A Critique of the Evidence Relating Diet and Coronary Heart Disease

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The following component part numbers comprise the compilation report:
ADP014598 thru ADP014630
A CRITIQUE OF THE EVIDENCE RELATING DIET AND
CORONARY HEART DISEASE

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It may be useful for me to review the problem of coronary heart
disease (CHD) from the special viewpoint of a nutritionist. While this
view may have some prejudice it seems relevant because of the frequent
association of diet with CHD and the widespread lay interest in the pro-
blem.

Coronary heart disease may seem to have risen like an epidemic
among us. It is a complicated task to determine whether this rise to
prominence is real or only made apparent by changing techniques. It
would be an interesting task for someone to relate the time course of the
prevalence of CHD to the marketing of electrocardiographs. To my
knowledge this has not been done. One might have expected a rise of
CHD when the ECG became available for diagnosis. Dr. Lew of the
Metropolitan Life Insurance Company has shown a remarkable explana-
tion for the distribution by states of coronary heart disease in the
United States (1)(2), (Fig. I and II). It must be clear that we see what
we look for.

A more subtle influence is that of "competing causes" (3). Even
when age specific rates are considered we may be baffled in understanding
the entire effect of the removal of diseases which typically kill at an
earlier age than does coronary heart disease.

The errors of reporting cause of death are well known (4). It is less
than even money that an autopsy will confirm the clinical impression and
only a small proportion of all deaths are followed by necropsy. Since
reporting causes of death, like ladies hats, tends to change with fashion
it is easily possible for the mortality rates to be strongly influenced by
the current fashion and this is conveniently done since the selection of
the first cause in the presence of multiple causes of death will determine
the final tabulations.

Finally we must concede that it is possible that an apparent rise of
prevalence of coronary heart disease is real and that this is a reflection
Design of Experiments

of the introduction of a new and potent causal factor that we must identify and adjust in order to control CHD.

The interest of nutritionists in this problem like their interest in most diseases stems from the ancient judgement that a man may be sick because of "something he et". This explanation has proved so attractive that we have a second epidemic, a scourge of nutritionists. These newcomers, coupled with the food industries, have made food and feeding a highly complicated and even dangerous business.

The essential series of hypotheses upon which most research is presently based may be shown as follows:

1. Diet
2. Hypercholesteremia
3. Atherosclerosis
4. Clinical Events

The evidence to support the first relationship is at best indecisive. The question was brought to prominence by A. Keys (5) who based this contention on a curious selection of food-mortality data of the World Health Organization (Fig. III). Aside from the fact that the hypothesis is based on tenuous population data that might as easily be explained in other ways (6) it has proven impossible to show in retrospective studies that persons with CHD eat differently than those without (Fig. IV).

The dietary behavior of 983 persons in the Framingham Study has been measured by Georgiana Pearson in the past four years (7)(8)(9). The reproducibility of the method whether by one person (Fig. V) or by a second observer (Fig. VI) is good. We are confident that these people were well classified but we can find no relationship between either cholesterol level (Table 1) or experience with CHD and the way these people eat. Morris, Marr and Heady (10) have found no diet-cholesterol disease relationship in their population of bank clerks (11). Their method of measuring diet does not reproduce quite as well as ours. (Table 2).

The entire problem is complicated by the prevailing imprecision of the measurement of cholesterol. Consider, for example, the data of Rivin (12) (Table 3) who compares hospital and commercial laboratories. We have compared several methods applied in a research setting (13) (Table 4). If one adds to this technical variation the considerable biological variation of serum cholesterol with time (14) it is clear that the
central element of the hypothesis may be so badly estimated that this disqualifies our most convenient index (Table 5).

We are at least as bad off in measuring atherosclerosis, the anatomical lesion we believe to be the basis for the clinical disorders. We cannot visualize these lesions in life and even after death to do more than make qualitative descriptions is difficult. You can appreciate that an element of probability determines whether the plaque is critically placed in the cardiovascular system.

The clinical manifestations of CHD are varied (Table 6). A disturbing number, disturbing at least for the biometrician, are completely occult events called "silent coronaries" because they do not cause important clinical signs. The cerebral events, strokes, are even more obscure because we have less precise ways to determine and localize these, having no equivalent for the ECG.

There are several prospective dietary studies under way which propose to change the experience with CHD by altering the diet. The dietary regimens of some of these are summarized in Table 7. The most ambitious of these called the National Diet Heart Disease Study is directed by Dr. Irvine Page and sponsored by the National Heart Institute (15). It is now in the feasibility phase, that is, the determination of whether families can be recruited, supplied with suitable food and kept under surveillance while consuming the diet for the measurement of cholesterol and the evaluation of cardiovascular disease status. If proven feasible, this experiment will be extended to larger numbers in order to answer the critical question--will dietary changes modify the course of CHD?

The smaller trials of diet, for example, that of Dayton at Los Angeles (16) and Rinzler with the Anti-Coronary Club (17) in New York have usually obtained about a 15% reduction of serum cholesterol in the best circumstances, that is, when the starting level is high. However, many subjects who do follow the diet do not respond and some who respond initially drift back up with time. We must conclude that dietary treatment, if effective, is a relatively impotent agent. We must conclude also that diet has been overemphasized as a cause of CHD and that dietary modifications are proving relatively ineffectual control measures.
Table 1

DIETARY INTAKES - AMERICANS 1957-58
FRAMINGHAM HEART STUDY
ARRANGED BY SERUM CHOLESTEROL LEVEL

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Calories</th>
<th>Fat g.</th>
<th>Protein g.</th>
<th>Chol. mg.</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Cholesterol</td>
<td>17</td>
<td>3127</td>
<td>149</td>
<td>113</td>
<td>703</td>
</tr>
<tr>
<td>Low Cholesterol</td>
<td>39</td>
<td>3487</td>
<td>163</td>
<td>126</td>
<td>721</td>
</tr>
<tr>
<td>Random Sample</td>
<td>133</td>
<td>3333</td>
<td>157</td>
<td>122</td>
<td>735</td>
</tr>
</tbody>
</table>
Table 2

COMPARISON OF REPEATABILITY FOR 2 METHODS OF MEASURING DIET

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Heady - Bank Clerks 1 week's weighed intake</th>
<th>Framingham research diet history</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r - consecutive weeks</td>
<td>r - 2 year interval</td>
</tr>
<tr>
<td>Calories</td>
<td>0.80</td>
<td>0.92</td>
</tr>
<tr>
<td>Protein (gm)</td>
<td>0.67</td>
<td>0.72</td>
</tr>
<tr>
<td>COH (gm)</td>
<td>0.84</td>
<td>0.90</td>
</tr>
<tr>
<td>Fat (gm)</td>
<td>0.79</td>
<td>0.88</td>
</tr>
</tbody>
</table>
Table 3

**Cholesterol Measurement**

Rivin, et al., J. A. M. A., 166:2108, 1959

**Values in Mgm%**

<table>
<thead>
<tr>
<th>Serum</th>
<th>Author</th>
<th>V. A.</th>
<th>Univ.</th>
<th>Commercial 1</th>
<th>Commercial 2</th>
<th>Commercial 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>529</td>
<td>479</td>
<td>480</td>
<td>598</td>
<td>513</td>
<td>411</td>
</tr>
<tr>
<td></td>
<td>487</td>
<td>418</td>
<td>541</td>
<td>500</td>
<td>451</td>
<td>318</td>
</tr>
<tr>
<td>B</td>
<td>260</td>
<td>240</td>
<td>255</td>
<td>291</td>
<td>273</td>
<td>183</td>
</tr>
<tr>
<td></td>
<td>273</td>
<td>233</td>
<td>296</td>
<td>263</td>
<td>272</td>
<td>191</td>
</tr>
<tr>
<td>C</td>
<td>218</td>
<td>213</td>
<td>275</td>
<td>312</td>
<td>255</td>
<td>180</td>
</tr>
<tr>
<td></td>
<td>249</td>
<td>220</td>
<td>288</td>
<td>252</td>
<td>246</td>
<td>172</td>
</tr>
</tbody>
</table>

Method: K-S, K-S, B1, B1, PSG, Sheftel
Table 4

<table>
<thead>
<tr>
<th>Level (mgm%)</th>
<th>N</th>
<th>X</th>
<th>T. E.</th>
<th>X</th>
<th>T. E.</th>
<th>X</th>
<th>T. E.</th>
<th>X</th>
<th>T. E.</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;210</td>
<td>15</td>
<td>188</td>
<td>6.4</td>
<td>180</td>
<td>5.6</td>
<td>179</td>
<td>7.7</td>
<td>237</td>
<td>3.2</td>
</tr>
<tr>
<td>211-274</td>
<td>15</td>
<td>232</td>
<td>4.1</td>
<td>228</td>
<td>5.7</td>
<td>225</td>
<td>8.8</td>
<td>288</td>
<td>3.2</td>
</tr>
<tr>
<td>275-499</td>
<td>14</td>
<td>368</td>
<td>5.2</td>
<td>384</td>
<td>7.6</td>
<td>340</td>
<td>15.1</td>
<td>452</td>
<td>12.9</td>
</tr>
<tr>
<td>&gt;499</td>
<td>15</td>
<td>672</td>
<td>7.7</td>
<td>667</td>
<td>10.4</td>
<td>643</td>
<td>26.9</td>
<td>837</td>
<td>14.2</td>
</tr>
<tr>
<td>all levels</td>
<td>59</td>
<td>365</td>
<td>6.0</td>
<td>365</td>
<td>7.6</td>
<td>347</td>
<td>17.1</td>
<td>454</td>
<td>14.2</td>
</tr>
</tbody>
</table>

Evaluation of Methods for Serum Cholesterol
Table 5

Serum Cholesterol Variation

68 men - measured twice weekly - 10 weeks

$S_T = \text{total variation} \quad S_E = \text{laboratory variation} \quad S_B = \text{biological variable}$

where $NS_B^2 = NS_T^2 - 1/2 NS_E^2$

$\bar{XS}_T = 20$

$\bar{XS}_E = 7$

$\bar{XS}_B = 13$

Then: For 95% assurance of effect $2 \times 20 = 40 \text{ mgm} \% \text{ minimum change.}$
Table 6

THE MANIFESTATIONS OF CORONARY HEART DISEASE

Of 100 Men with "Events"

30 drop dead
20 are "silent"
10 die a little later
40 recover
### Table 7

**DIETARY REGIMENS -- OBSERVED AND FAT RESTRICTED**

<table>
<thead>
<tr>
<th></th>
<th>Framingham (Men)</th>
<th>Page</th>
<th>Rinsler</th>
<th>Dayton</th>
<th>American Heart</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calories</td>
<td>3075</td>
<td>2000</td>
<td>2400</td>
<td>2430</td>
<td>2800</td>
</tr>
<tr>
<td>Protein (gm)</td>
<td>112</td>
<td>70</td>
<td>140</td>
<td>94</td>
<td>85</td>
</tr>
<tr>
<td>Fat (gm)</td>
<td>154</td>
<td>90</td>
<td>81</td>
<td>106</td>
<td>75</td>
</tr>
<tr>
<td>% Cal.</td>
<td>45</td>
<td>41</td>
<td>32</td>
<td>40</td>
<td>36</td>
</tr>
<tr>
<td>Cholesterol (migm)</td>
<td>705</td>
<td>&lt;200</td>
<td>200</td>
<td>380</td>
<td>200</td>
</tr>
<tr>
<td>PUS/S</td>
<td>0.3</td>
<td>1.5</td>
<td>1.0</td>
<td>1.7</td>
<td>1.1</td>
</tr>
</tbody>
</table>
Figure I

GEOGRAPHIC VARIATIONS IN ARTERIOSCLEROTIC HEART DISEASE
WHITE MALES, 1950

[Map showing geographic variations with color coding for different data ranges.]

Data of Enterline and Stewart, Reference 1.
Figure II
CORRELATION BETWEEN MORTALITY FROM ARTERIOSCLEROTIC HEART DISEASE AND INTERNISTS PER 100,000 WHITE PERSONS
United States 1950

<table>
<thead>
<tr>
<th>Region</th>
<th>Age-adjusted Death Rate per 100,000</th>
<th>Number of Internists** per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Middle Atlantic</td>
<td>273</td>
<td>12.6</td>
</tr>
<tr>
<td>New England</td>
<td>250</td>
<td>10.5</td>
</tr>
<tr>
<td>Pacific Coast</td>
<td>233</td>
<td>9.7</td>
</tr>
<tr>
<td>East North Central</td>
<td>214</td>
<td>7.3</td>
</tr>
<tr>
<td>South Atlantic*</td>
<td>193</td>
<td>7.6</td>
</tr>
<tr>
<td>West North Central</td>
<td>183</td>
<td>6.7</td>
</tr>
<tr>
<td>Mountain</td>
<td>179</td>
<td>6.5</td>
</tr>
<tr>
<td>West South Central</td>
<td>176</td>
<td>5.8</td>
</tr>
<tr>
<td>East South Central</td>
<td>160</td>
<td>4.5</td>
</tr>
</tbody>
</table>

* Excludes District of Columbia
** Includes cardiologists
Includes Coronary Heart Disease. Death rates age adjusted on basis of total U.S. population in 1950.

This material was published by E. A. Lew - Reference 2.
Figure III

DIET AND MORTALITY FROM HEART DISEASE IN
22 COUNTRIES 1951-53
MEN 55-59 YRS.

- Keys' Select 6
- 22 Available

DEATHS
1000

PERCENT

CALORIES FROM FAT  CALORIES FROM ANIMAL PROTEIN
OBSERVATION OF DIET PATTERN AND EXPERIENCE WITH CORONARY HEART DISEASE

<table>
<thead>
<tr>
<th>Observer</th>
<th>Association Observed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wilkinson</td>
<td>Michigan</td>
</tr>
<tr>
<td>Rosenman</td>
<td>California</td>
</tr>
<tr>
<td>Zukel</td>
<td>North Dakota</td>
</tr>
<tr>
<td>Mann</td>
<td>Massachusetts</td>
</tr>
<tr>
<td>Morris</td>
<td>London</td>
</tr>
<tr>
<td>Keys</td>
<td>Minnesota</td>
</tr>
</tbody>
</table>
I INTERVIEWER - 2 YEAR INTERVAL

- FIRST INTERVIEW
- SECOND INTERVIEW

$r = 0.88$

Figure V
Figure VI

- FIRST INTERVIEW
- SECOND INTERVIEW

DAILY FAT (GRAMS)

CASE NUMBER


