PAPERS AND SHORT REPORTS

High levels of energy expenditure in obese women

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Abstract

Total free living energy expenditure was compared in lean and obese women by the new doubly labelled water method and partitioned into basal metabolism and thermogenesis plus activity by whole body calorimetry. Average energy expenditure was significantly higher in the obese group (10·22 versus 7·99 MJ/day (2445 versus 1911 kcal/day); p<0·001) resulting from an increase in the energy cost of both basal metabolism and physical activity. Self recorded energy intakes were accurate in the lean subjects but underestimated expenditure by 3·5 MJ/day (837 kcal/day) in the obese group. Basal metabolic rate and energy expenditure on thermogenesis plus activity were identical in the two groups when corrected for differences in fat free mass and total body mass.

In the obese women in this series there was no evidence that their obesity was caused by a metabolic or behavioural defect resulting in reduced energy expenditure.

Introduction

Obese patients usually believe that their dietary energy intake is no higher than that of an equivalent lean person and frequently report an inability to lose weight with daily intakes of 6 MJ (1435 kcal) or less. The persistence of these claims together with the failure of most dietary surveys to detect hyperphagia in preobese or obese people has led to the hypothesis that obesity is caused by metabolic or behavioural defects which result in reduced energy expenditure.[1-3] There still, however, is no consensus on whether basal metabolism, thermogenesis, or activity patterns are abnormal. Even when abnormalities have been detected under controlled laboratory conditions their relevance in the overall energy balance equation has not been clear, since it has been impossible to measure total energy expenditure in free living people.

The recent doubly labelled water ($^2H_2{}^{18}O$) method now makes such measurements possible. We have used this new technique in conjunction with whole body calorimetry to test whether obese women have proportionately lower levels of energy expenditure than lean controls when following their normal patterns of activity.

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Present study

DOUBLY LABELLED WATER METHOD

The doubly labelled water method provides the first non-invasive technique for measuring total daily energy expenditure in free living people over extended periods. In principle, after oral dosing with the stable isotopes ^2H and ^{18}O the deuterium labels the body's water pool and the oxygen-18 labels both the water and bicarbonate pools, which are in rapid equilibrium through the carbonate dehydratase reaction. The disappearance rates of the two isotopes measure the turnover of water and water plus carbon dioxide, from which carbon dioxide production is calculated by difference. Energy expenditure is calculated from carbon dioxide production by classical indirect calorimetric equations. Full details of the principle, validation, and potential errors of the technique have been reported.[4-6] The calculated total error of the method (roughly ±5%) includes real biological day to day variations in energy expenditure.

A potential source of bias contained within this estimate of the error arises from the need to make an assumption concerning the proportion of water turnover which undergoes isotopic fractionation when evaporation occurs at epithelial surfaces. Elsewhere we assumed that half of each subject's water turnover was fractionated.[6] We now find that for normal adults in Britain an average of 40% is more appropriate and the results have been recalculated accordingly. This increases our previous estimates of energy expenditure by an average of 3·1%. In the absence of full data on the relative proportions of respiratory, sweating, and non-sweating epithelial water losses in lean and obese people under normal environmental conditions we have assumed in this study that 40% of water losses were fractionated in both the lean and obese groups. In the obese subjects, however, calculated surface area and measured energy expenditure were 21% and 28% higher than in the lean group and water turnover calculated from the deuterium disappearance rates was only 3% higher. The proportion of water fractionated may therefore have been greater in the obese than in the lean women. The maximum

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potential bias in energy expenditure introduced by using the same fractionation correction in each group was an overestimate of 4% for the obese subjects.

PROTOCOL

Energy expenditure during a protocol of fixed activity was measured by continuous whole body indirect calorimetry over periods of 36 hours, data from the initial 12 hour run in being discarded. The protocol was designed to represent a restful day and included eight hours' sleeping, one hour of lying awake (basal metabolic rate), one and a quarter to one and a half hours' standing (washing, making bed), half an hour of cycling, half an hour of stepping, and the remainder sitting down. The two exercises were at light work rates and for the obese subjects the stepping rate was adjusted for body weight. Subjects took a normal diet and were maintained close to energy balance or marginally underfed while in the calorimeter. Three lean subjects were studied overnight and for the assessment of basal metabolic rate only.

TABLE I—*Description of subjects*

Subject No	Age (years)	Height (cm)	Weight (kg)	% Of ideal body weight	Weight (kg)/ height (m)^2	Fat free mass (kg)	Occupation	Social class
				Lean group				
1	37	161	57·6	107	22·2	41·0	Civil servant	II
2	33	158	49·5	95	19·8	43·6	Various	II
3	31	163	55·7	100	20·9	42·9	Nurse	III Manual
4	23	165	56·2	97	20·7	41·5	Hospital clerk	III Manual
5	23	163	53·2	95	20·0	37·6	VDU operator	III Non-manual
6	32	158	49·7	95	19·9	35·0	Housewife	I
7	28	163	64·6	120	24·3	40·8	Part time cleaner	III Manual
8	26	160	60·6	112	23·7	43·5	Part time shop assistant	III Non-manual
9	24	156	59·0	113	24·3	41·9	Secretary	I
10	24	180	71·4	105	22·0	50·2	Housewife	III Manual
11	31	151	62·9	129	27·6	43·3	Housewife	II
12	29	150	51·0	106	22·7	35·3	Graduate student	I
13	38	170	56·4	92	19·5	40·7	Part time secretary	III Non-manual
Mean	29	161	57·5	105	22·1	41·3		
SD	5	8	6·3	11	2·4	3·9		
				Obese group				
14	32	161	74·9	139	28·9	44·4	Housewife	III Manual
15	27	160	88·6	164	34·6	47·5	Housewife	IV
16	40	168	120·1	201	42·6	60·6	Piano teacher	I
17	39	161	83·1	154	32·1	47·5	Housewife	I
18	36	164	80·5	142	29·9	48·8	Part time cleaner	IV
19	38	162	80·3	145	30·6	45·9	Part time playground supervisor	II
20	26	160	79·7	147	31·1	44·8	Part time care assistant	IV
21	37	169	82·4	137	28·8	48·4	Craft teacher	I
22	39	165	102·1	177	37·5	54·2	Sales executive	II
Mean	35	163	87·9	156	32·9	49·1		
SD	5	3	14·3	21	4·6	5·2		

Basal metabolic rate was measured under strictly controlled standard conditions—lying at complete physical rest immediately after being woken up, in thermoneutral conditions, and 13 hours after eating. Data from the initial five to 10 minutes of assessment were excluded if energy expenditure appeared to be raised owing to arousal. Results are presented as the average of up to four measurements made within two months. Subject 8 declined calorimetry and her basal metabolic rate was therefore predicted from standard equations based on weight and height. The coefficient of variation of duplicate measurements under these conditions was roughly 1% for the 24 hour period and 1·6% for basal metabolic rate.

After the calorimeter run each subject received an oral dose of 0·05 g ^2H_2O and 0·15 g $H_2{}^{18}O$ per kg body weight and refrained from eating or drinking for a four hour equilibration period. Urine samples were collected for the remainder of the dosing day and a single morning urine sample was collected by the subject at home for the next 14-31 days. At the end of the measurement period total body water was remeasured by giving a second dose of 0·05 g ^2H_2O per kg body weight in order to assess the changes in body composition. Isotopic enrichment of all urine samples was measured by isotope ratio mass spectrometry (VG Isogas) and the results calculated as described.[5-7] Body fat content was calculated from total body water by assuming that fat free mass has a water content of 73%.

Each subject recorded her food intake by weighing all foods and fluids over seven days for the lean group and over two periods of seven days for the obese group. The proportion of the isotope measurement period which was also covered by intake measurements averaged 41% (range 17-64%). Nutrient content and food quotient were calculated from food tables.[8] Food quotients were converted to the respiratory quotients necessary for the calculation of energy expenditure by accounting for changes in body composition over the measurement period.

SUBJECTS

Results are presented for nine obese and 13 lean women participating in studies of energy expenditure during pregnancy, lactation, and postpartum obesity (see table I). All subjects were recruited by advertisement. The obese subjects were selected from 97 respondents on the basis of a firm history that the onset of their obesity had been during a pregnancy or early postpartum period. Most had a clear family history of obesity (>30% of parents or siblings with obesity) and some reported restrained eating before their obesity. None of the obese subjects had any known metabolic or endocrinological cause for their obesity. All 22 subjects were healthy and none was pregnant or lactating when studied or taking any medications likely to influence energy intake or expenditure, including oral contraceptives. Subject 20 was a heavy smoker, subject 2 was a moderate smoker, and subjects 3 and 5 were light smokers.

The subjects were well matched for height, social class, and type of occupation (see table I). None was in full time manual employment. As a result of selecting the obese group for postpartum obesity the groups were poorly matched for age and parity. On average the obese women were five years older than the lean.

The cut off for obesity was set at 135% of ideal body weight, as defined by the Metropolitan Life Insurance Company tables.[9] When classified according to Quetelet's index (weight in kg/height^2 in m) three subjects were grade I obese, five grade II, and one grade III.[10] On this basis subject 11 would also have been classified as obese. Her body composition data, however, showed that she was muscular with a low body fat content, and she was therefore assigned to the lean group. Subject 10 was tall by comparison with the other subjects and, though lean, had a body weight approaching that of the lightest obese subject. Her energy expenditure was consequently high. No data were excluded from the analysis.

The study was approved by the Dunn Nutrition Unit's ethical committee.

Results

BASAL METABOLISM

Basal metabolic rate was significantly higher in the obese women (6·71 v 5·65 MJ/day (1605 v 1352 kcal/day); p<0·001), but this was entirely

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accounted for by their greater fat free mass (tables I and II). When expressed per kg fat free mass the difference in basal metabolic rate between the two groups was only 0·7%—lean 138 (SE 2), obese 137 (3) kJ/kg fat free mass/day (33·01 (SE 0·48) *v* 32·77 (0·72) kcal/kg fat free mass/day).

ENERGY EXPENDITURE IN WHOLE BODY CALORIMETER

On the fixed activity protocol imposed by the calorimeter timetable the obese women expended an average of 8·97 MJ (2146 kcal) daily compared with 7·42 MJ (1775 kcal) daily for the lean group ($p<0·001$; table II). This difference was largely, but not wholly, accounted for by the difference in fat free mass between the groups: when expressed as a multiple of their maintenance requirements the obese group had only a slightly higher expenditure than the lean group (1·336 (SE 0·019) *v* 1·297 (0·018) times basal metabolic rate). The residual difference was due to the extra cost of weightbearing activity, which is proportional to total body weight and not to fat free mass. The difference was relatively small because the main weightbearing activity (stepping) was adjusted to an equivalent work rate for the two groups, and the only other weightbearing activity was during the one and a quarter to one and a half hours of standing.

Other whole body calorimetric studies in this unit and elsewhere all show that total 24 hour energy expenditure under sedentary conditions is 25-35% greater than resting metabolism in lean and obese subjects alike.[11-13] Owing to their increased basal metabolic rate obese subjects therefore inevitably have a higher energy expenditure in the artificially controlled conditions of whole body calorimetry.

FREE LIVING ENERGY EXPENDITURE

Table II expresses total free living energy expenditure measured by the double isotope method as an average daily value over the 14-31 days. The obese women expended an average of 28% more energy than the lean controls (10·22 *v* 7·99 MJ/day (2445 *v* 1911 kcal/day); $p<0·001$). Use of a different fractionation correction for the obese group would not alter the conclusion that the obese women were using considerably more energy in normal life than the lean controls. The difference would remain highly significant.

The total amount of energy expended on dietary and thermoregulatory (and possibly adaptive) thermogenesis and on all obligatory and discretionary physical activity while the subjects followed their normal lifestyle may be calculated by subtracting maintenance expenditure—that is, basal metabolic rate—from isotopically measured total daily energy expenditure. Total daily energy expenditure minus basal metabolic rate averaged 2·26 (SE 0·24) MJ/day (541 (57) kcal/day) in the lean group and was 53% higher in the obese group—3·45 (0·33) MJ/day (825 (79) kcal/day; $p<0·01$) (table II). The wide

TABLE III—*Self recorded energy intakes (MJ/day). Values are geometric means*

Subject No	Dietary intake	Dietary intake ±balance	24 Hour total energy expenditure
		Lean group	
1	7·66	8·13	8·08
2	9·99	9·75	10·88
3	8·47	8·72	7·90
4	7·75	6·87	7·48
5	7·00	7·41	6·13
6	5·95	8·02	8·09
7	5·45	5·18	7·53
8	4·77†	5·40†	7·58
9	8·22	10·44	8·40
10	9·97	10·46	10·15
11	8·09	8·10	8·11
12			7·05
13	9·32	10·84‡	7·48
Mean	7·85	8·15	7·99
SE	0·46	0·55	0·32
		Obese group	
14	8·25	8·87	9·68
15	3·64†	7·55†	9·69
16	8·50	10·29	11·85
17	7·71	7·58	12·79
18	4·75	8·79	9·21
19	6·85	7·13	9·19
20	8·64	10·72	9·97
21	4·35	5·75	8·79
22	6·36		11·51
Mean	6·73	8·28	10·22**
SE	0·64	0·69	0·45

**Compared with lean group: $p<0·001$.
†Data excluded from means owing to poor subject compliance (as assessed by dietitian).
‡Balance data excluded. Subject ill before second total body water measurement.
Conversion: SI to traditional units—1 MJ≈240 kcal.

TABLE II—*Energy expenditure measured by whole body indirect calorimetry and double isotope technique*

Subject No	Basal metabolic rate (MJ/day)	24 Hour total energy expenditure (MJ)		Isotopic 24 hour total energy expenditure minus basal metabolic rate†	(24 Hour total energy expenditure minus basal metabolic rate)/body weight in kg (kJ/kg/day)
		Calorimeter	Isotope†		
			Lean group		
1	5·37	7·37	8·08	2·71	47
2	6·19	7·75	10·88	4·69	95
3	5·91	7·82	7·90	1·99	36
4	5·85	7·48	7·48	1·63	29
5	5·06	6·45	6·13	1·07	20
6	5·31	6·42	8·09	2·78	56
7	5·54	7·59	7·53	1·99	31
8	5·65‡		7·58	1·93	32
9	5·76		8·40	2·64	45
10	6·40	8·51	10·15	3·75	53
11	5·90		8·11	2·21	35
12	4·67		7·05	2·38	47
13	5·86	7·38	7·48	1·62	27
Mean	5·65	7·42	7·99	2·26	39
SE	0·13	0·22	0·32	0·24	5
			Obese group		
14	6·70	8·46	9·68	2·98	40
15	6·77	9·23	9·69	2·92	33
16	8·20	11·09	11·85	3·65	31
17	6·64	8·99	12·79	6·15	74
18	6·54	8·31	9·21	2·67	33
19	6·42	8·20	9·19	2·77	34
20	6·43	9·13	9·97	3·54	44
21	5·96	8·33	8·79	2·83	34
22	6·73	8·96	11·51	4·79	47
Mean	6·71**	8·97**	10·22**	3·45*	40
SE	0·21	0·30	0·45	0·33	4

Compared with lean group: *$p<0·01$. **$p<0·001$.
†Geometric means are presented owing to skewed distribution.
‡Predicted from Schofield *et al*.[14]
Conversion: SI to traditional units—1 MJ≈240 kcal. 1kJ≈0·24 kcal.

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range of values (total daily energy expenditure and total daily energy expenditure minus basal metabolic rate) may be accounted for by differences in patterns of discretionary activity. In the lean women the total daily energy expenditure minus basal metabolic rate ranged from 1·07 to 4·69 MJ/day (256 to 1122 kcal/day) with a coefficient of variation of 38·7%. The subject with the lowest value was on holiday at the time of measurement and admitted to being unusually inactive. The variation was lower in the obese group (coefficient of variation 28·7%), since the lowest observed expenditure on activity and thermogenesis was 2·67 MJ/day (639 kcal/day). This was 0·41 MJ/day (98 kcal/day) more than the average value for the lean group.

If we assume that the energy costs of the main components of total daily energy expenditure minus basal metabolic rate are roughly proportional to total body weight a direct comparison between the two groups may be made by expressing total daily energy expenditure minus basal metabolic rate with body weight as the denominator. This yielded average energy expenditures of 39 (SE 5) and 40 (4) kJ/kg/day (9·3 (1·2) and 9·6 (1·0) kcal/kg/day) in the lean and obese groups respectively, suggesting that the amount of discretionary activity performed was exactly the same in the two groups. This approach is necessarily approximate. However, any more elaborate attempt to subdivide total daily energy expenditure minus basal metabolic rate into the components of thermogenesis and activity will have the effect of increasing the calculated amount of physical activity in the obese group relative to the lean controls. For instance, if the energy cost of thermoregulatory thermogenesis was assumed to be negligible (since most of the measurements were made in the summer, and man regulates his microenvironment in order to avoid cold stress) and energy dissipated as dietary thermogenesis assumed to be 10% of the total energy intake, the residual energy expenditure attributable to activity would be 1·46 and 2·43 MJ/day (349 and 581 kcal/day), or 25 and 28 kJ/kg/day (6·0 and 6·7 kcal/kg/day), in the lean and obese groups respectively. If, as has been suggested on the basis of whole body calorimetry,[15] the thermogenic effect of food is actually lower in obese than in lean people then the calculated amount of energy expended on physical activity would be even greater in the obese group.

DIETARY INTAKE

Table III summarises the self recorded energy intakes for the two groups. Data from one subject in each group were excluded by the dietitian as being obviously unreliable. The remaining data yielded a mean value of 7·85 MJ/day (1878 kcal/day) in the lean group, which was only 2% lower than the measured energy expenditure. The changes in body composition over the isotope measurement period showed a small negative energy balance, and when this was accounted for the energy expenditure calculated from the intake and balance data (8·15 MJ/day; 1950 kcal/day) differed from the isotopically measured expenditure by only +2%. This close agreement in the lean group shows that dietary measurements are highly reliable in well motivated subjects with no reason for concealing their true intake. Agreement was not always good for each subject considered alone (coefficient of variation 16%), but this is to be expected given the known short term imbalances between intake and expenditure[16] and should not be interpreted as necessarily indicating error.

As in many studies of obese people, the average self recorded energy intake of the obese subjects was lower than in the lean group and averaged only 6·73 MJ (1610 kcal) daily. This was only 67% of the isotopically measured total daily energy expenditure and represented an underestimate of 3·49 MJ/day (835 kcal/day).

We could not discern whether this underestimation was due to underrecording or to dieting during the intake measurement period, since the measurements of intake and expenditure were not entirely simultaneous and the errors inherent in measuring short term changes in body composition tend to be large. Nevertheless, a mean negative energy balance of 1·75 MJ/day (419 kcal/day) was found in the obese group, confirming that some dieting was occurring and suggesting that both factors were present.

Discussion

This study found no evidence of energy sparing mechanisms in a group of women with established obesity. The combined use of whole body calorimetry and the doubly labelled water method has for the first time made it possible to assess differences in both basal metabolism and the total cost of activity and thermogenesis integrated over long periods in people following their normal patterns of activity. When appropriately corrected for fat free mass or total body weight each component of total energy expenditure appeared on average to be identical in the lean and obese subjects.

These results were obtained in a comparatively homogeneous subset of the obese population selected as having obesity with a postpartum origin and may not therefore be applicable to all obese people. Nevertheless, when interviewing subjects for the study it became clear that unequivocal histories of postpartum obesity were rare, so that possibly the metabolic and behavioural changes of pregnancy merely precipitated a maturity onset obesity in susceptible women. If this is correct the findings are probably representative of most overweight or moderately obese people in Britain whose obesity is of adult onset and has no known metabolic basis. The results should not, however, be extrapolated to grossly obese people whose physical movement has become seriously handicapped. They may also not be representative of people whose obesity began in childhood, since energy sparing mechanisms may exist in such people.[17]

The results from the lean subjects are important with respect to the aetiology of obesity, confirming our conclusion that secular trends in activity patterns in modern society have led to exceptionally low levels of energy expenditure in most people.[6] If these low levels are not recognised and matched by appropriate modifications of energy intake they will result in a positive energy imbalance, which may partly explain the trend towards increasing adiposity in affluent nations.[18] Reduced energy expenditure is also likely to precipitate frank obesity in a higher proportion of people who, for metabolic or other reasons, are predisposed to weight gain.

The results from the obese subjects, however, provide no explanation in terms of energy expenditure for individual susceptibility to obesity. It cannot be assumed on the basis of our findings in women with established obesity that preobese people would also fail to show energy sparing mechanisms, but such a conclusion does now seem likely. Firstly, the equivalence of basal metabolism between lean and obese people when expressed as a function of active tissue mass appears to be well established[15 19-21] and is further supported by our study. Garrow and Webster recently reanalysed data on basal metabolism holding fat free mass constant in order to test the possibility that preobese people have a low metabolic rate and acquire their high metabolic rate only when they become obese. They found that fatter people actually had a slightly higher metabolic rate per kg fat free mass than thin people, making it unlikely that they were more "energy thrifty" in the preobese state.[22] Secondly, if preobese people were less active than their lean counterparts it seems likely that this would be accentuated in the obese state (owing to fatigue and social pressures against active participation in sport) and would therefore have been readily detectable. Our study, however, suggested that the obese subjects were at least as active as the lean controls. Thirdly, though the possible existence of thermogenic defects in obese or preobese people remains controversial,[2] any such defect in our obese subjects must have had a negligible influence on total energy expenditure.

Possibly our most important finding is that the obese subjects must have been consuming an average of 2·22 MJ/day (531 kcal/day) more than the lean controls in order to sustain their obesity but that this would have been underestimated by almost 3·5 MJ/day (837 kcal/day) on the basis of dietary information alone. This emphasises that mild hyperphagia may quite easily exist, and remain undetected, in preobese subjects and removes the need to invoke energy sparing mechanisms to explain at least some forms of obesity. Metabolic or behavioural defects in appetite control mechanisms now seem a more likely explanation.

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Reasons for poor prognosis in British patients with cutaneous malignant melanoma

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Abstract

One hundred and twenty five patients presenting in the west of Scotland with primary cutaneous malignant melanoma answered a detailed questionnaire to establish whether there was any evidence of inappropriate delay in receiving surgical treatment for a new or changing pigmented lesion. The survey was carried out because of the relatively high proportion of patients in Scotland with melanoma presenting with primary lesions categorised as "thick, poor prognosis" and the poor five year survival figures as compared with many other countries.

Of the 125 patients questioned, only 20 (16%) had received appropriate surgical treatment within three months of becoming aware of a suspicious cutaneous pigmented lesion; 63 (50%) had received surgical treatment three to 12 months after first noticing such a change, and in 42 cases (34%) this interval was over one year. In 102 of 105 patients in whom the interval exceeded three months the patient alone was responsible for the delay; in only three cases was the family doctor partially at fault. No evidence of delay by the hospital service was identified. Because of these findings a public education campaign was launched in the west of Scotland in June 1985 with the aim of improving recognition of early malignant melanoma. In the next six months the proportion of patients in the west of Scotland with primary melanomas categorised as "thin, good prognosis" had risen from 38% to 62%, and the proportion with tumours categorised as "thick, poor prognosis" had fallen from 34% to 15%.

Introduction

In a recent extensive survey of incidence and survival statistics in patients with cutaneous malignant melanoma from centres in all parts of the world the overall five year survival rate for over 8000 patients presenting with stage I malignant melanoma (mainly during 1970-5) was 79%[1]—83% for women, 72% for men. This high figure contrasts with the 62% overall (65% for men, 53% for women) reported by the Scottish Melanoma Group for Scottish patients presenting in 1979.[2] Figures from England and Wales for the same period show an even poorer five year survival (58% for women, 44% for men).[3]

Analysis of data from individual centres in the comprehensive survey[1] showed that the highest five year survival rates occurred in centres where a large proportion of patients presented with primary melanomas categorised as "thin, good prognosis." It is well established that the most important prognostic factor for the individual patient with primary or stage I cutaneous malignant melanoma is the Breslow tumour thickness of the primary lesion.[4,5] This is calculated microscopically from the granular layer of the overlying epidermis to the deepest underlying melanoma cell. Most centres now categorise patients with primary cutaneous malignant melanoma as having a good, intermediate, or poor prognosis based on tumour thicknesses of under 1·5 mm (thin lesions), 1·5-3·5 mm (intermediate lesions), and over 3·5 mm (thick lesions) respectively.

The prognostic value of tumour thickness is proved by correlating it with five year survival. Thus in a series from Duke University of 2470 patients with melanoma the five year survival rate was 81%, and 58% of patients from that centre had primary tumours less than 1·5 mm thick.[6] Similarly, in 3025 patients reported from Sydney the five year survival rate was 79%, and 55% of those patients had tumours less than 1·5 mm thick.[7] By contrast, in the Scottish series of 1318 patients only 39% had primary tumours less than 1·5 mm thick at the time of surgical excision.[2] No comparable data are available for Breslow thickness measurements in a large series of melanomas from England and Wales.

These figures suggest that the poorer five year survival for British patients with primary malignant melanoma may be due at least in part to the smaller proportion presenting with thin tumours in the good prognosis category. It has been suggested that the "biological behaviour" of melanoma may differ throughout the world, possibly owing to the systemic effects of varying intensity of sunlight, and this has been advanced to explain the better survival figures in Sydney. Nevertheless, the fact that in Sweden (which is on a very similar latitude to Scotland) the five year survival figure is 80%, and 50% of Swedish patients present with tumours 1·5 mm or less in thickness,[8] suggests that geographical variations alone are unlikely to be the explanation for the poor Scottish figures.

We have therefore carried out a study designed to establish whether the relatively low proportion of patients presenting in

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