THE DISTRIBUTION OF BLOOD CHOLESTEROL IN CANCER

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(From the Littauer Fund for Cancer Research, Memorial Hospital, New York City)

Interest in the cholesterol content of the blood as a possible factor in carcinogenesis goes back many years to the work of Ludin (1), who postulated some relationship on the basis of histologic studies. This interest has been stimulated at intervals by work in various fields of cancer research. Harnes (2), for example, reported in 1929 that among rabbits inoculated with testicular carcinoma, those which were eventually to succumb to the disease showed a marked increase in whole blood cholesterol, an increase which was progressive to the time of death, while animals which recovered from the inoculation showed a progressive drop in blood cholesterol concentration. Bloor (3) similarly reported high concentrations of cholesterol in three or four patients with cancer, and Myers (4) in his general review of blood chemistry and its clinical significance made the statement that in the early stages of malignant disease the blood cholesterol is high. Denis (5), on the other hand, after a comprehensive study of blood cholesterol in many different pathological conditions concluded that the range of cholesterol concentrations in cancer is entirely normal, varying from 130 to 277 mg. per 100 c.c.; her normal range was 167 to 255 mg.

Studies of Roffo and Correa (6) on the cholesterol content of malignant tumors and normal tissue have led them to believe that accumulation of cholesterol in the tissues plays an important part in carcinogenesis.

Many attempts have been made to show that radiation of malignant growths brings about a change in concentration of cholesterol in the blood, and to associate such changes with radiation sickness. Certain authors, notably Burgheim (7) and Babarezy (8) report definite increases following radiation. On the contrary, Mahnert and Zacherl (9), Strauss (10), and Roffo (11) claim that radiation brings about a decrease in blood cholesterol, while Konrich and Scheller (12), Jacobs and Motojima (13),
Brunton (14), and Pohle and Sevringhaus (15) all report that there is no consistent change following radiation, or no change which is not within the limits of error of the method.

In the course of a study of the effect of radiation on blood cholesterol, Mattick and Buchwald (16) reported a relationship, previously noted by Levy-Dorn and Burgheim (17), which promised to be of some diagnostic significance. In 85 per cent of the 100 cases of cancer studied by them, the cholesterol content of the plasma was found to be higher than that of the whole blood, while 80 per cent of the healthy persons showed this relationship reversed. In a later study (18) of a number of other pathological conditions than cancer, they found a normal relationship in 67 per cent of the cases, while in 33 per cent the relationship was reversed as in cancer.

It seemed to the present writers that this finding, even though not as strictly diagnostic as the authors had at first hoped, was of considerable importance if it could be substantiated. The great number and variety of malignant tumors in all stages available at the Memorial Hospital made it possible to study this relationship in as representative a series as could be found, taking every precaution to have all results comparable. Since there is some disagreement at the present time as to the effect of recently ingested food on the concentration of cholesterol in the blood, it seemed wiser to take all bloods after an all-night fast, before breakfast. All bloods were accordingly so drawn, taken immediately to the laboratory, and kept on ice until they could be precipitated, which was always within an hour or two.

The estimation was carried out according to Bloor's (19) latest directions, with one slight modification. After making the alcohol-ether solution up to volume, it was poured into a flask containing 2 to 3 grams of solid calcium hydrate, shaken well, and filtered. This eliminated a good deal of the disturbing brown color of which many authors speak in connection with cholesterol determinations. This difficulty is entirely avoided if, further, the chloroform used for the final solution of the unknown, as well as the chloroform solution of the standard, is kept absolutely dry, small bottles being used for the desk supply to avoid contamination of main supplies by moisture of the air. In our series of estimations using this method we found that we could not count on less than 5 per cent variation between duplicates, though most of them agreed within 2 to 4 per cent.
It will be noted from the chart, where all the data have been given, that no consistent relationship was found between the concentration of cholesterol in plasma and in whole blood in cases of malignant neoplasms and of related blood diseases. Because of the experimental error inherent in the method, we have felt that those cases in which the ratio varied between 0.95 and 1.05 could be suitably interpreted as having equal concentrations in whole blood and plasma. With this in mind, we find a plasma/whole blood ratio greater than 1 in 32 per cent of the cases, less than 1 in 30 per cent, and equivalent concentrations in 38 per cent. The cases of benign neoplasms and the control cases are too few to lend themselves to statistical analysis, but it will be noted that the ratios are distributed rather than consistent.

Our study lends no support to the theory that the concentration of cholesterol in the blood is abnormal in cancer. Bloor and Denis have both given a range of normal blood cholesterol concentrations when the estimations were made by the method we have used. Bloor gives 210 to 220 mg. per cent as normal for men and 230 to 240 mg. for women. Denis found a wider range in normal cases, from 167 to 255 mg. per cent. Our figures for normal and non-malignant cases vary from 159 to 255 mg. per cent for whole blood, with a range from 124 to 350 mg. per cent in the cases of cancer. Of these however, only 9 were below 160 and only 2 above 260, and in neither instance with the high values is there any relationship to be discovered between the size of the lesion or the extent of metastases and the cholesterol content of the blood. The two very high figures were obtained in cases of carcinoma of the breast, but one of these had no metastases at all, while another case with a much larger tumor, and with metastases to lymph nodes, showed a cholesterol content in the blood of 166 mg. per cent, which is close to the lower limit. Since cholesterol is consistently low in anemia, the nine cases of low values in our series are very probably referable to this.

**Summary**

1. In a series of 63 cases of malignant tumors and allied blood diseases, we have found no constant relationship between the concentration of cholesterol in whole blood and in plasma.

2. We find that the cholesterol content of the blood is not increased above normal in the presence of cancer.
### Blood-Cholesterol Findings in Malignant Neoplasms, Blood Diseases Allied to Neoplasms, Benign Neoplasms, and Control Cases

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Metastasis</th>
<th>Cholesterol Mg %</th>
<th>Ratio</th>
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<tr>
<td></td>
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<tr>
<td>E. H.</td>
<td>64</td>
<td>♀</td>
<td>Melanoma of vulva, 2.5 × 2.5 cm., on left labium majus</td>
<td>None</td>
<td>259</td>
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<tr>
<td>S. F.</td>
<td>63</td>
<td>♂</td>
<td>Squamous carcinoma of ear, 1.5 cm., superficial. Wassermann</td>
<td>None</td>
<td>173</td>
</tr>
<tr>
<td>T. C.</td>
<td>72</td>
<td>♂</td>
<td>Basal-cell epitheloma of nose, 2 × 2 cm.; adenoid features</td>
<td>None</td>
<td>106</td>
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<tr>
<td>E. M. H.</td>
<td>58</td>
<td>♂</td>
<td>Carcinoma of floor of mouth, 4 × 4 cm., papillary type; leukoplakia</td>
<td>None</td>
<td>204</td>
</tr>
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<td>E. F.</td>
<td>63</td>
<td>♂</td>
<td>Squamous carcinoma of tongue, 4 × 3 cm., grade II</td>
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<td>218</td>
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<tr>
<td>P. F.</td>
<td>73</td>
<td>♂</td>
<td>Squamous carcinoma of tongue; leukoplakia; syphilis</td>
<td>Cervical lymph nodes</td>
<td>184</td>
</tr>
<tr>
<td>W. R.</td>
<td>66</td>
<td>♂</td>
<td>Transitional-cell carcinoma of nasopharynx, 3 sq. cm., grade II</td>
<td>Cervical lymph nodes</td>
<td>155</td>
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<tr>
<td>F. H.</td>
<td>69</td>
<td>♀</td>
<td>Epidermoid carcinoma of maxillary antrum</td>
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<td>147</td>
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<tr>
<td>T. S.</td>
<td>63</td>
<td>♂</td>
<td>Squamous carcinoma of buccal mucosa, involving both lips, 4 × 4 cm., infiltrating</td>
<td>Submaxillary and sub-meseral nodes</td>
<td>101</td>
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<tr>
<td>A. C.</td>
<td>63</td>
<td>♂</td>
<td>Squamous carcinoma of buccal mucosa, 5 × 5 cm., grade I, infiltrating; ulcerating; leukoplakia</td>
<td>Submaxillary node</td>
<td>175</td>
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<tr>
<td>G. R.</td>
<td>65</td>
<td>♂</td>
<td>Squamous carcinoma of lip, grade II, involving four-thirds of lip; also basal-cell epitheloma of ear</td>
<td>None</td>
<td>105</td>
</tr>
<tr>
<td>J. C.</td>
<td>69</td>
<td>♂</td>
<td>Squamous carcinoma of lip, grade I, 2 × 1 cm., superficial, papillary</td>
<td>None</td>
<td>104</td>
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<tr>
<td>J. L.</td>
<td>67</td>
<td>♂</td>
<td>Epidermoid carcinoma of larynx, grade II, sub-glottis, involving two-thirds of larynx; pulmonary tuberculosis</td>
<td>None</td>
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<tr>
<td>H. E.</td>
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<td>♂</td>
<td>Squamous carcinoma of esophagus, grade II, extensive, ulcerated</td>
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<td>170</td>
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<tr>
<td>S. T.</td>
<td>63</td>
<td>♂</td>
<td>Adenocarcinoma (mucocellulare) of cardia</td>
<td>Pancreas, diaphragm, esophageal, and aortic nodes</td>
<td>201</td>
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<tr>
<td>F. M.</td>
<td>68</td>
<td>♀</td>
<td>Carcinoma of cardia and lower esophagus</td>
<td>Gastric nodes</td>
<td>223</td>
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<tr>
<td>C. Y.</td>
<td>49</td>
<td>♀</td>
<td>Recurrent carcinoma of gallbladder, large</td>
<td>Liver</td>
<td>148</td>
</tr>
<tr>
<td>J. P.</td>
<td>60</td>
<td>♀</td>
<td>Colloid adenocarcinoma of rectum, bulky, fixed, ulcerated</td>
<td>Perirectal</td>
<td>161</td>
</tr>
<tr>
<td>E. H.</td>
<td>64</td>
<td>♂</td>
<td>Carcinoma of rectum (adenoma malignum), grade I, fixed, stenoting</td>
<td>Perirectal</td>
<td>148</td>
</tr>
<tr>
<td>M. F.</td>
<td>55</td>
<td>♂</td>
<td>Carcinoma of rectum (adenoma malignum), grade II, fixed, ulcerated, midrectum, bulky</td>
<td>Perirectal</td>
<td>227</td>
</tr>
<tr>
<td>V. B. P.</td>
<td>71</td>
<td>♂</td>
<td>Plasmid epidermoid carcinoma of anus, grade II, 4 × 4 cm.</td>
<td>None</td>
<td>230</td>
</tr>
<tr>
<td>T. M.</td>
<td>68</td>
<td>♂</td>
<td>Carcinoma of rectum (adenoma malignum), grade II, 4 × 4 cm., ulcerated, fixed</td>
<td>Perirectal</td>
<td>180</td>
</tr>
<tr>
<td>Age</td>
<td>Sex</td>
<td>Diagnosis</td>
<td>Metastasis</td>
<td>Cholesterol %</td>
<td>Ratio</td>
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<td>Whole Blood</td>
<td>Plasma</td>
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<td>Plasma/ WB</td>
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<tr>
<td>J. F.</td>
<td>56</td>
<td>o</td>
<td>Carcinoma of rectum (adenoma malignum), grade II, midrectum, bulky, ulcerated</td>
<td>Perirectal</td>
<td>193</td>
</tr>
<tr>
<td>C. W.</td>
<td>41</td>
<td>o</td>
<td>Squamous carcinoma of penis, grade I, papillary, bulky, involving glans, prepuce and shaft</td>
<td>Bilateral inguinal nodes</td>
<td>209</td>
</tr>
<tr>
<td>F. G.</td>
<td>28</td>
<td>o</td>
<td>Embryonal teratoma testis, grade IV, bulky</td>
<td>Perirenal nodes</td>
<td>179</td>
</tr>
<tr>
<td>E. R.</td>
<td>51</td>
<td>o</td>
<td>Carcinoma of prostate, in advanced stage, enormous tumor; anemia</td>
<td>Seminal vesicles; bone</td>
<td>203</td>
</tr>
<tr>
<td>H. G.</td>
<td>39</td>
<td>o</td>
<td>Wilms' adenomaurocoma of kidney, massive; anemia, cachexia</td>
<td>Lungs; ilium</td>
<td>200</td>
</tr>
<tr>
<td>R. F.</td>
<td>31</td>
<td>o</td>
<td>Adenocarcinoma of uterus (early); also ovarian cystic fibroma, 6 cm.</td>
<td>None</td>
<td>179</td>
</tr>
<tr>
<td>G. M.</td>
<td>40</td>
<td>o</td>
<td>Squamous carcinoma of cervix uteri, grade I, papillary, in advanced stage</td>
<td>Involves rectum and bladder</td>
<td>204</td>
</tr>
<tr>
<td>A. F.</td>
<td>57</td>
<td>o</td>
<td>Squamous carcinoma of cervix uteri, in advanced stage; cachexia</td>
<td>Parametria</td>
<td>211</td>
</tr>
<tr>
<td>M. S.</td>
<td>51</td>
<td>o</td>
<td>Plexiform epidermoid carcinoma of cervix uteri, grade II, advanced stage; anemia</td>
<td>Parametria; ilium</td>
<td>190</td>
</tr>
<tr>
<td>A. M.</td>
<td>51</td>
<td>o</td>
<td>Transitional-cell carcinoma of cervix uteri, grade III, bulky, in advanced stage</td>
<td>Uterine adenexa</td>
<td>161</td>
</tr>
<tr>
<td>A. D. J.</td>
<td>53</td>
<td>o</td>
<td>Plexiform epidermoid carcinoma of cervix uteri, grade II, in advanced stage; fixed</td>
<td>Posterior and left parametrium</td>
<td>171</td>
</tr>
<tr>
<td>G. B. R.</td>
<td>63</td>
<td>o</td>
<td>Adenocarcinoma of body of uterus, grade III, uterus enlarged, fixed</td>
<td>?</td>
<td>235</td>
</tr>
<tr>
<td>J. J. C.</td>
<td>70</td>
<td>o</td>
<td>Papillary epidermoid carcinoma of urinary bladder; three plum-sized tumors</td>
<td>None</td>
<td>190</td>
</tr>
<tr>
<td>M. B.</td>
<td>57</td>
<td>o</td>
<td>Anaplastic epidermoid carcinoma of urinary bladder, 3 cm., infiltrating</td>
<td>None</td>
<td>207</td>
</tr>
<tr>
<td>W. B. A.</td>
<td>45</td>
<td>o</td>
<td>Carcinoma of urinary bladder, ulcerated</td>
<td>None</td>
<td>226</td>
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<tr>
<td>M. O'K.</td>
<td>42</td>
<td>o</td>
<td>Carcinoma of breast in advanced stage</td>
<td>Lungs, axillary and supraclavicular nodes</td>
<td>207</td>
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<tr>
<td>M. T.</td>
<td>55</td>
<td>o</td>
<td>Carcinoma of breast (small-cell, infiltrating duct cancer), advanced stage</td>
<td>Lungs, skin, axilla, supraclavicular space</td>
<td>225</td>
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<td>B. S.</td>
<td>50</td>
<td>o</td>
<td>Carcinoma of breast, 5.5 cm., in advanced stage</td>
<td>Lungs, axilla, supraclavicular space</td>
<td>200</td>
</tr>
<tr>
<td>L. P.</td>
<td>48</td>
<td>o</td>
<td>Carcinoma of breast, 4.5 X 3.5 X 2.5 cm., confirmed by biopsy</td>
<td>None</td>
<td>308</td>
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<tr>
<td>R. V.</td>
<td>61</td>
<td>o</td>
<td>Carcinoma of breast (infiltrating; alveolar carcinoma of ducts), 2.5 X 2.5 X 2 cm.</td>
<td>None</td>
<td>244</td>
</tr>
<tr>
<td>S. L.</td>
<td>42</td>
<td>o</td>
<td>Carcinoma of breast, 4.5 X 3.5 X 2.3 cm.</td>
<td>Axillary lymph nodes</td>
<td>301</td>
</tr>
<tr>
<td>L. R.</td>
<td>33</td>
<td>o</td>
<td>Carcinoma of breast, 1.9 X 1.8 cm., enormous</td>
<td>Axillary lymph nodes</td>
<td>166</td>
</tr>
<tr>
<td>C. D.</td>
<td>40</td>
<td>o</td>
<td>Carcinoma of breast, colloid type, 2.5 X 2 X 1.5 cm.</td>
<td>Axillary lymph nodes</td>
<td>205</td>
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</table>
Blood-Cholesterol Findings in Malignant Neoplasms, Blood Diseases Allied to Neoplasms, Benign Neoplasms, and Control Cases (continued)

### MALIGNANT NEOPLASMS

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Metastasis</th>
<th>Cholesterol Mg %</th>
<th>Ratio</th>
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<td>Plasma</td>
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</tr>
<tr>
<td>M. B.</td>
<td>50</td>
<td>♀</td>
<td>Carcinoma of breast, (infiltrating duct cancer), 5 × 4.5 × 4 cm</td>
<td>None</td>
<td>202</td>
</tr>
<tr>
<td>V. J.</td>
<td>39</td>
<td>♀</td>
<td>Carcinoma of breast, 6 × 5 cm.</td>
<td>Axillary lymph nodes</td>
<td>206</td>
</tr>
<tr>
<td>A. R.</td>
<td>60</td>
<td>♀</td>
<td>Multiple myeloma involving skull, pelvis, scapulae, humeri, clavicles</td>
<td>Multiple lesions</td>
<td>153</td>
</tr>
<tr>
<td>L. G.</td>
<td>27</td>
<td>♀</td>
<td>Endothelial myeloma of rib</td>
<td>None found</td>
<td>202</td>
</tr>
<tr>
<td>F. G.</td>
<td>41</td>
<td>♀</td>
<td>Osteogenic sarcoma of ilium, enormous tumor of spindle-cell type</td>
<td>Longs</td>
<td>242</td>
</tr>
<tr>
<td>M. W.</td>
<td>38</td>
<td>♀</td>
<td>Carcinoma of thyroid, spindle and polyhedral-cell type</td>
<td>Cervical lymph nodes</td>
<td>181</td>
</tr>
<tr>
<td>L. A.</td>
<td>57</td>
<td>♀</td>
<td>Carcinoma of thyroid, lobulated, fixed; spindle-cell cancer, bulky, 10 × 10 × 8 cm.</td>
<td>Vertebral, manubrium</td>
<td>187</td>
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<tr>
<td>M. R.</td>
<td>37</td>
<td>♀</td>
<td>Neurogenic sarcoma of leg, grade II, 6 × 4 × 4 cm, fixed</td>
<td>None</td>
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<tr>
<td>P. A.</td>
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<td>♀</td>
<td>Neurogenic sarcoma of wrist, 2.5 × 1.5 × 1 cm, encapsulated; possible angio-endothelioma</td>
<td>None</td>
<td>206</td>
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<tr>
<td>A. S.</td>
<td>59</td>
<td>♀</td>
<td>Neurogenic myxosarcoma of groin, grade II; two nodules, 6 × 5 × 4 cm. and 8 × 7 × 5 cm.</td>
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<td>224</td>
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<tr>
<td>Z. E.</td>
<td>33</td>
<td>♀</td>
<td>Neurogenic sarcoma of arm, grade III, 11 × 7 cm, large</td>
<td>None</td>
<td>149</td>
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<tr>
<td>C. J.</td>
<td>27</td>
<td>♀</td>
<td>Hodgkin’s disease of spleen, mediastinum, neck and axilla</td>
<td>Multiple lesions</td>
<td>124</td>
</tr>
<tr>
<td>A. L.</td>
<td>40</td>
<td>♀</td>
<td>Hodgkin’s disease of axillae, groins, neck, bronchial nodes, vertebrae</td>
<td>Multiple lesions</td>
<td>200</td>
</tr>
<tr>
<td>E. S.</td>
<td>52</td>
<td>♀</td>
<td>Hodgkin’s disease of peri-oesal nodes only, confirmed by biopsy</td>
<td>?</td>
<td>175</td>
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### BLOOD DISEASES ALLIED TO NEOPLASMS

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<tr>
<td>S. M.</td>
<td>52</td>
<td>♀</td>
<td>Polycythemia vera</td>
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<tr>
<td>J. R.</td>
<td>57</td>
<td>♀</td>
<td>Lymphatic leukemia</td>
<td></td>
<td>228</td>
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<tr>
<td>M. L.</td>
<td>40</td>
<td>♀</td>
<td>Spleenomyelogenous leukemia</td>
<td></td>
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<tr>
<td>J. G.</td>
<td>32</td>
<td>♀</td>
<td>Spleenomyelogenous leukemia</td>
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### BENIGN NEOPLASMS

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<tr>
<td>J. McD.</td>
<td>44</td>
<td>♀</td>
<td>Lipoma of axilla, 9 × 8 cm.</td>
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<td>E. L.</td>
<td>20</td>
<td>♀</td>
<td>Fibro-adenoma of breast, 8 × 8 cm.</td>
<td></td>
<td>173</td>
</tr>
<tr>
<td>R. S.</td>
<td>26</td>
<td>♀</td>
<td>Fibro-adenoma of breast, 4.5 × 3.5 cm.</td>
<td></td>
<td>185</td>
</tr>
<tr>
<td>E. R.</td>
<td>44</td>
<td>♀</td>
<td>Cystosarcoma phylloides mammae, 8 × 4 × 3 cm.</td>
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<td>199</td>
</tr>
<tr>
<td>C. S.</td>
<td>57</td>
<td>♀</td>
<td>Fibromyoma of uterus, 6 × 6 cm.</td>
<td></td>
<td>255</td>
</tr>
<tr>
<td>S. W.</td>
<td>44</td>
<td>♀</td>
<td>Fibromyoma of uterus, 14 × 12 cm. Also benign adenomatous endometrial polyps</td>
<td></td>
<td>192</td>
</tr>
<tr>
<td>G. O.</td>
<td>42</td>
<td>♀</td>
<td>Fibromyoma of uterus, size of 3 months gestation</td>
<td></td>
<td>188</td>
</tr>
<tr>
<td>M. V.</td>
<td>40</td>
<td>♀</td>
<td>Fibromyoma of uterus, large</td>
<td></td>
<td>228</td>
</tr>
</tbody>
</table>

295
**Blood-Cholesterol Findings in Malignant Neoplasms, Blood Diseases Allied to Neoplasms, Benign Neoplasms, and Control Cases (continued)**

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Metastasis</th>
<th>Cholesterol Mg %</th>
<th>Ratio</th>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Whole Blood</td>
<td>Plasma</td>
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<tr>
<td>A. S.</td>
<td>64</td>
<td>♂ Osteomyelitis of mandible</td>
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<td>226</td>
</tr>
<tr>
<td>A. W.</td>
<td>41</td>
<td>♂ Chronic endocervicitis</td>
<td></td>
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<td>185</td>
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<tr>
<td>B. M.</td>
<td>28</td>
<td>♂ Chronic cystic mastitis</td>
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<td>199</td>
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<tr>
<td>J. B.</td>
<td>53</td>
<td>♂ Chronic interstitial mastitis</td>
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<tr>
<td>G. S.</td>
<td>51</td>
<td>♂ Gumma of breast</td>
<td></td>
<td>229</td>
<td>234</td>
</tr>
</tbody>
</table>

**Bibliography**

4. **Myers, V. C.**: Physiol. Rev. 4: 274, 1924.
5. **Denis, W.**: J. Biol. Chem. 29: 93, 1917.