Rapid communications

Oral glucose tolerance and ambient temperature in non-diabetic subjects

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Summary. When either a 960-kcal, 140-g carbohydrate meal, or a 75-g glucose load was ingested by non-diabetic Caucasians, the 2-h venous plasma glucose concentration was higher by 0.82 and 1.25 mmol/l, respectively, if the ambient temperature was 33 °C rather than 23 °C. It is likely that this is a result of relative 'arterialisation' of the venous blood. Even at 23 °C room temperature, use of the 'hot hand' technique to obtain 'arterialised' venous blood increases post-load glucose

levels in contralateral antecubital veins. If these observations apply to those acclimatised to the heat, they could affect the diagnosis of both diabetes and impaired glucose tolerance in the tropics.

Key words: Ambient temperature, glucose tolerance, tropical countries, hot hand technique, post-prandial glucose.

The prevalence of low glucose tolerance varies greatly around the world, with values of 40% or more among both the native American Pima Indians and the Micronesians in Nauru, compared to under 10% in many European communities [1, 2]. The incidence of Type 2 (non-insulin-dependent) diabetes has been estimated as 24 in nine British towns [3] compared to 1,540 in Nauru, both per 100,000 person years. The incidence among the Pima Indians has been reckoned to be 19-fold that among the population of Rochester, Minn, USA.

While high rates of diabetic tissue damage among both the American Indians [4] and the Nauruans indicate a high frequency of diabetes, there is much debate as to the possible role of as yet unidentified environmental factors in explaining observations such as the higher prevalence of diabetes among urbanised than rural Melanesians [5]. An important genetic effect has also been postulated, e.g. between Nauruans and Gilbertese.

Ability to limit the degree of hyperglycaemia after a glucose load, and to restore normal glucose levels, has long been involved in estimates of the prevalence of diabetes mellitus and the associated 'impaired glucose tolerance' [6]. Indeed, in several of the earlier studies, before the WHO Report [6], measurement of the fasting glucose concentration was often omitted. The venous glucose concentration 2 h after the test load was relied upon entirely, set against various current definitions of diabetes.

During a study of the metabolic response to meals eaten by both obese and normal-weight non-diabetic subjects at different environmental temperatures, we found higher antecubital venous plasma glucose concentrations in those in a warm room (33 °C) compared to those in a cooler one (23 °C), and now report those results and others prompted by them.

Subjects and methods

A standard meal was ingested by 22 non-diabetic subjects who had been recruited in two groups as either normal ($n=10$, 6 male) or overweight ($n=12$, 6 male). Their Body Mass Indices (BMI) (W/H^2 as kg/m^2) were <25.0 and >27.0 , respectively, and averaged 22.5 ± 1.6 and 31.3 ± 2.9 ; their ages were 47 ± 13 and 43 ± 13 years. The 75-g oral glucose load was given to 6 other non-obese subjects (5 male) with median BMI of 22.3 (range 19.0 to 25.6) and median age of 28 (range 19 to 57) years. Subjects travelled from home each day, after overnight fasting but drinking water ad libitum. At the hospital they rested for 30 min before taking a nutrient load, with antecubital vein blood drawn from an indwelling cannula 20, 10 and 1 min before ingestion, and half-hourly thereafter, with an additional sample just 15 min after the ingestion of a 75-g glucose load. The 960 kcal test meal contained 36 g protein, 31 g fat and 142 g carbohydrate, as well as 15 g cereal fibre, and was eaten within 15 min. When 75 g of glucose was taken dissolved in 300–350 ml water, it was drunk within 5 min; a further 50 ml of plain water was then drunk. The tests were performed in a thermostatically controlled room at a temperature of either 23 °C or 33 °C (± 0.5 °C), in randomised order.

On four occasions with two subjects arterialised venous blood was obtained from an indwelling intravenous cannula inserted retrograde at the wrist with the hand heated by air at 60 °C inside an insu-

Table 1. Plasma glucose concentrations (mmol/l) at times (min) after either the standard meal or the glucose load in non-diabetic subjects, means $\pm$ SD

		Time (min)					
		0	15	30	60	90	120
Standard meal							
Nonobese (<i>n</i> =10)	23 °C	4.87 $\pm$ 0.42		5.94 $\pm$ 1.68	5.25 $\pm$ 1.38	5.27 $\pm$ 0.83	5.27 $\pm$ 1.96
	33 °C	5.11 $\pm$ 0.45		8.49 $\pm$ 1.52	7.26 $\pm$ 1.51	6.30 $\pm$ 0.76	6.06 $\pm$ 0.41
Obese (<i>n</i> =12)	23 °C	5.06 $\pm$ 0.21		7.18 $\pm$ 0.56	6.22 $\pm$ 1.16	5.99 $\pm$ 0.74	5.90 $\pm$ 0.51
	33 °C	5.32 $\pm$ 0.51		8.33 $\pm$ 1.04	7.46 $\pm$ 1.29	6.88 $\pm$ 1.29	6.73 $\pm$ 1.01
75-g glucose load							
Non-obese (<i>n</i> =6)	23 °C	4.90 $\pm$ 0.15	6.12 $\pm$ 0.77	7.48 $\pm$ 1.05	5.71 $\pm$ 1.17	5.36 $\pm$ 1.25	5.11 $\pm$ 0.78
Non-obese (<i>n</i> =6)	33 °C	5.08 $\pm$ 0.30	6.53 $\pm$ 0.43	8.23 $\pm$ 1.45	8.16 $\pm$ 1.29	7.10 $\pm$ 0.66	6.37 $\pm$ 1.19

Table 2. Plasma glucose values of two non-diabetic non-obese male subjects from an antecubital vein (on one occasion), and from both an 'arterialised' wrist vein from a 'hot hand' and a contralateral antecubital vein (on another occasion), at two different temperatures

		Initial plasma glucose (mmol/l)	Increase in plasma glucose (mmol/l) at times (min) after oral glucose					
		0	15	30	60	90	120	
23 °C	Venous usual	5.0	-0.1	1.0	1.7	0.9	-0.2	
		5.1	0.8	2.8	0.8	0.5	-0.6	
	Arterialised venous	5.1	1.0	4.0	6.1	5.9	3.2	
		5.6	-	2.2	5.3	2.9	1.6	
	Contralateral venous	5.0	0.6	3.4	5.4	5.3	2.9	
		5.5	-	1.7	3.7	2.3	1.4	
	Venous usual	4.9	1.4	4.0	4.4	3.3	2.1	
		5.1	1.2	3.6	2.3	1.7	0.8	
33 °C	Arterialised venous	5.2	0.7	2.8	4.1	3.4	1.6	
		5.5	1.4	4.1	1.7	3.3	1.9	
	Contralateral venous	5.2	0.6	2.7	4.1	3.5	0.7	
		5.3	1.3	3.3	1.3	2.8	1.4	

lated cylinder. Antecubital venous blood was drawn contralateral to the hot hand.

Blood was centrifuged within 5 min of withdrawal, and before and during centrifugation was chilled at 0–1 °C. The plasma was frozen (–20 °C) until analysis by a hexokinase method.

Statistical analysis

The data were stored and analysed on the Oxford University ICL 2988 computer, using the procedures of the Biomedical Data Package. A three-factor repeated measures design for analysis of variance was used with one (obesity) between – and two (temperature and time) within – subject factors. The *p* values are for the main effect of temperature. Paired Student's *t*-tests were used for the differences between the two temperatures for the 2-h post-glucose values. Data are given as means $\pm$ SD.

Results

The plasma glucose results after the standard meal are given in Table 1, and it can be seen that in both the obese and the non-obese subjects the post-meal plasma glucose levels were higher in the warmer than in the cooler room ($p < 0.001$). The results for the 75 g oral glucose load to the non-obese non-diabetic subjects are also given in Table 1, and show a similar difference ($p < 0.002$). The difference at 2 h averaged 1.25 ± 1.21 mmol/l ($p = 0.05$).

Two non-obese male non-diabetic subjects underwent further 75 g oral glucose tests at both 23 °C and 33 °C. In these, the customary 'hot hand' technique [7] was used to obtain 'arterialised' venous blood, while antecubital venous blood was drawn from the other arm. Their results, together with their previous 'usual' glucose test, are listed in Table 2. The glucose concentration in the contralateral venous blood was less, but not greatly so, than in the 'arterialised' blood; indeed, it was not far above the 'usual' venous values at 33 °C, although there was a substantial difference between these values at 23 °C.

Discussion

It has long been known that venous blood obtained at the wrist of a 'hot hand' has a plasma glucose concentration that closely resembles that of arterial blood, both fasting and after an oral glucose load [8]. It is also well established that plasma glucose in antecubital venous blood is little lower than arterial in the fasting state, but much lower after an oral glucose load. In a particularly detailed study the mean transit time for blood through the forearm was estimated at 1.0 min under usual circumstances but just 0.3 min when the hand was heated, with irreversible fractional removal of glucose of 2.9% and 1.9% respectively [8].

What may not have been realised previously is the difference in antecubital venous glucose values ob-

tained when the same subject takes a nutrient load at an ambient temperature of 33 °C rather than 23 °C. If such an effect of elevated ambient temperature also occurs in those acclimatised to warm surroundings (and we already have good reason to believe so for the citizens of Pune, India [C.S. Yajnik, unpublished observations]), it could partly explain the very high prevalence of diabetes reported in certain tropical studies, or indeed in hot surroundings outside the tropics. The subjects in large population studies have not generally been conveyed to cool, air-conditioned surroundings for testing. The difference 2 h post-load in the antecubital values between tests at 23° and 33 °C increases when fasting glucose enters the diabetic range, e.g. around 4 mmol/l, with fasting blood glucose about 10 mmol/l [C.S. Yajnik and our own unpublished observations].

The population of the tropical countries is increasing, but even 10 years ago was reckoned to be at least 1600×10^6 [9]. If nutritional or genetic factors allow even 5% of these to approximate to the usual European or North American 'non-diabetic' level of glucose tolerance, then a decrease of 1 mmol/l in the 2-h venous glucose value could be reckoned to remove an assumption of unhealthy glucose tolerance from 10–15% of the 'at risk' population, i.e. at least 8 million people. No one doubts the problem that diabetes presents among the Pima Indians and the Nauruans; it is possible, however, that its prevalence is sometimes quantitatively exaggerated.

Our observations also question the validity of the arterio-venous differences measured between arterialed venous 'hot hand' and contralateral antecubital venous blood as the basis for calculation of muscular or peripheral uptake of substrates. The antecubital venous blood is different from what it would have been if no heat had been applied, so extrapolation from its values to the whole musculature or organism at the ambient temperature must be cautiously done, as previously noted [10]. The contralateral arm can be cooled to restore its blood flow to its level before the 'hot hand', but even then the pattern of blood flow may be different.

The oral 75-g glucose tolerance test has been reckoned to show greater variability than the intravenous

glucose tolerance test. Perhaps the ambient temperature affects the oral more than the intravenous test; this temperature is rarely recorded, let alone controlled. It certainly appears a potentially powerful influence on the results for post-load oral glucose venous levels obtained in hot countries.

Acknowledgements. We are very grateful to Ms S. Humphreys for biochemical analyses, to Ms B. Pim for nursing care of the subjects, to Ms V. Thursfield for statistical analysis, and to Ms D. Renton for preparation of the manuscript. We depend upon the Oxford Diabetes Trust for financial support of the Sheikh Rashid Diabetes Unit.

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Received: 9 April 1987

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