Free Rad. Res. Comms., Vol. 4, No. 2, pp. 99–103

Printed in Great Britain

THE METABOLISM OF LOW MOLECULAR WEIGHT HYDROCARBON GASES IN MAN

ANDRE M. VAN RIJ* and CHRIS R. WADE

Department of Surgery, Otago Medical School, Dunedin, New Zealand

(Received February 17th 1987)

The metabolism of ethane and pentane in man is demonstrated to occur from the uptake of an enriched atmosphere of these gases in a rebreathe spirometer circuit. Dithiocarb, an inhibitor of alkane metabolism, reduced uptake and increased the respiratory excretion of these gases. This effect was least marked for the slowly metabolised ethane. Therefore the endogenous production of ethane as measured by respiratory excretion is less affected. However pentane is rapidly metabolised and this limits the use of simple respiratory excretion of pentane as a measure of *in vivo* lipid peroxidation.

KEY WORDS: Pentane, ethane, lipid peroxidation, dithiocarb.

INTRODUCTION

The respiratory excretion of ethane and pentane has been used as a measure of *in vivo* lipid peroxidation.[1] These volatile low molecular weight hydrocarbon gases are products of the peroxidation and breakdown of (n-3) and (n-6) polyunsaturated fats respectively.[2] Studies using small animals housed in enclosed chambers have suggested that ethane and pentane are excreted quantitatively with lipid peroxidation in the breath. This method has now been used to investigate the effects of a variety of nutrients and drugs on lipid peroxidation.[3,4] The application of this in man has been recommended and attempted by some workers.[5,7] However, a difficulty which has been largely ignored in the interpretation of the results of the respiratory excretion of ethane and pentane, is the possible metabolism of these relatively inert gases. This has been demonstrated to occur in the rat model predominantly in the liver and is therefore greatly influenced by changes in liver function.[8]

In man, the focus of interest in studies of lipid peroxidation includes the action of drugs, nutrients and disease states. These may however significantly affect liver metabolism, for example, the effect of alcohol on liver metabolism and the study of lipid peroxidation induced by alcohol. Furthermore, the low rate of production and the high ambient levels of these gases present in the environment ideally necessitate a long sampling period.[9] This may be achieved either by the collection and extraction of large volumes of breath or by the use of a rebreathe system. In the latter approach particularly variations in metabolism would be critical.

For these reasons it has been necessary to determine whether low molecular weight hydrocarbons are metabolised in man and whether this can be measured to allow more meaningful assessment of ethane and pentane production.

*Correspondence to: Dr A.M. van Rij.

METHODS

The rate of metabolism of ethane and pentane in man was determined using a closed circuit rebreathe spirometer system.[9] Subjects were connected to the circuit through a two-way valve for periods up to two hours while the contained air was circulated by a motorised pump for complete mixing. At the beginning of the rebreathe period the ambient air in the spirometer circuit was enriched with a known mixture (45 nmol/l) of hydrocarbon gases (Alltech Associates, Deerfield, IL). Fifty millilitre samples of the rebreathed gases were removed in gas tight syringes at twenty minute intervals for analysis. The spirometer circuit and method of extraction, concentration and gas chromatographic analysis of these gases has been described previously.[9] In brief: the samples were concentrated by absorption at −130°C on Porasil-C (Alltech Associates). After desorption at 100°C, the gases were collected into a gas-tight syringe by flushing the column with 50 ml of N_2. C_2-C_5 hydrocarbons were measured on a Shimadzu R-1A gas chromatograph (Shimadzu, Tokyo, Japan) using a 3 m column

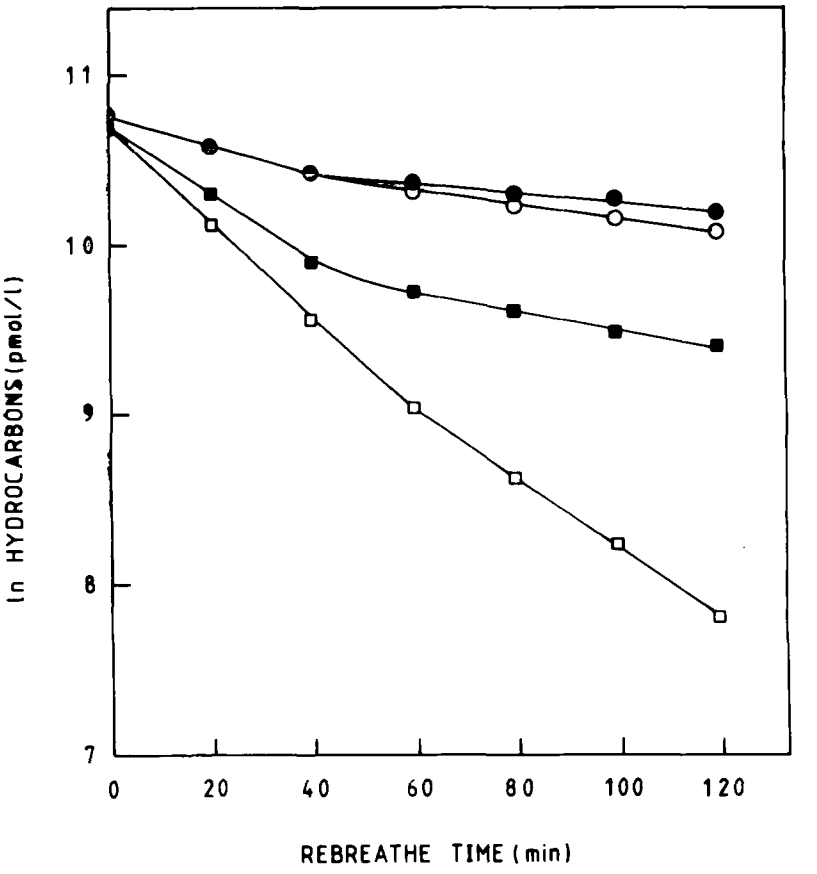

FIGURE 1 Ethane and pentane uptake over a two hour period from a rebreathe circuit containing 45 nmol/l hydrocarbon gases, before (Ethane ○, Pentane □) and after (Ethane ●, Pentane ■) dithiocarb administration to a single subject.

of n-octane/Porasil-C (Alltech Associates) and a flame ionisation detector. Separation was carried out at 25°C with an N_2 carrier gas flow of 20 ml/min. Following the intitial observations and to further confirm metabolism of these gases, the experiment was repeated after the oral administration of an inhibitor of hepatic alkane metabolism, diethyldithiocarbamate (dithiocarb, Dumex, Copenhagen, Denmark) 0.8 gm eight hourly for thirty-six hours.

Endogenous production of these hydrocarbons before and after the administration of Disulfarim was also measured using the method previously described by our group.[9] This includes a 1.5 hour preparatory equilibrating period breathing very low level hydrocarbon scrubbed air (< 0.1 pmol/l) to eliminate the effects of previous exposure to hydrocarbon contaminated environments.

RESULTS

The changes in the uptake of ethane and pentane in the rebreathe circuit over a two hour period are shown in Figure 1. The other gases propane and butane have intermediate profiles corresponding to their respective molecular weight. Logarithmic regressional analysis of the data shows that two exponential rate constants can be calculated for the gas uptakes.

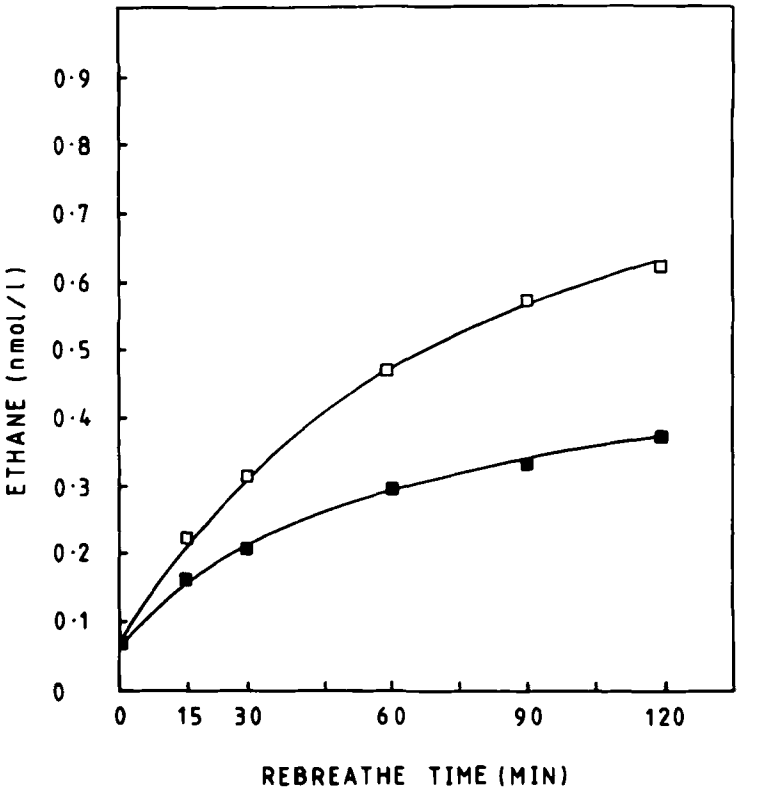

FIGURE 2 The respiratory excretion of ethane during a two hour rebreathe in a single subject before (■) and after (□) dithiocarb administration.

The first exponential is considered to reflect the early phase of rapid tissue uptake of the gases and is influenced predominantly by cardiac output, tissue blood flow and solubility coefficients, not unlike the distribution of some anaesthetic gases.[10] Only very rapid metabolism would be expected to be indicative of the metabolic rate. Consequently ethane metabolism is relatively slow ($T_{1/2}$ = 3.6 hours) while pentane is rapidly metabolised ($T_{1/2}$ = 45 minutes). Dithiocarb decreased the rate of gas uptake for all the gases as a result of decreased metabolism. This effect was more marked for pentane ($T_{1/2}$ = 2.0 hours) than for ethane ($T_{1/2}$ = 6.2 hours). The early pentane distribution was also affected presumably as a result of elevated tissue levels reached as a consequence of dithiocarb administration over the thirty-six hour period prior to rebreathing.

The effect of the inhibition of the metabolism and pentane was also clearly apparent on the endogenous production of these gases as measured by respiratory excretion over a two hour rebreathe (Figs 2 and 3). Ethane concentrations before and after dithiocarb administration were 370 pmol/l and 622 pmol/l respectively at the end of a two hour rebreathe. Similarly, pentane concentrations increased after dithiocarb treatment from 120 pmol/l to 1600 pmol/l.

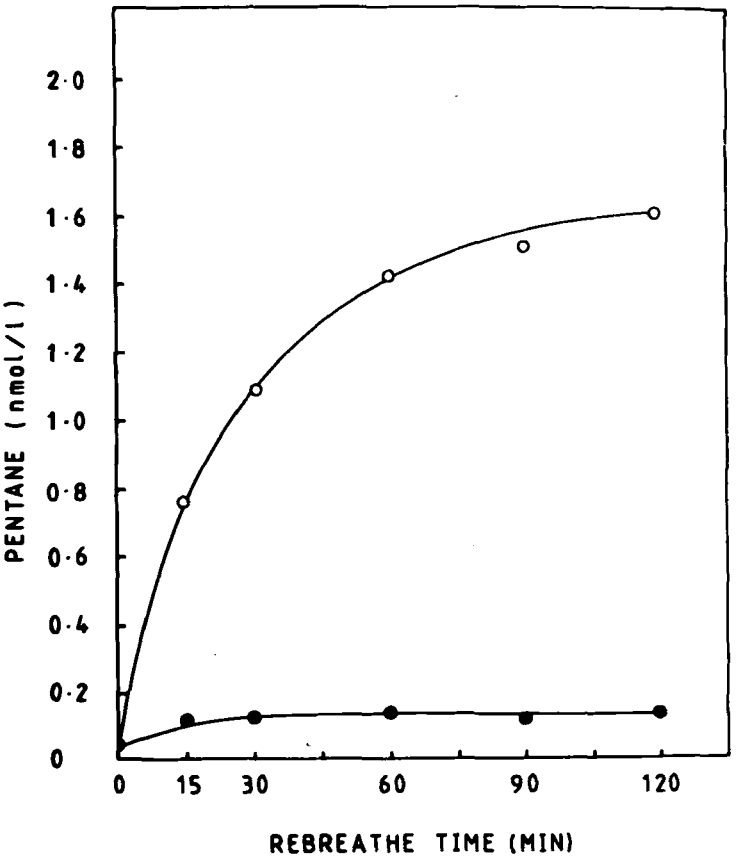

FIGURE 3 The respiratory excretion of pentane during a two hour rebreathe in a single subject before (●) and after (○) dithiocarb administration.

DISCUSSION

These observations demonstrate that low molecular weight hydrocarbons are metabolised in man. Our investigations suggest that this is probably via the hepatic mono-oxygenase system and by conversion to the correspoding alcohol and aldehyde and hence the effect of dithiocarb. Ethane metabolism in man is relatively slow and therefore endogenous production due to *in vivo* lipid peroxidation is less susceptible in individuals can reasonably be calculated from a respiratory excretion curve using the equation we have previously derived for ethane production.[9] For pentane the situation is more complicated as metabolism is rapid and this greatly affects the respiratory excretion, as shown by the fourteen-fold increase in pentane levels after dithiocarb treatment. Moreover, individual variation in metabolism may occur and the effects of drugs and diseases of interest must also be considered. This is unfortunate as pentane is derived from linoleic acid, the dominant (n-6) polyunsaturated fatty acid present in the body, and its production would be expected to more usefully reflect *in vivo* lipid peroxidation. To be able to measure pentane production in man the measurement of pentane metabolism is essential. Further investigations are in progress to provide a suitable derivation based on an inhalational pharmacokinetic model for the reliable measurement of pentane production as a measure of lipid peroxidation *in vivo* in man.

Acknowledgement

This work was supported by the New Zealand Medical Research Council.

References

1. Tappel, A.L. and Dillard, C.J. *In vivo* lipid peroxidation: measurement via exhaled pentane and protection by vitamin E. *Fed. Proc.*, **2**, 174–178, (1981).
2. Evans, C.D., List, G.R., Dolev, A.M.I. *et al.* Pentane from thermal decomposition of lipoperoxidase-derived products. *Lipids*, **2**, 432–434, (1967).
3. Kivits, G.A.A., Ganguli-Swarttouw, M.A.C.R. and Christ, E.J. The composition of alkanes in exhaled air of rats as a result of lipid peroxidation *in vivo*: Effects of dietary fatty acids, vitamin E and selenium. *Biochem. Biophys. Acta*, **665**, 559–570, (1981).
4. Burk, R.F., Ludden, T.M. and Lane, J.M. Pentane clearance from inspired air by the rat: Dependence on the liver. *Gastroenterol.* **84**, 138–142, (1984).
5. Dillard, C.J., Litov, R.E., Savin, W.M. *et al.* Effects of exercise, vitamin E and ozone on pulmonary function and lipid peroxidation. *J. Appl. Physiol.*, **48**, 927–932, (1978).
6. Prilipko, L.L., Orlox, O.N., Kagan, V.E. *et al.* Accumulation of gaseous lipid peroxidation products in the expired air in children during hyperbaric oxygenation. *Bull. Exp. Bio. Med.*, **96**, 1367–1369, (1984).
7. Moscarella, S., Caramelli, L., Mannaioni, P.E. *et al.* Effect of alcoholic cirrhosis on ethane and pentane levels in breath. *Boll. Soc. Ital. Sper.*, **60**, 527–533, (1984).
8. Frank, H., Hintze, T., Bimboes, D. *et al.* Monitoring lipid peroxidation by breath analysis: Endogenous hydrocarbons and their metabolic elimination. *Toxicol. Appl. Pharm.* **56**, 337–334, (1980).
9. Wade, C.R., Van Rij, A.M. *In vivo* lipid peroxidation in man as measured by the respiratory excretion of ethane, pentane and other low molecular weight hydrocarbons. *Analyt. Biochem.* **150**, 1–7, (1985).
10. Eger, II I.E.I. *Anaesthetic Uptake and Action.* Baltimore, 1981, pp 97–112.

Accepted by Dr. J.V. Bannister