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SYMPOSIUM ON 'COMPARATIVE ASPECTS OF FATTY ACID METABOLISM'

Fatty acid synthesis in liver and adipose tissue

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In general terms the pathways of fatty acid biosynthesis are qualitatively similar in the liver and adipose tissue of monogastric, ruminant and avian species. There are, however, interesting quantitative differences and this review will compare and contrast some aspects of fatty acid synthesis in these tissues both within and between species.

Relative importance of adipose tissue and liver as sites of lipogenesis

Fatty acid biosynthesis occurs in all animal tissues but the major sites are generally considered to be adipose tissue, liver and lactating mammary gland (see Romsos & Leveille, 1974*a*; Volpe & Vagelos, 1976). As a consequence of studies carried out principally during the 1950s and 1960s with laboratory rodents, the adipose tissue has come to be regarded as a more important lipogenic tissue than the liver in non-lactating animals; Masoro *et al.* (1949) reported that fatty acid biosynthesis was not impaired in hepatectomized rats and adipose tissue was identified as the major site of fatty acid synthesis in mice (Feller, 1954; Favarger, 1965; Jansen *et al.* 1966) and rats (Hausberger *et al.* 1954; Leveille, 1966, 1967). In these studies adipose tissue accounted for at least 50% and in some cases as much as 95% of the fatty acids synthesized.

Contradictory observations have also been reported in rats (Patkin & Masoro, 1964; de Freitas & Depocas, 1965; Gandemer *et al.* 1982) and mice (Hems *et al.* 1975; Hollands & Cawthorne, 1981; Rath & Thenen, 1980) where the liver was relatively more important than adipose tissue. The discrepancies may be due, at

least in part, to the use of ^{14}C-labelled substrates in early studies and it is generally considered that the incorporation of ^{3}H from [^{3}H]water, which can measure the rate of lipogenesis irrespective of the possible multiple carbon sources, would clarify some of these contradictions although the relative contributions of the liver and adipose tissue also depend upon the composition of the diet and feeding pattern (see pp. 268–269).

Similar contradictions apply to the role of human adipose tissue in fatty acid synthesis. Many of the results (Shrago *et al.* 1967, 1969, 1971; Patel *et al.* 1975; Shrago & Spenetta, 1976) but not all (Bray, 1969, 1972; Goldrick & McLoughlin, 1970; Goldrick & Galton, 1974) show that adipose tissue is not a major site of fatty acid biosynthesis. Clearly, a re-evaluation of the relative roles of liver and adipose tissue is required in relation to fatty acid synthesis in the human.

Although the liver and adipose tissue are generally regarded as the principal lipogenic tissues they usually contribute no more than 40% of the total synthetic rate in laboratory rodents. In this regard it has been demonstrated that the carcass, emptied of its organs and dissectable white adipose tissue and composed mainly of muscles and skeleton, shows a high rate of lipogenesis (Rath & Thenen, 1980; Hollands & Cawthorne, 1981). It has been suggested that the site of this carcass lipogenesis could be intermuscular fat-pads (Kannan *et al.* 1976) or adipocytes, either mature or immature, within or associated with red muscles (Hollands & Cawthorne, 1981).

The roles of the liver and adipose tissue in lipogenesis in domesticated species would seem to be more clearly defined. Adipose tissue is the major site of fatty acid synthesis in the non-lactating ruminant (see Vernon, 1980*a*). The in vivo studies of Ingle *et al.* (1972*a*) suggested that in non-lactating sheep, adipose tissue is responsible for more than 90% of fatty acid synthesis and this conclusion has been generally supported by in vitro studies in sheep, cattle and goats (Payne & Masters, 1971; Hood *et al.* 1972; Ingle *et al.* 1972*b*; Liepa *et al.* 1978). The pig (O'Hea & Leveille, 1969; Mersmann *et al.* 1973) and guinea-pig (Patel & Hanson, 1974) resemble the ruminant in this respect as their livers have a negligible capacity for fatty acid synthesis. In contrast, the liver is the major site of lipogenesis in all the avian species investigated (see Pearce, 1980).

From the above discussion it is clear that there are species differences with regard to the relative roles of liver and adipose tissue in lipogenesis. In addition, it has recently been reported (Rath & Thenen, 1980) that there are also strain differences within species; in these studies it was demonstrated that the relative contributions of liver and adipose tissue varied between different strains of mice (both lean strains and obese strains). Similarly, differences in the relative rates of fatty acid synthesis have been observed in adipose tissues from beef and dairy cattle (see Vernon, 1980*a*).

It has also been reported that there are differences in fatty acid synthesis between the various sites of white adipose tissue and also between white adipose tissue in general and brown adipose tissue. White adipose tissue sites occur in a number of well-defined anatomical locations and many reports indicate highly

significant differences in the rates of fatty acid synthesis between the different sites in pigs (Anderson *et al.* 1972) and rats (Bjornstorp *et al.* 1970; Jamdar, 1978; Fried *et al.* 1982). Further studies in this area are required to provide an overall assessment of the total contribution of white adipose tissue to the metabolism of the whole animal. Comparisons of fatty acid synthesis in white and brown adipose tissues have shown that in rats (Agius & Williamson, 1980) and mice (Rath *et al.* 1979; Trayhurn, 1981) the rate of synthesis is many times greater in the latter tissue. Fatty acids, synthesized *in situ*, may be the substrates oxidized during dietary-induced thermogenesis (Agius & Williamson, 1980; Weaire & Kanagasabai, 1982).

Pathways of fatty acid synthesis

Fatty acid synthesis is a cytosolic process utilizing acetyl CoA as an obligatory precursor. The acetyl-CoA may be derived from the citrate-cleavage pathway (Srere, 1959; Spencer & Lowenstein, 1962) or directly from acetate (Barth *et al.* 1972). In the citrate-cleavage pathway, acetyl-CoA, which is formed intramitochondrially from various precursors, cannot diffuse into the cytoplasm at a rate sufficient to support fatty acid synthesis and is transported through the mitochondrial membrane as citrate. This is the source of the major portion of acetyl-CoA in monogastric mammals and birds.

Although the citrate-cleavage pathway is of major importance in many monogastric mammals and birds, this may not be true of all species (see Jones & Wahle, 1980). Acetyl-CoA can also be formed from acetate by cytosolic acetyl-CoA synthetase and this is the major pathway in ruminant tissues (see Ballard *et al.* 1969).

Substrates for fatty acid synthesis

It is generally accepted that the relative rates of fatty acid synthesis from various substrates (glucose, pyruvate, lactate, acetate) vary markedly between species (Saggerson, 1974; Vernon, 1980*b*) in both liver and adipose tissue. In monogastric species such as the mouse and rat, and in avian species, where large amounts of glucose may be derived from the diet, glucose is a major source of C for fatty acid synthesis. The extent of glucose utilization depends upon the carbohydrate and lipid compositions of the diet, the diurnal rhythm and the associated feeding pattern. Conversely, herbivorous animals (guinea-pig, rabbit, ruminants) consume large quantities of plant structural polysaccharides. These materials are resistant to degradation by digestive enzymes and consequently herbivores generally obtain less glucose via digestion; in these animals glucose is less important than acetate and lactate in fatty acid synthesis.

The role of glucose as a lipogenic substrate in the liver of mice was questioned by Hems *et al.* (1975); these authors calculated that glucose only contributed 5–10% of the total fatty acids synthesized in *ad lib.*-fed animals. The contribution

of glucose relative to other precursors depends upon the nutritional status of the animal (fed, fasted, fasted–refed). In the force-fed mouse, glucose was reported to be the sole source of C for hepatic fatty acid synthesis (Baker *et al.* 1978) although in this in vivo study some of the glucose may have been converted to lactate and other intermediates by extra-hepatic tissues and hence converted to fatty acids via this indirect route.

In ruminant tissues it is well established that acetate, derived from rumen fermentation, is the major precursor for fatty acid biosynthesis and the rate of incorporation of acetate C into fatty acids in adipose tissues has been shown to be between 10 and 100 times greater than that of glucose C (Vernon, 1980*a*). Comparisons of fatty acid synthesis from [^{14}C]acetate and [^{3}H]water in sheep adipose tissue led to the conclusion that acetate was the precursor for essentially all the fatty acids produced (Vernon, 1976). The lack of utilization of glucose in fatty acid biosynthesis is reflected in the very low specific activities of ATP-citrate lyase, malate dehydrogenase (oxaloacetate-decarboxylating) ($NADP^+$) and pyruvate dehydrogenase in ruminant tissues (Ballard *et al.* 1972; Robertson *et al.* 1980).

There are, however, circumstances when glucose is used as a precursor for fatty acids by ruminants. Increased glucose availability in the diet and intravenous, intra-abomasal or intra-duodenal glucose infusion all result in increases in fatty acid synthesis from glucose and lipogenic enzyme activity in sheep liver and adipose tissue (Ballard *et al.* 1972; Pearce & Piperova, 1981; Piperova & Pearce, 1982). Similarly, glucose increases the rate of fatty acid synthesis in sheep adipose tissue pieces maintained in tissue culture for 24 h (Vernon, 1979; Robertson *et al.* 1981). Ruminant tissues, therefore, have some potential for utilizing glucose as a fatty acid precursor but acetate is preferentially accepted, even in the above situations, as the C source for lipogenesis. Investigations have been made to identify the rate-limiting step(s) in the conversion of glucose to fatty acids by ruminant adipose tissue. Robertson *et al.* (1981) reported that in isolated adipose tissue pieces neither ATP-citrate lyase nor pyruvate dehydrogenase limited fatty acid synthesis from glucose and recent studies indicate that the likely rate-limiting steps occur earlier in glycolysis; hexokinase, phosphofructokinase and pyruvate kinase have been suggested as steps which may have key roles in controlling the flux of glucose C to fatty acids (Smith & Prior, 1981; Robertson *et al.* 1982; Yang *et al.* 1982).

Lactate has been reported to be a significant lipogenic precursor for fatty acid synthesis in both sheep and cattle adipose tissue (Prior, 1978; Whitehurst *et al.* 1978). The negligible incorporation of radioactivity from [1-^{14}C]lactate into fatty acids suggests that the route of metabolism is via pyruvate dehydrogenase (Vernon, 1980*a*) and this is supported by the results of Smith & Prior (1981) which show that lactate is converted to fatty acids via citrate; the latter authors suggest that the activities of ATP-citrate lyase and malate dehydrogenase (oxaloacetate-decarboxylating) ($NADP^+$) are not rate-limiting in the conversion of lactate to fatty acids. The use of selective inhibitors has also shown acetyl-CoA carboxylase and fatty acid synthetase to be involved (Prior *et al.* 1981).

Changes in hepatic and adipose tissue fatty acid synthesis during post-natal and post-weaning growth

During the suckling period in rats and mice, the rate of fatty acid synthesis and the content of lipogenic enzymes of neonatal tissues is low; this has been attributed to the high fat content of maternal milk (Ballard & Hanson, 1967). On weaning there is usually a change from a low- to a high-carbohydrate diet and this results in a marked increase in fatty acid synthesis and lipogenic enzyme activity in both liver and adipose tissue (Ballard & Hanson, 1967; Taylor *et al.* 1967; Bazin & Lavau, 1982). During the post-weaning period the rate of fatty acid synthesis in different body tissues varies with age in both mice (Le Marchand-Brustel & Jeanrenaud, 1978; Rath & Thenen, 1980) and rats (Godbole & York, 1978; Gandemer *et al.* 1979, 1982). In both species similar results were obtained; fatty acid biosynthesis was low in both liver and adipose tissue during the suckling period and increased dramatically immediately after weaning. A similar post-weaning increase in adipose tissue fatty acid synthesis has been observed in the pig (Mersmann *et al.* 1973). Hepatic fatty acid synthesis and lipogenic enzyme activities remained high in the young adult rat (<3 months old) but were reduced in both dissectable adipose tissue and the 'rest of the carcass' which also contained adipose tissue depots (Gandemer *et al.* 1979, 1982).

Changes in lipogenic enzyme activity in both liver and adipose tissue have been investigated in sexually mature male and female rats. Although no differences were found in enzyme specific activities in adipose tissue (Gandemer *et al.* 1979) it was observed that, in liver, the enzyme activities were higher in females than in males (Webb & Bailey, 1975; Gandemer *et al.* 1979). The studies of Lockwood *et al.* (1970) suggest that both male and female sex hormones are involved in controlling the specific activities of these enzymes.

In avian species the situation is opposite to that in mammals during the immediate post-natal period. On hatching, the diet changes from the high-fat diet of the embryo to a high-carbohydrate cereal mash and the rate of hepatic lipogenesis increases rapidly on hatching and feeding (see Pearce, 1977). During this early post-natal period the specific activities of the hepatic lipogenic enzymes also increase rapidly. The increases in ATP-citrate lyase, acetyl-CoA carboxylase and fatty acid synthetase on hatching occur before food is provided, showing that they are independent of feeding, whereas malate dehydrogenase (oxaloacetate-decarboxylating) ($NADP^+$) does not increase in activity before feeding commences. In contrast, the activities of these enzymes, and also fatty acid biosynthesis in avian adipose tissue, remain low from the late embryonic stage until at least 4 weeks after hatching. Hepatic lipogenic enzyme specific activity has been observed to remain high until around 7 weeks of age and then decline to much lower levels between 10 and 22 weeks of age. With the onset of sexual maturity and the commencement of egg laying, hepatic lipogenic enzyme activities in the pullet increase to levels similar to those seen in early post-natal development (Pearce, 1971, 1972). Such increases in lipogenic enzyme activity are not found in cockerels

as a result of sexual maturity and are probably related to egg production and the related requirement for lipid in the laying hen (Pearce, 1971).

Effect of diet on fatty acid synthesis

The quantity and nature of ingested food have marked effects on the pathways of lipogenesis.

Periodicity of feeding. With regard to the quantity of food consumed it is well-established that the pattern of food intake, by meal-feeding, *ad lib.*-feeding, fasting, refeeding after a fast or force feeding, results in significant alterations in fatty acid synthesis in mammals (Leveille, 1972; Baker *et al.* 1978) and avian species (Pearce, 1974). Fasting and refeeding after a fast generally have similar effects on both liver and adipose tissue fatty acid synthesis; however, comparisons of the effects of meal-feeding and *ad lib.*-feeding in rats indicate that adipose tissue is the primary site of fatty acid synthesis in meal-fed animals (Leveille, 1972).

There are significant diurnal rhythms in fatty acid biosynthesis in both liver and adipose tissue of laboratory rodents with a marked increase in *ad lib.*-fed animals during the dark period (Hems *et al.* 1975; Cawthorne & Cornish, 1979; Cornish & Cawthorne, 1978; Kimura *et al.* 1970; Godbole & York, 1978). Rodents ingest most of their food during this period and so the variations in fatty acid synthesis may be due partly to alterations in the pattern of circulating substrates and hormones in response to feeding.

Effect of dietary fat and carbohydrates. The relative quantities of carbohydrate and lipid in the diet and the nature of these components have profound effects on fatty acid synthesis in both liver and adipose tissue. The fact that mammals can convert carbohydrate to fatty acids and deposit these as triglycerides in adipose tissue is well-established. Stetten & Boxer (1944) reported that, in rats fed on fat-free diets, 30% of the ingested carbohydrate was converted to fatty acids; similar effects were obtained in mice (Masoro *et al.* 1949). However, the inclusion of fat in the diet results in marked reductions in the rate of fatty acid biosynthesis from carbohydrate (Patkin & Masoro, 1964; de Freitas & Depocas, 1965).

The effects of dietary lipid on hepatic and adipose tissue fatty acid synthesis appear to depend upon the character of the lipid. Dietary saturated fat inhibits the activities of acetyl-CoA carboxylase (Volpe & Vagelos, 1976) and fatty acid synthetase (Knoche *et al.* 1973), whereas polyunsaturated fat controls the quantity of lipogenic enzymes in the liver (Musch *et al.* 1974; Flick *et al.* 1977; Toussant *et al.* 1981). Fewer investigations have been made to compare the effects of the type of dietary fat on adipose tissue metabolism but studies in the rat (Waterman *et al.* 1975; Knoche *et al.* 1973; Loriette & Lapous, 1976) and the pig (Waterman *et al.* 1975) indicate that saturated fat has a greater effect in suppressing fatty acid synthesis than unsaturated fat. Similar effects of dietary saturated fat have been observed in sheep, but in steers the provision of both saturated and unsaturated fat resulted in reduced adipose tissue fatty acid synthesis although the process was more sensitive to dietary polyunsaturated fat (Vernon, 1980*a*). There are clearly organ-specific as well as species-specific responses to the character of dietary fat.

The type of dietary carbohydrate also influences fatty acid synthesis. It is well-established that substituting sucrose or fructose for starch or glucose in the diet results in increases in lipogenesis in man (Anderson *et al.* 1963; Antar & Ohlson, 1965; Macdonald, 1965), rats (Nikkila & Ojala, 1965; Zakim *et al.* 1967) and domestic fowl (Grant & Fahrenbach, 1959; Pearce, 1970). The effects of sucrose feeding are due to its fructose moiety. In species such as the rat, where both liver and adipose tissue contribute to *de novo* fatty acid synthesis, dietary manipulations generally affect both tissues in a similar fashion. However, fructose feeding increases hepatic fatty acid synthesis but reduces synthesis in the adipose tissue (Romsos & Leveille, 1974*b*). This effect is also reflected in lipogenic enzyme activity in liver and adipose tissue (Bruckdorfer *et al.* 1972; Chevalier *et al.* 1972). It would, therefore, appear that glucose and starch are the precursors for adipose tissue fatty acid synthesis, whereas sucrose and fructose are precursors for hepatic fatty acid synthesis.

Effect of temperature on fatty acid synthesis

During cold exposure, homoeotherms increase heat production to maintain their body temperature. In this process, fatty acids are mobilized from white adipose tissue and oxidized by other tissues, particularly brown adipose tissue and muscle (Masironi & Depocas, 1961; Masoro, 1966; Jansky, 1973). Acute and chronic exposure of rats and mice to cold results in a significant increase in fatty acid synthesis in liver and white and brown adipose tissues (Rath *et al.* 1979; Trayhurn, 1979). It has been suggested that an increase in fatty acid synthesis may be an integral part of the biochemical response to a decrease in ambient temperature in that it provides a preferred substrate for oxidation and hence the acute thermoregulatory response (Rath *et al.* 1979).

Concluding remarks

It is clear from the above discussion that many factors affect the rates of fatty acid synthesis in the liver and adipose tissue; these, in turn, influence the relative contributions of liver and adipose tissue to total fatty acid synthesis. It is necessary to take these factors into account, particularly diet, age, physiological state, species and strain and their inter-relationships, when comparing tissue fatty acid synthesis both within and between species.

REFERENCES

Agius, L. & Williamson, D. H. (1980). *Biochem. J.* **190**, 477.
Anderson, D. B., Kauffman, R. G. & Kastenschmidt, L. L. (1972). *J. Lipid Res.* **13**, 593.
Anderson, J. T., Grande, F., Matsumoto, Y. & Keys, A. (1963). *J. Nutr.* **79**, 349.
Antar, M. A. & Ohlson, M. A. (1965). *J. Nutr.* **85**, 329.
Baker, N., Learn, D. B. & Bruckdorfer, K. R. (1978). *J. Lipid Res.* **19**, 879.
Ballard, F. J., Filsell, O. H. & Jarrett, I. G. (1972). *Biochem. J.* **126**, 193.
Ballard, F. J. & Hanson, R. W. (1967). *Biochem. J.* **102**, 952.

Ballard, F. J., Hanson, R. W. & Kronfeld, D. S. (1969). *Fedn Proc. Fedn Am. Socs exp. Biol.* **28**, 218.
Barth, C., Sladek, M. & Decker, K. (1972). *Biochim. biophys. Acta* **260**, 1.
Bazin, R. & Lavau, M. (1982). *J. Lipid Res.* **23**, 839.
Bjornstorp, P., Krotkiewski, M., Larsson, B. & Somlo-Szugs, Z. (1970). *Acta Physiol. Scand.* **80**, 29.
Bray, G. A. (1969). *J. clin. Invest.* **48**, 1413.
Bray, G. A. (1972). *J. clin. Invest.* **51**, 537.
Bruckdorfer, K. R., Khan, I. H. & Yudkin, J. (1972). *Biochem. J.* **129**, 439.
Cawthorne, M. A. & Cornish, S. (1979). *Int. J. Obesity* **3**, 83.
Chevalier, M. M., Wiley, J. H. & Leveille, G. A. (1972). *J. Nutr.* **102**, 337.
Cornish, S. & Cawthorne, M. A. (1978). *Horm. Metab. Res.* **10**, 186.
de Freitas, A. S. W. & Depocas, F. (1965). *Can. J. Biochem.* **43**, 437.
Favarger, P. (1965). In *Handbook of Physiology, Adipose Tissue*, Sect. 5, Chap. 4, p. 19. Washington DC: American Physiology Society.
Feller, D. D. (1954). *J. biol. Chem.* **206**, 171.
Flick, P. K., Chen, J. & Vagelos, P. R. (1977). *J. biol. Chem.* **252**, 4242.
Fried, S. K., Lavau, M. & Pi-Sunyer, F. X. (1982). *Metabolism* **31**, 876.
Gandemer, G., Pascal, G. & Durand, G. (1979). *Annls. Biol. anim. Biochem. Biophys.* **19**, 573.
Gandemer, G., Pascal, G. & Durand, G. (1982). *Int. J. Biochem.* **14**, 797.
Godbole, V. & York, D. A. (1978). *Diabetologia* **14**, 191.
Goldrick, R. B. & Galton, D. J. (1974). *Clin. Sci. Mol. Med.* **46**, 469.
Goldrick, R. B. & McLoughlin, G. M. (1970). *J. clin. Invest.* **49**, 1213.
Grant, W. C. & Fahrenbach, M. J. (1959). *Proc. Soc. exp. biol. Med.* **100**, 250.
Hausberger, F. X., Seymour, W. H. & Rutman, R. J. (1954). *J. biol. Chem.* **208**, 431.
Hems, D. A., Rath, A. & Verrinder, T. R. (1975). *Biochem. J.* **150**, 167.
Hollands, M. A. & Cawthorne, M. A. (1981). *Biochem. J.* **196**, 645.
Hood, R. L., Thompson, E. H. & Allen, C. E. (1972). *Int. J. Biochem.* **3**, 598.
Ingle, D. L., Bauman, D. E. & Garrigus, U. S. (1972*a*). *J. Nutr.* **102**, 609.
Ingle, D. L., Bauman, D. E. & Garrigus, U. S. (1972*b*). *J. Nutr.* **102**, 617.
Jamdar, S. C. (1978). *Biochem. J.* **170**, 153.
Jansen, G. R., Hutchinson, C. F. & Zanetti, M. E. (1966). *Biochem. J.* **99**, 323.
Jansky, L. (1973). *Biol. Rev.* **48**, 85.
Jones, C. T. & Wahle, K. W. J. (1980). *Biochem. Soc. Trans.* **8**, 289.
Kannan, R., Palmquist, D. L. & Baker, N. (1976). *Biochim. biophys. Acta* **431**, 225.
Kimura, T., Taizo, M. & Ashida, K. (1970). *J. Nutr.* **100**, 691.
Knoche, H., Esders, T. W., Koths, K. & Bloch, K. (1973). *J. biol. Chem.* **248**, 2317.
Le Marchand-Brustel, Y. & Jeanrenaud, B. (1978). *Am. J. Physiol.* **234**, E568.
Leveille, G. A. (1966). *J. Lipid Res.* **7**, 46.
Leveille, G. A. (1967). *Proc. Soc. exp. biol. Med.* **125**, 85.
Leveille, G. A. (1972). *Nutr. Rev.* **30**, 151.
Liepa, G. U., Beitz, D. C. & Linder, J. R. (1978). *J. Nutr.* **108**, 1733.
Lockwood, E. A., Bailey, E. & Taylor, C. B. (1970). *Biochem. J.* **118**, 115.
Loriette, C. & Lapous, D. (1976). *Experentia* **3**, 881.
Macdonald, I. (1965). *Am. J. clin. Nutr.* **16**, 458.
Masironi, R. & Depocas, F. (1961). *Can. J. biochem. Physiol.* **39**, 219.
Masoro, E. J. (1966). *Physiol. Rev.* **46**, 67.
Masoro, E. J., Chaikoff, I. L. & Dauben, W. G. (1949). *J. biol. Chem.* **179**, 1117.
Mersmann, H. J., Houk, J. M., Phinney, G., Underwood, M. C. & Brown, L. J. (1973). *Am. J. Physiol.* **224**, 1123.
Musch, K., Ojakian, M. A. & Williams, M. A. (1974). *Biochim. biophys. Acta* **337**, 343.
Nikkila, E. A. & Ojala, K. (1965). *Life Sci.* **4**, 937.
O'Hea, E. K. & Leveille, G. A. (1969). *J. Nutr.* **99**, 338.
Patel, M. S. & Hanson, R. W. (1974). *Mech. Aging Dev.* **3**, 65.
Patel, M. S., Owen, O. E., Goldman, L. I. & Hanson, R. W. (1975). *Metabolism* **24**, 161.
Patkin, J. & Masoro, E. J. (1964). *Can. J. Physiol. Pharmacol.* **42**, 101.
Payne, E. & Masters, C. J. (1971). *Int. J. Biochem.* **2**, 623.

Pearce, J. (1970). *Int. J. Biochem.* **1**, 306.
Pearce, J. (1971). *Biochem. J.* **123**, 717.
Pearce, J. (1972). *Comp. Biochem. Physiol.* **42**, 721.
Pearce, J. (1974). *Wlds. Poult. Sci. J.* **30**, 115.
Pearce, J. (1977). *Int. J. Biochem.* **8**, 269.
Pearce, J. (1980). *Biochem. Soc. Trans.* **8**, 295.
Pearce, J. & Piperova, L. S. (1981). *Proc. 12th Int. Cong. Nutr., San Diego,* p. 126.
Piperova, L. S. & Pearce, J. (1982). *Int. J. Biochem.* **14**, 351.
Prior, R. L. (1978). *J. Nutr.* **108**, 926.
Prior, R. L., Smith, S. B. & Jacobson, J. J. (1981). *Arch. Biochem. Biophys.* **211**, 202.
Rath, E. A., Salmon, D. M. & Hems, D. A. (1979). *FEBS Lett.* **108**, 33.
Rath, E. A. & Thenen, S. W. (1980). *Biochim. biophys. Acta* **618**, 18.
Robertson, J. P., Faulkner, A. & Vernon, R. G. (1980). *FEBS Lett.* **120**, 192.
Robertson, J. P., Faulkner, A. & Vernon, R. G. (1981). *Biochem. Soc. Trans.* **9**, 398.
Robertson, J. P., Faulkner, A. & Vernon, R. G. (1982). *Biochem. J.* **206**, 577.
Romsos, D. R. & Leveille, G. A. (1974*a*). *Adv. Lipid Res.* **12**, 97.
Romsos, D. R. & Leveille, G. A. (1974*b*). *Biochim. biophys. Acta* **360**, 1.
Saggerson, E. D. (1974). *Biochem. J.* **140**, 211.
Shrago, E., Glennon, J. A. & Gordon, E. S. (1967). *J. clin. Endocrin. Metab.* **273**, 679.
Shrago, E., Glennon, J. A. & Gordon, E. S. (1971). *Metabolism* **20**, 54.
Shrago, E. & Spennetta, T. (1976). *Am. J. clin. Nutr.* **29**, 540.
Shrago, E., Spennetta, T. & Gordon, E. (1969). *J. biol. Chem.* **24**, 2761.
Smith, S. B. & Prior, R. L. (1981). *Arch. Biochem. Biophys.* **211**, 192.
Spencer, A. F. & Lowenstein, J. M. (1962). *J. biol. Chem.* **237**, 3640.
Srere, P. A. (1959). *J. biol. Chem.* **234**, 2544.
Stetten, D. & Boxer, G. E. (1944). *J. biol. Chem.* **155**, 231.
Taylor, C. B., Bailey, E. & Bartley, W. (1967). *Biochem. J.* **105**, 717.
Toussant, M. J., Wilson, M. D. & Clarke, S. D. (1981). *J. Nutr.* **111**, 146.
Trayhurn, P. (1979). *FEBS Lett.* **104**, 13.
Trayhurn, P. (1981). *Biochim. biophys. Acta* **664**, 549.
Vernon, R. G. (1976). *Lipids* **11**, 662.
Vernon, R. G. (1979). *Int. J. Biochem.* **10**, 57.
Vernon, R. G. (1980*a*). *Prog. Lipid Res.* **19**, 23.
Vernon, R. G. (1980*b*). *Biochem. Soc. Trans.* **8**, 291.
Volpe, J. J. & Vagelos, P. R. (1976). *Physiol. Rev.* **56**, 339.
Waterman, R. A., Romsos, D. R., Tsai, A. C., Miller, E. R. & Leveille, G. A. (1975). *Proc. Soc. exp. biol. Med.* **150**, 347.
Weaire, P. J. & Kanagasabai, T. F. (1982). *Biochem. J.* **206**, 667.
Webb, J. R. & Bailey, E. (1975). *Int. J. Biochem.* **6**, 813.
Whitehurst, G. B., Beitz, D. C., Pothoven, M. A., Ellison, W. R. & Crump, M. H. (1978). *J. Nutr.* **108**, 1806.
Yang, Y. T., White, L. S. & Muir, L. A. (1982). *J. Anim. Sci.* **55**, 313.
Zakim, D., Pardini, R. S., Herman, R. H. & Sauberlich, H. E. (1967). *Biochim. biophys. Acta* **144**, 242.

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