PROCEEDINGS OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE **182,** 221–224 (1986)

Heritability of Plasma Cholesterol and Triglyceride Concentrations in Swine (42331)

WILSON G. POND, HARRY J. MERSMANN, AND LARRY D. YOUNG

U.S. Department of Agriculture, Agricultural Research Service, Roman L. Hruska U.S. Meat Animal Research Center, Clay Center, Nebraska 68933

Abstract. Three-hundred and eighteen female swine representing contemporary commercial swine breeds (34 Chester White, 43 Large White, 42 Landrace, 40 Yorkshire, and 159 four-breed crossbreeds) were used to evaluate genetic variation between and within breeds for levels of plasma cholesterol and plasma triglycerides. Blood was sampled from all pigs after a 16-hr fast at 154 days of age. Plasma cholesterol was measured in all pigs and triglycerides were measured in 232 pigs. Paternal half-sib heritabilities (h^2) for plasma cholesterol and plasma triglycerides were 0.45 $\pm$ 0.23 and 1.04 $\pm$ 0.32, respectively. Breed differences were not apparent for either trait. Phenotypic and paternal half-sib genetic correlations between the two traits were 0.16 and 0.66, respectively. Neither body weight nor backfat depth were important in affecting the estimate of h^2 for either trait. The relatively high h^2 of total plasma cholesterol and of total triglycerides offers the possibility of developing, through selection, populations of hypercholesterolemic or hypertriglyceridemic swine useful as models for studies directed toward further understanding of human cardiovascular disease.

The importance of plasma cholesterol concentration as a factor in coronary artery disease in humans is well documented (1, 2). The known forms of familial hyperlipidemia (Types I, II, III, IV, V) represent subsets of the population at risk of developing atherosclerosis (3). One might predict variable responses of a sample of the genetically widely diverse United States population to diets of differing composition, yet no such systematic study has been reported. The pig is accepted as an appropriate animal model for studying this relationship (4–9). The genetic diversity of the pig offers the opportunity of assessing interrelationships between genetic background and cardiovascular response to diet. Estimates of heritability of 0.25 (10) and 0.29 (11) for total serum cholesterol concentration in swine suggest that selection for this trait would be effective. The purposes of the present report are to determine the genetic variation in total plasma cholesterol and total plasma triglyceride among and within commercially available breeds of swine and their four-way crosses. The relationships between plasma concentrations of each of these constituents and body weight and body composition as indicated by subcutaneous backfat thickness were also estimated.

Materials and Methods. Three-hundred and eighteen contemporary female swine representing commercial swine breeds (34 Chester White, 43 Large White, 42 Landrace, 40 Yorkshire, and 159 four-breed crossbreeds) were used. All pigs were fed a standard maize–soybean meal type diet (16% protein, 3% fat, 0% cholesterol) *ad libitum* from weaning at 5 weeks of age. They were housed in 16 pens in one building. Blood was sampled (heparinized syringe) from the anterior vena cava of each pig at 154 days of age after a 16-hr fast, centrifuged, and the plasma stored at -15°C until analyzed for cholesterol and triglycerides. Cholesterol was determined by an enzymatic procedure (12) with cholesterol esterase and cholesterol oxidase to yield hydrogen peroxide which was reacted with phenol and 4-aminoantipyrine to yield a red color, detected spectrophotometrically (reagents obtained from Alpkem Corp., Clockamus, Oreg.). Triglycerides were determined after saponification as glycerol which was oxidized by periodate to yield formaldehyde which was detected colorimetrically after reaction with acetylacetone to yield diacetyldihydrolutidine (13). For triglycerides, only 232 samples were available for analysis (29 Chester White, 33 Large White, 28 Landrace, 29 Yorkshire, and 113 crossbred). Backfat (mean of three measurements 5 cm off the dorsal midline over the shoulder, midback, and rump) estimated ul-

0037-9727/86 $1.50

trasonically and body weight were recorded for each animal when blood was sampled (154 days).

Data were analyzed by least-squares procedures (14) with a model that included breed group, sire within breed group and dam within sire within breed group. Sire and dam were considered random. The effects of body weight and backfat thickness on plasma cholesterol and triglycerides were evaluated by adding them as covariates in separate models. Heritabilities and genetic correlations were calculated from estimated genetic variances and covariances based on sire components of variance. Phenotypic correlations were also estimated.

Results. Breed group means, analyses of variance, and heritability estimates based on sire components of variance are shown in Table I for plasma cholesterol and triglycerides. Sire ($P < 0.05$) and dam ($P < 0.01$), but not breed, affected plasma cholesterol. Body weight and backfat were not significant as covariates. Overall breed group means ± SE ranged from 109.8 ± 2.9 mg/dl for Landrace to 117.0 ± 3.2 mg/dl for Yorkshire with other breeds and crossbreeds intermediate (overall mean, 113.6 ± 1.4 mg/dl). The paternal half-sib estimate of h^2, 0.45 ± 0.23, is higher than literature estimates (10, 11).

Sire ($P < 0.01$) affected plasma triglycerides while, unlike the case with cholesterol, dam had no effect and the breed group effect was marginal ($P < 0.10$). Neither body weight nor backfat significantly affected components of variance compared with values obtained when no covariate was used in the analysis for either cholesterol or triglycerides. Crossbreeds had the lowest mean triglycerides (55.3 ± 4.1 mg/dl) and Yorkshires the highest (72.6 ± 7.4) with other breeds intermediate (overall mean = 64.6 ± 3.1 mg/dl).

As in the case of h^2 estimates for plasma cholesterol and triglycerides, the use of body weight or backfat as a covariate failed to affect phenotypic and genetic correlations between these two traits. The paternal half-sib genetic correlation was 0.66 ± 0.31 and the phenotypic correlation was 0.16, indicating a weak positive association between cholesterol and triglycerides in the population studied.

Discussion. The paternal half-sib estimate of 0.45 ± 0.23 for h^2 of plasma cholesterol obtained in this study is similar to the estimate of 0.39 obtained by Reetz *et al.* (11), but considerably larger than the estimate of 0.10 obtained by Rothschild and Chapman (10). Rothschild and Chapman (10) considered that their best estimate of h^2 was 0.29 based on regression of offspring on sire. Rothschild and

TABLE I. ANALYSES OF VARIANCE, HERITABILITY ESTIMATES, AND BREED GROUP MEANS FOR LEVELS OF CHOLESTEROL (mg/dl) AND TRIGLYCERIDES (mg/dl)[a]

		Cholesterol			Triglycerides	
Analysis of variance source	*df*	Mean square	Probability	*df*	Mean square	Probability
Breed group (BG)	4	492	0.31	4	3048	0.09
Sire within BG (S/BG)	46	396	0.05	43	1385	0.01
Dam within S/BG	67	253	0.01	40	540	0.23
Remainder	200	107		144	468	
Heritability estimate						
h^2 Paternal half-sib		0.45 ± 0.23			1.04 ± 0.32	
Breed group means ± SE (*N*)						
Yorkshire		117.0 ± 3.2 (40)			72.6 ± 7.4 (29)	
Landrace		109.8 ± 2.9 (42)			70.1 ± 6.7 (28)	
Large white		115.9 ± 3.0 (43)			68.5 ± 6.6 (33)	
Chester white		114.4 ± 3.4 (34)			56.6 ± 6.6 (29)	
Crossbreed		111.2 ± 1.8 (159)			53.3 ± 4.1 (113)	
Overall mean		113.6 ± 1.4 (318)			64.6 ± 3.1 (232)	

[a] Mean body weight was 82.4 ± 5.8 kg; mean total of three backfat probes was 51.8 ± 7.3 mm.

Chapman (10) used a population of 1441 unselected male, female, and castrated male Yorkshire pigs at 56 days of age that were progeny of parents selected for high or low serum cholesterol, while Reetz *et al.* (11) used 648 female German Landrace pigs averaging 100 kg body wt and raised as progeny groups at production testing stations in Germany. The variation in estimates of h^2 may be related to variation in age at measurement, breeds used, diets, sampling, or testing facilities. Heritability estimates of plasma or serum cholesterol in other species range from 0.30 in chickens (15) to 0.51 in mice (16–18) and 0.80 in cattle (19). There appear to be limited direct estimates of h^2 of plasma cholesterol in humans, although there are well-documented forms of genetically determined hyperlipidemia, of which Type II represents a subgroup known to have hypercholesterolemia. Genetic components, including polygenic effects as well as the mutant allele responsible for familial hypercholesterolemia may account for as much as 40% of the total variability in plasma cholesterol in humans (3). Elevated low density lipoprotein cholesterol (LDL) is particularly associated with an increased risk of coronary artery disease, but the heritability of LDL in humans is not clearly established.

No estimates are available of the heritability of LDL or other plasma lipoprotein fractions in swine. Rapacz *et al.* (20) reported genetic differences among swine in response of the aorta to a high fat diet; these differences were associated with genetic polymorphism, whereby swine either hetero- or homozygous for the Lpp_5 gene had a greater tendency to develop elevated LDL-lipid when fed a high fat diet than those with the Lpp_8 gene.

The relatively high h^2 of total plasma cholesterol observed in the present study offers the possibility of developing, through selection, populations of swine hyper- or hypocholesterolemic relative to unselected populations. Such animals would be useful models in studies directed toward human cardiovascular disease and in further efforts to characterize plasma lipoprotein fractions in hyper- and hypocholesterolemic swine with respect to genetic susceptibility to atherosclerosis and to interactions between plasma lipoprotein profile and coronary artery disease. Future efforts to develop hyperlipemic populations of swine should include measurements of LDL and HDL cholesterol as well as total cholesterol and triglycerides in the plasma and the changes in lipoprotein profile in response to diet.

The failure of body weight as a covariate to affect the heritability estimate for plasma cholesterol in the present study is in contrast to the observation of Rothschild and Chapman (10) in prepubertal pigs and of Weibust (16) and Eapen *et al.* (21) in mice at 60 days of age in which positive correlations between body weight and plasma cholesterol were recorded. Fasting serum cholesterol of pigs selected for six generations for rapid body weight gain and leanness was greater than that of pigs selected for slow weight gain and fatness (22). On the other hand, selection for body fatness in swine (23) is not necessarily associated with changes in plasma cholesterol or triglyceride (24), or in susceptibility to atherosclerosis (25).

We are unaware of data in swine for heritability of plasma triglyceride other than the current estimate. The high paternal half-sib estimate of $h^2 = 1.04 \pm 0.32$ suggests that rapid progress could result from selection for high or low plasma triglycerides in swine. The low genetic and phenotypic correlations between plasma cholesterol and triglycerides suggests that genetic control of the metabolism of these two lipid classes is not closely linked. These data in swine suggest that genetic selection for hypercholesterolemia in swine would not be accompanied by associated shifts in plasma triglycerides.

Hypertriglyceridemia and hypercholesterolemia in humans are not highly related in subgroups of hyperlipidemia (Types I, II, III, IV, V), in which each Type differs from others in the lipid profile. The correlation between plasma concentrations of cholesterol and triglyceride in the general population is not clearly defined.

The authors thank Jenell Dague and associates for animal care and blood sampling, Lei Yen and Denise Oschner for blood analyses, Debbie Stritzke for data analysis, and Sherry Hansen for typing the manuscript.

1. Levy RI, Feinleib M. Risk factors for coronary artery disease and their management. In: Braunwald E, ed. Heart Disease: A Textbook of Cardiovascular Medicine. Philadelphia, Saunders, 1980.
2. Kannel WB, Castelli WP, Gordon T, McNamara PM. Serum cholesterol lipoproteins and the risk of coronary

artery disease, the Framingham study. Ann Intern Med **74**:1, 1974.
3. Tamir I, Rifkind BM, Levy RI. Measurement of lipids and evaluation of lipid disorders. In: Henry JB, Ed. Clinical Diagnosis and Management by Laboratory Methods. Chap. 8. Philadelphia, Saunders, Vol I, 1979.
4. Pond WG. Nutrition and heart disease: The pig as an experimental model. In: Roberts HR, Dodds WJ, ed. Pig Model for Biomedical Research. Miaola, Taiwan, Pig Research Institute, pp43–59, 1982.
5. Dodds WJ. The pig model for biomedical research. Fed Proc **41**:247–256, 1982.
6. Ratcliffe HL, Lugenbuhl H. The domestic pig: A model for experimental atherosclerosis. Atherosclerosis **13**:133–136, 1971.
7. Goldsmith DPJ, Jacobi HP. Atherosclerosis in swine fed several types of lipid-cholesterol diets. Lipids **13**: 174–180, 1978.
8. Chapman MJ, Goldstein S. Comparison of the serum low density lipoprotein and of its apaprotein in the pig, rhesus monkey, and baboon with that in man. Atherosclerosis **25**:267–291, 1976.
9. Stanton HC, Mersmann HJ. Swine in Cardiovascular Research. Boca Raton, Fla., CRC Press, 1985, in press.
10. Rothschild M, Chapman AB. Factors affecting serum cholesterol in swine. J Hered **67**:47–48, 1976.
11. Reetz I, Wegner W, Feder H. Statistik, Erblichkeit und korrelative bindung einiger Merkmale des kreislaufsystems bei weiblichen mastschiveinen der deutscher Lanrasse II: Erblichkeitsgrade und Genfrequenzen. Zentralbl Veterinaermed Reihe A **22**:741–755, 1975.
12. Allain CC, Poon LS, Chan CSG, Richmond W, Fu PC. Enzymatic determination of total serum cholesterol. Clin Chem **20**:470–475, 1974.
13. Fletcher MJ. A colorimetric method for estimating serum triglycerides. Clin Chem Acta **22**:393–398, 1968.
14. Harvey WR. Least-Squares Analysis of Data with Unequal Subclass Numbers. US Dept of Agric, Agric Res Serv, H-4, 1975.
15. Cherms FL Jr, Wilcox PH, Schaffner CS. Genetic studies of serum cholesterol in the chicken. Poult Sci **39**:889–892, 1960.
16. Weibust RS. Inheritance of plasma cholesterol levels in mice. Genetics **73**:303–312, 1973.
17. Dunnington EA, White JM, Vinson WE. Selection for serum cholesterol voluntary physical activity, 56-day body weight and feed intake in randomized mice: I. Direct responses. Canad J Genet Cytol **23**:533–544, 1981.
18. Dunnington EA, White JM, Vinson WE. Selection for serum cholesterol voluntary physical activity, 56-day body weight and feed intake in randomized mice: II. Correlated responses. Canad J Genet Cytol **23**:545–555, 1981.
19. Stufflebean SE, Lasley J. Hereditary basis of serum cholesterol level in beef cattle. J Hered **60**:15–16, 1969.
20. Rapacz J, Elson CE, Lalich JJ. Correlation of an immunogenetically defined lipoprotein type with aortic intimal lipidosis in swine. Exp Molec Pathol **27**:249–255, 1977.
21. Eapen KJ, Goswami OB, Petlar SK. Inheritance of serum cholesterol and its relation to body weights in white mice. J Genet **60**:222–229, 1971.
22. Bakke H. Serum levels of cholesterol in lines of pigs selected for rate of gain and thickness of backfat. Acta Agric Scand **25**:14–16, 1975.
23. Hetzer HO, Harvey WR. Selection for high and low fatness in swine. J Anim Sci **26**:1244–1251, 1967.
24. Mersmann HJ, Pond WG, Yen JT. Plasma glucose, insulin and lipids during growth of genetically lean and obese swine. Growth **46**:189–198, 1982.
25. Pond WG, Mersmann HJ, Yen JT. Effect of obesity *per se* on plasma lipid and aortic responses to diet in swine. Proc Soc Exp Biol Med **179**:90–95, 1985.

Received December 10, 1985. P.S.E.B.M. 1986, Vol. 182.
Accepted February 28, 1986.