A joint meeting of the Nutrition Society and Sociedad Española de Nutrición was held at the University of Navarra, Pamplona, Spain on 8–11 September 1999

2nd Plenary Session: 'Body-weight balance and regulation'

Role of substrate utilization and thermogenesis on body-weight control with particular reference to alcohol*

Yves Schutz
Institute of Physiology, Faculty of Medicine, University of Lausanne, Rue du Bugnon 7, CH-1005 Lausanne, Switzerland

Alcohol (ethanol; EtOH) provides fuel energy to the body (29·7 kJ (7·1 kcal)/g, 23·4 kJ (5·6 kcal)/ml), as do other macronutrients, but no associated essential nutrients. The thermogenic effect of EtOH (on average 15 % of its metabolizable value) is much greater than that of the main substrates utilized by the body, i.e. fat and carbohydrates (CHO), suggesting a lower net efficiency of energy utilization for EtOH than for fat and CHO. EtOH cannot be stored in the body and is toxic, so that there is an obligatory continuous oxidation of EtOH and it becomes the priority fuel to be metabolized. In contrast to CHO, its rate of oxidation does not depend on the dose ingested. As with CHO intake, it engenders a shift in postprandial substrate utilization (decrease in fat oxidation), but by a non-insulin-mediated mechanism. A limited amount of EtOH can be converted to fatty acids by hepatic *de novo* lipogenesis (as occurs with high levels of CHO feeding) from acetate production, which inhibits lipolysis in peripheral tissues. There is no evidence that EtOH consumed under normoenergetic conditions (i.e. isoenergetically replacing CHO or fat) leads to greater body fat storage than fat or CHO. However, there is still a lack of experimental studies on the influence of EtOH on the level of spontaneous physical activity in man. This effect may well depend on the dose of EtOH consumed as well as other intrinsic factors.

Energy metabolism: Thermogenesis: Thermic effect of alcohol

Alcohol (ethanol; EtOH) contributes a significant proportion of the total energy intake in many countries. International studies indicate that the average *per capita* consumption of EtOH is of the order of 10–30 g/d, representing about 3–9 % of the daily energy intake (Westerterp *et al*. 1999). Epidemiological data generally show that EtOH is usually additional to the normal diet in moderate consumers (Camargo *et al*. 1987; Westerterp *et al*. 1999), whereas it largely substitutes for food intake in heavy drinkers (Thomson *et al*. 1988).

Chronic EtOH intake has a variety of toxic effects on body systems which have been well described (Lieber, 1993). Although moderate EtOH consumption seems to have a protective effect on CHD, this substrate is associated with an increased risk of chronic disease in adults (James & Ralph, 2000). On the basis of the lack of an epidemiological relationship between total EtOH consumption in non-alcoholic individuals and body weight (or BMI), it has been concluded, surprisingly, that EtOH energy does not count (Lieber, 1991; Westerterp, 1995). In addition, it is rather surprising that, as in certain epidemiological studies (Meyer *et al*. 1999), the results of simple subjective evaluation of EtOH consumption through a mailed questionnaire, combined with the collection of anthropometric factors (also obtained by mail), have been used to assess whether EtOH constitutes a risk factor for weight change and subsequent obesity (Suter *et al*. 1997)!

Today, the incidence of overweight and obesity appears to be increasing rapidly in most countries of the world, clearly demonstrating that the primary etiological factor of obesity development comes from environmental factors and behavioural changes (i.e. nutritional and physical activity factors) rather than from genetic factors. Among the nutritional influences on the regulation of body weight, high-energy foods (McCrory *et al*. 2000), elevated total fat intake, as well as a high value for exogenous fat : complex CHO, may play a role (Astrup *et al*. 1995). Obviously these

Abbreviations: CHO, carbohydrate; EtOH, alcohol (ethanol); MEOS, microsomal ethanol oxidizing system

Corresponding author: Dr Yves Schutz, fax +41 21 692 55 05, email Yves.Schutz@iphysiol.unil.ch

*The other papers presented at this meeting were published in *Proceedings of the Nutrition Society* (2000) **59** no. 3.

Downloaded from https://www.cambridge.org/core. University of Basel Library, on 11 Jul 2017 at 09:29:51, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0029665100000744

few isolated factors do not explain why the prevalence and incidence of obesity are rising in industrialized and emerging countries, but possibly a combination of factors (acting probably synergistically) may be responsible. The fall in spontaneous and work-related physical activity is undoubtedly involved, since it is known to have an important impact on body-weight regulation over the long term.

Whether or not the consumption of EtOH constitutes an additional risk factor in this context remains an open question. It has been hypothesized that EtOH may be involved in the development of excess body weight, primarily due to its effects on substrate oxidation (Suter *et al*. 1992). The present short review will mainly consider the metabolic effect of exogenous EtOH *v.* CHO intakes on substrate oxidation and storage, and hence on potential body-weight change.

Obesity, defined as an excess of body fat for size, results from a chronic state of positive fat balance, leading to triacylglycerol accumulation in adipose tissue. One logical and objective approach for evaluating the extent to which EtOH intake favours body-fat gain and weight gain can be considered on the basis of the potential influence of EtOH intake on overall fat balance (Schutz, 1999). The physiological fat balance equation can be written as:

Fat balance = (exogenous fat intake + endogenous net fat synthesis) − (total fat oxidation).

Endogenous fat synthesis corresponds to the process of *de novo* lipogenesis from EtOH, and total fat oxidation represents the sum of exogenous + endogenous fat oxidation. For simplicity, fat oxidation is considered separately from CHO oxidation, although it should be realized that fat and carbohydrate oxidation are not mutually independent (Frayn & Whitley, 1997). Using this simple equation, it can be anticipated that EtOH consumption constitutes a potential risk factor for body fat change, depending on the extent to which EtOH influences fat balance by the following factors:

1. passive overconsumption of energy in the form of fat when EtOH is co-ingested with food, i.e. increase in exogenous fat;
2. magnitude of thermogenesis of EtOH, i.e. net efficiency of energy utilization in intermediary metabolism;
3. decrease in total fat oxidation in the presence of EtOH and potential influence of EtOH on endogenous fat synthesis (*de novo* lipogenesis).

Effect of co-ingestion of alcohol on spontaneous energy (fat) intake

This topic has been reviewed by Tremblay (1999). When EtOH is consumed together with food it does not suppress the intake of other macronutrients taken in parallel, in order to compensate for its own energy value (Westerterp-Plantenga & Verwegen, 1999). In social drinkers EtOH is generally additional to the diet, and therefore promotes spontaneous overfeeding, particularly if the diet is rich in fat (Tremblay *et al*. 1995; Poppitt *et al*. 1996), although there are some exceptions (Foltin *et al*. 1993). Thus, the suppressive effect of EtOH on fat oxidation (described later, p. 513) is further amplified in the presence of exogenous fat intake, indicating that the combination of EtOH with fat is undesirable for body-weight maintenance.

Tremblay (1999) tested, under acute conditions, the potential effect of EtOH consumption on the subsequent suppression of energy intake under *ad libitum* conditions; a high-fat appetizer combined with EtOH engendered a net increase in total energy intake as compared with a low-fat appetizer of the same weight and energy density but containing no EtOH. It seems that in terms of control of substrate intake EtOH is not adequately 'sensed' as such by the body, perhaps because there is no form of tissue storage of EtOH in the postprandial phase (in contrast to CHO), except the quantitatively limited conversion into fatty acids (see p. 513).

To summarize, EtOH consumption does not have the potential to induce an equivalent reduction in spontaneous food intake. The high-fat diet seems to further disrupt the control of food intake when EtOH is co-ingested. The control of appetite with habitual EtOH intake in social drinkers remains an open question. Whether or not spontaneous overfeeding (even of a small magnitude) consistently occurs before satiety is reached when EtOH is integrated into a meal (or consumed before a meal) needs further study.

Thermogenesis of alcohol

The gross energy of EtOH is 29·7kJ (7·1kcal)/g and, due to the fact that the breath, sweat and urinary losses of EtOH are small, it is almost identical to its metabolizable energy value. Ingestion of macronutrients leads to an increase in heat production (postprandial thermogenesis or thermic effects of food) when exogenous substrates (including EtOH) are processed in intermediary metabolism and when the macronutrients are stored within the body tissues. The net efficiency of fuel utilization can be predicted from a knowledge of the efficiency of the biochemical pathways involved, or from measurement of the thermogenic response to acute substrate ingestion by indirect calorimetry. Thus, two approaches are possible:

1. stoichiometric calculations;
2. assessment of EtOH-induced thermogenesis.

Stoichiometric calculations are obtained from the ATP requirements, based on the biosynthetic and metabolic transformation pathways of the substrate, multiplied by the energy equivalent of ATP. This approach provides a 'minimal' value, since all the associated energetic costs incurred cannot be easily accounted for in this theoretical calculation.

Low doses of EtOH are mostly metabolized by the alcohol dehydrogenase pathway, whereas high EtOH doses leading to high blood EtOH concentrations are mainly metabolized in the microsomal EtOH oxidizing system (MEOS; Lieber, 1993); both metabolic pathways leading to the same intermediate metabolite, i.e. acetate production. The biochemical energetic efficiency of these two pathways based on ATP utilization is substantially different; by stoichiometry the thermogenic response of EtOH is

Downloaded from https://www.cambridge.org/core. University of Basel Library, on 11 Jul 2017 at 09:29:51, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0029665100000744

estimated to be 12 % of its energy value for the aldehyde dehydrogenase pathway and 27 % for the MEOS, indicating that the remaining part (i.e. 88 % and 73 % respectively) of the EtOH energy can be available to the body.

A number of experimental studies on the acute thermogenic effect of EtOH have been published in the last three decades (Rosenberg & Durnin, 1978; Weststrate *et al*. 1990, Suter *et al*. 1992, 1994; Sonko *et al*. 1994; Murgatroyd *et al*. 1996; Westerterp *et al*. 1999). These studies are somewhat controversial, since various experimental designs and conditions (duration of measurements, single bolus dose *v*. intravenous injection, type of subjects studied, gender etc.) and various doses as well as different EtOH presentations have been employed. From a summary table published by Westerterp *et al*. (1999) it can be seen that EtOH consumption results in a rise in heat production ranging from 2 to 4 % in thermogenesis studies of short duration (less than 1·5 h), and from 14 to 17 % in studies of longer duration (more than 4 h). In our study (Suter *et al*. 1994) we found that the EtOH-induced thermogenesis measured over the whole day averaged 22 % of the energy content of the ingested EtOH, whereas, as expected, it was lower (17 %) when the immediate response was assessed over 4 h with a single dose of EtOH. The thermogenic effect of EtOH was confined to the daytime period when EtOH was being metabolized, strongly supporting the concept that the thermic effect of EtOH is related to its metabolism. The values for EtOH-induced thermogenesis have been mostly reported for healthy non-alcoholic individuals (Rosenberg & Durnin, 1978; Weststrate *et al*. 1990; Suter *et al*. 1992, 1994; Sonko *et al*. 1994; Murgatroyd *et al*. 1996), so that the response may be different in subjects regularly consuming EtOH in excessive amounts and/or in patients with EtOH-induced pathology of the liver. In chronically alcoholic subjects the net efficiency of utilization of EtOH energy may be lower, as explained earlier, due to various mechanisms, in particular the preponderance of the MEOS, an induced hyperthyroid state or an impaired oxidative phosphorylation, as well as the effect of mitochondrial damage due to the toxic effect of EtOH and the intermediate compound acetaldehyde.

To summarize, the thermogenic effect of acute doses of EtOH assessed in resting healthy subjects represents approximately 15 % of the EtOH energy ingested (Sonko *et al*. 1994; Suter *et al*. 1994; Murgatroyd *et al*. 1996). This value is higher than the thermogenic effect of either CHO (5–8 % of energy value) or fat (2–3 %), but is within the range of the calculated theoretical thermogenesis of EtOH (12 % for the aldehyde dehydrogenase pathway and 27 % for the MEOS). There is little evidence that a large 'luxus consumption' exists with EtOH ingestion (Lands & Zakhari, 1991) and that the energy associated with EtOH therefore 'does not count' (Lieber, 1991).

Effect of alcohol on fat oxidation and on *de novo* lipogenesis

One major issue for body-weight regulation is the extent to which EtOH spares other substrates from oxidation. As schematically shown in Fig. 1, substrate oxidation (which provides ATP) depends on the rate of energy expenditure of the individual; four substrates (if one includes EtOH) provide energy through their individual rates of combustion, each having different RQ (the lowest being EtOH and the highest being CHO) and slightly different energy equivalents for ATP. Metabolic interconversions of substrates are possible through gluconeogenesis (from glucogenic amino acids, glycerol and lactate) and *de novo*

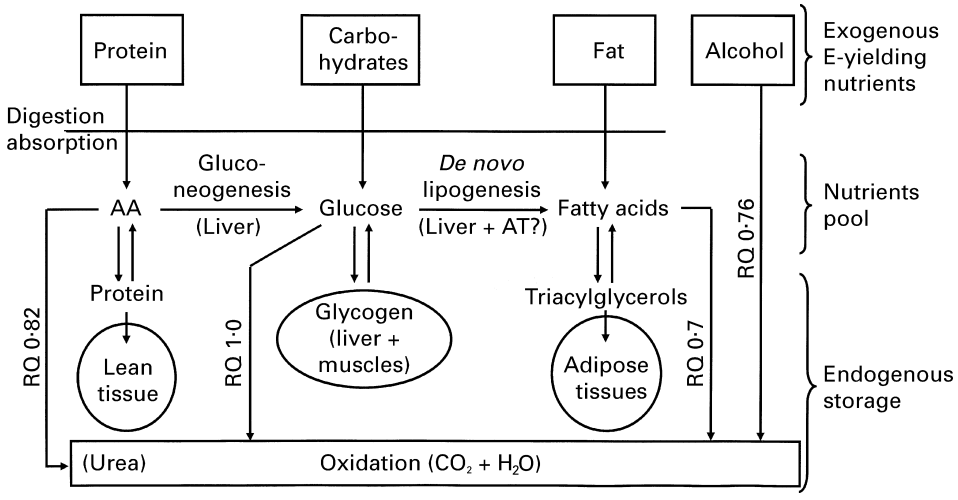

Fig. 1. Schematic simplified overview of the fate of exogenous substrates within the body and their metabolic interconversion by gluconeogenesis and *de novo* lipogenesis. Endogenous substrates are stored in different body pools, whose size and energy (E) density (kJ/g) are markedly different among the tissues storing these substrates. Alcohol, distributed in total body water after consumption, does not possess any storing pool as such, and only a limited proportion is converted into fatty acids by *de novo* lipogenesis. Note that endogenous substrates are constantly turning over at controlled rates which vary according to the nature of substrates, the type of organ and tissues considered and the nature and level of exogenous intake. AA, amino acids; AT, adipose tissue.

Downloaded from https://www.cambridge.org/core. University of Basel Library, on 11 Jul 2017 at 09:29:51, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0029665100000744

lipogenesis (from glucose and EtOH). Basically, in the studies in which the metabolic effect of EtOH has been explored, two types of experimental designs have been used: (1) isoenergetic substitution of EtOH for one or more of the other macronutrients (unchanged energy intake); (2) addition of EtOH to a maintenance diet (positive energy balance).

Comparison of EtOH fuel with CHO fuel is of some interest since CHO and EtOH are both rapidly utilized substrates, but compared with CHO the three key features of EtOH metabolism are: (1) the oxidation occurs predominantly in the liver; (2) there is no immediate storage mechanism in the body (such as glycogen for carbohydrate); (3) there is no feedback control rate of EtOH oxidation (as is the case for glucose). The key features of the metabolism of EtOH as compared with CHO are presented in Table 1. CHO contribute a large percentage of the total energy intake (typically more than 50 %), whereas this is not the case for EtOH in non-alcoholic individuals. CHO are a heterogeneous group of substrates consumed as solid food or drinks, whereas EtOH comprises a single molecule consumed mostly as a beverage, although sometimes mixed with food (e.g. in liqueur chocolates or cheese fondue). While EtOH is distributed in total body water, glucose is confined to extracellular fluids. There is no possible way to store exogenous EtOH in the body except by transforming its intermediate product (acetate) into fatty acids by hepatic *de novo* lipogenesis. In contrast, CHO can be stored rapidly in the postprandial phase in the form of hydrated glycogen in liver and muscles.

There are substantial differences among substrates in their energy value, magnitude of postprandial thermogenesis and hierarchy of substrate oxidation in the postprandial phase (Fig. 2). In addition, the satiating capacity of protein is greater than that of CHO and that of fat and EtOH. Although the notion that there is a hierarchy in the utilization of EtOH as compared with other substrates makes sense, it seems difficult to conceive that EtOH would totally suppress the oxidation of another substrate. Since there is a maximum oxidation rate of EtOH of approximately 0·1 g/kg fat-free mass per h (i.e. 2·9 kJ (0·7 kcal)/kg fat-free mass per h), approximately 50 % of the resting energy expenditure can be accounted for by EtOH oxidation (and substantially less when related to total energy expenditure, which includes physical activity). This factor indicates that, potentially, EtOH can transiently spare the oxidation of other substrates up to a maximum level of half the resting metabolic rate. This situation contrasts with the effect of CHO ingestion on CHO utilization and fat sparing in the postprandial phase.

A review of some experimental studies shows that the overall sparing of substrate in the presence of EtOH consumption varies among studies (Schutz, 1995) and types of designs. For CHO it ranges from 15 % for 'balanced' substitution studies to 43 % for complete CHO substitution. For fat it is approximately 30 % for both 'balanced' and complete substitution studies with one exception, where no sparing of fat was observed (Sonko *et al*. 1994). The effect of EtOH consumption on substrate oxidation is generally that both fat and CHO oxidation are reduced depending on whether it is a total or 'balanced substitution'. Currently, there is no consensus as to whether EtOH spares fat only, or a combination of fat and CHO, from oxidation. It should be mentioned that the interpretation of the effect of EtOH intake on the co-oxidation of other substrates may be difficult, since when EtOH totally isoenergetically replaces one substrate in the meal (e.g. complete substitution for CHO, such as in the study of Schutz, 1995) the absence of exogenous CHO as such (and not necessarily the specific effect of EtOH substitution) will engender an adaptive response aimed at lowering CHO oxidation in an attempt to reach a new CHO balance.

Naturally labelled substrates (e.g. rum for EtOH and sugar cane and maize for CHO) can be used to assess the pattern of change in exogenous oxidation by the measurement of the isotopic abundance of breath $^{13}CO_2$. Comparing acute CHO *v*. EtOH ingestion, CHO resulted in a sharp rise in ^{13}C enrichment in breath with a peak at 3 h, followed by a subsequent decline (Schutz, 1995). This finding is consistent with the rapid increase in CHO oxidation during the postprandial phase. With EtOH ingestion there was a completely different $^{13}CO_2$ breath pattern, with a slow continuous rise in $^{13}CO_2$ up to 8 h, consistent with the constant rate of hepatic EtOH oxidation.

Table 1. Major differences in the metabolism of carbohydrate (CHO) *v.* alcohol (EtOH) within the body

CHO	EtOH
Rapid substrate	Rapid substrate
High RQ (1·0)	Low RQ (0·66)
Energy density 16·7 kJ (4 kcal)/g	Energy density 29·7 kJ (7·1 kcal)/g 23·4 kJ (5·6 kcal)/ml)
No loss in urine and breath	Negligible losses in urine and breath
Source of energy for all cells (glucose)	Source of energy for liver only (acetate), initially
Endogenous synthesis and exogenous storage (as glycogen)	No endogenous synthesis and limited delayed storage as fatty acid
CHO ingestion leads to an increase in the rate of CHO oxidation and storage (dose dependent curve)	EtOH ingestion fails to increase the rate of EtOH oxidation (flat dose response, maximum response)
Fat sparing	Fat and carbohydrate sparing
Protein sparing	Increased protein flux

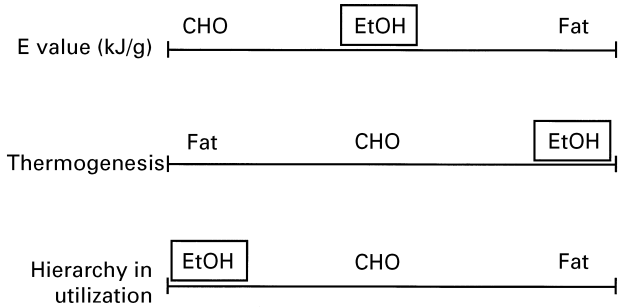

Fig. 2. Contrasting features of the energy (E) value (low to high), postprandial thermogenesis (an index of net inefficiency of energy utilization) and hierarchy in metabolic utilization (highest to lowest) of carbohydrate, fat and ethanol (EtOH).

Downloaded from https://www.cambridge.org/core. University of Basel Library, on 11 Jul 2017 at 09:29:51, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0029665100000744

EtOH consumed in addition to a normal diet is expected to lead to fat storage (as with excess CHO intake), since it spares fat from oxidation. Fig. 3 gives an overview of the basic mechanisms, explaining the increase in fat storage when EtOH is consumed in excess of energy requirements. Any substrate (CHO, fat, protein or EtOH) taken in excess of energy requirement over a prolonged period of time will ultimately lead to fat accumulation after a transitory period during which there is an adaptation in substrate utilization, which depends on the type and amount of substrates considered as well as endogenous factors. As mentioned previously, the key issue is to know which substrate is the easiest to consume spontaneously in excess in real life, EtOH, fat or both!

De novo lipogenesis

The nutritional conditions under which *de novo* lipogenesis has been measured in healthy individuals have been reviewed by Hellerstein (1999), and include acute studies with a single massive CHO load, isoenergetic and hyperenergetic high-CHO low-fat diets. The effect of potentially lipogenic substrates (such as fructose) have also been investigated. In terms of individual characteristics the effect of gender, menstrual cycle and excess body weight have also been studied. Mass isotopomer distribution analysis after isotopic labelling of metabolic precursors combined with indirect calorimetry permits the assessment of both whole-body lipid oxidation and hepatic *de novo* lipogenesis (Hellerstein, 1999). This technique has been recently used in a study of the effect of EtOH on *de novo* lipogenesis (Siler *et al*. 1999). Acute EtOH ingestion at a low dose (24 g) was shown to activate *de novo* lipogenesis in the liver of healthy male subjects. EtOH is first converted to acetate in the liver and, once released into the plasma, it is oxidized in proportion to its plasma concentration (Shelmet *et al*. 1988) and leads to an inhibition of lipolysis in adipose tissue, as evidenced by a decrease in free fatty acid and glycerol release. Whole-body lipid oxidation decreased by more than half in the presence of EtOH consumption.

The study of Siler *et al*. (1999) constitutes the first evidence of a stimulation of hepatic *de novo* lipogenesis by EtOH intake in human subjects. However, it should be noted that although the fractional contribution of *de novo* lipogenesis to VLDL-triacylglycerol-palmitate synthesis rose substantially (from 2 to 30 %), the absolute rate of lipogenesis in relation to the dose of EtOH ingested was on average less than 5 %. As a result, the major quantitative fate of exogenous EtOH consumption was complete oxidation to CO_2 and H_2O.

Other metabolic effects of alcohol

Acute administration of EtOH stimulates the sympathetic nervous system and alters hepatic glucose metabolism; it decreases blood glucose by decreasing hepatic glucose production (Delarue *et al*. 1997) through inhibition of liver gluconeogenesis. EtOH consumption also influences insulin sensitivity, but this effect depends on the amount of EtOH consumed (Razey *et al*. 1992). The effect of EtOH on protein metabolism has, up to the present time, received little attention and has not been thoroughly investigated in human subjects. In a classic well-controlled study performed more than two decades ago in a metabolic ward, isoenergetic replacement of food energy by EtOH, given in the form of wine or pure EtOH, resulted in a persistent negative N balance, suggesting an effect of EtOH on fat-free-mass losses (MacDonald & Margen, 1976). More recently, it was demonstrated that elevation of blood EtOH following social drinking increased leucine turnover (Berneis *et al*. 1997) and influenced hepatic protein metabolism (De Feo *et al*. 1995; Volpi *et al*. 1998). The effect of EtOH consumption on plasma leptin has not been investigated yet in human subjects.

Conclusions

First, analysis of the statistical relationship between EtOH intake and body weight (or BMI) derived from epidemiological studies cannot be used to judge whether EtOH

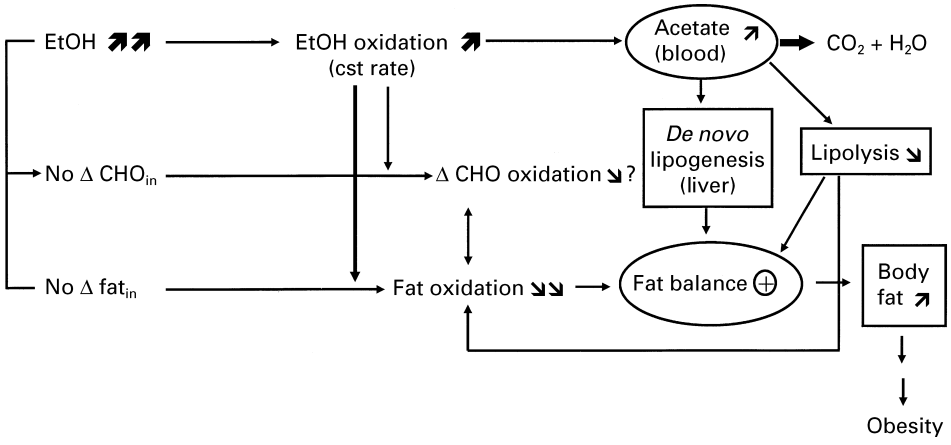

Fig. 3. Effect of exogenous alcohol (EtOH) consumption added to a mixed diet on fat utilization and *de novo* lipogenesis in man. ΔCHO_{in}, Δfat_{in}, change in carbohydrate and fat intake respectively; ΔCHO oxidation, change in carbohydrate oxidation; ⊕, positive; ↗↗,↗, increase which was relatively higher and lower respectively; ↘↘,↘, decrease which was relatively higher and lower respectively; cst, constant.

Downloaded from https://www.cambridge.org/core. University of Basel Library, on 11 Jul 2017 at 09:29:51, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0029665100000744

constitutes a risk factor for weight change. Muller (1999), highlighting that many studies are poorly controlled, recently pointed out that we still ignore the precise effect of EtOH on body weight despite one century of research. EtOH is utilized as a source of energy by the body and it should be taken into account in the energy budget: EtOH energy does count as with other metabolic fuels, but with a net efficiency of energy utilization (i.e. a thermogenic effect) intermediate between the values for CHO and protein. In addition, acute EtOH intake not only increases heat production, but, in contrast to other fuels, also leads to increased peripheral heat dissipation, thus resulting in a transitory negative thermal balance and a drop in body core temperature.

EtOH intake failed to modify the level of energy intake (in particular fat) but affects the rate of substrate oxidation by decreasing the oxidation of fat (and of CHO in certain circumstances). When EtOH is ingested in conjunction with a meal it rapidly becomes the priority fuel and temporarily displaces fat and CHO from oxidation, indicating a sparing effect. However, when the consumption of EtOH is taken under strict isoenergetic conditions, such as those in experimental studies where the total energy intake is 'clamped', there is only a transitory effect of EtOH on fat oxidation. After a certain time (i.e. over a 24 h period) the body reaches a new steady-state at which the proportion of macronutrients and EtOH oxidized corresponds to that ingested. Future studies should concentrate on the long-term effect of EtOH ingestion on energy, substrate and thermal balances. In contrast to the early feeding trials in which the effect of EtOH was examined, careful assessment of body composition should be also included. One component which has not been studied previously is spontaneous physical activity. Whether or not EtOH leads to a change in physical activity remains to be investigated. It seems essential to gain more information on the effect of EtOH ingestion taken in 'physiological' amounts and in a normal vehicle (wine, beer etc.) on total daily energy expenditure and spontaneous physical activity under free-living conditions.

References

Astrup A, Buemann B, Gluud C, Bennett P, Tjur T & Christensen N (1995) Prognostic markers for diet-induced weight loss in obese women. *International Journal of Obesity* **19**, 275–278.

Berneis K, Ninnis R, & Keller U (1997) Ethanol exerts acute protein-sparing effects during postabsorptive but not during anabolic conditions in man. *Metabolism* **46**, 750–755.

Camargo CA, Vranizan KM, Dreon DM, Frey-Hewitt B & Wood PD (1987) Alcohol, calorie intake, and adiposity in overweight men. *Journal of the American College of Nutrition* **6**, 271–278.

De Feo P, Volpi E, Lucidi P, Cruciani G, Monacchia F, Reboldi G, Santeusanio F, Bolli GB & Brunetti P (1995) Ethanol impairs post-prandial hepatic protein metabolism. *Journal of Clinical Investigation* **95**, 1472–1479.

Delarue J, Schneiter P, Henry S, Cayeux C, Jéquier E & Tappy L (1997) Effects of adrenergic blockade on hepatic glucose production during ethanol administration. *Clinical Physiology* **17**, 509–521.

Foltin RW, Kelly TH & Fischman MW (1993) Ethanol as an energy source in humans: comparison with dextrose-containing beverages. *Appetite* **20**, 95–110.

Frayn KN & Whitley HA (1997) Carbohydrate and fat balance: separate existences or an intimate relationship? *European Journal of Clinical Nutrition* **51**, 789.

Hellerstein MK (1999) De novo lipogenesis in humans: metabolic and regulatory aspects. *European Journal of Clinical Nutrition* **53**, S53–S65.

James WPT & Ralph A (2000) Alcohol: its metabolism and effects. In *Human Nutrition and Dietetics*, pp. 121–135 [JS Garrow, WPT James and A Ralph, editors]. Edinburgh: Churchill Livingstone.

Lands WE & Zakhari S (1991) The case of the missing calories. *American Journal of Clinical Nutrition* **54**, 47–48.

Lieber CS (1991) Perspectives: do alcohol calories count? *American Journal of Clinical Nutrition* **54**, 976–982.

Lieber CS (1993) A personal perspective on alcohol, nutrition, and the liver. *American Journal of Clinical Nutrition* **58**, 430–442.

McCrory MA, Fuss PJ, Saltzman E & Roberts SB (2000) Dietary determinants of energy intake and weight regulation in healthy adults. *Journal of Nutrition* **130**, 276S–279S.

MacDonald JT & Margen S (1976) Wine versus ethanol in human nutrition 1. Nitrogen and calorie balance. *American Journal of Clinical Nutrition* **29**, 1093–1103.

Meyer R, Suter PM & Vetter W (1999) Alcohol-risk factor for overweight. *Schweizerische Rundschau für Medizin Praxis* **88**, 1555–1561.

Muller MJ (1999) Alcohol and body weight. *Zeitschrift für Gastroenterologie* **37**, 33–43.

Murgatroyd PR, van de Ven ML, Goldberg GR & Prentice AM (1996) Alcohol and the regulation of energy balance: overnight effects on diet-induced thermogenesis and fuel storage. *British Journal of Nutrition* **75**, 33–45.

Poppitt SD, Eckhardt JW, McGonagble J, Murgatroyd PR & Prentice A (1996) Short-term effects of alcohol consumption on appetite and energy intake. *Physiology and Behavior* **60**, 1063–1070.

Razay G, Heaton KW, Bolton CH & Hughes AO (1992) Alcohol consumption and its relation to cardiovascular risk factors in British women. *British Medical Journal* **304**, 80–83.

Rosenberg K & Durnin JV (1978) The effect of alcohol on resting metabolic rate. *British Journal of Nutrition* **40**, 293–298.

Schutz Y (1995) Alcohol calories count the same as other calories. *International Journal of Obesity* **19**, Suppl. 2, 12–13.

Schutz Y (1999) Does the conversion of carbohydrate to fat contribute to obesity in humans? *Obesity Matters* **2**, 18–22.

Shelmet JJ, Reichard GA, Skutches CL, Hoeldtke RD, Owen OE & Boden G (1988) Ethanol causes acute inhibition of carbohydrate, fat, and protein oxidation and insulin resistance. *Journal of Clinical Investigation* **81**, 1137–1145.

Siler SQ, Neese RA & Hellerstein MK (1999) De novo lipogenesis, lipid kinetics, and whole-body lipid balances in humans after acute alcohol consumption. *American Journal of Clinical Nutrition* **70**, 928–936.

Sonko BJ, Prentice AM, Murgatroyd PR, Goldberg GR, van de Ven ML & Coward WA (1994) Effect of alcohol on postmeal fat storage. *American Journal of Clinical Nutrition* **59**, 619–625.

Suter PM, Hasler E & Vetter W (1997) Effects of alcohol on energy metabolism and body weight regulation: is alcohol a risk factor for obesity? *Nutrition Reviews* **55**, 157–171.

Suter PM, Jéquier E & Schutz Y (1994) Effect of ethanol on energy expenditure. *American Journal of Physiology* **266**, R1204–R1212.

Suter PM, Schutz Y & Jéquier E (1992) The effect of ethanol on fat storage in healthy subjects. *New England Journal of Medicine* **326**, 983–987.

Thomson M, Fulton M, Elton RA, Brown S, Wood DA & Olivier F (1988) Alcohol consumption and nutritient intake in middle-aged

Downloaded from https://www.cambridge.org/core. University of Basel Library, on 11 Jul 2017 at 09:29:51, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0029665100000744

Scottish men. *American Journal of Clinical Nutrition* **47**, 139–145.
Tremblay A (1999) The effects of exercise and alcohol intake on energy balance and food intake. In *Progress in Obesity Research*, pp. 423–429 [BG Ailhaud, editor]. London: John Libbey & Company Ltd.
Tremblay A, Buemann B, Thériault G & Bouchard C (1995) Body fatness in active individuals reporting low lipid and alcohol intake. *European Journal of Clinical Nutrition* **49**, 824–831.
Volpi E, Lucidi P, Cruciani G, Monacchia F, Santoni S, Reboldi G, Brunetti P, Bolli GB & De Feo P (1998) Moderate and large doses of ethanol differentially affect hepatic protein metabolism in humans. *Journal of Nutrition* **128**, 198–203.
Westerterp KR (1995) Alcohol calories do not count the same as other calories. *International Journal of Obesity* **19**, Suppl. 2, 14–15.
Westerterp KR, Prentice AM & Jéguier E (1999) Alcohol and body weight. In *Health Issues Related to Alcohol Consumption*, pp. 103–123 [I Macdonald, editor]. Oxford: Blackwell Press.
Westerterp-Plantenga MS & Verwegen CR (1999) The appetizing effect of an aperitif in overweight and normal-weight humans. *American Journal of Clinical Nutrition* **69**, 205–212.
Weststrate JA, Wunnink I, Deurenberg P & Hautvast JG (1990) Alcohol and its acute effects on resting metabolic rate and diet-induced thermogenesis. *British Journal of Nutrition* **64**, 413–425.

© Nutrition Society 2000

Downloaded from https://www.cambridge.org/core. University of Basel Library, on 11 Jul 2017 at 09:29:51, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0029665100000744