the case of wheat fed. In this case, it appears that quality of the pork may be more affected than composition of the fat, a distinction which must be made in various instances between characteristics of the adipose tissue and of the rendered or extracted fat.

Changes in butter fat brought about by feed are complicated by the presence of fat acids of low molecular weight which do not occur to any extent in the body fat or in the plant fats in feeds used by cattle. The changes in these acids naturally influence the changes in the others. In general, the mill feeds which are relatively high in ether extract when fed in large quantities, also blue grass pasture, tend to increase the iodine number (oleic acid content) and the per cent of volatile acids. Carbohydrate-rich feeds tend to produce the opposite effect.

The sustained interest in the subject of quality of animal fats is evidence of not only its importance but of continued progress in elucidating the many complex problems involved. On the one hand, there is need for a more adequate understanding of a biochemical process involved in fat formation in the animal body and on the other of the manufacture and standardization of the commercial product.

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INTERMEDIARY METABOLISM OF THE LIPIDS

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Abstract

The author reviews recent advancements in the study of the fate of lipids in metabolism. Brief discussions of the mechanism of absorption in the intestinal wall; of the role of lecithin, cephalin, sphingomyelin, and cholesterol in fat metabolism; of the metabolic changes in fats in the liver, and of the manner of oxidation of fats in the body, are presented.

This is not a general review but aims merely to deal with a few fields where recent investigations have turned up important material. Taking the metabolic events in order:

Absorption of Fat

In absorption from the intestine, it is now an accepted belief that there is a complete breakdown of the fat into the constituent glycerol and fatty acids, followed by resynthesis with apparently a rearrangement of the fatty acids in the molecule and possibly some chemical change—saturation or desaturation, or possibly dilution by fatty acids or fat from other sources. The sum of the changes results in a chyle fat somewhat different from the food fat. The change is toward the formation of a fat melting at about the animal's body temperature.

As in most other changes in fatty acid combination, phosphorization with formation of phospholipids is important as shown by the work of Sinclair (1) and Verzar and McDougall (2). There is little doubt that the fatty acids enter, to a considerable extent, into phospholipid combination in the epithelial cells of the absorbing surface of the intestine. In this connection, it is well to keep in mind the conception of Loew (3) who was one of the earliest to include the phospholipids in the theoretical scheme of fatty acid metabolism. His idea was that the phospholipid complex constitutes a framework to which the fatty acids are attached for purposes of transport and later combustion. The purpose of this combination in the intestine is for transport and possibly to lower the active mass of free fatty acids in the epithelial cells and thus hasten the diffusion from the intestine. The fatty acids thus attached to the framework are later, partly at least, shifted off again forming fat and probably cholesterol esters, two molecules of phospholipid contributing four fatty acids, three of which go to a fat molecule, the other to a cholesterol ester molecule (4). The stripped glycerophosphoric acid-choline complex can then take up more fatty acids. The percentage of phospholipid in the mucosa does not change much during fat absorption so that we have to assume either this fixed framework or a continuous passage out of the epithelium of phospholipid. The latter doesn't seem quite to fit the present facts since there is little increase of phospholipid in the thoracic duct lymph. On the other hand, the phospholipid of the blood plasma rises during fat absorption as does also the liver phospholipid, which may mean an absorption of the phospholipid directly into the blood stream. Moreover, this increased phospholipid in blood and liver contains the fatty acids being absorbed.

To what extent phosphorization takes place during these early stages of metabolism cannot be said. Most of the absorbed fat appears in the throacic duct, the blood and the liver as neutral fat, and undoubtedly most of it is transported as fat whether from the intestine or from the stores. It seems probable at present that the phosphorization is an accessory mechanism to speed the absorption of fat just as phosphorization increases the rate of absorption of dextrose (5). We cannot say to what extent phosphorization enters into the later stages of fatty acid metabolism. We don't yet know how the fat in the blood stream enters and leaves the stores nor whether, as Loew (3) and Leathes and Raper (6) believed, the fatty acids must be

changed to phospholipid for combustion. Recent evidence (7, 8), however, which is not uncontested (9) goes to show that the fatty acids in the phospholipid form are more easily burned than in the form of neutral fat.

Labelled Fatty Acids

A fruitful line of advance has been developed by the use of labelled fatty acids as practiced by Artom and Peretti (10) with iodized compounds, by Schoenheimer and Rittenberg (11) with deuterium compounds, and by Sinclair (12) with the highly unsaturated acids of cod liver oil and with elaidic acid. Deuterium and elaidic acid compounds have given especially clear-cut results. Schoenheimer and associates have shown definitely, among other facts, that desaturation and saturation of fatty acids *can* take place in the animal organism, and that exchange of fat in the depots may be ready and extensive—that in some cases (mice) it may be laid down and moved again after each meal. The ready mobility of the fat in the depots is emphasized in animals with fat deficiency as shown by Wesson and Burr (13). In their animals (rats), it was found that most of the glucose which would normally be burned was first transformed into fat and probably stored, only to be immediately removed and burned. The ready mobility of the stored fat, under some circumstances, is something we have not appreciated, since most of the earlier evidence goes to show that in animals in a normal state of nutrition fat may stay in the stores for a long time (14).

Sinclair (12) with elaidic acid has shown the participation of phospholipid in fatty acid metabolism, not only in intestinal absorption but also in transport in the blood, in the liver and in the tissues (muscles). He has been able in this way to differentiate between phospholipid which is strictly metabolic, i.e., phospholipid which carries fatty acids on their way to replace wear and tear or to combustion, and phospholipid which has other functions in the tissues, i.e., as an aid in carrying on the chemical and physicochemical processes going on in the cell or as composing part of the fixed framework of the tissues. The small amount of evidence at present accumulated would indicate that lecithin is the main metabolic form of the fatty acids, while cephalin has mostly other functions. Sphingomyelin, the other known phospholipid, begins to intrude itself on our attention, but so far the amount of work done on it is not sufficient to serve as a basis for speculation as to its function in metabolism.

Little can be said about the part played by cholesterol in the metabolism of the fatty acids. It enters into its relationship with them early and continues with them throughout their metabolic life. Cholesterol is absorbed from the intestine and during absorption it is in part esterified with the fatty acids there being absorbed. Free and esterified cholesterol are found in the thoracic duct lymph and in the blood plasma where the ester form of cholesterol composes ⅔ to ¾ of the total. Cholesterol ester is found only in small amounts in normal tissues, although it is found to accumulate in fatty livers. Sperry (15) has shown that there is a cholesterol esterase in the blood which apparently has as its function the complete esterification of the cholesterol. In the living animal the level of esterified cholesterol in plasma is kept rather closely at the fixed level already mentioned. The fatty acids combined with it are the most unsaturated of all the fatty acids in the blood. Some figures for iodine numbers of the fatty acids recently obtained by us (16) on human blood plasma are as follows: neutral fat fatty acids 102, phospholipid fatty acids 125, and cholesterol ester fatty acids 158. Cholesterol thus seems always to be combined with very unsaturated fatty acids but the purpose of this combination has not yet revealed itself. Perhaps one of its functions is to combine with and remove from active circulation the excess of the more unsaturated fatty acids.

The Liver in Fat Metabolism

Since the discovery of the fat deficiency disease of Burr and Burr (17), we have drifted away from Leathes' conception of the liver as a place where the fatty acids are desaturated. For one thing, the intestine has been found to have this power and, for another, the fact shown by Burr and Burr (18) that the organism cannot change oleic acid into the next unsaturated acid, linolic, literally to save its life. As Sinclair has pointed out in this connection, the state of things is not quite as serious as that, but the fact remains that the ability of the living organism to desaturate the fatty acids appears to be limited. One double bond can be introduced, as in oleic acid, without difficulty. It is the second one which seems to present the obstacle. However, acids of higher degrees of unsaturation, for example arachidonic and other longer chain acids, can apparently be formed as needed even though the apparently simpler ones cannot.

The most discussed feature of the fat metabolism of the liver is at present the conditions surrounding the fatty livers produced in a variety of ways. Best and Ridout (19) noted the condition in depancreatized dogs fed insulin. Various other workers have later found the same. Feeding of cholesterol (20) and cystine (21) has been shown to produce this condition which consists in an accumulation of fat and cholesterol esters in the liver. Feeding choline will cause the accumulation to disappear. There is apparently a block in the metabolism of fat at the liver. Of course, choline suggests phospholipid and the handiest explanation of the block is that choline is the limiting factor in the transformation of fat to phospholipid for transport. Best (personal communication), however, does not accept this explanation but thinks that the reason is more obscure. The question also is raised, "Why does the cholesterol ester accumulate with the fat and also disappear with it?" There is no answer except that phospholipid and cholesterol with its esters always seem to occur together and are apparently linked together in fat metabolism. Perhaps the process is the reverse of what we have mentioned earlier, i.e., one fatty acid from cholesterol ester plus three fatty acids from fat give two sets of two fatty acids for two molecules of phospholipid, the whole hinging on the use of phospholipid as the agent for more fat.

I had intended to talk on oxidation of the fatty acids but the time is up and so I can refer only briefly to a few points which seem significant in this connection. First of all, β-oxidation remains as the main method of reducing the long chains to CO_2 and H_2O whether it is true β-oxidation or a modified α-oxidation as suggested by Witzemann (22), a conception which fits better with the chemists' ideas of oxidation. The important fact is that the oxidation once started runs through the chain to complete destruction. The only fragments of the chain which ever remain are the four carbon residues, the acetone bodies. These occur only when

combustion of fat is forced by the failure of combustion of other fuel.

Other methods of oxidation have been claimed and some of these appear to be promising. Simultaneous oxidation at both ends of the chain as claimed by Verkade (23) is somewhat doubted as a general mechanism by Flaschenträger and Bernhard (24). Simultaneous oxidation at various points in the chain as suggested by Smedley-MacLean and Pearce (25) and Jowett and Quastel (26) seems probable under certain conditions. According to Flaschenträger and Bernhard, β-oxidation is possible only with the free COOH group and the purpose of ω-oxidation is to furnish COOH groups where these are lacking, e.g., when the fatty acid carboxyl is combined as it is in neutral fat. However, dicarboxylic acids are difficult to oxidize, the β-oxidations on the two ends interfering with each other. Protecting one carboxyl by an ester or amide group results in almost complete (90%+) disappearance. Quantitatively this ω-oxidation is not very important. Even with the 9 and 10 acids which yield the most, the excretion of dibasic acids in the urine is not over 2-3 per cent.

Deuel and associates (27) bring evidence to show that caprylic, capric, lauric and myristic acids give more than double the acetone body excretion when fed to rats as the lower fatty acids. Palmitic and stearic acids yield three of these fragments while odd-numbered acids give none.

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The Functions Of The Phospholipids In The Animal Body

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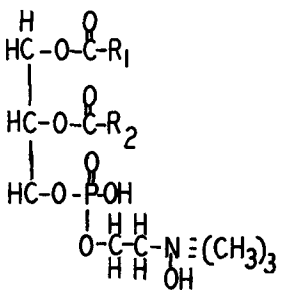
Abstract

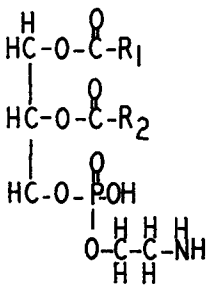
This paper deals with the bearing of some of the recent information on the three proposed functions of the phospholipids: that they are intermediary metabolites in fat metabolism; that they serve as an oxidation-reduction system; and that they are essential elements in cell structure. The rapid turnover of phospholipids in intestinal mucosa, liver and blood plasma indicates an active part in fat metabolism. The slow turnover in other tissues, notably skeletal muscle, points to a non-metabolic function. The amount of phospholipid present in various skeletal muscles is shown to be a function of the relative extent to which they are used. The adaptation seems to be a slow process since forced activity of a muscle produces a comparatively slight increase in phospholipid content.

Introduction

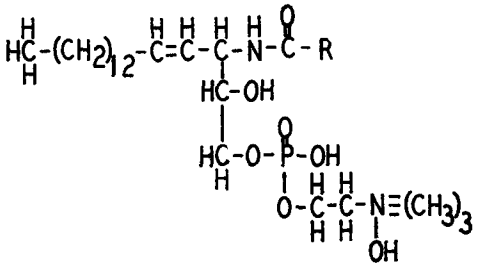
Before proceeding with a discussion of the functions of the phospholipids in the animal body, it is perhaps advisable to review very briefly their chemical nature. At the present time, three distinct types of phospholipids, the lecithins, the cephalins and the sphingomyelins, are recognized as occurring in mammals on which, thus far, most of the work has been done. The general formulae are as follows:



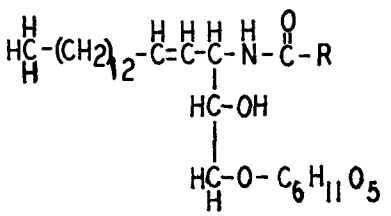
Lecithins



Cephalins



Sphingomyelins



Cerebrosides