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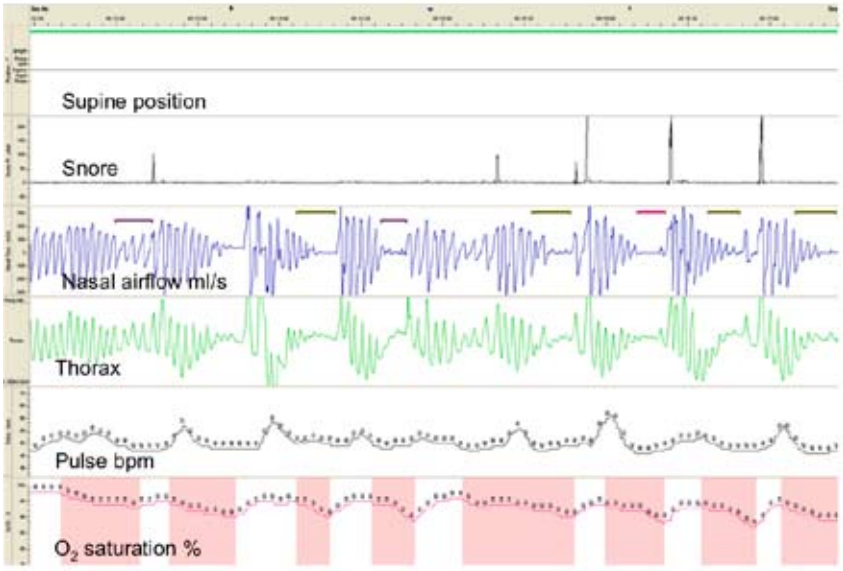
Sleep, sleep apnoea and sleep curtailment

Sleep apnoea is often unrecognised in people with diabetes. Effective treatment could improve glycaemic control and reduce cardiovascular risk.

Sleep, along with adequate exercise and a healthy diet, has been a casualty of the social, economic and working lifestyle changes of the twentieth century. Driven by the discovery and exploitation of electricity and its potential for lighting, driving motors and activating electronic devices the relationship between work and healthy leisure has been distorted. Entertainment systems can, but may not always, encourage physically inactive leisure and may be linked to undesirable snacking habits. Electric motors drive a multitude of domestic and work-place labour saving devices. Ubiquitous lighting may keep us awake for longer and the microchip has driven a large proportion of the working population into sedentary computer work-stations where the tasks can spill over into the home and even the holiday via the world-wide web and mobile communications. Wonderful though all of this may be from some perspectives it is doubtful if the consequences for everyone will be improved health.

Sleep curtailment, a reduction of the average amount of time spent in sleep, has been documented in the United States of America through cross-sectional surveys showing a reduction from eight down to seven hours in the thirty-five years up to 1995 with a further one hour reduction in about 30% of Americans, aged 30 to 64, from 1995 to 2004. Almost certainly driven by working and leisure lifestyles and commercial activity this one to two hour reduction of sleep duration (12 to 25%) coincides with the rising prevalence of obesity and diabetes in the United States (Knutson and Cauter, 2008). In susceptible individuals a number of mechanisms, some supported by experimental evidence, could result in increased risk of diabetes and obesity. Sleep loss may drive increased sympathetic nervous activity, increased evening cortisol levels and night-time growth hormone, thereby increasing insulin resistance. Sleep curtailment allows more time for eating, but through tiredness and lethargy may decrease overall energy expenditure. Sleep loss has been shown experimentally to raise ghrelin and lower leptin, driving a tendency to weight gain. Several cross-sectional surveys have shown links between poor sleep quality in people with type 2 diabetes and markers indicating worse glycaemic control and between less than seven hours sleep daily and increased risk of developing diabetes. An appreciable number of mostly cross-sectional epidemiological studies in both adults and children show an association between short sleep and higher body mass index (tabulated in detail in Knutson and Cauter, 2008). Other evidence shows that short sleepers are at increased risk of cardiovascular disease and recently Hall it al (2008) showed that sleep duration correlated with presence or absence of metabolic syndrome; shorter sleep duration was associated with abdominal obesity, higher blood glucose levels and higher blood triglyceride levels.

'Sleep loss has been shown experimentally to raise ghrelin and lower leptin, driving a tendency to weight gain.'



A sleep study showing two hypopneas and eight apneas followed by desaturation and stress reaction (pulse elevation) over 5 minutes in a 45 year old man with a BMI of 33.9 kg/m.m

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Sleep Apnoea Study…

Sleep apnoea (cessation of airflow at the mouth and nose for more than ten seconds occurring more than 30 times in a seven hour sleep) and obstructive sleep apnoea, OSA (airway obstruction causing sleep disturbance and episodes of low blood oxygen levels leading to systemic and pulmonary hypertension) occurs in people with obesity and without obesity, with diabetes and without diabetes. Risk factors for OSA include positive family history, male gender, smoking and alcohol use as well as overweight and obesity. Obstructive sleep apnoea causes excessive daytime sleepiness, snoring, falling asleep at work and while driving, and general fatigue. OSA also causes high blood pressure, poor concentration, forgetfulness, morning headaches and sexual dysfunction. A high proportion of stroke and non-fatal myocardial infarction patients give a history of OSA. In the non-obese with proven obstructive sleep apnoea the role of local deposits of adipose tissue may have been overlooked. Mortimore et al (1998) showed that while airway cross sectional area was reduced 73% in obese patients (mean BMI 34) with OSA a group of nine non-obese subjects (mean BMI 26) with OSA showed a 54% reduction of airway cross sectional area compared to control subjects. Scans showed that para-pharyngeal fat in a clearly defined zone was raised 158% in the obese OSA patients but it was raised 69% in the non-obese subjects compared to controls. This raises the interesting question of whether localised deposits of para-pharyngeal fat could be reduced in size by a weight reduction programmme in such non-obese OSA patients reduicing them from say BMI 26 to say 24 or 23. This study has not yet been undertaken. There is some evidence [see page 3] that weight reduction may be beneficial in improving symptoms in obese OSAS patients but the quality of the evidence is not as good as it should be and the SIGN working group noted that 'unfortunately sustained weight reduction is rarely achieved whatever resources are applied'. Good quality randomised controlled trials of weight loss and, more importantly, weight maintenance in managing OSAS are needed.

The prevalence of OSAS in a UK population of people with type 2 diabetes was estimated by West et al (2006) to be 23% overall compared to 6% in a community based study reported earlier. Despite the limitations of the study (discussed by Wilding 2006) West and colleagues drew attention to a possible 'epidemic' of OSAS which ought to be addressed by identifying and treating affected individuals. In those with diabetes additional mechanisms including autonomic dysfunction affecting respiratory function and responses to hypoxia may operate. Hypoxia may raise the output of pro-inflammatory cytokines from adipose tissue and lower adiponectin output. The increased sympathetic activity following frequent arousals may increase insulin resistance and impair beta-cell function. These and other mechanisms may account for the association of sleep apnoea with worse glycaemic control and worse cardiovascular risk in those with diabetes and OSAS. Wilding (2006) noted the need for further prevalence studies and determination of the characteristics of those who would benefit from treatment. Acquisition of the necessary good quality evidence to inform clinical practice may take several years. In the meantime the introduction of a few additional questions into the clinical history and the more frequent use of the Epworth sleepiness questionnaire are relatively simple steps to take. Indeed, if nearly one in four people with diabetes are affected by OSA a good case could be made for offering the questionnaire to all adult patients with type 2 diabetes.

References:

Knutson KL, Cauter EV Associations between sleep loss and increased risk of obesity and diabetes.
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Hall HH, Muldoon MF, Jennings R, Buysee DJ, Flory JD, Manuck SB Self-reported sleep duration is associated with the metabolic syndrome on midlife adults.
SLEEP 2008; 31(5): 635-643

Mortimore IL, Marshall I, Wraith PK, Sellar RJ, Douglas NJ. Neck and total body fat deposition in non-obese and obese patients with sleep apnoea compared with that in control subjects.
Am J Resp Crit Care Med 1998; 157: 280-283

West SD, Nicoll DJ, Stradling JR. Prevalence of obstructive sleep apnoea in men with type 2 diabetes.
Thorax 2006; 61:945-50

Wilding J. Diabetes and sleep apnoea: a hidden epidemic?
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The Epworth sleepiness questionnaire can be found at: http://www.patient.co.uk/showdoc/27001179/

And at: http://www.patient.co.uk/showdoc/40002436/ (accessed 14th January 2009

Footnote: OSAS = Obstructive Sleep Apnoea Syndrome = OSA + symptoms and psycho-social consequences

Weight Matters

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Use of Body Mass Index enables us to identify individuals who may require attention in terms of overall total body fat, but it is a crude measure which does not reflect fat distribution and may sometimes mislead us into believing that non-obese people may not have any fat related problems. Recognition of the role of adipose tissue as a source of pro-inflammatory cytokines and other signals, and evidence for local signalling to adjacent tissue raises the possibility of a role for local deposits of fat having disproportionate effects on disease risk.

Pericardial fat clearly has a local pro-inflammatory effect on adjacent coronary arteries mediated by cytokines. Local deposits in the high para-pharyngeal region may, despite their absolute small size have critical effects in causing airway obstruction (see above). Intra-femoral fat might signal locally to the region under the articular cartilage. All of these processes could occur in non-obese people.

There is evidence for an effect of energy supply on cytokine levels and in some clinical trials it may be difficult to unravel the effect of dietary energy reduction from body weight reduction in terms of which causes improvement – often it may be both. In view of the evidence for marginal energy restriction in reducing overall cardiovascular risk and in extending longevity we may be moving towards a new era in which, by whatever means (diet, drug therapy, surgical intervention), we marginally reduce dietary energy supply (by 10 to 20%) in order to achieve some therapeutic objectives.

'Current guidelines recognise that there is a place for weight loss in all patients with obesity and obstructive sleep apnoea.'

In this issue the focus is on sleep and sleep apnoea, an under-recognised problem, certainly in people with diabetes. Evidence for a benefit for weight reduction is incomplete and there is a need for more randomised controlled trials and acquisition of evidence for weight maintenance. The Cambridge Health and Weight Plan team is pleased to note that a randomised controlled trial of the Cambridge programme in patients with obstructive sleep apnoea will be taking place at the Karolinska Institute in Stockholm, Sweden throughout 2009.

In the meantime current guidelines recognise that there is a place for weight loss in all patients with obesity and obstructive sleep apnoea. Weight loss should also be encouraged in those already using continuous positive airway pressure (CPAP) as this may allow discontinuation of CPAP therapy.

Guidelines for management of obstructive sleep apnoea/hypopnoea in adults

In June 2003 The Scottish Intercollegiate Guidelines Network published guideline 73 'Management of Obstructive Sleep Apnoea/Hypopnoea in Adults'. This remains the definitive guideline for the UK, being endorsed by the British Thoracic Society, until the present time even though review was due in 2006 (see below). The guideline presented evidence based recommendations for diagnosis and management based on standard criteria. Methods of diagnosis were reviewed following discussion of definitions and symptoms. Subjective assessment of sleepiness using the validated Epworth Sleepiness questionnaire correlates weakly with OSAHS severity but remains the best available tool to assess the patient's own perception of his or her sleepiness [a score of more than 10/24 being indicative of a possible problem]. A review of diagnostic tools led to a recommendation that 'limited sleep studies to assess respiratory events are an adequate first-line method of diagnostic assessment'.

Treatment options reviewed included behavioural interventions, non-surgical options and surgical options. Behavioural interventions included smoking, alcohol and sedative use, and weight reduction. It was noted that there was a poor correlation between amount of weight reduction and clinical response but that a 10-15% reduction of body weight has been associated with improvements in desaturation index. The report noted that 'unfortunately sustained weight reduction is rarely achieved whatever resources are applied'. Despite lower levels of evidence the report recommended that 'Weight loss should be encouraged in all patients with obesity contributing to their OSAHS....Weight loss should also be encouraged as an adjunct to CPAP or intra-oral devices as it may allow discontinuation of therapy.'

Randomised controlled trials have established continuous positive airway pressure (CPAP) as the treatment with the firmest evidence base and the report recommended that 'CPAP is the first choice therapy for patients with moderate or severe OSAHS that is sufficiently symptomatic to require intervention'. However it was noted that CPAP is not always well tolerated – less than two hours use each night during the early weeks of use indicated a likelihood of long-term none compliance.

Intra-oral devices were deemed appropriate for snorers and people with mild OSAHS and for those unable to tolerate CPAP. Pharmacological therapy was judged as not recommendable as first line therapy for OSAHS. There were no randomised clinical trials comparing surgical treatments for OSAHS.

In 2007 the need for a SIGN guideline review was considered and two new areas were identified [APAP, auto-titration CPAP, and melatonin] and the majority of respondents recommended that selected elements of the guideline should be reviewed.

In line with this guidance the National Institute for Clinical Excellence recommended in March 2008 that:

CPAP is recommended as an option for adults with moderate or severe OSAHS, and

CPAP is only recommended as an option for treatment in adults with mild OSAHS if (a) they have symptoms affecting quality of life and if (b) lifestyle advice has been unsuccessful or is judged inappropriate.

Management of Obstructive Sleep Apnoea/Hypopnoea in Adults'. Guideline 73 The Scottish Intercollegiate Guidelines Network June 2003 see: http://www.sign.ac.uk/pdf/sign73.pdf (accessed 14th January 2009)

Proposed review of sign guideline consultation form Sign 73 see: http://www.sign.ac.uk/pdf/2007sleep.pdf (accessed 14th January 2009)

NICE guidance on CPAP can be found at: http://www.nice.org.uk/nicemedia/pdf/TA139UNG.pdf (accessed 14th January 2009)

Recommendation	Grade	Level of Evidence
All patients with suspected sleep apnoea (& partners) should complete an Epworth sleep questionnaire	**C** [A body of evidence including studies rated as 2+, applicable and consistent or extrapolated from evidence rated 2++]	**2+** [well conducted case control or cohort studies with low bias and moderate probability that relationship is causal], **3** [non-analytic studies: case reports, case reviews]
Limited sleep studies to assess respiratory events are a first-line diagnostic method	**B** [A body of evidence including studies rated 2++, applicable and consistent or extrapolated from evidence rated 1+-,1+]	**2+-** [well conducted case control or cohort studies with low bias and moderate/low probability that relationship is causal]
Weight loss should be encouraged in all patients with obesity contributing to their OSAHS. ... Weight loss should also be encouraged as an adjunct to CPAP or intra-oral devices as it may allow discontinuation of therapy	**C**	**1++** [high quality meta-analyses, systematic reviews of RCTs or RCTs with low risk of bias], **2+** [well conducted case control or cohort studies with low bias, **3** [non-analytic studies: case reports, case reviews]
CPAP is the first choice therapy for patients with moderate or severe OSAHS that requires intervention	**A** [At least one meta-analysis, systematic review of RCTs or RCT rated 1+-, applicable, or a body of evidence rated 1-, applicable and consistent]	**1++,** **1+** [well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias]
Low CPAP use (<2h/night) should lead to review	**C**	**2+,** **2++** [high quality systematic reviews of case control or cohort studies, high quality case control or cohort studies with low risk of confounding or bias]
Intra-oral devices are appropriate therapy for snorers and those with mild OSAHS	**A**	**1+,** **1-** [well conducted meta-analyses, systematic reviews of RCTs, or RCTs with high risk of bias], **1++**
Intra-oral devices are appropriate in those not tolerating CPAP	**B**	**1-**

Table constructed from: Management of Obstructive Sleep Apnoea/Hypopnoea in Adults'. Guideline 73 The Scottish Intercollegiate Guidelines Network June 2003

Footnote: OSAHS = Obstructive Sleep Apnoea/Hypopnoea Syndrome

What is the Cambridge Diet?

The term 'Cambridge Diet' is synonymous in the minds of many health care practitioners with very low-calorie diets (VLCDs). The Cambridge Diet was developed by Dr Alan Howard as a formula VLCD and indeed this remains the greater part of its present day usage. However about ten years ago it evolved into a more flexible series of dietary energy intake levels (1500, 1200, 1000, 810, 615, 415 kcal/d) allowing titration of energy intake against the client or patient's response. This is interesting historically because in the late nineteenth century a step-wise titration upwards of dietary energy was offered to people with diabetes following a fast to clear the urine of reducing sugars. Now, this remarkably precise titration process (precise because it includes formula food products rather than non-formula foods alone) can be applied with a step-wise reduction or increase of energy intake according to need. Very low calorie diets give the most effective weight losses but sometimes a part formula and part food diet can achieve remarkable weight loss. Dietary adherence tends to be less good at the higher energy intake levels and patients tend to be more hungry but nevertheless energy intake levels above 800kcal/d can give good results. The gradually accumulating scientific literature on the efficacy of VLCDs indicates that it is highly likely that the potential applications of VLCDs and part-food, part formula food low calorie diets [LCDs above 800kcals/d] will be more widely appreciated. The 2000's may well be the decade of bariatric surgery but the 2010s could be the decade of effective diets.

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Star Citation

Lojander J, Mustajoki P, Rönkä S, Mecklin P, Maasilta P. A nurse-managed weight reduction programme for obstructive sleep apnoea syndrome. J Internal Medicine 1998; 244: 251-255

This Study was designed to determine whether or not a department of respiratory medicine could run a cost-effective weight management programme for patients with obstructive sleep apnoea syndrome (OSAS) in moderately obese patients. Subjects were recruited on diagnosis of OSAS, but individuals with other major serious disease or those in whom immediate introduction of nCPAP (nasal continuous airway pressure) was necessary for occupational reasons (professional drivers) were excluded. Twenty-three men and one woman, aged 48 ± 7 years and weighing 110 ± 11kg [BMI 36 ± 3 kg/m2] were treated for 6 weeks with a very low-calorie diet [500kcal/d, Dietta-Mini®, MediFood Ltd., Finland] followed by 46 weeks of food based low calorie diet with a structured educational programme with weekly meetings for the first 14 weeks and monthly thereafter. Sleep studies were undertaken at baseline, after six weeks and at one year. A visual analogue scale was used to assess daytime somnolence.

	Baseline	**6 weeks (end of VLCD)**	**One year**
Subject no.	24	23	22
Weight kg	110 ± 11	97 ± 11*(↓12%)	99 ± 12*(↓10%)
BMI kg/m2	36 ± 3	31 ± 3*(↓14%)	31 ± 7*(↓14%)
Desaturations (4%)/h	30 ± 20	13 ± 12*(↓57%)	12 ± 14*(↓60%)
Desaturations (10%)/h	13 ± 18	4 ± 10*(↓69%)	4 ± 12*(↓69%)
Subject somnolence index	47 ± 30	28 ± 22**(↓40%)	37 ± 34**(↓21%)

$*p<0.005$ and $**p<0.05$ compared to baseline

Calculations based on the relative costs of providing nCPAP and the weight loss and maintenance programmes suggested that the weight and lifestyle programme cost about half of the cost of CPAP. The research team concluded that a nurse-managed programme combining VLCD with behavioural therapy in a secondary care setting was safe and cost-effective.

This study showed that it was possible to achieve improvement and maintain this for one year. This and other similar studies indicate that there is a need for a randomised controlled trial of VLCD followed by an effective weight maintenance treatment undertaken on a larger subject group. Ideally evidence for maintenance of weight and respiratory improvement beyond one year should be acquired.

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