KETONURIA IN THE ANTARCTIC: A DETAILED STUDY

By R. M. Lloyd

Abstract. A study was made of 11 healthy young men spending a year at a British station in the Antarctic. They partook of high- and low-fat diets, both at the station and in the field on manhauling or dog-sledge journeys. Measurements were made of energy expenditure and intake, and of the degree of cold exposure. Timed specimens of urine were collected each evening 2 hr. *post cibum* and the total ketone-body excretion rate was determined.

It was found that:

i. Polar sledgers may expend more than 7,000 kcal./day.
ii. The total ketone-body excretion rate for men at the station and not exposed to ketogenic factors was $3\cdot0 \pm 1\cdot2$ μmol./min.
iii. Energy expenditure, negative calorie balance and degree of exposure to cold were all positively and independently associated with total ketone-body excretion rates.
iv. There was no demonstrable relationship between daily intake of fat and ketonuria except when the subjects were in negative calorie balance. An intake of 285 g. of fat per day in the resting state did not produce ketosis.
v. There was no evidence of adaptation to sledging ketosis even after 7 months continuous sledging in the field.

Halley Bay (lat. 75°31′S., long. 26°44′W.) is the British Antarctic Survey's largest scientific station and during the year 1966–67 28 men wintered there. The station is buried, by the action of drifting snow, in the Brunt Ice Shelf. The weather in this area is very variable and temperatures range from −50° to 0° C.

Ketosis is a state of disordered metabolism of the body in which break-down of fat predominates and three "ketone" bodies accumulate, namely acetone, aceto-acetic acid and β-hydroxybutyric acid. The last-named is not a true ketone. Hence ketonuria is the excessive excretion of ketones in the urine.

The polar traveller is subjected to several factors which are said to cause ketosis or to influence its degree. Five factors were studied: exercise, calorie balance, fat intake, cold and adaptation.

Exercise, calorie balance and ketosis

Whereas most other nations working in the Antarctic use mechanized transport exclusively, the British still use dog teams and occasionally manhaul sledges. These two modes of travel involve a considerable degree of hard bodily exercise, particularly in mountainous territory and in deep soft snow. Sledging diets tend to provide insufficient calories and consequently calorie balance is often negative in the field. Courtice and Douglas (1936) demonstrated that exercise is ketogenic. This has been confirmed by many workers (Winkler and Hebeler, 1939; Sargent and Consolazio, 1951; Johnson and Passmore, 1960).

Cold and ketosis

Sledging is invariably undertaken in cold weather and many workers have shown that cold can cause or aggravate ketosis. The subject has been well reviewed by Masoro (1966).

Fat intake and ketosis

The polar sledger uses a sledging ration of high fat content to keep its weight low and the calorie yield high (vital to good sledging logistics). The normal sledging ration of the British Antarctic Survey, for instance, varies slightly from year to year but it yields about 4,100 kcal. and approximately 55 per cent of these calories come from fat. High-fat diets are said of themselves to cause ketosis, and Shaffer (1921) was of the opinion that the appearance of ketosis depended only upon the ratio of ketogenic (fat and protein) to antiketogenic (carbohydrate) fractions in the food metabolized. However, the problem is now known to be more involved (Passmore, 1961).

Adaptation to ketosis

Adaptation to starvation ketosis has been shown in Eskimos (Heinbecker, 1928, 1931, 1932). Two men living in New York who voluntarily ate a flesh-only diet, consisting almost entirely of fat and protein, for a year became ketotic continuously, but some adaptation occurred in that the degree of ketosis decreased after several months (McClellan and Du Bois, 1930). Sargent and Consolazio (1951) demonstrated in a series of men on ketogenic diets under survival conditions that ketosis tended to be less in the second week. Winkler and Hebeler (1939) were of the opinion that exercise is ketogenic in the unfit but not in a trained athlete. Thus some degree of adaptation to ketosis might be observed in a polar traveller.

Experimental

Eleven male subjects, including the author, were studied whilst about their normal work. All were volunteers, healthy and young, and of ages 22 to 29 years. Their weights varied from 62 to 96 kg.

Two of the subjects (T.H. and G.L.) were studied as they were nearing the end of a 7-month sledge journey. They were asked to record their daily mileages, the weather conditions and to supply evening urine samples on five consecutive days. They ate a normal, unrestricted sledging ration supplying about 4,100 kcal., approximately 50 per cent fat, boosted by a variable amount of chocolate. Their exact dietary intake was not measured owing to circumstances beyond the author's control.

The remaining nine subjects were observed during the winter at the station for 5 days on a high-fat diet (July) and 5 days on a low-fat diet (August). Seven of the nine were, in addition, studied in the field when sledging with dogs or manhauling. Each journey included 5 days on a high-fat diet and 5 days on a low-fat diet with an intervening period of at least 4 days on an *ad libitum* diet during which no observations were made. Four men (C.W., A.J., R.T., R.L.) did two such journeys, W.I. and R.S. did one journey and subject C.R. manhauled for 3 days but was forced to retire with lumbago. Two subjects, A.W. and B.S., were observed only at the station.

Throughout each 5-day survey, daily measurements were made of energy expenditure, dietary and energy intake, and degree of exposure to cold.

Energy expenditure

An estimate of the 24 hr. energy expenditure was made using the diary technique of Masterton and others (1957). Basal metabolic rates were calculated from the tables of Harris and Benedict (1919, p. 253–66).

Exposure to cold

The time spent outdoors each day was recorded for each individual and weather observations were made at noon and in the evening. Wind velocities (m./sec.) and dry-bulb temperatures in the shade (°C) were recorded at a height of 5 ft. (1·5 m.) above the snow. These two factors have been combined in a nomogram (Consolazio and others, 1951) to give the degree of "windchill"—a mathematical expression of the phenomenon whereby the chilling effect of a given air temperature is increased by a rise in wind velocity (Siple and Passel, 1945). The windchill scale (which is not linear) has been simplified for ease of analysis to a 0–8 scale (Table I). Windchills have been expressed in two ways: first, as the evening windchill, and secondly, as the mean of the noon and evening windchills. Cold exposure has also been assessed by measuring the time spent out-of-doors, as temperatures never rose above 0° C. None of these methods takes account of the insulative value of the protective clothing worn and is far from being ideal.

Adaptation to ketosis

Evidence for adaptation has been looked for first by comparing the incidence of ketonuria on successive sledge journeys on an individual basis, comparing days of similar calorie balance. Four subjects only could be studied in this way—C.W., R.T., A.J., and R.L. The second method has been to note whether or not ketonuria occurred in the men who had been sledging for 7 months.

TABLE I. THE WINDCHILL SCALE AND A SIMPLIFIED VERSION

Windchill (kcal./$m.^2$/hr.)*	*State of comfort*	*Simplified windchill (arbitrary scale)*
25–75	Hot	–
75–150	Warm	–
150–300	Pleasant	0
300–490	Cool	1
490–695	Very cool	2
695–900	Cold	3
900–1,100	Very cold	4
1,100–1,305	Bitterly cold	5
1,305–1,665	Exposed flesh freezes, travel disagreeable	6
1,665–2,130	Exposed flesh freezes in 1 min., travel dangerous	7
2,130–2,500	Exposed flesh freezes in 30 sec.	8

* Approximations only. From the nomogram of Consolazio and others (1951, fig. 62).

Diets and energy intake

The four diets used in this survey were designed by the author in the Antarctic using information from the tables of McCance and Widdowson (1960) and from Andrew Lusk & Co. (London), the packers and suppliers of all the foods used. The subjects agreed to adhere strictly to the diets and to note any food that could not be eaten.

Collection and storage of urine specimens

Bladders were emptied before the evening meal and specimens of urine were collected approximately 2 hr. after each evening meal, the secretion of the specimen being timed to the nearest minute and its volume measured to the nearest 5 ml. Thus the excretion rate of each specimen could be calculated. 10 ml. aliquots were placed in screw-capped polythene bottles, carefully labelled and allowed to freeze. The samples were kept frozen at $-20°$ C, or below, until analysed in Liverpool.

Estimation of urinary total ketone bodies

Total ketone bodies (acetone, aceto-acetic acid and β-hydroxybutyric acid) in the urine were analysed by the method of Paterson and others (1967) with some modifications: 1 oz. (28·4 ml.) "Universal" screw-capped bottles were used; protein precipitation was considered unnecessary as none of the specimens contained protein; acetone standards of 2, 4 and 6 mmol. were prepared, and with 0·5 cm. cuvettes, Beer's law was obeyed over this range of concentrations. Combining the urine flow rate and the total ketone-body concentrations enabled the results to be expressed as total ketone-body excretion rates in μmol./min.

RESULTS

The upper limit of normal for the excretion rate of total ketone-bodies in this study has been taken as 5·0 μmol./min. (Johnson and others, 1958) even though the specimens were not obtained as these authors recommended, i.e. when the subjects were in the post-absorptive state. Close agreement with this figure was found when the data were examined for men who had not been exposed to ketogenic factors, i.e. when they were at the station, on the low-fat diet, in positive calorie balance and spending no more than 2 hr./day out-of-doors. These criteria were fulfilled in 33 out of 193 subject days. The mean value for the total ketone-body excretion rate was 3·0 μmol./min. with a standard deviation of 1·2 μmol./min., giving an upper limit of normal of 5·4 μmol./min. The distribution of the data was found to be "normal" when plotted on arithmetical probability paper. Taking the upper limit as 5·0 μmol./min., all of the subjects became ketotic on at least one occasion; out of 160 subject days on which for one reason or another ketonuria might have been expected to occur, ketonuria was observed on 72 occasions.

Exercise, dietary intake, calorie balance and ketosis

The average energy expenditure for the group was found to be:

2,310 kcal./day on sledging lie-up days.
3,540 kcal./day at the station.
3,970 kcal./day whilst sledging (all days).
4,390 kcal./day on active sledging days only.

Energy expenditures in excess of 7,000 kcal./day were occasionally found on sledging journeys.

The four diets were:

Low fat (station) 3,500 kcal., 30 per cent as fat, about 113 g. fat/day.
High fat (station) 3,500 kcal., 60 per cent as fat, about 225 g. fat/day.
Low fat (sledging) 4,400 kcal., 30 per cent as fat, about 142 g. fat/day.
High fat (sledging) 4,400 kcal., 60 per cent as fat, about 285 g. fat/day.

Tea and coffee were unlimited but the milk and sugar for the drinks came from the daily allocation.

If the data for all the subjects are pooled, it is found that energy expenditure and total ketone-body excretion rate are strongly correlated and the association is positive, i.e. the incidence of ketonuria increases as energy expenditure rises ($r = +0·60$ and $P<0·001$, highly significant; Fig. 1). In the calculation of these data all degrees of negative and positive calorie balance, no matter how small, were included. This relationship is found also in eight out of the

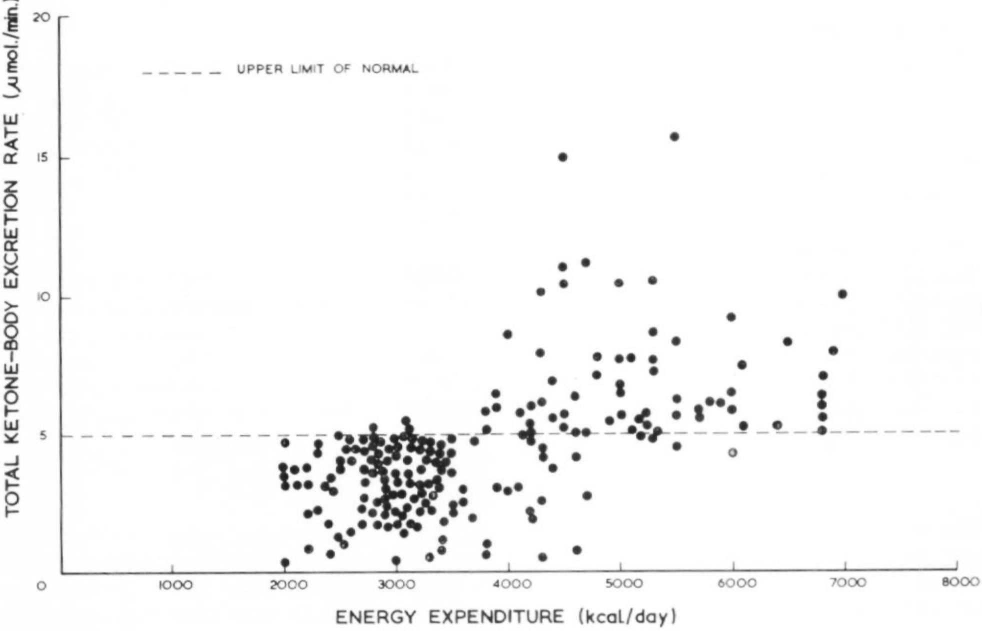

Fig. 1. Correlation between total ketone-body excretion rate and energy expenditure.

nine subjects at the individual level (Table II). The close association between energy expenditure and total ketone-body excretion rate is well shown by the results of the χ^2 test ($\chi^2 = 95 \cdot 32$, $P < 0 \cdot 001$, highly significant; Table III).

If the calorie balance is considered (the difference between the fixed calorie intake and the variable energy expenditure), a very similar association is found between negative calorie balance and total ketone-body excretion rate ($r = 0 \cdot 58$, $\chi^2 = 99 \cdot 24$, $P < 0 \cdot 001$, highly

TABLE II. CORRELATION COEFFICIENTS (r) AND THEIR SIGNIFICANCE (P) BETWEEN TOTAL KETONE-BODY EXCRETION RATES AND ENERGY EXPENDITURE, CALORIE BALANCE, ELAPSED TIME OUT-OF-DOORS, AND FAT INTAKE
(The number of pairs of observations are shown in parentheses. N-2 degrees of freedom have been used thoughout.)

Subject	*Function*	*Total ketone-body excretion rate* *v* *Fat intake* (g./day)	*Total ketone-body excretion rate* *v* *Daily elapsed time out-of-doors* (min.)	*Total ketone-body excretion rate* *v* *Energy balance* (plus or minus kcal./day)	*Total-ketone body excretion rate* *v* *Energy expenditure* (kcal./day)
R.L.	*r*	0·00	+0·68	−0·76	+0·80
(30)	*P*	>0·05	<0·001	<0·001	<0·001
C.W.	*r*	+0·25	+0·52	−0·41	+0·42
(30)	*P*	>0·05	<0·01	<0·05	<0·05
A.J.	*r*	+0·27	+0·49	−0·69	+0·65
(30)	*P*	>0·05	<0·01	<0·001	<0·001
R.T.	*r*	+0·31	+0·37	−0·56	+0·61
(30)	*P*	>0·05	<0·05	=0·001	<0·001
R.S.	*r*	+0·26	+0·69	−0·57	+0·62
(20)	*P*	>0·05	<0·001	<0·01	<0·01
W.I.	*r*	+0·31	+0·50	−0·25	+0·57
(20)	*P*	>0·05	<0·05	>0·05	<0·01
C.R.	*r*	+0·37	+0·63	−0·62	+0·75
(13)	*P*	>0·05	<0·05	<0·05	<0·01
B.S.	*r*	+0·26	+0·63	−0·68	+0·69
(10)	*P*	>0·05	=0·05	<0·05	<0·05
A.W.	*r*	0·00	+0·19	−0·16	+0·16
(10)	*P*	>0·05	>0·05	>0·05	>0·05
Collectively	*r*	+0·09	+0·51	−0·58	+0·60
(193)	*P*	>0·05	<0·001	<0·001	<0·001

$P > 0 \cdot 05$, not significant.
$P < 0 \cdot 05$, significant.
$P < 0 \cdot 001$, highly significant.

significant; Table III, Fig. 2). It can be seen from Table IV that on a sledge journey the incidence of ketonuria in subjects C.W., A.J., R.T. and R.L. for days of negative calorie balance (32/39) is significantly greater than for days of positive calorie balance (5/41) and $\chi^2 = 36 \cdot 3$, $P < 0 \cdot 001$, highly significant. For the same four subjects the incidence of ketosis at the station was significantly greater for days in negative calorie balance (9/13) than for days of positive calorie balance (2/27), where $\chi^2 = 13 \cdot 9$ and $P < 0 \cdot 001$, highly significant.

The question now arises as to whether it is the degree of energy expenditure which is important in ketogenesis or the degree of negativity of the calorie balance, because on a fixed intake it is found that high energy expenditure is invariably accompanied by calorie deficit. To investigate this problem the data were examined for days on which the energy expenditure lay within ± 10 per cent of the two calorie intake levels, 3,500 and 4,400 kcal./day. 43

TABLE III. VALUES AND SIGNIFICANCE OF χ^2 FOR SEVERAL VARIABLES (BASED ON 193 PAIRS OF DATA). THE DIVISIONS BETWEEN "HIGH"- AND "LOW"-ENERGY EXPENDITURE, ETC., ARE ARBITRARY BUT CONSIDERED REASONABLE

χ^2 *calculated between total ketone-body excretion rate* (< and ⩾ 5 μmol./min.) *and the following:*	χ^2 (using Yates's (1934) correlation)	*P*	*Overt association*
1. Energy expenditure (< and ⩾ 3,500 kcal./day)	95·32	<0·001	Positive
2. Calorie balance (negative and positive kcal./day)	99·24	<0·001	Negative
3. Evening windchill (< and ⩾ 4 units)	18·63	<0·001	Positive
3A. Evening windchill (positive calorie balance only)	0·05	>0·05	Positive
4. Mean of noon and evening windchill (< and ⩾ 4 units)	6·47	<0·05	Positive
4A. Mean of noon and evening windchill (positive calorie balance only)	0	>0·05	0
5. Daily time spent outdoors (min.) (< and ⩾ 350 min./day)	48·88	<0·001	Positive
5A. Daily time spent outdoors (positive calorie balance only)	4·13	<0·05	Positive
6. Fat content of diet (< and ⩾ 150 g. fat/day)	3·53	>0·05	Positive
6A. Fat content of diet (positive calorie balance only)	2·55	>0·05	Positive
6B. Fat content of diet (negative calorie balance only)	5·04	<0·05	Positive

P >0·05, not significant.
P <0·05, significant.
P <0·001, highly significant.

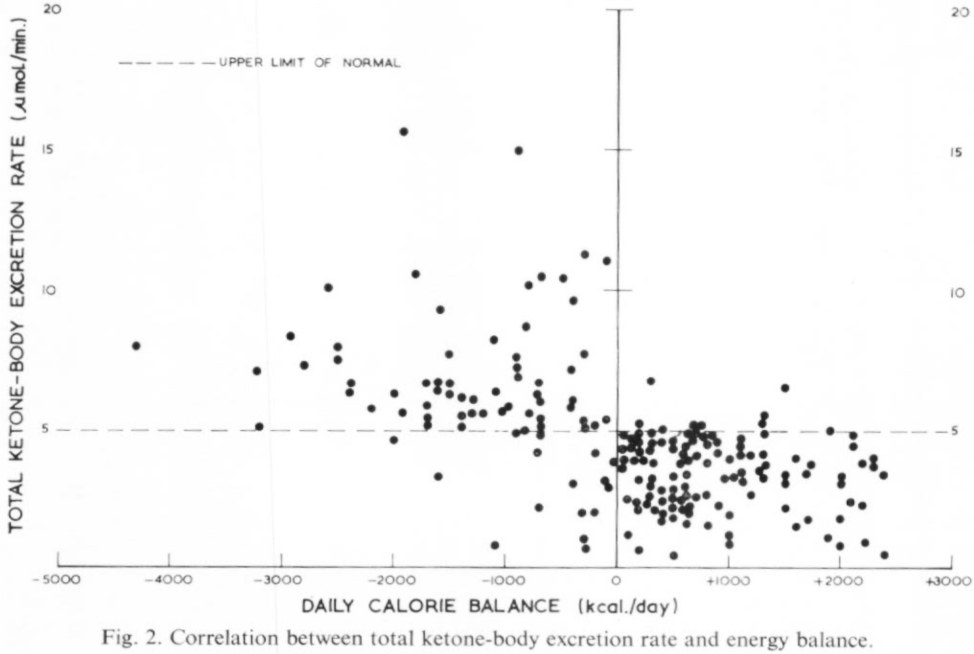

Fig. 2. Correlation between total ketone-body excretion rate and energy balance.

subject days of "neutral" calorie balance occurred. The incidence of ketonuria when in neutral calorie balance at about 4,400 kcal./day (10/19) is found to be significantly higher than when in neutral calorie balance at about 3,500 kcal./day (1/24); $\chi^2 = 14{\cdot}30$, $P<0{\cdot}001$, highly significant.

TABLE IV. ADAPTATION TO SLEDGING; INCIDENCE OF KETONURIA ON SUCCESSIVE SLEDGING JOURNEYS
(Of the fractions, the numerator shows the number of days on which ketonuria occurred and the denominator shows the number of days on which observations were made.)

Subject	Days of positive calorie balance		Days of negative calorie balance	
	First journey (date)	Second journey (date)	First journey	Second journey
R.L.	0/2 (January 1966)	1/10 (March 1966)	7/8	—
C.W.	2/2 (February 1966)	0/3 (October 1966)	7/8	5/7
A.J.	0/10 (March 1966)	0/3 (October 1966)	—	7/7
R.T.	0/3 (March 1966)	2/8 (September 1966)	5/7	1/2

Unfortunately, because of the fixed calorie intakes, it is not possible to calculate from the data what the incidence of ketosis is for negative and positive calorie balances for a given energy expenditure—in other words, to apply the converse of the above test.

Ketonuria and fat content of diet

No correlation was demonstrable between daily fat intake and total ketone-body excretion rate (Tables II and III, Fig. 3) either at the individual level or for the pooled data. It was found whilst "lying-up" in a tent during bad weather ketonuria did not appear even though 285 g. of fat were consumed per day with the high-fat diet.

If, however, the pooled data are divided into days of positive and negative calorie balance, it is found that fat intake is positively associated with total ketone-body excretion rate in the negative balance group ($\chi^2 = 5 \cdot 04$, $P < 0 \cdot 05$, significant), but not in the positive balance group ($\chi^2 = 2 \cdot 55$, $P > 0 \cdot 05$, not significant).

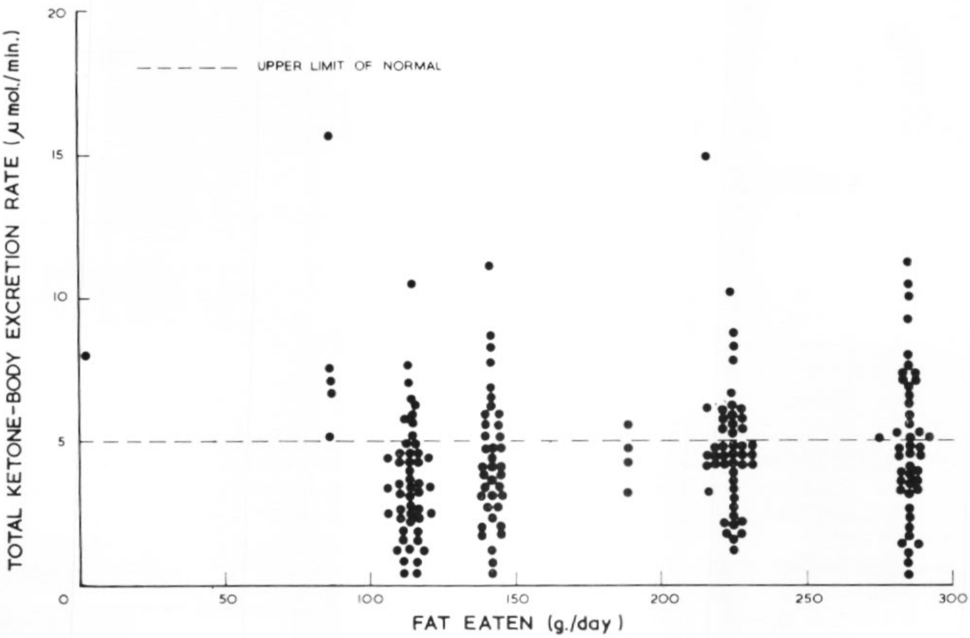

Fig. 3. Correlation between total ketone-body excretion rate and fat content of diet.

Ketonuria and cold

It will be seen in Table III that the mean noon and evening windchill is positively associated with total ketone-body excretion rate, and a stronger association is found when evening windchill alone is considered. The strongest association is between the time spent out-of-doors and total ketone-body excretion rate ($\chi^2 = 48 \cdot 88$, $P < 0 \cdot 001$, highly significant, $r = +0 \cdot 51$) (Fig. 4).

If the factor of calorie deficit is excluded, i.e. only days of positive calorie balance are considered, it is found that total ketone-body excretion rate is weakly associated with the time spent out-of-doors, but not at all with windchill (Table III).

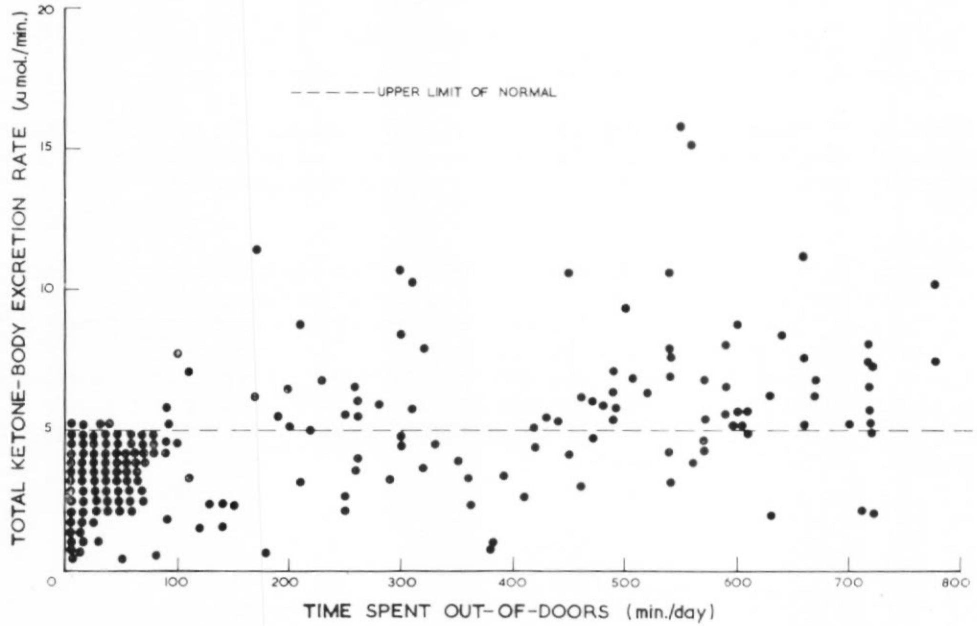

Fig. 4. Correlation between total ketone-body excretion rate and time spent out-of-doors.

Adaptation to ketosis

Consideration of Table IV shows that there is no clear evidence to suggest that ketonuria is less on a second sledge journey.

Subjects G.L. and T.H., during their period of study, sledged between 9 and 20 miles/day (14·5 and 32·2 km./day) (a good daily average for the Halley Bay area) in very cold conditions. G.L. showed ketonuria (as judged by Ketostix*) on three occasions out of five, and T.H. on one day out of five. These two subjects did not time their urine secretion and so their samples were not analysed quantitatively.

Discussion

The expected occurrence of ketonuria in the Antarctic was observed.

The close agreement between the upper limit of normal for total ketone-body excretion rate described in this investigation and that of Johnson and others (1958) is of interest, for it might be thought on theoretical grounds that their value for the post-absorptive state would be the higher in view of the greater duration of fasting, about 13 hr. as opposed to 2 hr. The present results suggest that it makes little difference whether samples for urinalysis are collected 2 hr. after the evening meal or in the post-absorptive state.

* Manufactured by Ames Co., Stoke Poges, England.

The calorie values of the station and sledging diets (decided before the investigation was undertaken) correspond closely with the mean daily energy-expenditure levels for the group at the station and on active sledging days.

The very high correlation between energy expenditure and the excretion rate of total ketone-bodies suggests that hard exercise is an important factor in the aetiology of ketonuria. Muir (1966), in a similar study, related ketosis to individual variations in activity. Sledging involves several repeated bouts of exercise during the course of the day (the usual procedure is to sledge for 50 min. and to rest for 10 min.), and it would appear that the effects are additive. This is in agreement with an aspect of the work of Courtice and Douglas (1936), who found that a 10 mile (16 km.) walk in the fasting state is ketogenic, the ketosis appearing in the resting state if the exercise is continuous. A second walk increased the eventual degree of ketosis. They also discovered that if, instead of a continuous 10 mile (16 km.) walk, a rest was taken after each 4 miles (6·4 km.), the ketosis appeared earlier and was not abolished by further exercise.

In contrast, Sargent and Consolazio (1951) found that ketosis, occurring during Army trials in winter, was independent of energy expenditure. Furthermore, Sargent and others (1958) found that the ketogenicity of any diet was reduced by an increase in the daily work load but they admitted that their evidence was very slight.

It was found that, for a subject in neutral calorie balance, ketonuria was significantly commoner at an energy-expenditure level of 4,400 kcal./day than at 3,500 kcal./day. This might suggest that it is the increase in energy output, as well as the development of a negative calorie balance state, that is important in producing ketosis.

The close relationship between negative calorie balance and ketonuria could imply that relative starvation causes ketosis as does actual starvation. This is the likely explanation of "spontaneous" ketosis of pregnancy in animals and of the increased susceptibility to ketosis of women in labour (Paterson and others, 1967).

When calorie deficit is excluded, the finding that the total ketone-body excretion rate is associated with the time spent out-of-doors suggests that the factor of exposure to cold is a further minor influence on the aetiology of ketonuria in the Antarctic. This supports the suggestion that of itself cold is ketogenic (Johnson and Sargent, 1958). Sargent and Consolazio (1951) were the first to point out that ketosis is commoner in the cold.

It would appear from the results that, despite the high fat content of the high-fat sledging ration, ketosis did not occur in the resting state but only when energy expenditure became high, and that a high fat intake increases the chance of becoming ketotic when in calorie deficit. It could be argued that the 285 g. of fat did not cause ketonuria on lie-up days because it was not absorbed to any extent. Masterton and others (1957) found in the Arctic that of a diet containing 270 g. fat 96 per cent was absorbed.

Evidence is presented here that adaptation to exercise-induced ketosis did not occur, but it does not exclude the possibility of adaptation.

Most of the findings in this survey can thus be explained by the calorie-deficiency hypothesis of the causation of ketosis (Mayes, 1962) as opposed to the hypothesis of Freund (1965) and Freund and Weinsier (1966), who regarded ketosis as being due to a specific lack of carbohydrate at the cellular level.

In conclusion, it may be said that in the polar sledger, ketosis is associated with both high energy expenditure and with calorie deficit. This ketosis is also aggravated by exposure to cold and by the necessity of eating large amounts of fat when in negative calorie balance. There was no clear evidence to support adaptation to ketosis, but not enough evidence to disprove the possibility.

ACKNOWLEDGEMENTS

I should like to thank the Director of the British Antarctic Survey, Sir Vivian Fuchs, for making this study possible; Dr. O. G. Edholm, of the Medical Research Council, and Dr. W. H. Taylor, of the Department of Chemical Pathology, The United Liverpool Hospitals, and their respective staffs for their enormous help and encouragement. I am also indebted to Mr. M. C. K. Tweedie, of the Department of Medical Statistics, University of Liverpool, and most of all to the cheerful co-operation of my colleagues in the Antarctic.

MS. received 10 December 1968

REFERENCES

CONSOLAZIO, C. F., JOHNSON, R. E. *and* E. MAREK. 1951. *Metabolic methods*. St. Louis, C. V. Mosby Company.

COURTICE, F. C. *and* C. G. DOUGLAS. 1936. The effects of prolonged muscular exercise on the metabolism. *Proc. R. Soc.*, Ser. B., **119**, No. B815, 381–439.

FREUND, G. 1965. The calorie deficiency hypothesis of ketogenesis tested in Man. *Metabolism*, **14**, No. 9, 985–90.

————. *and* R. L. WEINSIER. 1966. Standardized ketosis in Man following medium chain triglyceride ingestion. *Metabolism*, **15**, No. 11, 980–91.

HARRIS, J. A. *and* F. G. BENEDICT. 1919. A biometric study of basal metabolism in Man. *Publs Carnegie Instn*, No. 279, 266 pp.

HEINBECKER, P. 1928. Studies on the metabolism of Eskimos. *J. biol. Chem.*, **80**, No. 2, 461–75.

————. 1931. Further studies on the metabolism of Eskimos. *J. biol. Chem.*, **93**, No. 2, 327–36.

————. 1932. Ketosis during fasting in Eskimos. *J. biol. Chem.*, **99**, No. 1, 279–82.

JOHNSON, R. E. *and* R. PASSMORE. 1960. Interrelations among post-exercise ketosis (Courtice-Douglas effect), hydration and metabolic state. *Metabolism*, **9**, No. 5, 443–51.

————. *and* F. SARGENT. 1958. Some quantitative interrelationships among thermal environment, human metabolism and nutrition. *Proc. Nutr. Soc.*, **17**, No. 2, 179–86.

————., ————. *and* R. PASSMORE. 1958. Normal variations in total ketone bodies in serum and urine of healthy young men. *Q. Jl exp. Physiol.*, **43**, No. 4, 339–44.

McCANCE, R. A. *and* E. M. WIDDOWSON. 1960. *The composition of foods*. 3rd edition. London, Her Majesty's Stationery Office. (M.R.C. Special Report Series, No. 297.)

McCLELLAN, W. S. *and* E. F. DU BOIS. 1930. Clinical calorimetry. XLV. Prolonged meat diets with a study of kidney function and ketosis. *J. biol. Chem.*, **87**, No. 3, 651–68.

MASORO, E. J. 1966. The effect of cold on the metabolic use of lipids. *Physiol. Rev.*, **46**, No. 1, 67–101.

MASTERTON, J. P., LEWIS, H. E. *and* E. M. WIDDOWSON. 1957. Food intakes, energy expenditures and faecal excretions of men on a polar expedition. *Br. J. Nutr.*, **11**, No. 3, 346–58.

MAYES, P. A. 1962. A calorie deficiency hypothesis of ketogenesis. *Metabolism*, **11**, No. 8, 781–99.

MUIR, A. L. 1966. Ketosis on a polar expedition. *J. Physiol., Lond.*, **184**, 70*P*–72*P*.

PASSMORE, R. 1961. On ketosis. *Lancet*, **i**, No. 7182, 839–43.

PATERSON, P., SHEATH, J., TAFT, P. *and* C. WOOD. 1967. Maternal and foetal ketone concentrations in plasma and urine. *Lancet*, **i**, No. 7495, 862–65.

SARGENT, F. *and* C. F. CONSOLAZIO. 1951. Stress and ketone body metabolism. *Science, N.Y.*, **113**, No. 2944, 631–33.

————., JOHNSON, R. E., ROBBINS, E. *and* L. SAWYER. 1958. The effects of environment and other factors on nutritional ketosis. *Q. Jl exp. Physiol.*, **43**, No. 4, 345–51.

SHAFFER, P. A. 1921. Antiketogenesis. II. The ketogenic antiketogenic balance in Man. *J. biol. Chem.*, **47**, No. 2, 449–73.

SIPLE, P. A. *and* C. F. PASSEL. 1945. Measurements of dry atmospheric cooling in subfreezing temperatures. *Proc. Am. phil. Soc.*, **89**, No. 1, 177–99.

WINKLER, H. *and* F. HEBELER. 1939. Über den Milchsaure- und Ketonkörperanstieg im Blut bei intensiver und ungewohnter körperlicher Arbeit. *Klin. Wschr.*, **18**, Nr. 17, 596–98.

YATES, F. 1934. Contingency tables involving small numbers and the χ^2 test. *Suppl. Jl R. statist. Soc.*, **1**, No. 2, 217–35.