Of the six women with cancer other than carcinoma of the breast, three had ovarian cancer with oophorectomies, and three had different types of cancer. Two of these women had relatively normal levels for VLDL and HDL2. The other four women had very high VLDL levels, combined in three cases with unusually
# TABLE 1 — LIPOPROTEINS IN SERA FROM NORMAL SUBJECTS AND PATIENTS WITH CANCER

## A — Women

| Lipoproteins (mg/100 ml serum) | Normal women | Women with breast cancer | Men with various types of cancer | Children with various types of cancer |
|-------------------------------|--------------|--------------------------|---------------------------------|--------------------------------------|
|                               | Group W-NO   | Group W-CF               | Primary operable                 | Advanced inoperable                  |
| No. of analyses               | 86           | 72                       | 3                               | 20                                   | 6                                    |
| VLDL^a                        |              |                           |                                 |                                      |                                       |
| Mean                          | 12           | 7                        | 102^b                           | 103                                 | 84                                   |
| Range                         | 0—55         | 0—28                     | 63—132                         | 0—260                                | 8—161                                |
| ± S.D.                        | ±11          | ±9                       | ±36                             | ±60                                  | ±35                                  |
| p                             |              |                           | <0.001                          | <0.001                               | <0.001                               |
| (HDL1)^c                      |              |                           |                                 |                                      |                                       |
| Mean                          | 45           | 49                       | 18                              | 74                                   | 95                                   |
| Range                         | 5—143        | 5—134                    | 13—22                           | 15—162                               | 38—123                               |
| ± S.D.                        | ±30          | ±29                      | ±5                              | ±48                                  | ±33                                  |
| p                             |              |                           | <0.05                           | <0.02                                | <0.001                               |
| HDL2^d(S1 4—0)               |              |                           |                                 |                                      |                                       |
| Mean                          | 120          | 52                       | 84                              | 51                                   | 61                                   |
| Range                         | 45—275       | 10—134                   | 59—126                          | 8—98                                 | 21—93                                |
| ± S.D.                        | ±56          | ±28                      | ±37                             | ±30                                  | ±29                                  |
| p                             |              |                           | <0.001                          | <0.05                                | <0.001                               |
| HDL3^e                        |              |                           |                                 |                                      |                                       |
| Mean                          | 126          | 126                      | 87                              | 111                                  | 134                                  |
| Range                         | 62—255       | 53—270                   | 62—115                          | 49—165                               | 85—188                               |
| ± S.D.                        | ±30          | ±36                      | ±27                             | ±34                                  | ±36                                  |
| p                             |              |                           | <0.02                           |                                      |                                       |

## B — Men

| Lipoproteins (mg/100 ml serum) | Normal Men | Men with various types of cancer | Normal children | Children with various types of cancer |
|-------------------------------|------------|---------------------------------|-----------------|--------------------------------------|
|                               | Group M-NO | Group M-CF                       |                 |                                      |
| No. of analyses               | 4          | 7                                | 8               | 3                                   | 11                                   |
| VLDL^a                        |            |                                  |                 |                                      |                                       |
| Mean                          | 43         | 197                              | 230             | 122                                 | 114                                  |
| Range                         | 40—46      | 73—296                          | 156—418         | 0—216                               | 10—264                               |
| ± S.D.                        | ±2         | ±91                              | ±95             | ±99                                  | ±99                                  |
| p                             |            | 0.001                            | 0.001           |                                      |                                       |
| (HDL1)^c                      |            |                                  |                 |                                      |                                       |
| Mean                          | 39         | 56                               | 116             | 63                                   | 51                                   |
| Range                         | 10—68      | 20—105                          | 38—276          | 59—68                                | 14—82                                |
| ± S.D.                        | ±31        | ±36                              | ±31             | ±5                                  | ±31                                  |
| p                             |            | 0.05                             | 0.05            |                                      |                                       |
| HDL2^d(S1 4—0)               |            |                                  |                 |                                      |                                       |
| Mean                          | 97         | 26                               | 23              | 65                                   | 19                                   |
| Range                         | 70—122     | 16—46                           | 15—53           | 60—72                                | 0—48                                 |
| ± S.D.                        | ±26        | ±14                              | ±13             | ±6                                  | ±17                                  |
| p                             |            | 0.001                            | 0.001           | 0.001                                | 0.001                                |
| HDL3^e                        |            |                                  |                 |                                      |                                       |
| Mean                          | 148        | 142                              | 120             | 217                                  | 106                                  |
| Range                         | 112—187    | 91—212                          | 51—173          | 118—314                              | 61—155                               |
| ± S.D.                        | ±33        | ±42                              | ±39             | ±98                                  | ±37                                  |
| p                             |            | 0.05                             |                 |                                      |                                       |

^a D < 1.006 g/ml.  
^b Nos. in italics are significantly different from those in Groups W-NO, M-NO, or normal children.  
^c Sf 3—0, D < 1.063 g/ml.  
^d HDL2 (Sf 4—0), D < 1.125 g/ml.  
^e HDL3, D < 1.21 g/ml.
### TABLE 2 – LIPOPROTEINS IN SERA FROM NORMAL WOMEN RELATED

| Subjects | Mean | Range | ± S.D. | Mean | Range | ± S.D. |
|----------|------|-------|--------|------|-------|--------|
| W-CF: Women with | | | | | | |
| 21—(1)^d | 0 | 0—14 | ± 5 | 88 | | |
| 8—(10) | 5 | 0—36 | ± 11 | 70 | 49—89 | ± 16 |
| 16—(9) | 11 | 0—11 | ± 4 | 43 | 23—49 | ± 13 |
| 27—(10) | 3 | 0—12 | ± 4 | 42 | 23—63 | ± 19 |
| 24—(11) | 3 | 0—27 | ± 5 | 27 | 15—45 | ± 11 |
| Averages | 10 | 0—28 | ± 5 | 26 | 15—35 | ± 6 |
| Group W-NO: Women with little | | | | | | |
| 12—(10) | 10 | 0—37 | ± 9 | 168 | 137—215 | ± 23 |
| 6—(9) | 14 | 0—18 | ± 10 | 135 | 106—176 | ± 20 |
| 4—(10) | 9 | 0—23 | ± 10 | 124 | 103—147 | ± 19 |
| 11—(11) | 25 | 0—55 | ± 10 | 105 | 79—128 | ± 21 |
| 15—(5) | 5 | 0—9 | ± 2 | 105 | 89—113 | ± 21 |
| 18—(11) | 10 | 0—28 | ± 2 | 93 | 69—118 | ± 21 |
| Averages | 12 | | | 122 | | |

- ^a^ D < 1.006 g/ml.
- ^b^ D < 1.125 g/ml; HDL₂ is the main component. Subjects are listed in decreasing order of this
- ^c^ D < 1.210 g/ml.
- ^d^ Nos. in parentheses represent weeks of samples; 1 blood sample/week.

### TABLE 3 – LIPOPROTEINS IN SERA FROM

| Subjects | D < 1.006 g/ml | D < 1.063 g/ml |
|----------|----------------|----------------|
|           | S_r 400—100^a| VLDL^b| S_r 3—0 (HDL₁) |
| 1. Choriocarcinoma | 0 | 23 | 38 |
| 2. Lung cancer | 4 | 145 | 104 |
| 3. Neuroblastoma | 40 | 161 | 122 |
| 4. Ovarian carcinoma | 0 | 76 | 123 |
| 5. Ovarian carcinoma | 0 | 8 | 77 |
| 6. Ovarian carcinoma | 0 | 91 | 107 |
| Averages | 7 | 84 | 95 |

- ^a^ Spectrum of components with the lowest densities in the VLDL fraction.
- ^b^ (VLDL)—(S_r 400—100) components, i.e., components with S_r rates < 100 or those with the
TO INCIDENCE OF CANCER IN THEIR IMMEDIATE FAMILIES

| HDL$_3$ c | Relatives with cancer (periods, yr) |
|-----------|-------------------------------------|
|           | Mean ± S.D. | 0 | 5 | 10 |

**Family histories of cancer**

|   |         |     |     |
|---|---------|-----|-----|
| 142 | 93–149  | ±20 |     |
| 121 | 97–178  | ±27 |     |
| 152 | 93–149  |     |     |
| 107 | 88–119  | ±14 |     |
| 110 | 54–134  | ±23 |     |
| 118 | 98–170  | ±22 |     |
| 99  | 75–131  | ±21 |     |

**or no family histories of cancer**

|   |         |     |     |
|---|---------|-----|-----|
| 143 | 110–174 | ±22 |     |
| 122 | 95–141  | ±16 |     |
| 124 | 98–159  | ±21 |     |
| 133 | 87–152  | ±21 |     |
| 110 | 62–151  | ±33 |     |
| 127 | 81–156  | ±20 |     |

component.

WOMEN WITH 4 DIFFERENT TYPES OF CANCER

(mg/100 ml serum)

|       | $S_f$ 20–12 | $S_f$ 12–4 | $S_f$ 4–0 (HDL$_2$) | HDL$_3$ |
|-------|-------------|------------|---------------------|---------|
| $D < 1.125$ g/ml | 0 | 0 | 93 | 85 |
| $D < 1.21$ g/ml | 21 | 71 | 34 | 158 |
|       | 0 | 0 | 21 | 138 |
|       | 0 | 16 | 78 | 188 |
|       | 0 | 17 | 85 | 115 |
|       | 12 | 21 | 52 | 121 |
|       | 6 | 21 | 61 | 134 |

highest densities in the VLDL fraction.
**TABLE 4 – LIPOPROTEINS IN SERA FROM NORMAL MEN RELATED TO INCIDENCE OF CANCER IN THEIR IMMEDIATE FAMILIES**

| Lipoprotein fractions (mg/100 ml serum) | \( D < 1.006 \text{ g/ml} \) | \( D < 1.125 \text{ g/ml} \) | \( D < 1.21 \text{ g/ml} \) |
|----------------------------------------|------------------------------|------------------------------|------------------------------|
| Subjects                               | \( S_f 400-100^a \) | VLDL\(^b\) | HDL\(_2\)\(^c\) (\( S_f 4-0 \)) | HDL\(_3\) |
| Group M-CF: Men with family histories of cancer | | | | |
| M. O.                                  | 4  | 99  | 46  | 124  |
| U. M.                                  | 0  | 73  | 39  | 212  |
| L. A.                                  | 5  | 264 | 27  | 157  |
| B. R.\(^d\)                            | 4  | 296 | 17  | 115  |
| G. E.                                  | 28 | 247 | 16  | 91   |
| G. R.\(^d\)                            | 72 | 200 | 10  | 153  |
| Averages                               | 19 | 197 | 26  | 142  |

Group M-NO: Men with little or no family histories of cancer

| H. O.                                  | 0  | 42  | 122 | 160  |
| G. R. E.                               | 0  | 40  | 117 | 112  |
| B. A.                                  | 0  | 43  | 80  | 187  |
| M. A. C.                               | 0  | 46  | 70  | 131  |
| Averages                               | 43 | 97  | 148 |

\(^a\) Spectrum of components with the lowest densities in the VLDL fraction.
\(^b\) (VLDL) = \( S_f 400-100 \) components, i.e., components with \( S_f \) rates < 100 or those with the highest densities in the VLDL fraction.
\(^c\) Subjects are listed in decreasing order of this component.
\(^d\) Propositi who subsequently developed cancer. Values for G. R. are averages of 2 experiments.

**TABLE 5 – LIPOPROTEINS IN SERA FROM**

| Lipoprotein fractions |
|-----------------------|
| \( D < 1.006 \text{ g/ml} \) |
| \( S_f 400-100^a \) | VLDL\(^b\) |
| 1. Parotid and gastro-intestinal cancer | 4  | 296 |
| 2. Melanoma\(^c\) | 72 | 200 |
| 3. Melanoma | 46 | 418 |
| 4. Leiomyosarcoma | 59 | 205 |
| 5. Colon carcinoma | 42 | 174 |
| 6. Chronic myelocytic leukemia | 38 | 156 |
| 7. Epidermoid broncho-genic carcinoma\(^d\) | 0  | 165 |
| Averages | 37 | 231 |

\(^a\) Spectrum of components with the lowest densities in the VLDL fraction.
\(^b\) (VLDL) = \( S_f 400-100 \) components, i.e., components with \( S_f \) rates < 100 or those with the highest densities in the VLDL fraction.
\(^c\) Means of 2 experiments.
\(^d\) Receiving X-ray treatments at time of sampling.
low levels of HDL₂. The average value for HDL₂ in these patients, however, was still significantly lower than the average for women in group W-NO. (Tables 1A and 3.)

The mean values for the lipoprotein HDL₂ were consistently and significantly lower in both women with cancer and women in group W-CF than in the women in group W-NO.

**Normal Men and Men with Cancer**

Nearly all the subjects in group M-CF had high values for VLDL and low values for HDL₂. (Tables 1B and 4.) Two of these men developed cancer (bronchogenic carcinoma and melanoma) within five years of the beginning of this study.

By contrast, all the men in group M-NO had low values for VLDL, more normal levels of HDL₂ and no incidence of cancer to date.

As in the women studied, the pattern of lipoprotein levels in men with cancer was more similar to that of the men in group M-CF (high levels of VLDL and low levels of HDL₂) than to that of the men in group M-NO.

However, the men with cancer did have somewhat higher levels of one class ($S_f$ 400-100) of VLDL than the men in group M-CF. (Tables 1B and 5.)

**Normal Children and Children with Cancer**

In all the normal children one class of VLDL was absent ($S_f$ 400-100) while most of the children with cancer had higher than normal values for the $S_f$ 400-100 component of VLDL.

All the HDL₂ values in the children with cancer were lower than in any normal subject (Tables 1B and 6) and HDL₂ was completely absent in the sera of two of the sick children.

**DISCUSSION**

It appears that each healthy person has a characteristic pattern for lipoproteins in serum taken during fasting. In these people the concentrations of HDL and especially HDL₂ are affected mainly by hormone levels so the concentrations may be quite different in men and women (normal values for HDL₂ are lower in men) and in premenopausal and postmenopausal women. In the serum of pa-

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### Table: Men with Different Types of Cancer

| $D < 1.063$ g/ml | $D < 1.125$ g/ml | $D < 1.21$ g/ml |
|-----------------|-----------------|-----------------|
| $S_f 3-0$ (HDL₁) | $S_f 20-12$ | $S_f 12-4$ | $S_f 4-0$ (HDL₂) | HDL₃ |
| 38              | 12              | 6               | 17               | 115  |
| 45              | 6               | 6               | 20               | 153  |
| 93              | 10              | 60              | 22               | 119  |
| 151             | 30              | 42              | 53               | 153  |
| 92              | 0               | 0               | 16               | 131  |
| 115             | 0               | 60              | 15               | 51   |
| 276             | 0               | 23              | 19               | 100  |
| 116             | 8               | 28              | 23               | 117  |

*est densities in the VLDL fraction.
patients with cancer, however, regardless of age or sex, the HDL₂ was significantly lower than in comparable normal people. The levels of VLDL were greatly increased in patients with cancer, especially in the men who have higher normal values for VLDL. Generally, patients with decreased HDL₂ have a tendency toward increased VLDL. The increase in VLDL which had been noted in men with coronary artery disease or after a high carbohydrate diet had not previously been described as an effect of cancer.³⁹

HDL₁, a component which varies little in normal subjects, was increased in the adults with cancer.³⁹ Of possible significance may be the differences in the lipid compositions of HDL₁ and HDL₃ between normal women and women with advanced cancer.

Specifically, however, HDL₃ was the lipoprotein class most consistently affected by cancer.

In view of the recent reports linking abnormal lipoprotein metabolism with several inherited diseases ¹¹,¹³ it seems significant that the normal subjects with low values for HDL₂ also have an unusually high incidence of cancer in their families; in fact, four of these thirteen subjects developed cancer during this study.

**SUMMARY**

Serum lipoprotein levels were measured in normal subjects and in patients with cancer. All normal adult subjects were classified according to the amounts of high-density lipoprotein-2 in their sera. It was observed that subjects with low

| TABLE 6 – LIPOPROTEINS IN SERA FROM | Lipoprotein fraction... |
| Subjects | SF 400–100 | VLDL |
| Normal | | |
| Subjects | SF 400–100 | VLDL |
| 1 | 0 | 0 |
| 2 | 0 | 216 |
| 3 | 0 | 149 |
| Averages | | 122 |
| Children with | | |
| 1. Malignant reticuloendotheliosis | 0 | 36 |
| 2. Chronic reticuloendotheliosis | 45 | 174 |
| 3. Acute leukemia | 56 | 264 |
| 4. Lymphoma | 33 | 209 |
| 5. Lymphangiomatosis | 0 | 10 |
| 6. Hodgkin's disease²,³ | 0 | 34 |
| 7. Myelomonocytic leukemia³,⁴ | 34 | 69 |
| Averages | 24 | 114 |

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* Spectrum of components with the lowest densities in the VLDL fraction.
* (VLDL) = (SF 400–100) components, i.e., components with SF rates < 100 or those with the
* Means of 2 experiments.
* Subjects 6 and 7 are the only females.
* Means of 4 experiments.
NORMAL CHILDREN AND CHILDREN WITH CANCER

|                  | $D < 1.063$ g/ml | $D < 1.125$ g/ml | $D < 1.21$ g/ml |
|------------------|------------------|------------------|-----------------|
|                  | $S_f 3-0$ (HDL$_1$) | $S_f 20-12$ | $S_f 12-4$ | $S_f 4-0$ (HDL$_2$) | HDL$_3$ |
| children         |                  |                  |                  |                  |        |
| 68               | 0                | 0                | 72               | 118              |
| 59               | 0                | 0                | 63               | 218              |
| 61               | 0                | 0                | 60               | 314              |
| 63               | 0                | 0                | 65               | 217              |
| different types of cancer |                  |                  |                  |                  |        |
| 82               | 0                | 24               | 15               | 100              |
| 71               | 0                | 0                | 48               | 154              |
| 81               | 0                | 17               | 0                | 75               |
| 17               | 0                | 0                | 27               | 155              |
| 14               | 8                | 23               | 0                | 112              |
| 23               | 11               | 3                | 14               | 61               |
| 67               | 0                | 0                | 30               | 88               |
| 51               | 3                | 10               | 19               | 106              |

Values also had a pronounced positive history of cancer in close blood relatives. The only significant difference between the groups of normal women was a substantially lower amount of the high-density lipoprotein-2 in those with positive family histories of cancer. Normal men with family histories of cancer also had decreased values for high-density lipoprotein-2 and, in addition, had elevated levels of the very-low-density lipoproteins.

Values for the high-density lipoprotein-2 in patients with cancer were significantly below those obtained from normal subjects without a positive family history of cancer. In some patients, notably children with acute leukemia and lymphangiomatosis, the high-density lipoprotein-2 was absent.

Twenty-three normal subjects were questioned in detail and given physical examinations at the beginning of the project and at five years and questionnaires only at ten years. Four normal subjects (2 men and 2 women) of the 13 with positive family histories of cancer had very low values for high-density lipoprotein-2. They have since developed cancer. The 2 men also had markedly elevated values for the very-low-density lipoproteins. None of the 10 people with normal levels for high-density lipoprotein-2 and little or no incidence of cancer in the family developed cancer within the same time period.

This study suggests a positive association between abnormal lipoprotein biochemistry (particularly decreased HDL$_3$), familial relationship and the possibility of developing cancer.
References

1. Barclay, M.; Calathes, D. N.; DiLorenzo, J. C.; Helper, A., and Kaufman, R. J.: The relation between plasma lipoproteins and breast carcinoma: Effect of degrees of breast disease on plasma lipoproteins and the possible role of lipid metabolic aberrations. Cancer 12: 1163-1170, 1959.

2. Barclay, M., et al.: Serum lipoproteins and human neoplastic disease. Clin. Chim. Acta 10: 39-47, 1964.

3. Higazi, A. M.; Ata, A. A.; Abdel-Rahman, Y. M.; Malek, A., and Mansour, K.: Electrophoretic pattern of serum proteins and lipids in leukemias. J. Egypt Med. Ass. 49: 679-691, 1966.

4. Kellen, J.: The serum beta-lipoproteins in different human malignant diseases. Neoplasma 15: 139-143, 1968.

5. Miller, B. J., and Erij, L.: The serum proteins and lipoproteins in patients with carcinoma and in subjects free of recurrence. Surg. Gyenc. & Obstet. 102: 487-491, 1956.

6. Nanawa, I. G., and Tsintsadze, T. M.: Changes in serum lipoproteins in patients with breast cancer. Tr. Nauchn.-Issled. Inst. Onkol. Gruz. SSR. 1: 119-145, 1961.

7. Ohya, A.: Immunochemical analysis of human serum lipoprotein. Studies on the immunochemical behavior of human sera from patients with hypertension or cancer. Juzen Igakukai Zasshi 64: 397-408, 1969.

8. Barclay, M.: Lipoprotein class distribution in normal and diseased states. In: Nelson, G. J. (ed.), Blood Lipids and Lipoproteins: Quantitation, Composition and Metabolism, Ed. 1, vol. 1. New York: John Wiley and Sons, Inc., 1971. [In press]

9. Nichols, A. V.: Human serum lipoproteins and their interrelationships. Advances Biol. Med. Phys. 11: 109-158, 1967.

10. DeLalla, O. F.; Elliott, H. A., and Gofman, J. W.: Ultracentrifugal studies of high-density serum lipoproteins in clinically healthy adults. Am. J. Physiol. 179: 333-337 1954.

11. Farquhar, J. W., and Ways, P.: Abetalipoproteinemia. In: Stanbury, J. B.; Wyngaarden, J. B., and Fredrickson, D. S. (eds.), The Metabolic Basis of Inherited Disease. Ed. 2. New York: McGraw-Hill Book Company, 1966. Pp. 509-522.

12. Fredrickson, D. S.: Familial high-density lipoprotein deficiency: Tangier disease. In: Stanbury, J. B.; Wyngaarden, J. B., and Fredrickson, D. S. (eds.), The Metabolic Basis of Inherited Disease. Ed. 2. New York: McGraw-Hill Book Company, 1966. Pp. 486-508.

13. Fredrickson, D. S.; Levy, R. I., and Lees, R. S.: Fat transport in lipoproteins: An integrated approach to mechanisms and disorders. New Eng. J. Med. 276: 34-42, 94-103, 148-156, 215-225, 273-281, 1967.

14. Fredrickson, D. S.; Levy, R. I. and Lindgren, F. T.: A comparison of heritable abnormal lipoprotein patterns as defined by two different techniques. J. Clin. Invest. 47: 2446-2457, 1968.

15. Schettler, G., and Kahlke, W. In: Schettler, G. (ed.), Lipids and Lipidoses. New York: Springer-Verlag, Inc., 1967. Pp. 213-239.