Hereditary Obesity: Relation to Serum Lipoproteins and Protein Concentrations in Swine

By Lena A. Lewis, Ph.D., and Irvine H. Page, M.D.

The importance of heredity in determining the cholesterol, lipoprotein, and plasma protein levels has received insufficient attention. All of these have a greater concentration in the blood of short-fat (mesomorphic), castrate, male, miniature pigs than in long-lean (ectomorphic) animals. These differences seem to persist even when weight changes and growth are rapid. We believe that some of the wide variability of blood lipid levels in human beings is due to genetic factors in the heterogeneous human population on varied diets.

In the hereditary obese-hyperglycemic syndrome of mice, hypercholesterolemia occurs.1 However, association of hypercholesterolemia with hereditary obesity in other species is not well documented. The present studies were made on miniature swine of the long-lean and short-fat strains to determine any association between body build and cholesterol-lipoprotein levels.

**METHODS AND MATERIAL**

Six dwarf swine, bred at the University of Minnesota and classified as long-lean or short-fat strains, were obtained when 12 weeks of age.* They were castrate males and had been immunized against cholera. They were fed a diet of ground oats, corn, and SMA formula† with multivitamins and extra vitamin D. Blood samples were taken every 2 weeks. Serum lipoproteins were determined ultracentrifugally at a density of 1.21, with KBr-NaCl as described by Lewis, Green, and Page.2 Serum proteins were determined by the moving-boundary-electrophoresis method of Tiselius as modified by Longworth,2 with phosphate buffer at pH 7.8 and ionic strength of 0.16 μ. Cholesterol was measured by the method of Abell and associates,4 free cholesterol by the Sperry and Webb5 method, and phospholipids by the Youngburg and Youngburg technic.6 Total protein was determined by the biuret method as modified by Sols.7

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From the Research Division of the Cleveland Clinic Foundation and the Frank E. Bunts Educational Institute, Cleveland, Ohio.

* Obtained from Dr. David C. England, Hormel Foundation, to whom we are indebted.

† Contains cow’s milk protein, 1.5 per cent; lactose, 7 per cent; fat, 3.5 per cent; minerals and vitamins; and 20 calories per ounce. It is produced by Wyeth Laboratories, Philadelphia, Pa.

**RESULTS**

The electrophoretic serum protein patterns of pigs showed clearly resolved albumin, α1-, β- and γ-globulin fractions (fig. 1). The total protein concentration of the fat pigs was higher than that of the lean animals, due largely to a higher albumin and β-globulin concentration. These differences persisted throughout the 9-month study, which covered a period of rapid growth for the pigs. The average total protein of the lean pigs at 14 weeks of age was 4.50, and at 34 weeks was 5.88 Gm./100 ml., while for the fat pigs it was 4.81 and 6.73 Gm./100 ml.

Both strains of pigs showed an increasing concentration of γ-globulin with growth, that of the lean pigs from 0.69 at 14 weeks to 0.91 at 34 weeks of age, and of the fat pigs from 0.42 to 1.04 Gm./100 ml. The concentration of α2-globulin for both strains was similar and showed no consistent change during the study.

The total serum cholesterol of the fat pigs was higher than that of the lean, with an average of 149 and 106 mg./100 ml. of serum, respectively, at 14 weeks; and 176 and 126 mg., respectively, at 34 weeks. The concentration of phospholipid phosphorus of the fat pigs was also higher, averaging 7.3 mg./100 ml. at 14 weeks and 8.6 mg. at 34 weeks; while that of the lean pigs was 4.9 and 6.4 mg./100 ml., respectively.

The early studies were made on serum obtained approximately 5 hours after feeding to permit frequent feeding of the young animals.
Later, samples were collected 18 hours after food ingestion.

The lipoprotein pattern of the pig (fig. 1) showed varying amounts of poorly resolved, very low density $-S > 400$ material (i.e., chylomicrons), low density $-S 70-400$ and $40-70$ components, clearly defined fractions with flotation rates between 25–40 and 15–25, and high density fraction $-S 1–10$. The concentration of $-S 15–25$ is greater than in most other species that have a component with a similar flotation rate. The difference between the fasting and nonfasting lipoprotein patterns was a reduction of the very low density $-S > 400$ component in the fasting samples.

The low density lipoproteins are present in greater concentration in the fat than in the lean animals, as are the $-S 15–40$ fractions. The high density, $-S 1–10$, fraction was of similar concentration in both strains. A protocol on fat pig No. 5 and lean No. 6 (tables 1 and 2) shows the persistent differences between the 2 strains throughout the 9 months of study.

The concentration of the $-S 15–40$ components of both strains increased during the period of study. The average concentration of $-S 15–40$ of the lean pigs at 14 weeks of age was 105 mg. and at 34 weeks was 206 mg./100 ml., while that of the fat animals was 129 mg. and 286 mg., respectively. Changes in concentration of the other components could not be correlated with age.

The long-lean pigs gained an average of 0.9 Kg. weekly in body weight during the first 20 weeks, while the short-fat animals averaged 1.7 Kg. (fig. 2). Since aureomycin in low con-
centration has been shown to increase the rate of weight gain of swine, this antibiotic was added to the diet in the amount of 100 mg./10 lbs. of dry feed. With this supplement, the weight gain of the lean pigs for the next 10 weeks was accelerated to 2.1 Kg./week, and of the fat to 2.0 Kg. Despite the accelerated weight gain, the lean pigs retained their characteristic long-lean look as compared to the fat ones (fig. 3). The differences in serum protein, cholesterol, and lipoproteins also persisted.

**DISCUSSION**

The changes in the serum protein pattern of the pigs during growth, i.e., increased albumin and γ-globulin concentration, are similar to those occurring in young dogs from the time of weaning until full growth.

The differences observed in serum protein and lipoprotein pattern of the 2 strains of pigs are found at a young age and persist. This indicates the permanence and importance of hereditary factors in establishing the protein-lipoprotein spectrum.

The finding of differences in lipoprotein and cholesterol concentration in 2 strains of pigs of similar age and on identical diets may help to explain the great range of normal values found in the heterogeneous human population on varied diets. The results indicate the inadmissibility of using different strains of animals for protein or lipoprotein studies without careful determination of their normal levels.

**Table 1.—Electrophoretic Serum Protein Fractions with Phosphate Buffer pH 7.8, Ionic Strength 0.16 by Moving Boundary Method, of Fat and Lean Miniature Pigs**

<table>
<thead>
<tr>
<th>Date</th>
<th>Pig #5; Short-Fat Strain</th>
<th>Pig #6; Long-Lean Strain</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total protein</td>
<td>Albumin</td>
</tr>
<tr>
<td>8/11/54</td>
<td>5.03</td>
<td>2.83</td>
</tr>
<tr>
<td>9/23/54</td>
<td>5.49</td>
<td>3.15</td>
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<tr>
<td>10/21/54</td>
<td>6.11</td>
<td>3.35</td>
</tr>
<tr>
<td>1/5/55</td>
<td>6.68</td>
<td>4.00</td>
</tr>
<tr>
<td>3/3/55</td>
<td>7.05</td>
<td>3.72</td>
</tr>
<tr>
<td>3/31/55</td>
<td>6.96</td>
<td>4.01</td>
</tr>
</tbody>
</table>

**Table 2.—Serum Lipoprotein, Cholesterol, and Phospholipid Concentrations of Miniature Swine (Short-Fat #5 and Long-Lean #6) During Growth**

<table>
<thead>
<tr>
<th>Date</th>
<th>Pig #5; Short-Fat Strain</th>
<th>Pig #6; Long-Lean Strain</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>mg./100 ml. of serum</td>
<td>Hours after ingestion of food</td>
</tr>
<tr>
<td></td>
<td>Total cholesterol</td>
<td>Free cholesterol</td>
</tr>
<tr>
<td>8/11/54</td>
<td>125</td>
<td>25</td>
</tr>
<tr>
<td>9/23/54</td>
<td>234</td>
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<td>45</td>
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<tr>
<td>3/31/55</td>
<td>159</td>
<td>33</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Date</th>
<th>Pig #6; Long-Lean Strain</th>
</tr>
</thead>
<tbody>
<tr>
<td>8/11/54</td>
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<td>10/21/54</td>
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<td>1/5/55</td>
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<td>105</td>
</tr>
<tr>
<td>3/31/55</td>
<td>118</td>
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</table>
globulinemia in a series of patients and suggested that the syndrome may be due to congenital or to acquired factors, as one of the patients had no lymphocyte abnormalities and relatives of both sexes manifested hypergamma-globulinemia. The finding of agammaglobulinemia in siblings by Brem and Morton also lends support to the hypothesis that \(\gamma\)-globulin formation may be genetically influenced.

The long-lean pigs could be considered an ectomorph type, while the short-fat animals have many of the characteristics associated with the mesomorph. Our data on pigs are not unlike those on human beings, where the ectomorph has lower levels of cholesterol than the mesomorph (Gertler and White).

Appreciable numbers of swine show arteriosclerotic lesions, approximately 13 per cent at 1 to 2 years of age and 25 per cent at 2 to 3 years. Any relation between the incidence of lesions and the somatotype to which the swine belonged would be of great interest.

**SUMMARY**

Electrophoretic serum protein fractions, ultracentrifugally determined lipoproteins, and cholesterol, have been estimated on 6 castrate male, miniature swine, 3 of the long-lean (ectomorph) and 3 of the short-fat (mesomorph) strain. Higher concentrations of total serum protein, albumin, cholesterol, and lower density, \(-S > 400, 40-400,\) and \(20-40,\) lipoproteins are present in fat pigs than in lean pigs. These differences persist throughout the period of rapid growth, when the relative rate of weight gain is similar and the diets are identical. The importance is emphasized of physical habitus or somatotype in the establishment of serum lipoprotein and protein patterns, in animals of like species but different genetic strain.

**SUMMARIO IN INTERLINGUA**

Esseva estimate le concentrationes seral de (1) le fractiones proteinie (in studios electrophoretic), (2) le lipoproteinas (post ultracentrifugation), e (3) le cholesterol in 6 castrate porcos mascule del racia “miniatura.” Tres del animales representava un lineage longe e magre
LEWIS AND PAGE

(ectomorphe), e 3 esseva de un lineage curte e grasse (mesomorphe). Le porcos grasse—in comparation con le porcos magre—habeva plus alte total concentrationes seral de proteina, albumina, e cholesterol e plus basse densitates lipoproteinic (—S > 400, 40–400, e 20–40). Iste differentias persisteva durante le periodo de rapide crescentia con dietas identic e simile valores relative del augmento de peso. Es sublineate le importancia del typo physic (i.e. del somatypo) in determinationes del valores seral de lipoproteinas e proteinas in animales del mesme specie sed de varie lineas genetic.

ACKNOWLEDGMENT

We wish to thank Dr. Stanton M. Hardy, Lederle Laboratories Division, American Cyanamid Company, for the aureomycin used and Dr. George E. Farrar, Jr., Wyeth Laboratories, for the SMA formula fed the pigs.

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REFERENCES


The physician without physiology and chemistry flounders along in an aimless fashion, never able to gain any accurate conception of disease, practising a sort of popgun pharmacy, hitting now the malady and again the patient, he himself not knowing which.—William Osler. Teaching and Thinking. Montreal M. J., 1895.
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