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Alcohol, snoring and sleep apnoea

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SUMMARY We studied the effect of alcohol ingestion on sleep-induced breathing abnormalities and arterial oxyhaemoglobin saturation in seven patients with a range of sleep-induced upper airway occlusion. The characteristics of each patient's sleep-induced breathing abnormality was established on one or more control all-night studies, and then a further all-night study was done immediately following alcohol ingestion. Alcohol increased the duration and frequency of the occlusive episodes in five patients with obstructive sleep apnoea, and resulted in a marked increase in the degree of hypoxaemia in the first hour of sleep. In two patients with benign chronic snoring, alcohol induced frank obstructive sleep apnoea during the first hour of sleep. We suggest that the increased tendency to develop obstructive apnoea after alcohol is the result of alcohol-induced oropharyngeal muscle hypotonia, while the increased duration of obstructive apnoeas is the result of alcohol-induced depression of arousal mechanisms.

The syndrome of sleep-induced upper airway obstruction is common.[1-3] The characteristic features of the disorder have been described extensively,[4] and a clear picture of its pathophysiology has emerged.[5-7] Suction collapse of the oropharyngeal airway occurs with the onset of sleep. Despite inspiratory efforts by the respiratory muscles, there is no airflow, and progressive asphyxia ensues. After 30 to 120 seconds there is a transient arousal from sleep with resumption of airflow through the upper airway. The cycle may be repeated 200-400 times each night, and profound hypoxaemia may occur.[5 7] Patients with this disorder have a characteristic history of snoring, usually for many years, and excessive daytime sleepiness. Many develop right heart failure and cardiac arrythmias, and a variety of symptoms have been attributed to central nervous system malfunction (for example memory loss, personality changes, frank dementia). All of these problems are believed to result from the sleep fragmentation and recurrent hypoxaemia.

In a study of 30 patients over a two year period we have found a strong clinical correlation between the severity of the disorder and alcohol consumption. The families of such patients frequently report that nocturnal snoring and apnoeic episodes are invariably worse after alcohol intake. The purpose of this study was to examine the acute effects of alcohol intake on breathing during sleep in a group of patients with different degrees of upper airway obstruction during sleep, ranging from chronic heavy snorers to severe continuous obstructive sleep apnoea.

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Methods

Patients Seven patients were selected for this study on the basis of a diagnostic all-night sleep study done 1-6 months previously. The aim of this selection was to allow us to identify the effects of alcohol on the broad spectrum of sleep-induced upper airway obstruction. This spectrum was divided into three categories:

(a) Three patients with obstructive sleep apnoea. One of these patients KF, a 30-year-old male (wt 116% ideal), had severe disease with repetitive episodes of complete upper airway obstruction during sleep. He had a history of heavy habitual snoring since puberty and a two year history of excessive daytime sleepiness. His wife had noted that his snoring and apnoea were worse at weekends after alcohol intake. The other two patients (GM, CW, weights 123%, 127% ideal respectively) had intermittent episodes of complete obstruction associated with mild degrees of nocturnal hypoxaemia. Both had long histories of noisy snoring but only mild excessive daytime sleepiness. None of these patients was regarded as alcoholic, although each drank moderately (range 200-300 gm alcohol/week).

(b) Two patients, FM and RT, (age 56 and 53 years, weights 126%, 97% respectively) had a long history (> 20 years) of habitual and heavy snoring (that is partial upper airways occlusion in sleep). These patients were included because habitual and heavy snoring is

known to be a forerunner of obstructive sleep apnoea.[8] Neither patient had clinical excessive daytime sleepiness. Neither patient drank alcohol regularly; both drank only on social occasions.

(c) Two patients with obstructive sleep apnoea complicating chronic obstructive lung disease. These patients, AC (age 56, wt 132% ideal), and WB (age 52 wt 119% ideal) were heavy smokers and alcohol drinkers and both had numerous hospital admissions for increasing daytime somnolence and cor pulmonale; for each patient the degree of lung function abnormality was never sufficient to account for the cor pulmonale and respiratory failure. At the time of the present study daytime lung function was: for AC, FEV_1/VC, 0·6 1/1·3 1, residual volume 130% predicted and a functional residual capacity of 93% predicted. For WB the values were 2·9 1/3·4 1, 133% and 122% respectively. Awake arterial blood gases breathing room air were: PO_2 47 mmHg, PCO_2 55 mmHg, pH 7·36 for AC, and 60, 47 and 7·43 respectively for WB. Both of these patients were known to drink heavily at various times (for example up to 300 gm alcohol/day).

All-night sleep studies Each of the seven patients had a number of all-night sleep studies following abstention from alcohol for at least two days. First an all-night diagnostic study established the pattern and severity of abnormality; this was done 3-6 months prior to the present study. At the time of the present study, an all-night study was done as a control study. If the sleep-related breathing abnormalities differed significantly from the original diagnostic study a further control study was done and served as a basis for comparison with the alcohol study. On the following night (6.00-9.00 pm) the subject drank wine or beer under supervision, to an amount equivalent to the maximum he would drink on social occasions. The amount was measured and expressed as gm of alcohol/kilogram body weight. A further all-night sleep study was then done. To control possible effects of posture, all subjects were asked to sleep in the supine position. This posture was maintained on both control and test nights for at least the first hour of sleep. All sleep studies began between 9.30-10.00 pm and continued for 7-8 hours. Sleep was monitored with two channels of electroencephalogram (EEG) (C_4/A_1, C_3/A_2), two channels of electrooculogram (EOG) and submental electromyogram (EMG). Electrocardiogram and heart rate were monitored continuously. Arterial oxyhaemoglobin saturation was measured continuously with a fibre optic ear oximeter (Hewlett Packard 47201A) and chest wall and abdominal movements (that is diaphragm motion) were recorded with a circumferential inductance device ("Respitrace", Ambulatory Monitoring Inc, Ardsley, NY, USA). Airflow at the nose and mouth was measured with thermistors. All signals were recorded with a Grass model 78-16 channel EEG polygraph system. Sleep was staged according to standard criteria.

Respiratory variables calculated were apnoea durations, minimum arterial oxyhaemoglobin saturations during apnoea, and apnoea index (number of apnoeas/hour of sleep). In addition, the degree of arterial oxyhaemoglobin desaturation was calculated quantitatively with a method similar to that described by Slutsky and Strohl.[9] In this analysis values of arterial oxyhaemoglobin saturation less than 50% were set at 50% because the instrument readings are inaccurate below this level.[10] Average values of saturation were obtained for each epoch of 1·0 minute, and the amount of time during sleep spent at any given level of arterial oxyhaemoglobin saturation was then calculated and expressed in percent. These values were then integrated to give the cumulative distribution function representing the amount of time that the subject spent at or below a given level of saturation.

This study was approved by the Ethics Review Committees of the Royal Prince Alfred Hospital, and the University of Sydney, and all patients gave informed consent.

Results

In all seven patients studied, alcohol exacerbated the sleep-induced breathing abnormalities, and to a variable extent caused worsening of arterial blood oxygenation during sleep. The effects of alcohol were dose related, and occurred during the first 1-2 hours of sleep following alcohol intake. In most patients the pattern of breathing and blood oxygenation had returned to control levels in the second half of the night. In all subjects, while drowsy and during periods of sleep in which there was no upper airway occlusion, the arterial oxyhaemoglobin saturation was persistently lowered (range 3-4%) after alcohol intake when compared to the control nights. Data from the control nights are summarised in table 1. Data from the first hour of sleep after alcohol and for the equivalent period on the control night are summarised in table 2.

Table 1 *Summary of disordered breathing in sleep on control nights*

Patient	*Duration of apnoea (s)*		*n*	*Apnoeic index*	*Time (min) in apnoea/hour*	*Lowest SaO_2% during apnoea*	
	Mean ± SE	*Range*				*Mean ± SE*	*Range*
KF	27 ± 0·5	15-40	190	32	14	88 ± 0·5	78-93
GM	26 ± 1·0	15-56	367	57	25	89 ± 0·5	74-95
CW	25 ± 1·0	15-39	42	8	3	92 ± 0·5	88-93
FM	—	—	0	0	0	—	—
RT	—	—	0	0	0	—	—
AC	25 ± 1·0	15-66	89	14	6	83 ± 0·5	54-89
WB	33 ± 3·0	15-67	28	4	2	61 ± 3·0	50-88

Table 2 *Summary of disordered breathing in the first hour of sleep* for control (C) and test (T) nights*

Patient		*Duration of apnoea (s)*		*Aponeic index*	*Time spent in apnoea (min)*	*Lowest SaO_2% during apnoea*	
		Mean ± SE	*Range*			*Mean ± SE*	*Range*
KF	C	28 ± 1·0	15-40	32	15	88 ± 0·5	83-93
	T	46 ± 1·0	18-56	47	36	54 ± 1·0	50-69
GM	C	21 ± 2·0	15-28	11	4	92 ± 0·5	91-94
	T	32 ± 3·0	15-54	21	11	87 ± 1·0	80-93
CW	C	26 ± 2·0	16-39	15	6	92 ± 0·5	91-93
	T	28 ± 1·0	17-37	30	14	88 ± 0·5	83-91
FM	C	—	—	0	0	—	—
	T	37 ± 1·0	15-47	62	38	80 ± 4·0	71-91
RT	C	—	—	0	0	—	—
	T	28 ± 3·0	15-47	13	6	92 ± 0·5	90-95
AC	C	17 ± 0·5	15-21	12	3	82 ± 1·0	73-85
	T	32 ± 3·0	16-81	86	45	52 ± 1·5	50-64
WB	C	28 ± 4·0	16-50	15	7	70 ± 3·0	53-82
	T	36 ± 6·0	15-65	9	5	59 ± 3·0	50-75

*For the first hour of sleep on both nights the sleep stage was stage I/II non-rapid-eye-movement (NREM) sleep in patients KF, GM, CW, AC and WB. Both FM and RT had periods of stage III/IV NREM sleep during the first hour on the control night, but only stage I/II on the test night. None of the patients had rapid-eye-movement sleep in the first hour on control or test nights.

(a) *Obstructive sleep apnoea* Alcohol had two distinct effects: first, the durations of apnoea were prolonged and greater degrees of arterial oxyhaemoglobin desaturation occurred (fig 1); second, alcohol increased the incidence of obstructive apnoeas (table 2). For example, in patient KF alcohol caused a significant increase in apnoea durations ($p < 0{\cdot}001$, unpaired *t* test) and a profound worsening of hypoxaemia. The all-night slow records of arterial oxyhaemoglobin saturation for both control and alcohol nights for KF are shown in fig 2 and the cumulative data for the first hour of sleep are shown in fig 3. On both nights this patient's upper airway occlusion was clearly posture-dependent such that complete occlusion (and progressive hypoxaemia) occurred only in the supine

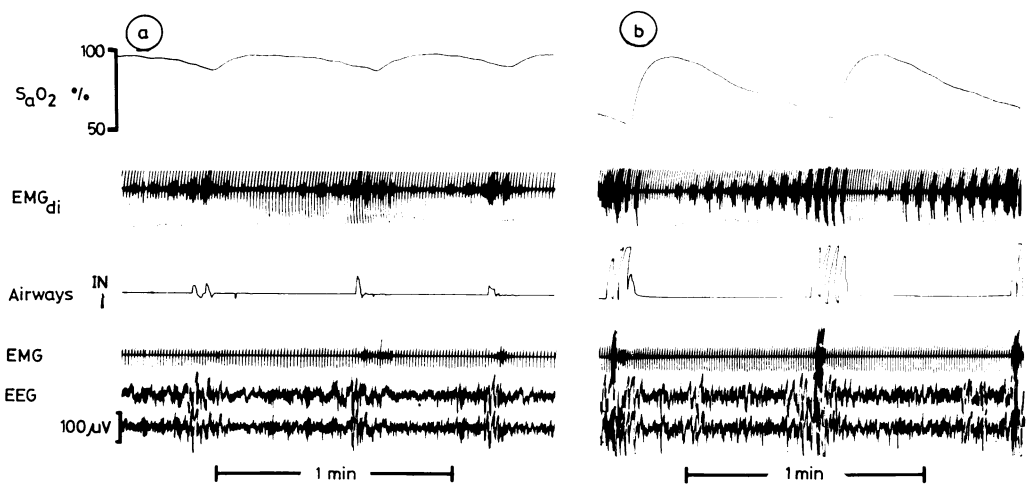

Fig 1 *Polygraph records from a patient (KF) with obstructive sleep apnoea demonstrating the effect of alcohol ingestion on the duration of apnoea and degree of arterial oxyhaemoglobin desaturation. SaO_2, saturation; EMG_{di}, electromyogram of diaphragm recorded with subcostal surface electrodes; Airflow, airflow at the nose and mouth; EMG, electromyogram of submental muscles; EEG, electroencephalogram (C_4/A_1, C_3/A_2). Panel A, typical record from the first hour of the control night. Panel B, typical record from the first hour of the alcohol night. Note the characteristic features of obstructive apnoea; inspiratory efforts without airflow at the nose and mouth, progressive asphyxia and transient arousal with resumption of oronasal airflow. Note the marked increase of apnoea duration and oxyhaemoglobin desaturation after alcohol.*

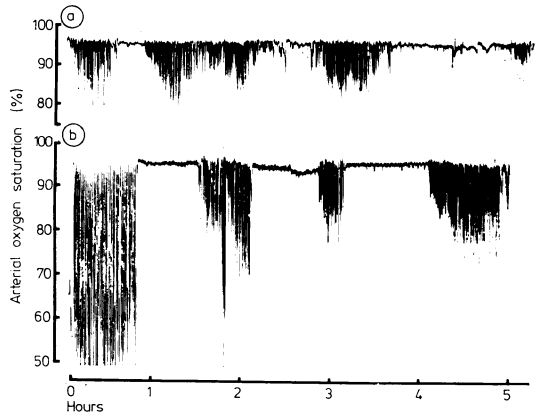

Fig 2 *All-night slow records of arterial oxyhaemoglobin saturation from a patient with obstructive sleep apnoea (KF). A, control night; B, alcohol night. Note the profound hypoxaemia in the first hour of sleep following alcohol ingestion. On both nights apnoeic apisodes occurred only while the patient slept in the supine posture. The discrepant fall in saturation near hour 2 in Trace B is an artifact resulting from disconnection of the ear probe.*

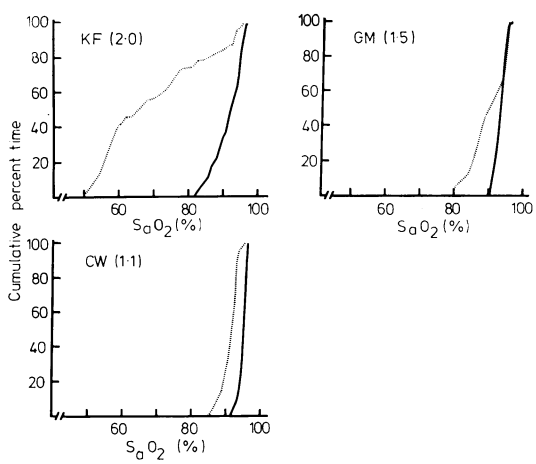

Fig 3 *Cumulative distribution functions of arterial oxyhaemoglobin saturation for the first hour of sleep in the three patients with obstructive sleep apnoea. Control night, continuous line; alcohol night, interrupted line. Each point on the distribution function indicates the percentage time spent at or below a given arterial oxyhaemoglobin saturation. Numbers in bracket represent the dose (gm/kg body wt) of alcohol consumed prior to sleep on the test night.*

position. However, alcohol clearly induced a profound worsening of blood oxygenation in the first hour of sleep after alcohol intake, with repetitive oximeter readings below 50% saturation.

For GM and CW, the major effect was to increase the number of apnoeas (from 11 to 21, and 15 to 30 per hour respectively, table 2). In addition the apnoeas were longer and the minimum arterial oxyhaemoglobin saturations lower, so that for the first hour of sleep there was considerably more hypoxaemia after alcohol (figs 2 and 3). For patient GM the variables of apnoea durations and apnoea index for the first hour of the control night were different to those for the whole night (tables 1 and 2). This difference resulted from a marked increase of severity of obstructive apnoea during episodes of REM sleep, a phenomenon described elsewhere.[5 7] Because on each of the control studies the REM episodes occurred late in the night the all-night average data showed greater abnormality than the first hour. On the alcohol night REM sleep also occurred much later in the night.

(b) *Chronic snorers* These two patients had no episodes of complete upper airway occlusion during the control nights despite sleeping in the supine position (table 1). Despite loud continuous inspiratory snoring both patients sustained normal levels of arterial oxyhaemoglobin levels. Following alcohol intake both patients developed frank upper airway obstructive apnoea with a typical pattern of inspiratory efforts without oronasal airflow (table 2). The all-night slow recordings of arterial oxyhaemoglobin saturation for the control and test nights for FM are shown in fig 4, and the cumulative oxyhaemoglobin saturation data for the first hour of sleep of both FM and RT are shown in fig 5.

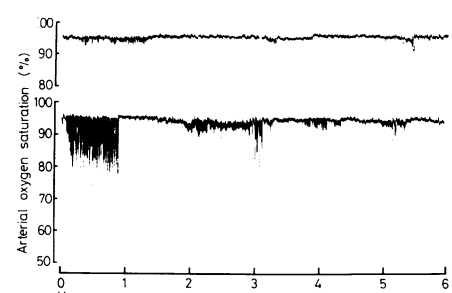

Fig 4 *All-night slow records of arterial oxyhaemoglobin saturation from a chronic snorer (FM). A, control night; B, alcohol night. Although continuous snoring occurred on the control night, there were no episodes of obstructive apnoea and no oxyhaemoglobin desaturation. Note the repetitive episodes of desaturation in the first hour of sleep following alcohol; these resulted from obstructive apneoas.*

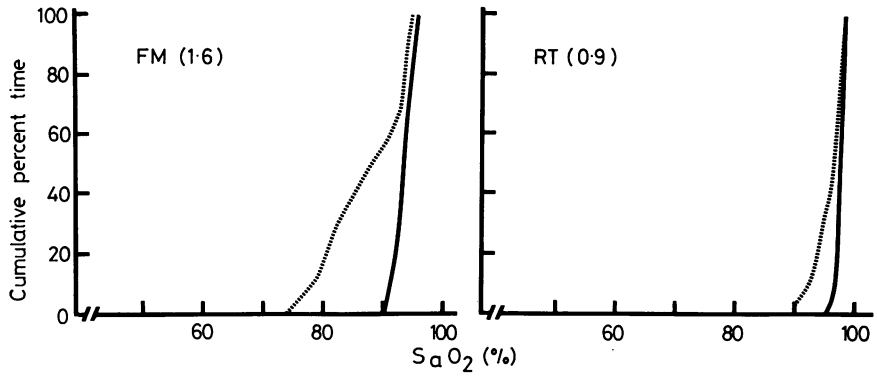

Fig 5 *Cumulative distribution functions of arterial oxyhaemoglobin saturation during the first hour of sleep for the two patients with chronic snoring. Control nights, continuous line; alcohol nights, interrupted line. Numbers in brackets, alcohol intake (gm/kg body wt).*

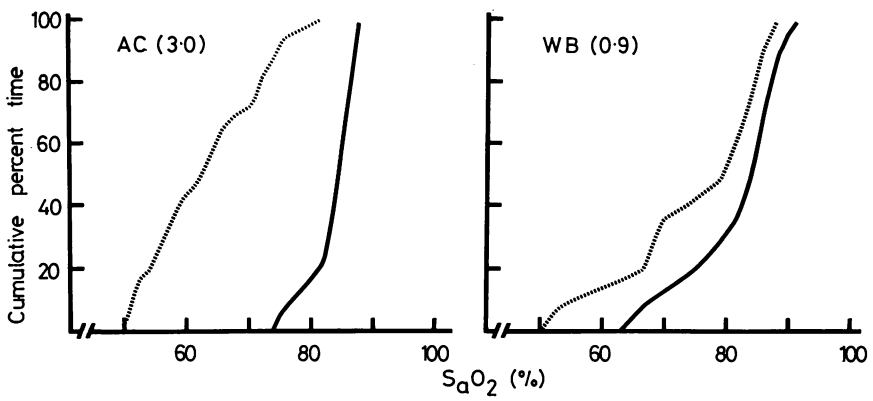

Fig 6 *Cumulative distribution functions of arterial oxyhaemoglobin saturation during the first hour of sleep for the two patients with chronic obstructive lung disease and obstructive apnoea. Control nights, continuous line; alcohol nights, interrupted line. Numbers in brackets, alcohol intake (gm/kg body wt).*

(c) *Lung disease and sleep apnoea* Alcohol intake caused longer obstructive apnoeas and lower levels of arterial oxyhaemoglobin saturation (table 2). Overall, alcohol produced a profound degree of hypoxaemia over the first hour of sleep (fig 6); for example 50% of the first hour of sleep was spent at or below an arterial oxyhaemoglobin saturation of 62% for AC and 79% for WB, compared to 84% for both patients on the control nights. Surprisingly the number of complete apnoeic episodes decreased in the first hour of sleep after alcohol for WB. However, this patient spent most of this time with virtually continuous partial upper airway obstruction (heavy snoring) with sustained low levels of oxyhaemoglobin saturation. When he did develop periods of complete upper airway occlusion they were longer than the control episodes (table 2).

Discussion

Our results established that alcohol consumption may have profound effect on breathing and arterial blood oxygenation during sleep in patients with obstructive sleep apnoea by causing longer apnoeic episodes and lower levels of arterial oxyhaemoglobin saturation. While these results are of no surprise to clinicians who manage this disorder, they confirm and extend the brief report of two patients by Guilleminault.[11] Our major new finding was that alcohol intake can induce obstructive sleep apnoea in subjects with otherwise benign chronic snoring. That such changes were most obvious in the first hour of sleep is consistent with the time-course of alcohol metabolism.

Two separate effects of alcohol were identfiied. First, alcohol clearly increased the duration of apnoeic episodes. We have postulated previously that the crucial event terminating obstructive apnoeas is the arousal induced by asphyxia;[5] arousal from sleep causes a return of tone in the muscles of the tongue, soft palate and pharynx, and so opens the oropharyngeal airway. Since acute brain depression and reduction of awake ventilatory responses to asphyxia are well recognised results of alcohol intake,[12 13] it is not surprising that the arousal response to asphyxia is depressed with consequently longer apnoeic durations. The depression of the arousal mechanisms was clearly dose-

dependent; lower levels of arterial oxyhaemoglobin saturation and longer apnoeas occurring in the patients who drank more alcohol (figs 2, 5). What is surprising was the profound levels of hypoxaemia seen in some patients (fig 2).

The second major effect of alcohol was that it promotes upper airway occlusion during sleep. The patients with mild obstructive apnoea clearly had more episodes of obstruction in the first hour of sleep on the test night (table 2). However, this effect of alcohol was particularly obvious in the chronic snorers; on the control night both of these subjects snored continuously during sleep, but had no episodes of complete upper airway occlusion; after alcohol, both subjects developed periods of frank obstructive sleep apnoea (fig 4, table 2). The likely explanation of this observation is that alcohol reduces muscle tone in sleep; this is consistent with the neural depression caused by alcohol. The current explanation of why upper airway occlusion occurs during sleep in this disorder, is that such patients have a mechanically narrow upper airway (either congentially or acquired, due to tissue enlargement, tonsils, adenoids, or fat deposits). The loss of muscle tone which occurs in sleep further reduces the area of the oropharyngeal airway. To sustain adequate inspiratory airflow, greater suction pressures are required; at some critical point the collapsing suction pressures overcome the supporting effects of tissue elastic components and muscle tone, and the tongue, soft palate oropharyngeal walls are sucked together, completely occluding the airway. It is obvious that any additional reduction of muscle tone (such as induced by alcohol) will promote upper airway occlusion.

A fundamental question about the disorder of obstructive sleep apnoea remains unanswered; is there any underlying neuromuscular defect? That is, is there excessive loss of muscle tone during sleep, or is the obstruction simply the combination of a mechanical narrowing in combination with a normal degree of sleep-induced muscle relaxation? Whereas some favour the latter explanation,[6] Guilleminault *et al*[14] have provided evidence from electromyographic recordings of pharyngeal muscles that there is an excessive loss of muscle tone. Although our study does not provide an answer to this question, it does demonstrate that an acute neuromuscular abnormality (presumed alcohol-induced muscle tone loss), can precipitate frank obstructive sleep apnoea in predisposed individuals (that is chronic snorers). A long history (often of the order of 20 years) of habitual and heavy snoring is characteristic of patients with obstructive sleep apnoea. The development of complete upper airway occlusion is usually a much more recent event and is often noted by the spouse as a change from continuous snoring, to a pattern of repetitive loud, gasping snoring breaths separated by silent periods (that is apnoeas). Chronic snoring is clearly a forerunner of the disease. Snoring itself is indicative of partial obstruction within the upper airway. While in some patients the additional factor which eventually precipitates complete oropharyngeal occlusion in a chronic snorer is readily identified (for example increasing obesity), in most it is not. Whether that additional factor is simply loss of muscle tone with age, or the presence of a specific neurological defect, our study emphasises the important role of the central nervous system in this disorder. While alcohol-induced neuromuscular depression is the most likely explanation of our findings, alcohol-induced vasomotor changes could also play a role.[15] Nasal airway mucosal engorgement with rhinorrhoea following the intake of alcohol may increase the airway resistance which will favour oropharyngeal occlusion, since it necessitates greater suction pressures downstream during inspiration.

Regardless of mechanisms, our results have major implications for the disorder of obstructive sleep apnoea, and for the problem of alcohol-related brain damage. It is obvious how alcohol intake plays a major negative role in the progress of this disease. Less obvious is the possibility that such alcohol induced changes of breathing and oxygenation is a cause of brain damage. Whereas thiamine deficiency is established as a cause of Wernicke's encephalopathy,[16] the cause of the more common brain damage syndrome of diffuse cortical loss is unclear.[16 17]

Chronic snoring is a particularly common problem. One recent estimate in a European community placed its incidence at 19%.[18] Likewise, obstructive sleep apnoea is common; the same study estimated the level at approximately 4% incidence. Because these disorders are so common, and because our study clearly demonstrated marked deterioration of arterial blood oxygenation in these patients, we suggest that asphyxia during sleep is a major cause of alcohol related brain damage. Although it is not possible to define the level of arterial oxyhaemoglobin saturation which would cause permanent brain, and other tissue damage, it seems highly likely that the profound degree of hypoxaemia induced by alcohol in some of our subjects would cause damage (figs 2, 3, 6). Levels below 50% arterial oxyhaemoglobin saturation seen in KF, WB and AC, correspond to partial pressures in the range of 20-30 mmHg, levels at which the oxygen content of the arterial blood can only be described as precariously low. The occurrence of brain (and other tissue)

hypoxia depends on a number of variables; oxygen utilisation and delivery. Delivery depends in turn on blood flow, the oxygen carrying capacity of the blood (for example haemoglobin content, and the nature of the haemoglobin), and partial pressures of oxygen in arterial blood. Hypoxic tissue damage is in turn a time-dependent process. Thus no single value for arterial oxyhaemoglobin saturation can indicate when tissue is damaged. The cyclic nature of the hypoxic insult further complicates evaluation; however, when the SaO_2 of the first hour of sleep was integrated with respect to time (fig 3), it can be seen that 60% of that first hour in patient KF was spent at or below a SaO_2 of 70%. In normal volunteers objective evidence of brain malfunction (that is EEG and psychomotor tests) occurs at this level.[19]

The two patients who had lung disease in combination with obstructive sleep apnoea add a further dimension to the problem. Because of their abnormal blood gases (that is lowered awake PaO_2 of 47 and 60 mmHg), the occurrence of obstructive apnoea led to much more rapid falls in SaO_2 and an overall greater level of desaturation in sleep after alcohol (fig 6, table 2). Furthermore, these patients depend on load compensating respiratory reflexes (particularly chemoreceptor reflexes) to sustain the increased muscle effort needed. Depression of chemoreceptors[12 13] will lead to a reduced ventilation (as suggested by the overall reduction of saturation in our patients, even when quitely awake), with a consequent reduction of oxygen partial pressure. Clearly, the combination of snoring or obstructive sleep apnoea, underlying lung disease, and alcohol ingestion will produce marked worsening of arterial oxyhaemoglobin levels in sleep, and may be causative factors in the development of alcohol related brain damage.

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