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Altounyan address

Respiratory dreams and nightmares

Neil J Douglas

Roger Altounyan played a major part in the development of inhaled prophylactic therapy for asthma. He pioneered the development of sodium cromoglycate by testing this agent, and many others, on his own asthma. His connection with my theme today is somewhat tenuous, and the best I could find relates to the fact that, as a child, he was the role model for Roger in Arthur Ransom's *Swallows and Amazons* in which appears:

"Susan said 'Roger, you had better go to sleep.' There was no answer. Roger was already asleep".[1]

While this somnolence was due to childhood exertion, I wish to focus on the sleep apnoea/hypopnoea syndrome as a major cause of somnolence in adults and children.

Epidemiology

The recognition of the sleep apnoea/hypopnoea syndrome (SAHS) was initially greeted by considerable scepticism in Britain. In 1981 the condition was reported as being "uncommon" in Britain by Professor David Flenley and Ian Oswald, respectively, leading figures in respiratory medicine and sleep in the country.[2] Subsequent events have shown this to be false and respiratory clinics throughout the country are now being inundated by patients. Prevalence figures from around the world are now showing that about 3–6% of men and 1–2% of women in middle age have both irregular breathing during sleep and sleepiness.[3–5] This has led to the suggestion that sleep apnoea "has an impact on society that rivals that of smoking".[6] One of the interesting facts to come out of these prevalence studies is that there are 6–8 times as many patients who have an increased frequency of irregular breathing during sleep but who are not sleepy during the daytime. It is not clear why this is the case, nor whether this is a genuine difference in the pathophysiological process or a differing threshold for identification of symptoms. Further work is required in this area.

Mechanism

The sleep apnoea/hypopnoea syndrome results from recurrent upper airways obstruction during sleep. The factors promoting the obstruction include obesity, retrognathia, and alcohol (fig 1). On average, patients with SAHS have narrower upper airways when awake than normal subjects, but there is considerable overlap.[7–9] We have recently investigated whether patients with SAHS may have impaired neuromuscular control of the upper airway by assessing the reflex electromyographic response to negative upper airway pressure in patients with SAHS and age matched normal non-snorers.[10] The results showed that the normal subjects and those with sleep apnoea had similar baseline electromyograms of their upper airway dilator muscles but that the patients with SAHS had impaired responses to negative pressure compared with normal subjects ($p < 0.001$).

Another factor that we have recently investigated is the familial nature of sleep apnoea. We did not wish to investigate whether sleep apnoea in obese patients was familial, as obesity is itself familial. We therefore investigated whether SAHS in patients with body mass indices of < 30 kg/m^2 tended to run in families. Full polysomnography was performed in 51 first degree relatives of non-obese patients with SAHS and 51 age, sex, height, and weight matched controls drawn from a general practice register. The relatives of the patients with SAHS had significantly more irregular breathing during sleep[11] and they also had narrower upper airways when this was assessed by acoustic reflection. Lateral cephalometry showed that the maxillae and mandibles of the relatives were retroposed compared with the normal subjects (fig 2), and this posterior displacement resulted in the narrowing of the upper airways. Thus, there is a strong familial – and probably genetic – component

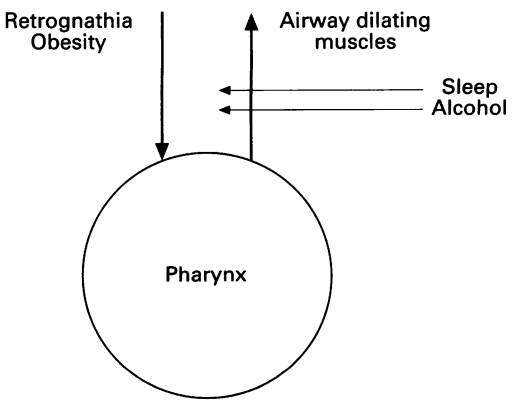

Figure 1 Schematic diagram of the mechanisms of upper airway obstruction.

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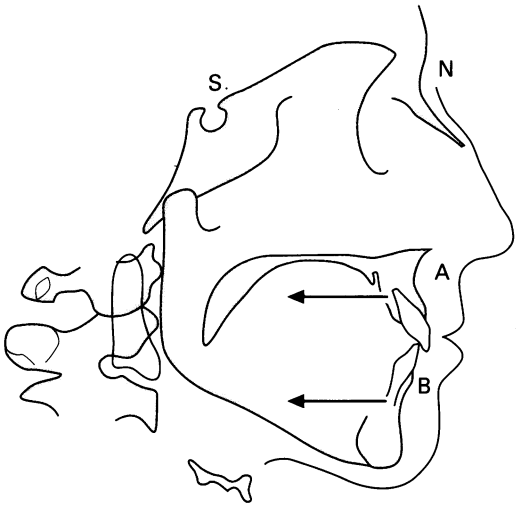

Figure 2 Schematic diagram of facial structure showing retroposition of mandible and maxilla in families with the sleep apnoea/hypopnoea syndrome. A = maximal maxillary indentation; B = maximal mandibular indentation; S = sella; N = nasion.

to SAHS in non-obese patients with the syndrome, and this observation has subsequently been confirmed also for obese patients with SAHS.[12 13]

We have also examined the disposition of adipose tissue in the neck and around the pharynx of non-obese patients with SAHS in comparison with age and weight matched controls. These patients have a greater quantity of fat in the neck than the controls and, in particular, have increased fat pads lateral to the pharynx.[14] This finding is similar to that previously reported for obese patients with SAHS when compared with weight matched controls.[15]

Associations of sleep apnoea

One of the most clearly proven risks of SAHS is an increased frequency of road traffic accidents, the rate of which is probably about double that in normal subjects.[16] This increased frequency may rise up to ninefold for single vehicle accidents[16] – the type of road traffic accidents which classically occur when drivers fall asleep at the wheel.

Hypertension is another well documented associated condition. There is no doubt that the arterial blood pressure rises repetitively during the night with the repeated apnoeas. Recent evidence indicates that this surge in blood pressure is part of the arousal response.[17] It is not small and, in some patients, both systolic and diastolic pressure double with each arousal. This doubling of blood pressure hundreds of times per night every night for years or even decades may contribute to the likely – but not proven – increase in cardiovascular and cerebrovascular morbidity and mortality associated with the condition.[18] While this nocturnal hypertension is well documented, the situation for blood pressure across the 24 hour period is less clear. One recent population based study[19] strongly suggests that patients with SAHS have an increased frequency of hypertension and that this effect is independent of obesity, sex, or age. However, another study has indicated that, although patients with irregular breathing do, on average, have high blood pressures, this effect might be slight once adjustment has been made for age, sex, obesity, alcohol consumption, and smoking.[20]

Although many have likened SAHS to the sudden infant death syndrome (SIDS), until recently there have been few data connecting these two conditions. As part of our survey into the familial nature of non-obese SAHS, we asked the relatives of our patients with SAHS and their matched normal subjects to indicate whether there had been any unexpected and unexplained sudden infant deaths in their families. A significantly higher number of cases of SIDS occurred in the families of patients with SAHS than in the control families ($p < 0.005$).[21] These relatively soft data require further clarification.

Diagnosis

I believe three aspects of diagnosis will be the focus of attention over the next few years. Firstly, emphasis will shift from identifying apnoeas and hypopnoeas to the identification of events causing pathophysiological sequelae. This will involve the identification of arousals, the final common pathway for sleepiness, impaired driving and cognitive performance, hypertension, and increased cardiovascular and cerebrovascular morbidity. Classically, arousal has been determined by electroencephalographic (EEG) criteria, but recent evidence indicates that this is imperfect. Surges in blood pressure can occur in response to external stimuli in which no cortical EEG change can be detected either by visual inspection or by computer analysis.[22] We have recently shown that daytime sleepiness can result from "disturbing nocturnal sleep" by repeated sounds, the intensity of which was titrated to produce no visible change on the EEG but a rise in blood pressure.[23] I believe that considerable attention will be focused on the development of cardiovascular or respiratory markers of arousal which have the potential to be not only more sensitive, but also cheaper and more robust than EEG markers.

The second major area in which new developments will occur will be in the identification of respiratory events that cause the so called upper airways resistance syndrome.[24] This condition has been recognised using oesophageal pressure monitoring, a technique which is relatively invasive and expensive. A non-invasive method of determining episodes where the upper airways resistance increases is by examining the inspiratory flow time profile[25] – that is, the development of flattening of the inspiratory flow curve indicating flow limitation. This technique needs to be examined closely to resolve whether all clinically significant episodes of increased upper airways resistance can be detected non-invasively.

The third area which needs to be developed is the incorporation of devices which can determine the presence of periodic limb movement disorder into equipment used for limited sleep studies. Increasingly, hypersomnolent patients will have diagnostic tests performed in

the home. Such techniques are capable of diagnosing most – but not all – patients with SAHS.[26] However, those patients with negative domiciliary tests need to be referred for in-laboratory sleep studies if they have major symptoms. One of the few conditions that can be diagnosed better, at present, in the sleep laboratory than at home is periodic limb movement disorder which may occur in 5–15% of somnolent patients.[26] There is therefore a need to incorporate leg movement detectors into limited sleep study equipment.

Treatment

Continuous positive airway pressure (CPAP) therapy in SAHS is one of the most effective and satisfying treatments in any branch of medicine. It is capable of transforming a patient's life overnight, converting him from being sleepy, incapable of productive work, and dangerous on the road into a normal human being. As such, it is much more effective than that used in most parts of respiratory or general medicine. In a recent placebo controlled crossover study we showed that CPAP improves symptoms, sleepiness, vigilance, driving simulator performance, cognitive function, quality of life, and mood in patients with a wide variety of apnoea + hypopnoea frequencies ranging from 7 to 129 per hour.[27] A more recent study[28] has suggested that similar improvements can be obtained in many patients with relatively low frequencies of irregular breathing during sleep – that is, 5–15 apnoeas + hypopnoeas per hour slept.

These results were obtained in carefully controlled trials, but do not address what actually happens in clinical practice. We have therefore recently surveyed the first 250 patients to be started on CPAP in Edinburgh – a further 400 have since received CPAP therapy. The group surveyed reported significant improvements in a wide range of functions, including sleepiness, concentration, ability to drive distances, ability to perform work, general health, and time off work.[29] We also endeavoured to investigate their frequency of road traffic incidents, comparing their reported frequency of incidents before and after CPAP. There was a significant decrease in near miss road traffic incidents reported after CPAP therapy ($p < 0.0001$), but there was no significant difference in the frequency of minor or major road traffic accidents – although these analyses were based on relatively small amounts of data.

Services

The rapidly rising rate of referral in patients who may have SAHS represents both a strength and a threat to respiratory medicine. The strengths are obvious in that the combination of a large number of patients with highly effective treatment is a very powerful case for increasing resources. Many of the threats relate to the potential for mismanaging these patients, particularly when insufficiently trained individuals are involved.

The development of a rational and well organised sleep medicine service poses a challenge to British medicine, as it does to all other countries around the world. I believe the most effective solution will be the establishment of regional centres which collaborate closely with district general hospitals (fig 3) and through them to family practice.

In the future it is likely that most diagnoses of SAHS – and, hopefully, periodic limb movement disorder – will take place in the community or at district hospital level using limited sleep study equipment. There is a plethora of such equipment being developed at present, but the limiting factor is not so much the equipment but the skills of the individuals who use it. In many centres in Britain physicians using such equipment are learning "on the hoof", often from the manufacturers of the equipment, and this is not a satisfactory process. Physicians have a healthy scepticism about the claims of drug companies for their products yet many have not developed this scepticism about complex, but often highly fallible, equipment. The most important item in the development of a local sleep service is to have trained personnel who understand the limitations of the diagnostic approach being used. The Royal College of Physicians of London in 1993 concluded that "all respiratory physicians should train for three months in a sleep centre",[30] and further went on to indicate that respiratory physicians should train "for 12 months if running a sleep laboratory". Neither of these recommendations has been enacted and it is imperative that the British Thoracic Society ensures that these become part of the curricula required for the certification of specialist training. Local hospitals with adequately trained medical and nursing staff should readily be able to perform limited diagnostic sleep studies and also follow up of patients on CPAP therapy. With the development of local expertise and improvement of automatic CPAP titration devices, it is likely that, in the near future, most CPAP titration will be able to take place in local hospitals. However, before this occurs, not only must the staff be trained, but there must be adequate staffing levels to provide early support for patients on CPAP, adequate equipment levels to present the full range of masks to the patients to achieve a satisfactory fit, and some consortium arrangements need to be reached to achieve maximal discounts by bulk purchasing of CPAP equipment.

The regional centres are at present the main location for diagnosis of sleep apnoea and for CPAP education and titration. These roles will diminish as more local services take them over,

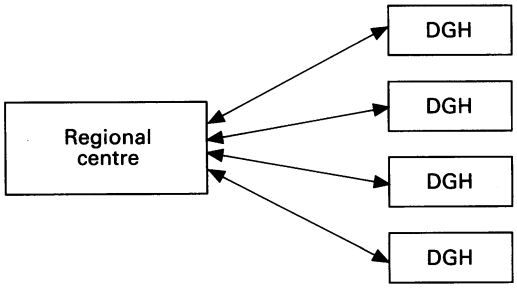

Figure 3 Design of hospital services.

leaving the regional centres to diagnose and manage the more complex patients with a combination of sleep apnoea and other respiratory or medical conditions or more unusual causes for daytime sleepiness, and to determine which patients might benefit from surgery for their sleep apnoea. Increasingly, the regional centres will also be involved in management of patients who require nocturnal intermittent positive pressure ventilation.

Respiratory nightmares

LACK OF EDUCATION

There is a genuine problem at all levels in the medical profession of lack of knowledge of sleep medicine. In a recent survey carried out by the British Sleep Society and analysed by Dr Greg Stores it was found that 71% of medical schools had teaching on sleep in their respiratory medicine courses and 29% had teaching on sleep in their general medical courses. These seemingly reasonable figures have, however, to be seen in the context that the median duration of teaching of sleep in respiratory medicine was two minutes and in general medicine zero minutes. Of even more concern was the fact that 67% of those organising courses in respiratory medicine felt that enough time was given to sleep medicine, the equivalent figure for general medicine being 60%. Until all undergraduates in all medical schools realise the morbidity and mortality associated with sleep disorders, there will be no major improvement in the standards of care provision for patients with such disorders in the community. This lack of education in sleep medicine holds equally true for basic medical and higher specialist training in the UK and also for continuing medical education for physicians, general practitioners, and other specialists.

QUALITY OF CARE

There are many horror stories circulating about inadequate delivery of care to patients with sleep disorders. I have personally seen three patients, each from a different hospital, who have been started on CPAP by being given a CPAP machine and the only available mask and told to take it home and try it. In none of the cases was there any attempt at mask fitting, CPAP education, or CPAP titration. This should not happen. There is evidence that the patient's use of CPAP over the first few days after its initiation predicts their subsequent use, and it proved difficult to reverse the anti-CPAP feelings that these three patients had developed. The risk is that one is denying patients therapy which may radically alter their lives. The fact that one of these patients was an air traffic controller and another a bus driver emphasises how important it is to give optimal treatment so that the patient becomes alert.

NON-PURCHASE OF SERVICE

There have already been threats from two regions of England that sleep services may be deleted from the list of purchases. Continuing examples of inadequate care will strengthen the case of the purchasers to take such cost saving decisions. Unfortunately there is still the element of the music hall joke about snoring hanging over sleep apnoea, and this makes it particularly important for us to demonstrate that the service is being delivered effectively with a high quality product. We must also strive to document very carefully the costs and benefits of the service provided.

CESSATION OF RESEARCH

The domination of molecular and cellular medicine for monies from research bodies poses a major threat to sleep medicine which, as yet, is not strong in these areas. As far as I can determine, the Medical Research Council has spent no money on sleep apnoea or related conditions over the last three years at least. The largest charitable body supporting research in the United Kingdom – The Wellcome Trust – has spent about £120 000 out of its expenditure of one billion pounds on medical research over that period – representing 0.01% of its spend on a condition with a prevalence of around 3%. Clearly, the academic sleep community is not getting its message through to those controlling research expenditure. There are senior respiratory physicians who remain unconvinced of the importance of sleep apnoea and this must be rectified.

Respiratory dreams

RESPIRATORY DOMINANCE

Respiratory physicians must ensure that they are major players in the provision of sleep services. They should be the team leaders in the regional centres, coordinating inputs from neurologists, psychiatrists, dentists, ENT surgeons, and faciomaxillary surgeons. In district general hospitals they again should be the team leaders, although the multidisciplinary approach will not always be relevant. Respiratory medicine did not take a proactive stance in the development of intensive care unit services in the UK and has lost these services mainly to other specialties. In many areas respiratory medicine has also lost HIV medicine and risks losing the medical oncology of lung tumours. We must not make the same mistake over sleep medicine.

INCREASED AWARENESS

The respiratory community must increase knowledge about sleep apnoea and related conditions, both within the profession and to the general public. This will require a coordinated approach over many years.

FUNDING

We have to ensure that the clinical services for sleep medicine are adequately funded and of high quality. We must also ensure that an appropriate level of research funding becomes available for good projects in sleep related medicine.

BETTER TREATMENT

Although CPAP is one of the most effective treatments available in medicine, it is relatively obtrusive and not ideal for long term commu-

nity use. More work needs to be done on other approaches, including a critical appraisal of the use of dental repositioning devices and surgical approaches. I am continually amazed that drug companies have failed to get into this area as it must be possible to develop a drug to increase upper airway muscle tone locally. Such a product would have wide sales, not only to the 3–6% of the public with SAHS but also to the 20–50% who snore. To the best of my knowledge no programme of drug development is taking place in this area at present.

Role of the British Thoracic Society

The British Thoracic Society should act to address these issues. Indeed, I believe that most of the standing committees of the BTS should be acting now to ensure that the respiratory community maximises this opportunity. The Education Committee must take on the challenge of undergraduate and postgraduate ignorance of sleep medicine; the Public Education Committee should address the lack of knowledge in the community and among health purchasers and should target legislators involved in health care and transport issues to stress the importance of sleep problems and thus ensure adequate levels of funding; the Manpower and Training Committee needs to ensure that training curricula follow the Royal College of Physicians of London's guidelines on sleep medicine, and this should be enacted through the Respiratory Specialty Advisory Committee. The Manpower and Training Committee also needs to ensure that sufficient numbers of respiratory physicians are trained to meet the increasing number of consultants being appointed with an interest in sleep medicine, and the Standards of Care Committee has a critical role in agreeing guidelines for the provision of sleep services in Britain. Without these guidelines pirate operators will move into the area, providing inadequate services which will not only result in patients receiving poor care but will also tarnish the image and thus fundability of the legitimate sleep services. The Research Committee should coordinate research between sleep centres to develop multicentre trials, and the Academic Committee should address the issue of why inadequate research funding is being allocated to sleep medicine. The only major committee of the British Thoracic Society without a clear mandate relating to sleep medicine is the Tobacco Committee, although even here decreasing tobacco consumption will decrease snoring and probably also decrease sleep apnoea.

I close by asking the Council of the British Thoracic Society to ensure that these issues are addressed as this opportunity to strengthen respiratory medicine and improve patient care and research quality should not be missed.

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