Midfacial Segment Pain: Implications for Rhinitis and Sinusitis

Nick S. Jones, MD, FRCS

Address
Department of Otorhinolaryngology, Head and Neck Surgery, Queen's Medical Centre, University Hospital, Nottingham, NG7 2UH United Kingdom.
E-mail: nick.jones@nottingham.ac.uk

Current Allergy and Asthma Reports 2004, **4:**187–192
Current Science Inc. ISSN 1529-7322

During the past decade, studies on facial pain have shown that there is a distinct group of patients who have a form of facial neuralgia that has all the characteristics of tension-type headache, except that it affects the midface; it is called midfacial segment pain. The pain is described as a feeling of pressure, although some patients might feel that their nose is blocked when they have no nasal airway obstruction. Midfacial segment pain is symmetric, and it might involve areas of the nasion (the root of the nose), under the bridge of the nose, on either side of the nose, the peri- or retro-orbital regions, or across the cheeks. There might be hyperesthesia of the skin and soft tissues over the affected area. Nasal endoscopy and CT scans are typically normal. Most patients with this condition respond to low-dose amitriptyline, but noticeable improvement might require up to 6 weeks.

Introduction

Patients with facial pain often make a self-diagnosis of "sinusitis," because they know that their sinuses lie within the face. In the medical literature, rhinologic causes of facial pain include acute infective rhinosinusitis—typically preceded by an upper respiratory tract infection, and often short-lived. Chronic infective rhinosinusitis has been assumed to be the most common cause of most patients' chronic facial pain, but with the advent of nasal endoscopy and computerized tomography, along with the finding that many patients' symptoms of facial pain persist after endoscopic sinus surgery, [1•,2••,3] it has become apparent that this is not the case. It is notable that more than 80% of patients with purulent secretions visible at nasal endoscopy have no facial pain [2••]. Many patients who report intermittent symptoms of facial pain, which they think is due to infection, and who visit a clinic when they are symptomatic, are not found to have any evidence of infection, and another neurologic cause for their pain is often responsible. In cases of facial pain secondary to genuine sinusitis, there are usually endoscopic signs of disease [4]. These patients almost invariably have coexisting symptoms of nasal obstruction, hyposmia, and/or a purulent nasal discharge [5]. In this group with genuine sinusitis, endoscopic sinus surgery has been shown to alleviate facial pain in 75% to 83% of cases [2••,6•]. Other causes of facial pain include atypical forms of migraine [7], cluster headache, paroxysmal hemicrania [8], and atypical facial pain [9••,10].

Proposed Theories for the Etiology of Rhinologic Pain

Some workers have hypothesized that rhinologic causes other than infection can cause facial pain, including the presence of contact points and vacuum pain. These theories have been repeatedly quoted in the literature, with little critical evaluation.

In 1908, Sluder described "sphenopalatine neuralgia" as a cause of an ipsilateral, boring, burning facial pain beginning along the lateral side of the nose and in the eye, forehead, orbit, temporal, and mastoid regions, constant or paroxysmal, associated with lacrimation, rhinorrhea, injected conjunctiva, and sometimes involving the cheek [11]. Sluder's definition did not describe a single entity but a diverse symptom complex. He never reported a patient presenting with a combination of all the features he described. Since his description, the symptom complex has been categorized as cluster headache [12,13], although the previous name still enters the literature, disregarding the efforts of the medical community to rationalize terminology [14]. The term Sluder's Syndrome is often used loosely, and it is best avoided, because his description differs from most clinical entities.

Sluder also described a different type of frontal pain that he attributed to "vacuum" headaches, which could produce ocular symptoms [15]. These symptoms were not associated with pus or a contact point, and the pain was relieved by applying astringents in the area of the middle meatus. In resistant cases, Sluder found that removal of the middle turbinate helped, but the pain returned in 2 to 3 years.

There is no good evidence that a vacuum within a blocked sinus can cause protracted pain. Transient facial pain in patients with other symptoms and signs of rhinosinusitis can occur with pressure changes when flying, diving, or skiing, but this resolves as the pressure within the sinuses equalizes through perfusion with the surrounding

vasculature. Silent sinus syndrome, which is due to a blocked sinus with resorption of its contents to the extent that the orbital floor prolapses into the maxillary sinus, causes no pain [16].

Nasal polyposis that is sufficient to block sinus ostia rarely causes facial pain, unless there is coexisting infection with a purulent discharge [5].

The theories that implicate contact points as a cause of facial pain originate from McAuliffe *et al.* [17], who described stimulating various points within the nasal cavity and paranasal sinuses in five individuals and said that both touch and faradic current caused referred pain to areas of the face. They illustrated this in diagrams that have been reproduced in many texts [18]. These findings have been used to support theories that mucosal contact points within the nasal cavity can cause facial pain [19], although McAuliffe's studies did not, in fact, describe contact point–induced facial pain. McAuliffe's work has recently been repeated in a controlled study and was found not to produce the referred pain that he described [20]. The prevalence of contact points has been found to be the same in an asymptomatic population and a symptomatic population, and when they were present in symptomatic patients with unilateral pain, they were also present in the contralateral side to the pain in 50% of patients [21].

Stammberger and Wolf [22] postulated that variations in the anatomy of the nasal cavity result in mucus stasis, infection, and, ultimately, facial pain. They also stated that mucosal contact points might result in the release of the neurotransmitter peptide substance P, a recognized neurotransmitter in nociceptive fibers. Although this hypothesis was published 15 years ago, there has been no in vitro or in vivo work to substantiate it. For a contact point to be credible as a cause of facial pain or headache, it should be a predictor of facial pain in the entire population [23]. Another observation is that nowhere else in the body does mucosa-mucosa contact cause pain, which makes it unlikely that mucosa-mucosa contact results in the release of substance P–producing pain.

Other authors have embraced these concepts to explain how pain might be induced by anatomical variants, such as a concha bullosa [24–27] or a pneumatized superior turbinate touching the septum [28]. The description of the presence of anatomical "abnormalities," such as a concha bullosa, a paradoxical middle turbinate, or a large ethmoid bulla, is a misnomer, as these are variations that occur in asymptomatic populations. Case-controlled studies examining the prevalence of anatomical variations in patients with rhinosinusitis and asymptomatic control groups have shown no significant differences [29•]. It seems probable that in most case series in the literature describing surgery for anatomical variations in patients with facial pain, positive results following surgery result from the effect of cognitive dissonance [30•] or from surgery-altering neuroplasticity within the brainstem sensory nuclear complex [31•]. This is supported by the finding that the effect of surgery on the pain is more often partial than complete, and any response is relatively short-lived, lasting no longer than a few weeks or months, and rarely as much as 1 year.

Endoscopic sinus surgery (ESS) has been advocated by a few workers for facial pain in the absence of endoscopic or CT evidence of sinus disease or anatomical variations [32,33]. Boonchoo [33] performed ESS on 16 patients with headache and negative sinus CT scans, and reported total resolution of pain in 10 patients and partial resolution in the other six. Cook *et al.* [32] advocated ESS on patients with facial pain, which also occurred independent of episodes of rhinosinusitis, with no CT evidence of sinus pathology. Twelve of the 18 patients who underwent surgery in their series had a significant reduction in pain severity; however, it is very significant that the authors describe "complete elimination of symptoms was not accomplished in any patient." They had no evidence of ostiomeatal obstruction. If the cause of their pain was due to an anatomical abnormality or ostial obstruction, it might be anticipated that surgery would cure the symptoms of pain. This was not the case. Similarly, Parsons and Batra [34] retrospectively described 34 patients with headaches who had contact points removed and found that although there was a 91% decrease in intensity and an 84% decrease in frequency, 65% had persisting symptoms. The partial reduction in the pain could be the effect of surgical trauma on the afferent fibers going to the trigeminal nucleus, which might alter the nucleus and its threshold for spontaneous activity for up to several months [3,31•]. Therefore, the evidence in support of the theories that persistent pain is caused by contact points or a blocked sinus in the absence of any infection is poor.

Patients whose primary complaint is headache or facial pain are less likely to have evidence of rhinosinusitis than those who have nasal symptoms [35], and those without nasal symptoms are very unlikely to be helped by nasal medical or surgical treatment [2••].

Great efforts have been made to categorize facial pain into diagnostic categories based on symptoms, signs, or etiology. The aim has been to develop an understanding of the etiology and, through this, find the most effective treatment for each group [12]. Some diagnoses have relatively tight descriptions, such as trigeminal neuralgia, but even with these, there are no diagnostic tests. The current classification is undermined to some extent because, in practice, a large proportion of patients cannot readily be classified into one or more of the distinct diagnostic groups. The selection of treatment then becomes based on the category that best resembles the patient's symptoms and the treatment that works best in that group.

Recent Advances

The ideas from the Copenhagen group [36,37,38••,39•,40] on tension-type headache have resulted in a model that might be relevant to many other patients with facial pain.

Table 1. Midfacial segment pain

Definition of midfacial segment pain
• A symmetric sensation of pressure or tightness. Some patients might say that their nose feels blocked, although they have no nasal airway obstruction.
• Involves the areas of the nasion, under the bridge of the nose, either side of the nose, the peri- or retro-orbital regions, or across the cheeks. The symptoms of tension-type headache often coexist.
• There might be hyperesthesia of the skin and soft tissues over the affected area.
• Nasal endoscopy is normal.
• CT of the paranasal sinuses is normal (note that 33% of asymptomatic patients have incidental mucosal changes on CT).
• The symptoms can be intermittent (<15 d/mo) or chronic (>15 d/mo).
• There are no consistent exacerbating or relieving factors.
• There are no nasal symptoms (note that approximately 20% of most populations have intermittent or persistent allergic rhinitis that may occur incidentally in this condition).

Essentially, these theories expound central sensitization of the trigeminal nucleus from either prolonged nociceptive input from a peripheral injury; surgery or inflammation; pericranial myofascial nociceptive input; or psychological or neurologic factors that can reduce supraspinal inhibition. This concept offers a broader perspective and is a more inclusive method for interpreting our patients' conditions. Other workers have described different mechanisms that can produce central sensitization through neural plasticity and have endeavored to explain the phenomenon of hyperalgesia and how pain can persist [31•,41].

The overlap between the various recognized conditions causing facial pain is greater than might appear from the current texts that classify them. Many patients who could readily be classified into one of the established defined groups also have additional features, such as neuropathic, myofascial, migrainous, or supraspinal characteristics to their pain [42••]. The Headache Classification Committee of the International Headache Society [12] endeavored to circumvent this problem by simply placing the patients' disorders in order of importance. However, this system does not allow the addition of other "characteristics," as opposed to an additional diagnosis, that might help in the patient's management, as there are clearly large areas of overlap between many patient's symptoms and their response to treatment. For example, separating headaches from facial pain is an artificial division because many conditions involve both the head and the face [10].

Midfacial segment pain has all the characteristics of tension-type headache, with the exception that it affects the midface (Table 1). Patients describe a feeling of pressure, heaviness, or tightness, and they might feel that their nose is blocked, but they have no airway obstruction. The symptoms are symmetric and might involve the nasion, the bridge of the nose, either side of the nose, and the peri-orbital region, retro-orbitally or across the cheeks. The forehead and occipital region might also be affected simultaneously in approximately 60% of patients. There are no consistent exacerbating or relieving factors, and patients often take a range of analgesics but have no, or a minimal effect, with the exception of ibuprofen, which might help a few to a minor extent. The symptoms are initially episodic, but are often persistent by the time patients are seen in secondary care. They might be convinced that their symptoms are due to sinusitis, because they know that their sinuses lie under this area, with the exception of the bridge of the nose. They might have been treated for a long period with antibiotics and topical nasal steroids, and a few patients have had some transient response on occasions that might be related to the placebo effect or cognitive dissonance, but these are inconsistent. Patients' symptoms are not worse with routine physical activity, and rarely interfere with the patient getting to sleep.

Patients often describe tenderness on touching the areas of the forehead or cheeks, leading them to think there is underlying inflammation of the bone. However, on examination, there is hyperesthesia of the skin and soft tissues in these areas, and gently touching these is enough to cause discomfort, with no evidence of underling bony disease. This is similar to the tender areas over the forehead and scalp seen with tension-type headache. Patients might indicate that the skin of the infraorbital margin region or cheeks swells up, but there are no objective signs; this symptom might relate to an alteration in sensation in this area.

Nasal endoscopy is normal. Because approximately one in three asymptomatic people have incidental changes on CT scans, this might confuse the picture. A trial of maximal nasal medical treatment, including oral and nasal steroids and a broad-spectrum antibiotic with anaerobic cover, fails to help their symptoms. Most patients with this condition respond to low-dose amitriptyline, but usually require up to 6 weeks of 10 mg (occasionally 20 mg) at night before it works. Amitriptyline should then be continued for 6 months before stopping it, and the 20% whose symptoms return when they stop it need to restart it if the pain returns. Patients need to be warned of the sedative effects, even at this low dose, but they can be reassured that tolerance usually develops in the first few days. It is our practice to inform patients that amitriptyline is also used in higher doses for other conditions, such as nocturnal enuresis and depression, but its effectiveness in midfacial segment pain is unrelated to its analgesic properties, which would take effect much more quickly and normally would require 75 mg. It is often reassuring for patients to know the dose used for depression is some seven or more times the dose used in tension-type headache or midfacial segment pain. Other serotonin reuptake inhibitors are not effective (again as in tension-type headache). If amitriptyline fails, relief might be obtained from neurontin, propranolol, carbamazepine, and, occasionally, sodium valproate.

In a proportion of patients, there are migrainous features, and a triptan might help acute exacerbations. This is analogous to the overlap between tension-type headache and migraine described in the neurologic literature [12,43–46]. It seems likely that the underlying pathology in midfacial segment pain is similar to that in tension-type headache. The etiology of this type of pain is uncertain, but Olesen's theory [38••,47], which integrates the effects of myofascial afferents, the activation of peripheral nocioceptors, and their convergence on the caudal nucleus of trigeminal, along with qualitative, changes in the central nervous system, provides one of the best models. There is also a suggestion that there is a downregulation of central inhibition from supraspinal impulses due to psychological stress and emotional disturbances. A higher proportion of these patients have myofascial pain, irritable bowel, and fatigue than that found in the normal population, although many appear to be healthy individuals. Other mechanisms have been proposed that include sensitization of peripheral myofascial receptors, sensitization of second-order neurons at the spinal or trigeminal level, sensitization of supraspinal neurons, or decreased antinociceptive activity from supraspinal structures [48]. The trigeminal caudal nucleus is the major relay nucleus for head and neck pain, and it seems that supraspinal excitatory input contributes to intense neuronal activation, resulting in a generalized increase in sensitivity of the nociceptive pathways, both centrally and peripherally. Midfacial segment pain might be a state of trigeminal neuronal hypersensitivity and pain facilitation. Olesen's model is attractive, as it might explain much of the clinical picture of midfacial segment pain [38••]. For example, the skin and soft-tissue hyperesthesia that accompanies the pain might be due to the hypersensitivity of the pain pathways, as mentioned earlier. It is of interest that if surgery is mistakenly performed as a treatment for midfacial segment pain, the pain might abate temporarily, only to return after several weeks to months. When patients with midfacial segment pain undergo septal or sinus surgery, there is no change in approximately 33%; in 33% symptoms are worsened; and in the remaining 33%, the pain is abated, but only for a few weeks, and rarely for more than a few months. It is as though the surgical stimulus alters the "balance" of neuronal activity in the trigeminal caudal nucleus for a short time. It is possible that the placebo effect or cognitive dissonance might also be responsible for a temporary symptomatic improvement. These effects cannot explain the benefit of amitriptyline, because the placebo effect normally subsides within months [30•].

The term midfacial segment pain avoids the use of the term "tension," which often results in a long and relatively unproductive discussion with patients about the role of stress in their condition.

Sinogenic Pain

Acute sinusitis usually follows an acute upper respiratory tract infection and is usually unilateral, intense, associated with pyrexia and unilateral nasal obstruction, and characterized by a purulent discharge. Chronic sinusitis is, however, usually painless, with episodes of pain occurring during acute exacerbations, which are often precipitated by an upper respiratory tract infection, or when there is obstruction of the sinus ostia by polyps, when pus is present [5]. The pain is often a unilateral, dull ache around the medial canthus of the eye, although more severe facial pain can occur; in maxillary sinusitis, toothache often occurs. An increase in the severity of pain on bending forward is traditionally thought to be diagnostic of sinusitis, but this is nonspecific, because many types of facial pain and headache are made worse by this.

The key points in the history of sinogenic pain are an exacerbation of pain during an upper respiratory tract infection, an association with rhinologic symptoms, and a response to medical treatment. Examination of the face is often normal in patients with chronic sinusitis. Facial swelling is usually due to other pathology, such as dental sepsis. If a diagnosis of sinusitis has been made and the patient has not responded to treatment, nasendoscopy is very helpful, if not essential, in making the diagnosis of sinusitis. A normal nasal cavity, showing no evidence of middle meatal mucopus or inflammatory changes, makes a diagnosis of sinogenic pain most unlikely, particularly if endoscopy is carried out when the patient is in pain or had pain within the previous few days. On occasion, it is useful to review the patient and repeat the nasendoscopy when they have pain, to clarify the diagnosis.

Atypical Facial Pain

This has been a diagnosis of exclusion, and care must be taken in reaching it, even when the patient has received previous opinions and no pathology has been identified. The history is often vague and inconsistent with widespread pain extending from the face onto other areas of the head and neck. The pain might move from one part of the face to another between consultations, and other symptoms, such as "mucus moving" in the sinuses, are often described. Some patients have completely fixed ideas about their condition and will not be convinced otherwise, regardless of the weight of evidence to the contrary. Pain is often described in dramatic terms. Many of these patients have a history of other pain syndromes, and their extensive records show minimal progress, despite having been prescribed various medications. They might have undergone previous sinus or dental surgery treatment, but the onset of their pain usually preceded any intervention, which helps differentiate it from postsurgical neurogenic pain [49]. Many patients with atypical facial pain exhibit significant psychological disturbance or a history of depression and are unable to function normally as a result of their pain. The management of such patients is challenging, and confrontation is nearly always counterproductive. A good starting point is to reassure the patient that you recognize that they have genuine pain, fol-

Table 2. Key points in avoiding an incorrect diagnosis of sinusitis in facial pain

- If facial pain and pressure are the primary symptoms, sinus disease in the absence of any nasal symptoms or signs is unlikely.
- A patient with facial pain in addition to nasal obstruction, a loss of sense of smell, and the following symptoms: worse with a cold, flying, or skiing, might be helped by nasal medical or surgical treatment.
- The pain of most patients seen in a rhinology clinic is due to causes other than sinusitis.
- Patients with normal nasal endoscopies are unlikely to have pain due to rhinosinusitis.
- Patients with a normal CT scan are unlikely to have pain due to rhinosinusitis (note that approximately 33% of asymptomatic patients have incidental mucosal changes on CT, and, therefore, radiographic changes alone are not diagnostic of symptomatic rhinosinusitis).
- Patients with purulent secretions and facial pain are likely to benefit from treatment directed at resolving their rhinosinusitis. Paradoxically, only a minority of patients with purulent rhinosinusitis at endoscopy have facial pain.
- If it is not possible to make a diagnosis at the first consultation, it is often helpful to ask the patient to keep a diary of symptoms, have a trial of medical nasal treatment, and review the patient again.
- Surgery done for pain in patients with no objective signs of paranasal sinus disease has no effect in 33%, makes the pain worse in 33%, and, although it can help reduce the pain for the remaining 33%, the improvement rarely lasts more than a few months.
- It is important to defer making a diagnosis in studies of facial pain until at least a12-month period has elapsed, because a response to treatment is often an important factor in confirming the cause. This is because the effect of cognitive dissonance, or of surgery altering neuroplasticity within the brainstem sensory nuclear complex, might have a temporary effect that can last a year [3].

lowed by an empathetic consultation with an explanation. Drug treatment involves a gradual build-up to the higher analgesic and antidepressant levels of amitriptyline (75–100 mg) at night. It might be possible, in a sympathetic way, to make such patients aware that psychological factors might play a role in their condition, and referral to a clinical psychologist might be helpful in some circumstances.

Conclusions

Most patients who present to an otorhinolaryngology clinic with facial pain and headaches believe they have "sinus trouble." There is an increasing awareness among otorhinolaryngologists that neurologic causes are responsible for a large proportion of patients with headache or facial pain [50,51]. We believe that patients with facial pain who have no objective evidence of sinus disease (endoscopy negative, CT negative), and whose pain fails to respond to medical antibiotic/steroid therapy aimed at treating sinonasal disease, are very unlikely to be helped by surgery, particularly in the medium and long term (Table 2).

A comprehensive examination, including nasendoscopy, is highly desirable if medical nasal treatment has failed to help, to identify significant pathology before making or refuting a diagnosis of sinusitis. Midfacial segment pain, which has all the characteristics of tension-type headache, except that it affects the midface, is a common cause of facial pain (Table 1).

References and Recommended Reading

Papers of particular interest, published recently, have been highlighted as:

- • Of importance
- •• Of major importance

1.• Tarabichi M: **Characteristics of sinus-related pain.** *Otolaryngol Head Neck Surg* 2000, **122:**84–87.

An honest study of 82 patients who underwent sinus surgery for facial pain showing that 1 year after surgery, 38% had pain without any evidence of sinusitis.

2.•• West B, Jones NS: **Endoscopy-negative, computed tomography–negative facial pain in a nasal clinic.** *Laryngoscope* 2001, **111:**581–586.

A large study of patients attending a rhinology clinic with more than a 2-year follow-up that illustrates many of the points made in this review in clinical practice.

3. Jones NS, Cooney T: **Facial pain and sinusitis.** *Rhinology,* In press.
4. Hughes R, Jones NS: **The role of endoscopy in outpatient management.** *Clin Otolaryngol* 1998, **23:**224–226.
5. Fahy C, Jones NS: **Nasal polyposis and facial pain.** *Clin Otolaryngol* 2001, **26:**510–513.
6.• Acquadro MA, Salman SD, Joseph MP:. **Analysis of pain and endoscopic sinus surgery for sinusitis.** *Ann Otol Rhinol Laryngol* 1997, **106:**305–309.

A study of 252 patients who underwent sinus surgery, 48% of whom had preoperative pain. After surgery, pain had lessened in 85%, but 10% had worse pain.

7. Daudia A, Jones NS: **Facial migraine in a rhinological setting.** *Clin Otolaryngol* 2002, **27:**521–525.
8. Fuad F, Jones NS: **Is there an overlap between paroxysmal hemicrania and cluster headache?** *J Laryngol Otol* 2002, **27:**472–479.
9.•• Jones NS: **Facial pain and headache.** In *Scott Brown's Otolaryngology,* edn 6, vol 4. Edited by Kerr A, Mackay IS, Bull TR. Butterworths: London; 1996:1–10.

A thorough review on facial pain, including a practical strategy about which questions in the history are of practical importance.

10. Jones NS: **The classification and diagnosis of facial pain.** *Hosp Med* 2001, **62:**598–606.
11. Sluder G: **The role of the sphenopalatine ganglion in nasal headaches.** *N Y Med J* 1908, **87:**989–990.
12. The Headache Classification Committee of the International Headache Society: **Classification and diagnostic criteria for headache disorders, cranial neuralgia and facial pain.** *Cephalalgia* 1988, **8:**1–96.
13. Ahmed S, Jones NS: **What is Sluder's neuralgia?** *J Laryngol Otol* 2003, **117:**437–443.
14. Puig CM, Driscoll CLW, Kern EB: **Sluder's sphenopalatine ganglion neuralgia-treatment with 88% phenol.** *J Rhinol* 1998, **12:**113–118.
15. Sluder G: *Headaches and Eye Disorders of Nasal Origin.* London: Henry Kimpton; 1919:57–85.
16. Wesley RE, Johnson JJ, Cate RC: **Spontaneous enophthalmos from chronic maxillary sinusitis.** *Laryngoscope* 1986, **96:**353–355.

17. McAuliffe GW, Goodell H, Wolff HG: *Experimental Studies on Headache: Pain from the Nasal and Paranasal Structures. Research Publication.* New York: Association for Research in Nervous and Mental Disease; 1943:185–208.
18. Wolff HG: **The Nasal, Paranasal and Aural Structures As Sources of Headache and Other Pain.** In *Headache and Other Head Pain.* New York: Oxford University Press; 1948:532–560.
19. Gerbe RW, Fry TL, Fischer ND: **Headache of nasal spur origin: an easily diagnosed and surgically correctable cause of facial pain.** *Headache* 1984, **24:**329–330.
20. Abu-Bakra M, Jones NS: **Does stimulation of the nasal mucosa cause referred pain to the face?** *Clin Otolaryngol* 2001a, **26:**403–432.
21. Abu-Bakra M, Jones NS: **The prevalence of nasal contact points in a population with facial pain and a control population.** *J Laryngol Otol* 2001b, **115:**629–632.
22. Stammberger H, Wolf G: **Headaches and sinus disease: the endoscopic approach.** *Ann Otol Rhinol Laryngol* 1988, **143:**3–23.
23. Hennekens CH, Buring JE: *Epidemiology in Medicine.* Boston: Little Brown; 1987:294–295.
24. Clerico DM, Fieldman R: **Referred headache of rhinogenic origin in the absence of sinusitis.** *Headache* 1994, **34:**226–229.
25. Blaugrund SM: **The nasal septum and concha bullosa.** *Otolaryngol Clin North Am* 1989, **22:**291–306.
26. Morgenstein KM, Krieger MK: **Experiences in middle turbinectomy.** *Laryngoscope* 1980, **90:**1596–1603.
27. Goldsmith AJ, Zahtz GD, Stegnjajic A, Shikowitz M: **Middle turbinate headache syndrome.** *Am J Rhinology* 1993, **7:**17–23.
28. Clerico DM: **Pneumatized superior turbinate as a cause of referred migraine headache.** *Laryngoscope* 1996, **106:**874–879.
29.• Jones NS: **A review of the CT staging systems, the prevalence of anatomical variations, incidence of mucosal findings and their correlation with symptoms, surgical and pathological findings.** *Clin Otolaryngol* 2002, **27:**11–17.
This review summarizes most of the clinical and radiologic studies examining the prevalence of anatomical variations in symptomatic and asymptomatic populations.
30.• Homer J, Jones NS, Sheard C, Herbert M: **Cognitive dissonance, the placebo effect and the evaluation of surgical results.** *Clin Otolaryngol* 2000, **25:**195–199.
A review of the theories behind cognitive dissonance and the placebo effect in clinical practice.
31.• Sessle BJ: **Acute and chronic craniofacial pain: brainstem mechanisms of nociceptive transmission and neuroplasticity, and other clinical correlates.** *Crit Rev Oral Biol Med* 2000, **11:**57–91.
A review of the brain stem mechanisms that relate to craniofacial pain.
32. Cook PR, Nishioka GJ, Davis WE, McKinsey JP: **Functional endoscopic sinus surgery in patients with normal computed tomography scans.** *Otolaryngol Head Neck Surg* 1994, **110:**505–509.
33. Boonchoo R: **Functional endoscopic sinus surgery in patients with sinugenic headache.** *J Med Assoc Thai* 1997, **80:**521–526.
34. Parsons DS, Batra PS: **Reported functional endoscopic sinus surgical outcomes for contact point headaches.** *Laryngoscope* 1998, **108:**696–702.
35. Rosbe KW, Jones KR: **Usefulness of patient symptoms and nasal endoscopy in the diagnosis of chronic sinusitis.** *Am J Rhinol* 1998, **12:**167–171.
36. Jensen R, Olesen J: **Tension-type headache: an update on mechanisms and treatment.** *Curr Opin Neurol* 2000, **13:**285–289.
37. Bendtsen L: **Central sensitization in tension-type headache: possible pathophysiological mechanisms.** *Cephalalgia* 2000, **20:**486–508.
38.•• Olesen J: **Clinical and pathophysiological observations in migraine and tension-type headache explained by integration of vascular, supraspinal and myofascial inputs.** *Pain* 1991, **46:**125–132.
A great contribution toward explaining the pathogenesis of tension-type headache.
39.• Jensen R: **Pathophysiological mechanisms of tension-type headache: a review of epidemiological and experimental studies.** *Cephalalgia* 1999, **19:**602–621.
An excellent paper on the pathophysiology of tension-type headache from the Copenhagen group that has done so much to improve our knowledge of this condition.
40. Olesen J, Rasmussen BK: **Classification of primary headaches.** *Biomed Pharmacother* 1995, **49:**446–451.
41. Ren K, Dubner R: **Central nervous system plasticity and persistent pain.** *J Orofac Pain* 1999, **13:**155–163.
42.•• Graff-Radford SB: **Facial pain.** *Curr Opin Neurol* 2000, **13:**291–296.
A good, contemporary review of the current thoughts on the mechanisms causing facial pain placed in a practical context.
43. Rasmussen BK, Jensen R, Schroll M, Olesen J: **Interrelations between migraine and tension-type headache in the general population [see comments].** *Arch Neurol* 1992, **49:**914–918.
44. Leston JA: **Migraine and tension-type headache are not separate disorders.** *Cephalalgia* 1996, **16:**220–222.
45. Marcus DA: **Migraine and tension-type headaches: the questionable validity of current classification systems [see comments].** *Clin J Pain* 1992, **8:**28–36; discussion 37–38.
46. Silberstein SD: **Tension-type headaches.** *Headache* 1994, **34:**S2–S7.
47. Jensen R., Olesen J: **Tension-type headache: an update on mechanisms and treatment.** *Curr Opin Neurol* 2000, **13:**285–289.
48. Bendtsen L, Jensen R, Olesen J: **Quantitavely altered nociception in chronic myofacial pain.** *Pain* 1996, **65:**259–264.
49. Khan O, Majumdar S, Jones NS: **Facial pain after sinus surgery and trauma.** *Clin Otolaryngol* 2002, **27:**171–174.
50. Acquadro MA, Salman SD, Joseph MP: **Analysis of pain and endoscopic sinus surgery for sinusitis.** *Ann Otol Rhinol Laryngol* 1997, **106:**305–309.
51. Ruoff GE: **When sinus headache isn't sinus headache.** *Headache Q* 1997, **8:**22–31.