Feature

Dietary protein: Does type influence cholesterolemia?

The following article was prepared by M.K. Foley, D.C. Beitz and J.W. Young of the Nutritional Physiology Group, Department of Animal Science, Iowa State University, Ames, Iowa, at the request of George Liepa of Texas Woman's University, Associate Editor for JAOCS *News for Vegetable Proteins.*

The American public is concerned about heart disease and plasma cholesterol concentration. This concern is illustrated by articles such as the cover story of the March 26, 1984, *Time* (1) or the feature in the October 19, 1987, *Newsweek* (2), in which much of the blame for heart disease and hypercholesterolemia is put on dietary cholesterol and consumption of saturated fat. No mention is made of any possible role of dietary protein in human hypercholesterolemia.

With the goal of reducing the incidence of heart disease, the American Heart Association recommends decreasing consumption of saturated fat but makes no recommendation about the type of dietary protein to consume (3). Does the type of dietary protein affect cholesterolemia? Research has been done with many species of animals in an attempt to determine if protein plays a role in cholesterolemia. This article summarizes relevant research for those species.

Rabbits

Nearly 30 years ago, research showed that rabbits easily become hypercholesterolemic and develop atherosclerosis without addition of dietary cholesterol (4,5). Consequently, many researchers have used the rabbit as a model in atherosclerosis research. Carroll (6) presents results of consumption of 22 different proteins (11 animal, 11 plant) on the cholesterol concentration of rabbit plasma. There is a spectrum of plasma cholesterol concentrations, with egg yolk protein being the most cholesterolemic and faba bean protein being the least. Other studies (7,8) also have found that animal proteins are hypercholesterolemic relative to plant proteins. Many researchers who attempt to understand this effect of protein use casein and soy protein as protein sources.

Hypercholesterolemia from the consumption of casein occurs in rabbits without addition of cholesterol to the diet (9–16). Katan et al. (16) found a significant correlation between hypercholesterolemia and aortic plaque development. The extent of plaque development and the log of time-averaged serum cholesterol concentration were correlated at r=.56. It also has been reported (9,17) that soy protein, which is hypocholesterolemic compared with casein, caused fewer aortic lesions than did feeding casein to rabbits.

Both casein and soy protein are hypercholesterolemic (50% and 125%, respectively) in rabbits one day after changing from a basal chow diet (18). The serum cholesterol concentration continued to increase for two weeks, but after four weeks, the hypercholesterolemic effect of soy protein had decreased.

Feeding soy protein results in a faster plasma cholesterol turnover and a decreased size of the primary cholesterol pool (11). Part of the increased turnover of cholesterol can be attributed to increased fecal excretion of cholesterol as a result of consumption of soy diets (9,11,19) and increased absorption of cholesterol from casein diets (11). In comparison with casein, soy protein also increased bile acid excretion in feces (9,11,19).

Casein consumption increased the low-density lipoprotein (LDL) cholesterol concentration (10,12,18). It also increased apoprotein-E concentration in intermediate-density lipoprotein (IDL), very-low-density lipoprotein (VLDL) and LDL (20), and decreased hepatic binding of apoprotein-B and apoprotein-E (10).

To determine if young rabbits were more susceptible than adult ones to the hypercholesterolemic effect of casein, West et al. (21) compared young and adult rabbits and found that in only one of three replications were young rabbits more susceptible to casein. They also found that adult rabbits had no significant difference in cholesterolemic response to casein or soy protein. In succeeding periods with the same rabbits, a less cholesterolemic response was found from changing protein types.

Kritchevsky (7) hypothesized that hypercholesterolemia is caused by the dietary ratio of lysine to arginine. To test his hypothesis, he and others (7,17,20) fed diets of soy protein, casein, soy protein + lysine (equivalent to lysine to arginine ratio of casein) and casein + arginine (equivalent to lysine to arginine ratio of soy protein). The results of these experiments were equivocal. Addition of arginine to casein decreased the hypercholesterolemic effect; the addition of lysine to soy protein increased plasma cholesterol to a concentration intermediate between casein and soy protein (7,17). Huff and Carroll (20) found that addition of lysine and arginine to soy protein and casein diets had no effect on cholesterol concentration.

When rabbits were fed amino acid mixtures resembling amino acid compositions of soy protein, sunflower protein, egg yolk protein or casein, their serum cholesterol concentration resembled that of rabbits fed intact proteins. Soy and sunflower amino acid mixes gave slightly greater values than did the corresponding intact proteins (21, 22). When enzymatically hydrolyzed casein and soy protein were fed, no difference was found between hydrolyzed and intact proteins (the free to total amino-N ratio is 0.37 for the soy protein) (22). A second study by the same researchers (14) found a 2.3-fold increase in serum cholesterol when soy protein with a free to total amino-N ratio of 0.47 was fed. They did state that the different ratios would not explain completely the difference in results.

Replacement of casein with soy protein caused serum cholesterol concentration to decrease (22). When the protein in the diet was 75% casein and 25% soy protein, the resulting serum cholesterol concentration was between that from either protein alone. When the mixture was 50:50, the serum cholesterol concentration was equal to that of soy protein alone.

The possibility of interactions of other nutrients with the type of protein has been investigated. Bauer and Covert (12) found that addition of sucrose augments hypercholesterolemic effects of casein diets. Kritchevsky et al. (23) added cellulose, wheat straw or alfalfa fiber to casein or soy protein diets to test for interaction of fiber and protein. Cellulose and wheat straw have equal effects on serum cholesterol, whereas alfalfa was hypocholesterolemic for both protein types. Alfalfa fiber eliminated differences between soy protein and casein diets for serum cholesterol. Interactions of protein with minerals were proposed when Van der Meer et al. (13) found that a high-calcium diet decreased the hypercholesterolemic effect of casein while not affecting blood cholesterol concentration of rabbits fed soy protein. Allotta et al. (24) hypothesized that the large amount of phosphorylation of casein interferes with trace mineral absorption, especially zinc and copper, which then alters cholesterol metabolism of animals.

In summary, the concentration of plasma cholesterol of rabbits is highly sensitive to the type of dietary protein. Rabbits seem more susceptible to hypercholesterolemia from casein (or other animal proteins) than from soy (or other plant proteins).

Rats

Rats fed casein do not consistently show the hypercholesterolemia found in rabbits. In weanling rats fed 10% protein and no cholesterol, plasma cholesterol concentration was inversely proportional to protein quality (25). The authors found feeding wheat gluten and soy protein to be hypercholesterolemic when compared with casein and egg whites. This hypercholesterolemia is contrasted to results of Yadav and Liener (26), in which 8.3% or 15% protein and 2% cholesterol were fed to young rats. They found that casein and an amino acid mixture corresponding to casein were both hypercholesterolemic compared with soy protein or an amino acid mixture corresponding to soy protein, and all diets were hypercholesterolemic compared with navy bean flour. Others (27,28) found cottonseed and soy proteins to be hypocholesterolemic relative to casein in rats that were not fed cholesterol. In contrast, Neves et al. (29) found no consistent differences in plasma cholesterol concentration of young rats fed animal proteins (casein, lactalbumin or egg albumin) and plant proteins (soy or alfalfa). Most published reports on effects of dietary casein and soy protein, however, show that in rats, as in rabbits, casein is hypercholesterolemic relative to soy protein (16,30–45).

The effect of the type of dietary protein on blood cholesterol concentration was seen both with (16,26, 32–37) and without (27,28,34,38–41) added dietary cholesterol. There were some cholesterolemic differences between adding and not adding cholesterol to the diets. Raheja and Linscheer (42) fed either soy protein or casein with and without adding 1% cholesterol and 0.5% cholic acid and found a greater hypercholesterolemic response to diets with cholesterol and cholic acid. Adding cholesterol often increased VLDL cholesterol concentration (32,33,35,43), but with no additional cholesterol fed, increases occurred both in VLDL (41,44) and high-density lipoprotein (HDL) (27, 28,44). Park et al. (27) found that plant proteins cause a higher proportion of HDL cholesterol to total cholesterol.

Rats, like rabbits, seem to have a differential responsiveness with age. In a comparison of immature and mature rats, the fractional esterification rate of free cholesterol was lower in mature rats, but net turnover of plasma cholesteryl esters and fecal excretion of neutral sterols was greater in immature rats (27). Lefevre and Schneeman (25) found the opposite cholesterolemic response with weanling rats fed a low-protein diet (10% protein) and hypothesized that it was caused by the low protein concentration limiting growth, thus causing different results than those found by others who either fed greater percentages of protein (27) or used older rats (26).

Rats, like rabbits, seem to have a differential responsiveness with age.

Several researchers have shown that the percentage of protein fed to rats affects the cholesterolemic response to type of protein. The hypercholesterolemic effect of casein was enhanced by increasing the percentage of casein in the diet, whereas the percentage of soy protein did not affect serum cholesterol (32,33). As in rabbits, the hypercholesterolemic effect of casein in the diet of rats was decreased by replacing casein with soy protein (33).

When effects of casein and soy

protein were compared, the concentration of cholesterol in liver paralleled serum cholesterol concentration (33); blood triacylglycerol concentration was greater from diets containing casein (38,40,41), and lymph cholesterol was nearly equal (45). Soy protein caused a greater rate of removal of cholesterol from blood, a decrease in the extracellular cholesterol pool and greater steroidogenesis (38). Furthermore, soy protein caused lower intestinal apoprotein A–I concentration in blood and lesser de novo synthesis of apoprotein A–I (45). Casein increased protein concentration in VLDL, LDL and HDL, whereas the addition of dietary cholesterol eliminated the increase (39). This protein increase in lipoprotein fractions led to an increase in the ratio of protein to cholesterol (39).

Soy protein fed to rats caused a more rapid turnover of blood cholesterol (38,40), an increased fractional esterification rate of plasma cholesterol (27), and a greater fractional catabolic rate of blood cholesterol (40) than did casein. When no cholesterol was fed, soy protein also caused increased excretion of neutral sterols (27,34,38) and decreased absorption of cholesterol from the intestine (38). If cholesterol was fed, no difference was found in cholesterol absorption (41, 43). The type of dietary protein did not change bile acid production because neither flow rate nor concentration of bile acids was found different in liver perfusate (46).

Effects of supplementing dietary soy protein with lysine and dietary casein with arginine also have been investigated in rats; inconsistent data resulted. Mokady and Liener (30) found that supplementation of specific proteins with amino acids did not affect the cholesterolemic properties of intact proteins, whereas others (16,28,31,41) found that addition of the same amino acids did modify cholesterolemic properties of the protein. Adding lysine to soy protein increased blood triacylglycerol concentration (28, 31,41), increased serum apolipoprotein-E concentration (31), and increased lipid absorption (44). Casein plus arginine decreased blood triacylglycerol concentration (28,31,41), serum cholesterol concentration (16) and lipid absorption (44). Feeding a mixture of amino acids equivalent to soy protein had no effects on cholesterol absorption, steroid excretion, and plasma cholesterol turnover but caused a decrease in extracellular cholesterol because of decreased cholesterol production (38).

Proteins also affect hormones and enzymes associated with cholesterol homeostasis. Glucagon concentration in plasma was not affected by feeding casein but addition of arginine to casein increased glucagon concentration (31). Dietary casein increased insulin concentration, and addition of arginine to casein decreased insulin (31,42). For cholesterol-free diets, rats fed casein had less 7-α-hydroxylase activity when compared with rats fed soy protein. When cholesterol was added to the diet, casein increased the activity of 7-α-hydroxylase (35). Proteins supplemented with lysine (soy) or arginine (casein) decreased and increased, respectively, the activity of the 7-α-hydroxylase (44). In diets without added cholesterol, 3-hydroxy-3-methylglutaryl-CoA reductase, the rate-limiting enzyme in cholesterol synthesis, was greater in the intestine of rats fed soy protein compared with that of rats fed casein (45), but both diets decreased the activity of this enzyme compared with the control (43).

Sirtori et al. (35) presented a summary of the effects of the type of dietary protein on cholesterol homeostasis in the rat. Hepatic regulation of cholesterol metabolism in rats is affected differently by plant and animal proteins. Animal proteins are hypercholesterolemic compared with plant proteins. Older rats are more sensitive to type of dietary protein with and without additional cholesterol in the diet.

Swine

Swine fed high-cholesterol diets containing either mixed plant (soy:corn:wheat, 50:25:25) or mixed animal protein sources (casein: albumin, 90:10) have a significantly lesser concentration of serum cholesterol from plant proteins (47).

Pigs fed a high-cholesterol diet with either soy protein or casein as the protein source had 50% less serum cholesterol from soy protein than from casein (48). Without added cholesterol being fed, Cho et al. (49) found no differential effects of protein, but with added cholesterol, both soy protein and casein diets increased serum cholesterol, with casein increasing it more. When swine were fed low-cholesterol diets and either soy protein or ground beef (50,51), soy protein or casein (52), and soy protein or egg white protein (53), no effects were found on plasma cholesterol concentration. Pond et al. (54) fed 8% and 16% soy protein and found that 8% protein resulted in increased plasma cholesterol, which is similar to results found with weanling rats fed low-protein diets (25). When pigs liberally were fed soy protein and ground beef in a low-cholesterol diet (0.09%), plasma cholesterol was increased over that of a conventional diet, and ground beef increased plasma cholesterol significantly more than did soy protein (55).

Soy protein, in comparison with beef protein, increased cholesterol concentraton in the liver (52), viscera (51), aorta (51), carcass (51) and skeletal muscle (55) of pigs. Other workers found no effects on liver cholesterol (51,53) and an increase in heart cholesterol from feeding ground beef (54). Pigs fed soy protein had 50% increased ileal excretion of neutral sterols and increased excretion of bile acids (56). Egg white protein, compared with soy protein, decreased fractional catabolic rate and irreversible loss of LDL cholesterol and LDL protein (53).

Swine seem to be hypercholesterolemic when fed animal proteins in high-cholesterol diets (greater than 0.1%), but they do not seem to be hypercholesterolemic when fed low-cholesterol diets (less than 0.1%).

Other animal models

Rhesus monkeys were fed a sequence of different diets, each for 13 to 17 weeks, to evaluate effects of dietary protein on plasma cholesterol concentration. When a commercial diet was changed to a soy protein diet with 0.1% cholesterol, a significant increase of serum cholesterol occurred. The diet for the monkeys then was changed to a casein diet with 0.1% cholesterol; a further increase in serum cholesterol resulted. This casein diet was followed by a soy-protein diet with 0.1% cholesterol, which decreased serum cholesterol. Changing back to the casein diet again increased serum cholesterol concentration. Large individual variation in responsiveness was found with a correlation of initial hypercholesterolemia and subsequent cholesterolemic protein responses (57).

Mice showed a hypercholesterolemic response when either soy protein or casein was added to the diet (42,58,59). Only one of the three reports, however, showed soy protein to be hypocholesterolemic in comparison with casein (58). The other two reports found no difference between the diets (42,59); this may be attributable to age differences because the dietary protein effect was found only with weanling mice. There were mixed results on liver cholesterol content because the two research groups that used male mice reported increased liver cholesterol from feeding soy protein (58,59). The other group, which used female mice, found increased liver cholesterol from feeding casein (42). One of the groups reported increased secretion of biliary cholesterol as a result of feeding casein (42), whereas another group reported decreased bile acid secretion as a result of feeding casein (58). Some of the differing results seem explainable by differences of age and sex.

Calves fed skim milk powder or liquid soybean extract for 14 weeks had no differences in serum cholesterol concentration (60). Calves fed low- or high-protein diets for 15 weeks had greater concentrations of neutral lipids, especially cholesterol, with the low-protein diet (61).

Hamsters fed casein or soy protein gave varied cholesterolemic results. Beynen and Schouten (62) found that casein increased plasma cholesterol by 50% over soy protein, whereas Duffy et al. (63) and Mahfouz-Cercone et al. (64) found no difference in serum cholesterol concentration in response to the same proteins. Mahfouz-Cercone et al. (64) reported hypercholesterolemia in hamsters when changing from a commercial chow to casein, soy or cottonseed protein, but they found no difference between the effects of the three proteins. Richmond et al. (65) also found no change in serum cholesterol between dietary cottonseed protein and casein. There was an increase in biliary cholesterol from casein (63-65) and no change in liver cholesterol content among the three treatments (62).

Gerbils fed supplemental cholesterol seem susceptible to hypercholesterolemia from casein (66). When guinea pigs are fed casein or soy protein, either with or without added cholesterol, an increase in serum cholesterol occurs. When they are fed added cholesterol, casein tends to cause greater serum cholesterol concentration than soy protein (67).

Turkeys fed soy protein had greater plasma cholesterol concentration than turkeys fed beef (68). Lofland et al. (69) observed that differences in serum cholesterol in pigeons were influenced by types of both protein and fat. They found that animal protein, when fed with butter and partly hydrogenated vegetable oil, was hypercholesterolemic compared with wheat gluten, but margarine or corn oil reversed this effect. Mol et al. (70) and Hevia and Visek (71) found no difference between soy protein and casein in chickens fed cholesterol-free diets. Terpstra et al. (72) also found no cholesterolemic differences from soy protein or casein diets containing large amounts of cholesterol; they reported that both proteins, when fed above daily requirements, were able to prevent some of the hypercholesterolemia from feeding cholesterol. Kritchevsky et al. (73) found that replacing casein with soy protein decreased serum cholesterol concentrations in chickens fed very high dosages of cholesterol (3%).

Humans

Results of human studies on the type of dietary proteins have been highly equivocal. Much of the variation in results may be explained by by difficulties in controlling dietary intakes of people.

Elliot (74) reviewed 14 studies in which replacing animal proteins with plant proteins decreased the plasma cholesterol concentration of hypercholesterolemic people. Sirtori et al. (75) found hypocholesterolemic effects when replacing a standard low-lipid diet with a soy protein diet in 42 hypercholesterolemic in-patients, regardless of the addition of dietary cholesterol. They found that 18 out-patients did not have the same amount of response, which possibly was because of difficulty in maintaining dietary compliance. Gaddi et al. (76) found that hypercholesterolemic children also responded to dietary substitution of plant for animal protein and noted a 22% decrease in total cholesterol after eight weeks. Shorey et al. (77), on the other hand, found no effect on plasma cholesterol in mildly hypercholesterolemic people when replacing animal with soy protein.

Van Raaij et al. (78) (with 69 normocholesterolemic volunteers) and Grundy and Abrams (79) (with one mildly hypercholesterolemic and 13 normocholesterolemic volunteers) also found no difference in plasma total cholesterol concentration of volunteers fed either soy protein or animal protein diets. Van Raaij et al. (78) found that soy protein decreased LDL cholesterol and increased HDL cholesterol concentrations. The general conclusion is that no consistent type of protein effect is demonstrated on the concentration of plasma cholesterol of normocholesterolemic persons. Hypercholesterolemic individuals seem to respond with a decrease in plasma cholesterol concentration when soy protein is substituted for casein.

Summary

Hypercholesterolemia from specific dietary proteins has been found in many species. Casein is hypercholesterolemic relative to soy protein in rabbits, rats, Rhesus monkeys and gerbils. Swine and chickens are susceptible to a hypercholesterolemic effect from casein when fed high concentrations of dietary cholesterol. Mice, hamsters and pigeons respond equivocally, whereas calves show no differences in cholesterolemia when fed plant or animal proteins. Young rats fed low-protein casein diets and turkeys fed ground beef become hypocholesterolemic when fed casein rather than soy protein. In the species that become hypercholesterolemic when fed casein, soy protein causes hypocholesterolemia by way of increased cholesterol turnover, fractional esterification rate and fecal cholesterol excretion.

ACKNOWLEDGMENTS

This is Journal Paper No. J-12895 of the Iowa Agriculture and Home Economics Experiment Station, Ames, Iowa, Project 2735.

REFERENCES

1. Wallis, C., *Time 123*(13):56 (1984).
2. Clark, M., M. Hager, L. Drew and P. King, *Newsweek 110*(16):94 (1987).

3. *The American Heart Association Diet*, American Heart Association, Dallas, TX, 1985.
4. Lambert, G.F., J.F. Miller, R.T. Olson and D.V. Frost, *Proc. Soc. Exp. Biol. Med. 97*:544 (1958).
5. Malmros, H., and G. Wigand, *Lancet 2*:749 (1959).
6. Carroll, K.K., *Fed. Proc. 41*:2792 (1982).
7. Kritchevsky, D., *J. Am. Oil Chem. Soc. 56*:135 (1979).
8. Hamilton R.M.G., and K.K. Carroll, *Atherosclerosis 24*:47 (1976).
9. Lo, G.S., R.H. Evans, K.S. Phillips, R.R. Dahlgren and F.H. Steinke, *Ibid. 64*:47 (1987).
10. Havel, R.J., *Annu. Rev. Physiol. 48*:119 (1986).
11. Huff, M.W., and K.K. Carroll, *J. Lipid Res. 21*:546 (1980).
12. Bauer, J.E., and S.J. Covert, *Lipids 19*:844 (1984).
13. Van der Meer, R., H. DeVries, C.E. West and H. DeWaard, *Atherosclerosis 56*:139 (1985).
14. Woodward, C.J.H., and K.K. Carroll, *Br. J. Nutr. 54*:355 (1985).
15. Beynen, A.C., K.E. Scholtz, L.F.M. Van Zutphen and C.E. West, *J. Nutr. 113*:1204 (1983).
16. Katan, M.B., L.M.H. Vroomen and R.J.J. Hermus, *Atherosclerosis 43*:381 (1982).
17. Kritchevsky, D., S.A. Tepper and J.A. Story, *Fed. Proc. 37*:7 (1978).
18. Terpstra, A.H.M., and F.J. Sanchez-Muniz, *Atherosclerosis 39*:217 (1981).
19. Kuyvenhoven, M.W., C.E. West, R. Van der Meer and A.C. Beynen, *Ibid. 116*:1395 (1986).
20. Huff, M.W., and K.K. Carroll, *Ibid. 110*:1676 (1980).
21. West, C.E., K. Devring, J.B. Schutte and A.H.M. Terpstra, *J. Nutr. 112*:1287 (1982).
22. Huff, M.W., R.M.G. Hamilton and K.K. Carroll, *Atherosclerosis 28*:187(1977).
23. Kritchevsky, D., S.A. Tepper, D.E. Williams and J.A. Story, *Ibid. 26*:397 (1977).
24. Allotta, G.C., S. Samman and D.C.K. Roberts, *Br. J. Nutr. 54*:87 (1985).
25. Lefevre, M., and B.O. Schneeman, *Nutr. Rep. Int. 28*:1369 (1983).
26. Yadav, N.R., and I.E. Liener, *Ibid. 16*:385 (1977).
27. Park, M-S.C., B.J. Kudchodkar and G.U. Liepa, *J. Nutr. 117*:30 (1987).
28. Park, M-S.C., and G.U. Liepa, *Ibid. 112*:1892 (1982).
29. Neves, L.B., C.K. Clifford, G.O. Kohler, D. De Fremery, B.E. Knuckles, C. Cheowtirakul, M.W. Miller, W.C. Weir and A.J. Clifford, *Ibid. 110*:732 (1980).
30. Mokady, S., and I.E. Liener, *Ann. Nutr. Metab. 26*:138 (1982).
31. Sugano, M., N. Ishiwaki, Y. Nagata and K. Imaizumi, *Br. J. Nutr. 48*:211 (1982).
32. Terpstra, A.H.M., G. Van Tintelen and C.E. West, *Atherosclerosis 42*:85(1982).
33. Terpstra, A.H.M., G. Van Tintelen and C.E. West, *J. Nutr. 112*:810 (1982).
34. Nagata, Y., K. Imaizumi and M. Sugano, *Br. J. Nutr. 44*:113 (1980).
35. Sirtori, C.R., G. Calli, M.R. Lovati, P. Carrara, E. Bosisio and M.G. Kienle, *J. Nutr. 114*:1493 (1984).
36. Beynen, A.C., A.H.M. Terpstra, C.E. West and G. Van Tintelen, *Nutr. Rep. Int. 28*:363 (1983).
37. Thatcher, C.D., N.L. Jacobson, J.W. Young and M.J. Richard, *Nutr. Res. 4*:1013 (1984).
38. Nagata, Y., N. Ishiwaki and M. Sugano, *J. Nutr. 112*:1614 (1982).
39. Lefevre, M., and B.O. Schneeman, *Ibid. 114*:768 (1984).
40. Lovati, M.R., L. Allievi and C.R. Sirtori, *Atherosclerosis 56*:243 (1985).
41. Vahouny, G.V., I. Adamson, W. Chalcarz, S. Satchithanandam, R. Muesing, D.M. Klurfeld, S.A. Tepper, A. Sanghui and D. Kritchevsky, *Ibid. 56*:127 (1985).
42. Raheja, K.L., and W.G. Linscheer, *Ann. Nutr. Metab. 26*:44 (1982).
43. Cohn, J.S., W.G. Kimpton and P.J. Nestel, *Atherosclerosis 52*:219 (1984).
44. Vahouny, G.V., W. Chalcarz, S. Satchithanandam, I. Adamson, D.M. Klurfeld and D. Kritchevsky, *Am. J. Clin. Nutr. 40*:1156 (1984).
45. Tanaka, K., K. Imaizumi and M. Sugano, *J. Nutri. 113*:1388 (1983).
46. Sugano, M., K. Tanaka and T. Ide, *Ibid. 112*:855 (1982).
47. Forsythe, W.A., E.R. Miller, G.M. Hill, D.R. Romsos and R.C. Simpson, *Ibid. 110*:2467 (1980).
48. Kim, D.N., K.T. Lee, J.M. Reiner and W.A. Thomas, *Exp. Mol. Pathol. 29*:385 (1978).
49. Cho, B.H.S., P.O. Egwin and G.O. Fahey Jr., *Atherosclerosis 56*:39 (1985).
50. Baldner-Shank, G., Effect of type of fat and protein on cholesterol and lipid metabolism of pigs, Ph.D Dissertation, Iowa State University, Ames, IA, 1986 (University Microfilms order number 87-03767).
51. Walsh, L.S., K.D. Wiggers, M.J. Richard and N.L. Jacobson, *Nutr. Res. 3*:557 (1983).
52. Richard, M.J., A.D. Julius and K.D. Wiggers, *Nutr. Rep. Int. 28*:973 (1983).
53. Walsh-Hentges, L.S., D.C. Beitz, N.L. Jacobson, A.D. McGilliard and J.J. Veenhuizen, *Lipids 20*:735 (1985).
54. Pond, W.G., J.-T. Yen, H.J. Mersmann and W.M. Haschek, *J. Nutr. 116*:1116 (1986).
55. Diersen-Schade, D.A., M.J. Richard, D.C. Beitz and N.L. Jacobson, *Ibid.115*:1016 (1985).
56. Beynen, A.C., C.E. West, J. Huisman, P. van Leeuwen and J.B. Schutte, in *Cholesterol Metabolism in Health and Disease: Studies in Netherlands*, edited by A.C. Beynen, M.J.H. Geelan, M.B. Katan and J.A. Schouten, Ponsen & Looijen, Wageningen, The Netherlands, 1985, p. 145.
57. Terpstra, A.H.M., C.E. West, J.T.C.N. Fennis, J.A. Schouten and E.A. Van der Veen, *Am. J. Clin. Nutr. 39*:1 (1984).
58. Roy, D.M., and B.O. Schneeman, *J. Nutr. 111*:878 (1981).
59. Weinans, G.J.B., and A.C. Beynen, *Nutr. Rep. Int. 28*:1017 (1983).
60. Beynen, A.C., L.G.M. Van Gils, K.E. Scholz and C.E. West, *Ibid. 27*:757 (1983).
61. Coccordrilli, G.D. Jr., P.T. Chandler and C.E. Polan, *J. Dairy Sci. 53*:1627 (1970).
62. Beynen, A.C., and J.A. Schouten, *Nutr. Rep. Int. 28*:835 (1983).
63. Duffy, A.M., N.M. DiMarco and G.U. Liepa, *Ibid. 31*:1319 (1985).
64. Mahfouz-Cercone, S., J.E. Johnson and G.U. Liepa, *Lipids 19*:5 (1984).
65. Richmond, A.S., N.M. DiMarco, M.G. Stroebel and G.U. Liepa, *Nutr. Rep. Int. 30*:1069 (1984).
66. Forsythe, W.A. III, *J. Nutr. 116*:1165 (1986).
67. Terpstra, A.H.M., G. Van Tintelen and C.E. West, *Nutr. Rep. Int. 25*:725 (1982).
68. Williams, J.E., D.G. Wagner, R.H. Thayer, L.E. Walters, G.W. Horn, J.J. Guenther and G.R. Waller, *Fed. Proc. 39*:336 (abstract) (1980).
69. Lofland, H.B., T.B. Clarkson, L. Rhyne and H.O. Goodman, *J. Athero. Res. 6*:395 (1966).
70. Mol, M.A.E., R.C. DeSmet, A.H.M. Terpstra and C.E. West, *J. Nutr. 112*:1029 (1982).
71. Hevia, P., and W.J. Visek, *Ibid. 109*:32 (1979).
72. Terpstra, A.H.M., J.B. Schutte and C.E. West, *Atherosclerosis 46*:95 (1983).
73. Kritchevsky, D., W.C. Grant, M.J. Fahrenbach, B.A. Riccardi and R.F.J. McCandless, *Arch. Biochem. Biophys. 75*:142 (1958).
74. Elliott, J.G., *Nutrition Overview, Vol. 2*, Protein Technologies International, St. Louis, MO (1987).
75. Sirtori, C.R., E. Gatti, O. Mantero, F. Conti, E. Agradi, E. Tremoli, M. Sirtori, L. Fraterrigo, L. Tavazzi and D. Kritchevsky, *Am. J. Clin. Nutri. 32*:1645 (1979).
76. Gaddi, A., G.C. Descovich, G. Noseda, C. Fragiacomo, A. Nicolini, G. Montanari, G. Vanetti, M. Sirtori, E. Gatti and C.R. Sirtori, *Arch. Dis. Child. 62*:274 (1987).
77. Shorey, R.L., B. Bazam, G.S. Lo and F.H. Steinke, *Am. J. Clin. Nutr. 34*:1769 (1981).
78. Van Raaij, J.M.A., M.B. Katan, J.G.A.J. Hautuast, R.J.J. Hermus, *Ibid. 34*:1261 (1981).
79. Grundy, S., and J.J. Abrams, *Ibid. 38*:245 (1983).