The “old school” definition of fibromyalgia (FM) used to be a sleep disorder that produced muscle pain. It was a textbook phenomenon identified by Harvey Moldofsky, M.D., of Toronto, Canada, of awake-like brain waves (alpha) interspersed throughout sleep and could be documented by a sleep study using an electroencephalogram (EEG). This alpha-EEG was noticed in other medical conditions, so it carried little weight as a diagnostic tool. In fact, for the past ten years the sleep disorder concept of FM, as well as chronic fatigue syndrome (CFS), has been shelved. Today, the focus is primarily on the symptom of pain.

Sophisticated tools are being used to study FM pain and its many symptoms that are somehow linked to the plethora of scientific findings associated with the syndrome. Research is further complicated by the fact that individuals with FM/CFS are a diverse group of patients.

But, what if FM/CFS was not so complicated? What if the unifying element among patients relates to structural abnormalities in the airways—from the tip of the nose to the bronchial tubes entering the lungs? Sounds too good to be true, doesn’t it? More studies are needed, but in the meantime, Fibromyalgia Network will let you decide whether researchers have stumbled upon the solution to the FM equation as we bring you back to the classroom to learn the basics of sleep, and the most crucial element of life itself: the ability to breathe.

‘Refresher Course’ in Breathing

Breathing occurs so automatically, it’s easy to overlook. Air from the environment (containing 21% oxygen) is inhaled through the nose, travels down the wind-pipe (trachea) and into the lungs where oxygen is exchanged for carbon dioxide (the by-product of respiration), which is then exhaled. The process is simple: the lungs expand to draw in air and they contract to expel it. Along the way, however, a number of structural and physiological defects may place a damper on this simple, rhythmic process. Also, some people are less fortunate than others, possessing several of these glitches and causing a greater resistance to airflow. As a result, the breathing “system” for each person is uniquely shaped by genetics (e.g., structure) and the environment (e.g., allergens).

The best way to point out the common problems that may interfere with breathing is through the use of illustrations. In Diagram A, a cross-sectional drawing of the nose, mouth and throat highlights the path that air must follow from the nose to the entrance of the trachea (wind-pipe). Diagram B contains a sketch of an open mouth showing how the tonsils, adenoids, tongue and other structures may impede airflow. Obviously, anything that restricts the size of the airway opening (including swelling from infections or allergens), could potentially lead to breathing difficulties.

As you examine Diagrams A and B, keep in mind the list below of structural defects that may interfere with breathing, especially during sleep when the head is in the reclined position (see Diagram C).

- Small nostrils and/or wide (deviated) septum
- Excessive cartilage in the nose
- Large, swollen turbinates (often due to allergens or infections)
- Upward arched hard palate
- Long, dangling soft palate (uvula)
- Small nasopharynx or oropharynx
- Large tongue in comparison to chin size (e.g., recessed chin)
- Narrow upper maxillary bone (smaller than normal distance between back molars)
- Tonsils and/or adenoids present (especially if swollen due to
Protruding discs; soft tissue injury (e.g., whiplash)

Enlarged thyroid gland (e.g., Graves’ disease with goiters and Hashimoto’s) may increase scar tissue.

In addition to the above, the masseter muscle that stretches from the upper cheek bone to the lower jaw bone is often tight or knotted in people with FM. Taut masseter muscles will draw the jaw up and back towards the throat, especially when laying down. This may reduce the size of the oropharynx, and the same is true of other tight muscles around the face or neck.

**Past Assignments**

FM patients often say they wake up stiff and achy. This would make sense if the oxygen supply to the muscles was impaired during the night. Yet, people with Obstructive Sleep Apnea Syndrome (OSAS), who have airflow blockages occurring at least 5-10 times per hour, usually don’t have widespread pain. Their primary symptoms are morning headaches and daytime fatigue. FM/CFS patients have these symptoms, and many more. Could another sleep disorder explain this?

**Bonifacio Alvarez Lario, M.D.**, of Spain addressed this question and published a follow-up report in 1996. He found that the level of blood oxygenation dropped significantly during the night in 28 FM patients (all female), compared to 15 healthy controls. Patients did not meet the criteria for OSAS, but they did spend a significant portion of the night with their blood oxygen concentration well below optimal levels. Lario suggested that alterations in breathing during sleep reduced muscle tissue oxygenation. This in turn produced morning pain and other FM/CFS symptoms.

Three years later, **Margherita Sergi, M.D.**, of Italy published a report on a possible link between nighttime breathing and FM. An erratic breathing pattern was found in 15 out of 17 female FM patients, compared to 2 of the 17 controls. Again, the interrupted sleep pattern did not meet the criteria for OSAS, but it did produce twice as many arousals per hour in the patient group compared to the controls. The amount of disturbed breathing during the night in FM patients correlated with symptoms of daytime fatigue and pain. Pulmonary volumes were the same in the two groups, reducing the likelihood that the findings were caused by tight chest wall muscles.

The investigators suspected that the breathing pattern could be caused by upper airway resistance (or flow restrictions) in the nose and throat regions, but discounted this possibility because many of the patients did not snore. Although snoring is always present OSAS (the loud vibrating noise produced when the airway tissues collapse), researchers in recent years have documented that snoring is not a prerequisite for Upper Airway Resistance Syndrome (UARS).

**UARS School of Thought**

If you take the structures in the nose and throat (Diagrams A and B), and place them in a supine sleeping position (Diagram C), it is clear to see how the airways can become obstructed—partially (UARS) or fully (OSAS). The size of the airway is one major factor, but the characteristics of the surrounding tissue (such as the strength of the muscles and the amount of fat deposits in the area) also plays a role. For many people with airway restrictions, difficulty sleeping and a variety of symptoms reminiscent of FM/CFS will develop.

As the lungs expand to suck in air, there is so much resistance in the airway that it takes much more effort to draw in each breath. This is hard on the heart, which is why physicians check for OSAS. Unfortunately, methods for testing UARS have only recently been developed, so this disorder is often overlooked.

Over ten years ago, scientists began studying people with UARS. Researchers placed a small sensor device in the nasal passage to measure the amount of resistance in the airway.
UARS could be identified. As with any “new” entity in medicine, UARS is the subject of “put-downs” because many doctors believe that OSAS is the only sleep-disordered breathing condition that exists. UARS challenges this traditional way of thinking, just as fibromyalgia challenges the concept of real pain without obvious tissue disease! UARS and FM/CFS have more in common than just symptoms.

If the sleep disorder of FM/CFS might really be that of UARS, why haven’t you been tested for it? In today’s world, apnea remains King ... and there appears to be little room for a Queen. Most physicians have been taught (and still may believe) that apnea is the only sleep-related breathing disorder that warrants further testing. The health insurance industry further promotes this mindset by not covering sleep studies for the sole purpose of diagnosing UARS, although many labs are capable of performing the necessary measurements. However, symptoms of chronic insomnia and suspicion of OSAS are usually sufficient grounds for ordering a sleep evaluation.

Christian Guilleminault, M.D., at the Stanford Sleep Center in California, has directed a large number of the studies on UARS. He discovered that UARS patients have a higher frequency of structural abnormalities in their upper airway than those without UARS, and has looked at blood pressure, age, gender, and menopause as predisposing risk factors for the condition.

FM Study Scores A+

Due to the similarities between UARS and FM, sleep researcher Avram R. Gold, M.D., at SUNY-Stony Brook in New York, collaborated with Joan Broderick, Ph.D., to determine how often UARS occurred in 28 women diagnosed with FM. Half of the patients were recruited from their sleep center in Stony Brook, NY, and the other half were enrolled from a previous “survey type” FM study that had nothing to do with sleep. The investigators of the study wanted to include FM patients who had not sought help for their sleep difficulties.

Evaluation of the airflow dynamics in all FM patients was compared to that of 11 female UARS patients who had been identified by previous research projects. Between the overnight sleep lab data and the physical findings about the airflow openings, the study revealed that 27 of the 28 FM patients met the criteria for UARS. The FM group averaged 30 arousals per hour, which was similar to that found in the UARS group. In addition, application of nasally administered continuous positive airway pressure (CPAP) to overcome the resistance to air flow provided proof that the frequent arousals were due to the airway resistance. After three weeks on nasal CPAP, a substantial reduction in FM symptoms (ranging from 23-47%) was achieved.

Despite dramatic symptom improvements, only 36% of the patients placed on CPAP were still using it nine months later. Although it may seem odd that patients would discontinue a therapy that helped them, there are many valid reasons why FM patients halted CPAP.

Two-thirds of the patients in the study had rhinitis (at least two of the following symptoms: chronic nasal stuffiness, post-nasal drip or nasal allergies). When chronic sinus problems exist, it increases nasal resistance and impairs one’s ability to breathe nasally. Other situations that prevented the CPAP usage included skin rashes caused by the device’s mask, inability to vary sleep position, and difficulty breathing against a positive pressure. Many could not fall asleep while breathing against a steady stream of pressurized air, because the effort required to exhale kept them awake. Fortunately, CPAP is not the only way to treat UARS.

OSAS or UARS? ... depends on how you grade them

The foregoing study described the high prevalence of UARS in women with FM. What about the overlap between OSAS and FM? In 1993, Kimberly May, M.D., looked for sleep apnea in patients with FM (92 females and 25 males). The incidence of OSAS was low in the women (2%), but it turned out to be exceptionally high (44%) in the group of men with FM. She concluded that sleep apnea may be a marker for undiagnosed FM in men. In addition, when the apnea was identified and treated, half of the patients showed significant improvement in their sleep and FM symptoms.

Therapies targeting OSAS and UARS can produce a dramatic reduction in symptoms, so they are important to identify. The distinguishing features of OSAS and UARS are indicated in Diagram D. UARS involves a restriction in airflow during sleep, produces an alpha-EEG sleep pattern similar to that found in FM, and causes more frequent arousals than OSAS. In fact, studies in recent years have documented that individuals with UARS exhibit many symptoms in common with FM, such as daytime fatigue, difficulty falling asleep (insomnia), headaches, irritable bowel syndrome, and bruxism (teeth grinding caused by unconscious jaw movements during sleep). Even low blood pressure, which is a frequent sign of orthostatic intolerance, and cold extremities, are significantly more common in people with UARS.

OSAS and UARS are at two ends of the spectrum of sleep-disordered breathing, but OSAS occurs more often in men while the prevalence of UARS is greater in women. The blood oxygen levels typically dip below 88% several times an hour in
OSAS patients, but there is no evidence of alpha-EEGs or awake-like brain waves intruding upon deep sleep—a finding in patients with UARS. This alpha-EEG in UARS suggests that the brain is in a constant state of arousal, even during sleep, and this could be why the two syndromes exhibit different symptoms. Conversely, the blood oxygen levels in UARS patients hover between 88-92% throughout the entire night (a phenomenon observed in the FM studies by both Lario and Sergi). OSAS and UARS are bad for one’s health, but UARS tends to be more destructive to the sleep process. This may also explain why UARS patients have more symptoms, which happen to overlap with those found in FM/CFS patients. It is quite possible that many diagnosed with FM or CFS also have UARS, but they are not being treated for the latter.

### Learning From Children

How can researchers be certain that sleep-disordered breathing is caused by airway restrictions and not by aging, hormones, or other factors? The answer to this comes from sleep studies performed on children ages 2 to 12. Guilleminault analyzed the medical records of 400 youngsters who had undergone overnight sleep tests because their parents noticed irregular breathing patterns during sleep. He compared them to 60 age-matched healthy kids who did not have any signs of sleep-disordered breathing. This latter group served as controls and were subsequently evaluated by an overnight sleep test for comparison purposes.

All 400 of the children with breathing problems were referred to an ear, nose and throat (ENT) specialist for treatment. Many of them had their tonsils and/or adenoids removed, but the choice of therapy was left up to the ENT. Three months after therapy, 55 children still had symptoms of sleep-disordered breathing, but none met the adult criteria for OSAS. Guilleminault re-graded their sleep study charts according to less strict criteria for OSAS (e.g., pediatric guidelines) and 31 patients received the OSAS score. The other 24 patients were scored as UARS.

The OSAS group was slightly older than the UARS children and consisted of more boys than girls. Of interest, close to 50% of the UARS group had already been diagnosed with attention deficit hyperactivity disorder. All 55 children were treated more aggressively (adenoids and tonsils removed; turbinates cut back), and almost all symptoms went away.
In a separate study, Guilleminault evaluated children in this same age group to determine why OSAS develops in a child as opposed to UARS. Children with the structural features outlined on page 12 were more likely to have sleep-disordered breathing. Those who had high blood pressure tended to meet the pediatric guidelines for OSAS, while those with low blood pressure (less than 80/60) tended to have UARS. This difference implies that the autonomic nervous system is dysfunctional in both conditions. However, the nervous system is responding to the airway resistance by two different mechanisms, generating two separate conditions. Both studies underscore the fact that OSAS and UARS begin very early in life.

**Next Assignment: Treatments**

Treatments for UARS vary from invasive surgeries to simple, self-administered remedies. Typically, multiple approaches are needed and sometimes the best place to start is with a sleep study to determine if you have UARS, and if so, its severity. Even if you don’t have UARS, learn the best methods for keeping your airways clear so that breathing difficulties don’t compound your sleep disorder, pain, and other symptoms.

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Insomnia and Obstructive Sleep Apnea Syndrome (OSAS) are the two most common sleep disorders. The overlap between the two is substantial (40% of people with OSAS battle insomnia).\textsuperscript{1} The reverse is also true: many people with insomnia also exhibit some form of sleep-disordered breathing (apnea and the newly identified Upper Airway Resistance Syndrome or UARS). Despite the apparent link between the two conditions, they have remained on two sides of a rift, with insomnia on one side, and sleep-disordered breathing on the other.

Barry Krakow, M.D., director of a sleep center in Albuquerque, NM, explained in his 2004 editorial how insomnia is usually pushed aside to be viewed from a purely psychological perspective (i.e., a defect that should be treated by mental health professionals).\textsuperscript{2} Conversely, OSAS is judged as a “real” disease that is rigorously investigated and treated by pulmonary specialists. Referring to this division, Krakow says, “It’s as though the right hand doesn’t know what the left hand is doing.”

Now that the tracks have been laid to make a connection between insomnia and sleep-disordered breathing, sleep medicine is at a crossroads. Which direction should sleep experts go? Krakow recommends that sleep doctors consider sleep-disordered breathing and insomnia as two sides of the same coin.

Breathing difficulties during sleep, particularly UARS, may be the cause of most cases of insomnia. Unfortunately, most doctors are only on the lookout for OSAS, and are unaware of UARS. Christian Guilleminault, M.D., of Stanford University, has shown that the common profile for people with OSAS cannot be applied to UARS. The typical person with OSAS is an overweight, middle-aged man. But what about those who are younger, female, and not overweight? These people are rarely referred to sleep centers for overnight studies. If they have UARS, it will go undetected and untreated. In fact, these people will likely be given sleeping pills or sent to psychotherapy (a common approach to treating chronic insomnia), but neither will correct a person’s airflow limitations during sleep.

So, what are the implications for fibromyalgia (FM) patients? UARS has been documented in a diverse group of people with a variety of primary symptom complaints, such as young children and teenagers with attention deficits, as well as adults with fatigue, irritable bowel, trouble sleeping, headaches, and the widespread pain of FM.\textsuperscript{3} Since not all FM patients fit the “OSAS profile,” it is important for treating physicians to recognize that airflow can be restricted by a number of mechanisms, and not simply the one that produces OSAS.

If UARS is a likely cause of insomnia, and OSAS is on the flip side of the “insomnia coin,” does this mean that there may also be a connection between UARS and OSAS? Recently, Guilleminault published an article reflecting the progress made in the field of UARS over the past ten years.\textsuperscript{4} He indicates that people with UARS usually have structural abnormalities that restrict airflow, while OSAS is neurological in nature. They appear to be two distinct syndromes, but research shows that, over time, UARS may actually become OSAS. Guilleminault writes, “... nonrecognition of the syndrome (UARS) and the anatomic abnormalities surrounding the upper airway responsible for its symptoms will lead to complications and perhaps even development of OSAS.”

According to Guilleminault, “A study looking at the long term evolution of UARS has been done.” The evolution from UARS to OSAS was slow, but 6-7% of patients in the five-year study developed OSAS. This soon-to-be published study could be highly significant, given that OSAS develops over many decades.

The expansion of FM sleep research to include UARS is good news. However, one of the major obstacles for detecting UARS with a high degree of accuracy is that patients must swallow a small transmitter to measure the pressure in the esophagus during sleep. The device is tiny and inexpensive, but is seldom used outside the realm of UARS research (i.e., it is not used to evaluate apnea ... not even for research). Fortunately, a less expensive (but less accurate) tool for detecting UARS was developed. In the meantime, sleep studies that evaluate people with insomnia, UARS, and mild OSAS may all lead to a better understanding of the nighttime frustrations faced by millions of patients with FM/CFS.

References:
If you manage to sleep an extra hour or two, is it a waste of valuable time? What if you are overwhelmed with work and decide to cut your sleep time short in order to get things done? Given that FM/CFS patients are often exhausted and feeling short-changed on time, these are important questions. Certainly, you want to do what is best for your health. Recognizing the connection between sleep and health, patients who responded to a non-drug Fibromyalgia Network survey rated maintaining a consistent sleep routine as the third most effective self-help measure for controlling symptoms.

Toying with Sleep

Two studies indicate that extra sleep should not be viewed as optional, but rather, as a priority for healthy living and maximizing daytime function. The first study looked at the effects of modestly restricting the sleep of 25 healthy subjects (who had no sleep complaints) for one week. For the purpose of comparison, the participants were first observed in an overnight sleep lab for four days, with no changes to their sleep schedule. Then, every day for one week, the subjects (13 men and 12 women) were awakened after only six hours of sleep. The participants were not allowed to nap and were told to stick to their regular schedules.

After just one week of this relatively modest (25%) sleep restriction, the subjects’ performance on various tests measurably declined. This corresponded with significant changes in the body’s production of several important substances. Among these, cytokine chemicals IL-6 and TNF—produced by the immune system but secreted through nerve endings—were both increased during the day. Cytokines are markers of systemic inflammation and are known to cause symptoms of pain and fatigue. Not surprisingly, they have been found to be elevated in patients with FM. Cortisol, an alerting hormone, was also impacted by the sleep restriction. While the total amount of cortisol produced was unaffected, it peaked two hours earlier in the morning following the pattern of a two-hour decrease in sleep.

Since reducing sleep time has serious consequences, does sleeping more have a positive impact? A recent study examined the benefits of increased sleep time. College students (ages 18 to 23) were allowed to ignore their alarm clocks and sleep in (on average an extra hour). After eight days, researchers found that in comparison to baseline values, the extended sleep led to substantial improvements in daytime alertness, reaction time, vigor, fatigue, and mood.

Insomnia

Cytokines IL-6 and TNF are both fatigue-inducing substances, so their production during the daytime can greatly hinder a person’s performance. Ordinarily, their peak secretion is around 9 p.m., which explains why people get sleepy at this time of night. A study looking at people with chronic insomnia found that IL-6 production shifted to the middle of the day (2 to 3 p.m.), while TNF secretion was elevated throughout the daytime hours. In a separate report, the same research team also found that cortisol was overproduced in people with insomnia, so even if they wanted to fall asleep, this arousing hormone could keep them awake. A major drawback of both of these studies: Upper Airway Resistance Syndrome (UARS) during sleep was not evaluated in the patients with insomnia.

Apnea

There is evidence that insomnia may be caused by airway resistance (e.g., UARS). If this is the case, and if insomnia and apnea are on different sides of the same coin (see previous article), then logically, there must be some connection with cytokines and apnea. As it turns out, there is! Daytime levels of IL-6 are elevated in people with apnea, which could explain their daytime fatigue (IL-6 causes fatigue in insomnia patients too). After a one-month treatment of apnea patients with Continuous Positive Airway Pressure (CPAP), which kept the airways open at night so that patients could obtain restful sleep, the levels of IL-6 were significantly decreased. A recent study found that administering CPAP to FM patients who also met the criteria for UARS substantially reduced their pain and fatigue. One can speculate that, like the apnea patients, symptom improvements in UARS and FM should coincide with a drop in cytokines.

In the previous Network newsletter, we reported that Continuous Positive Airway Pressure (CPAP) reduced the symptoms of FM pain, fatigue, sleep disorder, and gastrointestinal disturbances by 40 to 50%—a success rate unmatched by any other therapy. Avram Gold, M.D., at Stony Brook University in New York was the lead author.\(^1\) When Fibromyalgia Network asked Dr. Gold about his approach for reducing the symptoms of FM, he emphasized, “I do not treat FM; I DO treat flow limitation during sleep in FM patients.”

Even after months of follow-up, the success rate does not improve. Why might this be? Three-quarters of the FM patients in Gold’s study had chronic allergic rhinitis (AR) and Gold suspects that the “high rate of poor nasal breathing in FM” could be partially responsible for limited treatment success. “I cannot rule out, however, that some other mechanism is also playing a role in causing the symptoms of FM.”\(^2\)

“I am quite convinced that when the work is done, it will demonstrate that inspiratory flow limitations during sleep are the unrecognized cause of much human suffering,” says Gold. “Six years of working with women with UARS (Upper Airway Resistance Syndrome) has convinced me of that.”

What are the primary approaches used for treating UARS, which in turn should improve FM/CFS? Therapies for UARS may be divided into four categories in order of increasing cost and invasiveness: (1) Inexpensive/ Self-Help Strategies, (2) CPAP, (3) Oral Appliances, and (4) Nasal Surgery.

### Inexpensive/ Self-Help Strategies

Aggressive treatment of nasal congestion tops the list for benefiting your breathing at night. Sleeping position is also important. Laying on one’s back will force the base of the tongue and other structures to fall back and occlude the airway. Ideally, a person should sleep on their side, with a cervical neck support to keep the trachea straight.\(^3\) A tennis ball or something similar can be attached to the back of a nightshirt to prevent people from sleeping on their back. Weight loss has long been promoted for the treatment of sleep apnea, but recent research shows that it is of little benefit.\(^3\)

### CPAP

CPAP is considered the first-choice therapy for UARS because the pressure setting can be individualized. It consists of a snug-fitting nasal mask with tubes connecting it to a machine that pressurizes the air flowing into the nose for breathing. Two types of machines are available, one which automatically adjusts the amount of pressure according to need, and another which produces a “fixed” pressure throughout the night. The auto CPAP delivers a lower average pressure and may be preferred by some patients. However, sudden changes in air pressure may cause frequent arousals, so if you find you cannot acclimate to one type of machine, try the other one before giving up.\(^4\)

“Patients can sleep with nasal CPAP at home in any position they like,” says Gold. Only during the sleep study, when the pressure setting is determined, must patients sleep on their back. “The airway is most collapsible in this position.”

If you already have insomnia, you may think the CPAP machine will keep you awake. Gold says that patients are often prescribed Ambien to help them adjust to sleeping with a mask and that symptoms of insomnia actually improve over time.

### Oral Appliances

Patients who are unable to tolerate CPAP due to difficulties with the mask, such as skin rash or problems breathing through the nose, may have greater success with oral appliances. These devices are designed to bring the lower jaw forward during sleep and were developed as an alternative to CPAP for patients with apnea. Impressions of your upper and lower teeth are used to make appliances out of plastic. They are not as effective as CPAP at preventing the airways from collapsing, but for people with mild airflow limitations (UARS and mild apnea), these devices may work well.\(^5\) A study involving mild apnea patients indicates that they often prefer the appliance over the CPAP machine, so they may represent your next-best option.\(^6\)

Four key points about oral devices include: (1) dentists specializing in sleep medicine and temporomandibular disorders are most likely to customize an appliance for you, (2) if your physician is not aware of a provider, The American Academy of Dental and Sleep Medicine’s Web site at [www.dentalsleepmed.org](http://www.dentalsleepmed.org) may be
helpful, (3) sore teeth and jaw in the morning are common side effects that should wear off shortly after removing the device...contact your provider for adjustments if your jaw pain or sleep worsens, and (4) major medical insurance companies often pay for oral appliances as “durable medical supplies.”

**Nasal Surgery**

The fatigue of FM/CFS is usually not viewed in relationship to chronic inflammation of the nasal or sinus tissues (e.g., rhinosinusitis or AR). A recent study by Alexander Chester, M.D., of Georgetown University, may help change this often overlooked cause of fatigue! At the October 2004 meeting of the American Association for CFS, Chester posed the question: “Does functional endoscopic sinus surgery reliably improve the fatigue associated with chronic rhinosinusitis?” He presented a review of the medical literature, showing that the fatigue levels greatly improve in patients after this form of surgery.7,8,9

What type of surgery is Chester referring to? It’s an outpatient procedure and the only form of surgery that Dr. Gold advocates for his patients. “It is surgery to improve nasal breathing (trimming back the turbinates, correction of deviated nasal septum, removal of polyps),” says Gold. “These procedures reduce nasal resistance and at the very least, they can improve a patient’s compliance with nasal CPAP.” The procedure also improves sleep and reduces daytime fatigue due to enlargement of the airway. Aside from this approach, other forms of surgery are generally considered a last resort.

**Sleep Studies:**

*When & How they should be done*

Typically, overnight sleep studies are only ordered if a person is suspected of having apnea, so people with insomnia seldom undergo a sleep study. This is particularly true for non-obese women. Fortunately, UARS is gaining recognition.

**Criteria:** Asking Gold if any persistent symptoms should prompt doctors to order a sleep study, he responded: “Fatigue/sleepiness...PERIOD. In my experience (since 1999), it is rare to find a patient with this symptom who does not have inspiratory flow limitations (e.g., UARS) during sleep.” When asked if other tests could take the place of an overnight sleep study, Gold’s answer was “no.” This is because large drops in blood oxygen levels (a detectable sign for most apnea patients using a portable device) don’t occur in UARS.

**Finding a Sleep Center:** If your doctor prescribes a sleep study, you will need to locate a sleep center. According to Gold, the best screening question is: “Do you make the diagnosis of UARS?”! The most accurate method of detecting UARS requires patients to swallow a tiny pressure sensor, but this tool is used primarily in the research setting. Fortunately, Gold points out a new alternative that is capable of detecting most cases of UARS. “Today, there is a new tool for measuring airflow during sleep that simplifies the detection of mild flow limitation. It is a nasal/oral transducer.” Only 25% of sleep centers have this device, so inquire about it before scheduling a study.

**Insurance Coverage:** “All of our patients have their studies covered by their insurers (as well as their treatment) using the code 780.53 (sleep apnea with fatigue) and sometimes 780.51 (sleep apnea with insomnia),” says Gold. “All of these patients have fatigue/sleepiness and many have mild snoring. In cases where the patient does not snore, the physician can write a letter to the insurance company citing my recent paper in SLEEP and Dr. May’s paper from 1993.1,10 I explain to the company that if we can get this woman on CPAP (or similar therapy), less money will be spent on medications and doctor’s visits. She will also be more alert behind the steering wheel and less likely to have an auto accident that could be a very expensive affair. These letters are remarkably effective.”

**Study Preparation:** Many patients fear that in order to undergo a sleep study, they must go off all of their medications. Barry Krakow, M.D., who routinely evaluates patients for UARS, indicates that “people should not change their sleep regimen for the study unless narcolepsy is suspected.” Otherwise, Krakow says that sleep doctors first want to evaluate patients “as is.” This includes bringing in all of your pillows and other comforts to best mimic your home environment.

After The Network published the UARS article in the last issue, no physician or researcher in the FM field has commented about it. Gold suspects that “the medical community is uncertain of what to make of this” (referring to UARS) because it contradicts current opinions. He adds that more studies are needed to strengthen the concept that flow limitations during sleep could cause or be partially responsible for FM/CFS. Yet, Gold believes that with new medical ideas, “the tail can wag the dog. Patients demanding answers will lead their physicians to learn new knowledge.”

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It turns out that a stuffy nose can be detrimental to the quality of your sleep. Recent research reveals that nasal congestion leads to daytime drowsiness. Allergic rhinitis (AR), the medical term for sneezing and nasal congestion, is a risk factor for developing sleep apnea, as well as its cousin, Upper Airway Resistance Syndrome (UARS). AR causes serious sleep disruption, which in turn leads to excessive sleepiness, decreased alertness, concentration deficits, irritability, and a diminished quality of life. Job performance and learning skills may also be impaired.

The vast majority of patients with FM/CFS put up with the chronic nuisance of AR. In fact, the symptom cycles of FM and AR are strikingly similar. FM symptoms fluctuate over a 24-hour period in a cycle that was documented by researcher Harvey Moldofsky, M.D., of Toronto, Canada. A graph of this cycle is superimposed over the AR symptom cycle below. The pattern of the fatigue-enhancing cytokine shift (as described on the previous page for insomnia/apnea) is also shown for comparison.

AR can exacerbate anyone’s sleep problems. For people with FM/CFS who are already tired and struggling to get a good night’s sleep, a better understanding of what causes AR and how to treat it is essential.

**Stuffy Nose and Sleep**

While it is possible that an allergen in your bedroom is causing you to wake up congested, there is a more likely cause of this symptom. Waking up each morning with a stuffy nose is part of the AR symptom cycle. Researchers have shown that AR symptoms peak between 5-6 a.m., whereas they may be less bothersome around 3 p.m. Morning stuffiness is usually about 20% worse than any of your daytime nasal symptoms.

Several factors may make your stuffy nose worse in the early morning hours. First, the nasal cavity swells up when you are laying down, causing nighttime secretions to accumulate. Second, your cortisol levels are the lowest at night. Cortisol is known for its role in suppressing the immune system, so at low levels, immune substances are more likely to be released, causing nasal inflammation and congestion. Third, the nervous system promotes an expansion of the blood vessels at night, which leads to swelling of sinus tissues.
fatigue? A study indicates that people rarely voice strong complaints about their stuffy nose, especially if it isn’t that bad in the doctor’s office in the middle of the day.* If you have a chronic runny nose or wake up to nasal congestion in the morning, make a point of addressing this symptom at your next doctor’s visit.

**Sinus Irritants ... are also found in FM**

The many sinus irritants involved in AR are listed in the table below, along with a brief description of their effects on sleep and nasal obstruction. Cells within the nasal cavity, called mast cells, can cause congestion and induce sleep-disruption by releasing their irritating contents into the nearby tissues. Examples include prostaglandins, histamine, cytokines, leukotrienes, and neurotransmitters involved in pain, such as substance P and nerve growth factor. Although a link between AR and FM is not established, University of Minnesota neuroscientist Alice Larson, Ph.D., is investigating the role of mast cells in FM. Her interest in these cells was piqued after working with I. Jon Russell, M.D., Ph.D., at the University of Texas at San Antonio, to document the three- and fourfold increases in substance P and nerve growth factor (respectively) in the spinal fluid of patients with FM.

A scientific meeting on FM, sponsored by the National Institutes of Health, Larson discussed her work that shows cromolyn solution prevents mast cells from releasing their contents, even under conditions that would normally trigger them into action. Therefore, cromolyn-based nasal sprays (such as over-the-counter NasalCrom) may minimize the symptoms of AR. More details about Larson’s mast cell research can be found on the Web site for the American Fibromyalgia Syndrome Association (AFSA) at www.afsafund.org.

The possibility of a relationship between leukotrienes and FM has not been studied. Yet, out of all of the nasal irritants produced by AR, these substances cause the most congestion. Two new drugs that block the action of leukotrienes have been approved for prescription sale in the United States. As you will read in the section below, they should benefit your sleep to a greater extent than drugs that target histamine.

### Treatments for Breathing

Now that the ties between AR and disturbed sleep have been explained, it’s time to make sure that your nighttime breathing is as effortless as possible! At first, decongestants might seem like the ideal treatment. Nasal sprays in this category, such as Afrin, take only 10 minutes to clear the upper airways. They work by shrinking the blood vessels and drying up the tissue. The downside is that they make congestion worse if used for more than four days (they are strictly to be used for one or two nights, if at all). Oral decongestants, such as pseudoephedrine (e.g., Sudafed), will clear your passages in 30 minutes, but they are stimulating agents that destroy sleep and cause drying of the nasal membranes, which aggravates chronic AR.

Usually, when people think of allergies, they think of antihistamines. Unfortunately, histamine in the brain plays a major role in maintaining wakefulness, so medications that interfere with its actions may cause sedation. The “first-generation” antihistamines, such as Benadryl, are able to cross the blood-brain barrier and induce sleepiness as well as cognitive dysfunction. Even if you choose to take these agents only at bedtime, they won’t curb nasal stuffiness in the morning because they...

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### Sinus Irritants

<table>
<thead>
<tr>
<th>Irritant</th>
<th>Effects on Sleep</th>
<th>Increases Congestion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histamine</td>
<td>Balances sleep/wake cycle</td>
<td>Slightly</td>
</tr>
<tr>
<td>Leukotrienes</td>
<td>Increase deep level sleep</td>
<td>Yes</td>
</tr>
<tr>
<td>Inflammatory Cytokines (e.g., IL-1, TNF)</td>
<td>Associated with sleep disruption</td>
<td>—</td>
</tr>
<tr>
<td>Prostaglandins</td>
<td>Sleep-promoting</td>
<td>Yes</td>
</tr>
<tr>
<td>Substance P *</td>
<td>Interferes with sleep</td>
<td>Yes</td>
</tr>
<tr>
<td>Nerve Growth Factor *</td>
<td>Interferes with sleep</td>
<td>Yes</td>
</tr>
</tbody>
</table>

* Reported elevated in FM patients

All of the above are released from mast cells. For more information, visit the American Fibromyalgia Syndrome Association (AFSA) Web site at www.afsafund.org. AFSA is an all-volunteer charity, whose overhead expenses are paid for by Fibromyalgia Network. This enables AFSA to spend over 90% of its contributions directly on research. Contribute Online, or print out the order form to mail in your contribution to AFSA today.
only work for 4–5 hours. Besides, they dry out the nasal passages and provide minimal help with congestion (they primarily relieve symptoms of sneezing and itching). If you elect to use this category of meds, avoid the popular cold-season combinations that include decongestants that are detrimental to sleep.

“Second-generation” antihistamines have been purposefully designed to work outside of the brain, so they don’t cause as much sedation. However, this side effect depends on the percentage of the drug that crosses the blood-brain barrier. For example, fexofenadine (Allegra) doesn’t cross the blood-brain barrier at all, while 30% of Zyrtec passes through. For this reason, Zyrtec is best taken at bedtime. This class of histamines can provide 24-hour relief and does not cause as much drying. Antihistamines in general do not effectively relieve nasal congestion, but certain brands may be better than others. Zyrtec and Clarinex (not the same as OTC Claritin) have been shown to be the most effective drugs in this class for relieving congestion.1,7

Nasal sprays are another treatment option, and are usually supplemental in AR therapy. Four categories of nasal sprays exist: antihistamines, steroids, cromolyn-based mast cell stabilizers, and saline solutions. The latter two are available over-the-counter. The role of cromolyn (e.g., NasalCrom) was discussed in the previous section. Saline solutions, such as Ocean Spray, simply keep the sinus membranes moist and help flush the irritants out of the nose. A study comparing antihistamine and steroid nasal sprays (azelastine versus flunisolide) demonstrated the superiority of dilute steroid solutions for treating AR.8 In particular, the steroid was shown to best reduce congestion and improve sleep. One drawback of steroid sprays, however, is that they take up to two weeks to reach their full effectiveness. These sprays are usually administered twice daily. Due to the cyclic nature of AR (worse in the morning and evening), it is optimal to use the spray immediately upon waking and then again before bedtime.

The newest class of AR medications work by blocking the effects of the leukotrienes. Two such drugs have been approved for prescription sale in the United States: Singular (montelukast) and Accolate (zafirlukast), but only Singular has specific approval for treating AR. Both have been shown to be superior to other AR meds available in pill form, particularly for reducing nasal congestion and enhancing sleep.3 Reduced nasal resistance and increased airflow rates found in patients taking these medications may be responsible for the improvements in sleep, especially since upper airway resistance appears to be the primary cause of insomnia.

## The Ideal Therapy

If money and insurance issues weren’t factors, what would be the ideal therapy for treating chronic nasal congestion and related AR symptoms? Singular is the best orally acting medication. If side effects are not tolerable, the next best is Accolate. A steroid nasal spray can also be used to enhance breathing, which ought to lead to better sleep. Using a nasal saline solution to flush and moisten the sinus membranes is useful no matter what pharmacological approach is tried. Also, mast cell stabilizers, such as over-the-counter NasalCrom spray, have a high safety record and are an alternative option for people who cannot tolerate steroid sprays. A second-generation antihistamine may help with itching, watery eyes, or a runny nose. Zyrtec and Clarinex are the best two meds in this

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**Medication Options**

### Decongestants (Oral and Nasal)

**Oral:**
- Pseudoephedrine (Sudafed)*

**Nasal Sprays:**
- Oxymetazoline (Afrin, Dristan)*
- Phenylephrine (Alconefrin, Neo-Synephrine, Vicks Sinex, etc.)*

### Antihistamines (Oral)

**First-Generation:**
- Diphenhydramine (Benadryl)*
- Chlorpheniramine (ChlorTrimeton, Sinu-Tab)*
- Clemastine (Tavist)*
- Triprolidine (Actifed, Allephed)*

**Second-Generation:**
- Loratadine (Claritin, Alavert)*
- Desloratadine (Clarinex)
- Fexofenadine (Allegra)

### Leukotriene Blockers (Oral)

- Montelukast (Singular)
- Zafirlukast (Accolate)

### Nasal Sprays

**Antihistamine:**
- Azelastine (Astelin)

**Steroid:**
- Budesonide (Rhinocort)
- Flunisolide (Nasalide, Nasarel)
- Fluticasone (Flonase)
- Mometasone (Nasonex)
- Triamcinolone (Nasacort)

**Mast Cell Stabilizer:**
- Cromolyn Solution (NasalCrom)*

**Moisturizer:**
- Saline Solution (Ocean, Ayr, etc.)*

*Available over-the-counter
category because they also treat nasal congestion. Take the time to find the AR treatment regimen that works for you. Your sleep is important, and breathing easier at night is the key to functioning better during the day.

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Q&A on UARS

Most questions on Upper Airway Resistance Syndrome (UARS) have been answered on the pages that follow. Below are answers to the remaining inquiries.

Q How would Hyperbaric Oxygen Therapy affect UARS? What about changes in barometric pressure?
A HBOT was found effective for treating FM and likely does so by reducing UARS (it increases the inspiratory air pressure), but it is expensive. We previously reported that FM symptoms flared when the barometric pressure dropped. In light of UARS, this makes sense because lower atmospheric pressure also exacerbates airflow resistance.

Q Are there any medicines to treat UARS?
A Drugs that increase serotonin (e.g., many antidepressants commonly prescribed for FM) may “slightly” aid UARS and mild apnea. Mirtazapine (Remeron), a sedating med that boosts serotonin may help as well, but causes substantial weight gain.

Q Do age or hormones influence UARS?
A Yes, during childhood and especially puberty, the tongue grows, thereby reducing the airway size and precipitating UARS in predisposed individuals. After menopause, the airway tissues may sag, increasing the incidence of UARS and apnea. Estrogen replacement minimizes this latter phenomenon.

Additional comments: (1) gasping for breath may be a sign of apnea or UARS, (2) grinding teeth at night highly correlates with the presence of UARS, (3) morning stiffness in FM and fluid retention in female apnea patients both respond to treatment with CPAP, (4) if a previous sleep study has ruled out apnea, this does not necessarily rule out UARS, and (5) Lin Chen, M.D., of Philadelphia, PA, looked at the charts of 135 FM patients and found that apnea was present in 20% of the women and 32% of the men. She suspects that the remaining patients may have had UARS, and comments: “These data provide additional reasons to consider sleep studies in fibromyalgia.”

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