MÆDICA - a Journal of Clinical Medicine

REVIEW

MAEDICA – a Journal of Clinical Medicine
2026; 21(2): 504-515
https://doi.org/10.26574/maedica.2026.21.2.504

Nose- and Sinus-related Neuralgia Syndromes: a Narrative Review with Proposed Diagnostic and Management Algorithm

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ABSTRACT

Objective: *Nose- and sinus-related neuralgia syndromes (NSNS) constitute a constellation of clinical entities characterized by persistent pain in the distribution of nerves from the nasal cavity and paranasal sinuses. Various characterizations and management approaches have been reported in the literature, yet no universally accepted definition exists. The aim of this study is to provide a narrative synthesis of relevant studies and to propose a structured algorithm for the diagnosis and management of this intriguing clinical entity.*

Materials and methods: *A narrative review informed by a structured database search was conducted using Medline (*via *PubMed), Scopus and manual searching, with no restrictions on publication date.*

Results: *Since Sluder's first description in 1908, a number of related syndromes have been reported in the literature, each with partially overlapping clinical features and diagnostic criteria, including anterior ethmoidal nerve syndrome, anterior ethmoidal neuralgia, sphenopalatine neuralgia, syndrome of the olfactory fissure, nasociliary neuralgia (Charlin's syndrome), collectively reflecting the complex and ambiguous nature of these disorders. While the anterior ethmoidal nerve is central to the syndrome, other nerves innervating the lateral nasal wall and nasal pyramid skin are also implicated in the associated headache. Complex pathophysiological mechanisms contribute to the chronic pain. Clinically, the syndrome is characterized by the absence of a specific sinonasal disease; pain may vary in localization, be uni- or bilateral, and can be associated with mucosal engorgement, intranasal contact points, or a history of facial trauma. A thorough history, clinical examination, nasal endoscopy, imaging of the nasal cavity and paranasal sinuses, recognition of the frequent association with endonasal contact points and the topical anesthetic test remain fundamental to the diagnosis of NSNS. Management options include conservative and surgical approaches.*

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Article received on the 9th of March 2026 and accepted for publication on the 18th of June 2026

Conclusion: *The existing literature on NSNS consists exclusively of small, uncontrolled case series and expert opinion spanning over a century, with no randomized controlled trials or prospective comparative studies, reflecting a persistent evidence gap that limits definitive conclusions about diagnosis and treatment. In this review, a practice-oriented diagnostic and management algorithm is proposed. Prospective controlled studies are needed to validate and refine these recommendations.*

Keywords: facial pain, neuralgia, anterior ethmoidal nerve, nasociliary neuralgia, contact point headache, sinus headache, sinonasal headache, Sluder's neuralgia.

INTRODUCTION

Nose- and sinus-related neuralgia syndromes (NSNS) is an umbrella term used to describe chronic pain in the distribution of the anterior ethmoidal nerve and other nerves from the nasal and paranasal areas receiving innervation from the ophthalmic and the maxillary divisions of the trigeminal nerve. Head pain is primarily transmitted via the trigeminal nerve, though clinical manifestations can vary depending on the site of trigeminal injury or dysfunction. Activation of the trigemino-vascular system within the cranium represents a final common pathway for many primary headaches. In contrast, the extracranial sensory endings of the trigeminal nerve may serve either as the origin of pain or as the pathway conveying extracranial head pain (1, 2).

Neuropathic pain, resulting from a lesion or disorder of the somatosensory nervous system, is a prevalent chronic pain condition that significantly affects the quality of life and can be experienced along the whole body. It can manifest with a variety of sensations and is commonly described as burning, shooting, prickling, tingling, squeezing, or freezing (3).

The anterior ethmoidal nerve syndrome is a syndrome of chronic neuropathic pain that is believed to arise from the irritation of the terminal fibers of the anterior ethmoidal nerve. Most commonly, it can resemble sinus-related discomfort, but it may also manifest as headache, occasionally of the migrainous type (2). Similar names, but also varying descriptions of similar syndromes can be found in the literature throughout the decades, the commonest ones being anterior ethmoidal nerve syndrome, anterior ethmoidal neuralgia, lower half headache of nasal origin, sphenopalatine neuralgia, Sluder's syndrome, syndrome of the olfactory fissure and nasociliary neuralgia or Charlin's syndrome (2).

The wide range of historical characterizations of the syndrome, along with the different diagnostic criteria and treatment modalities that have been proposed still pose a diagnostic challenge in contemporary clinical practice to the clinician when it comes to the management of headache with sinus character, but with no apparent pathology from the examination of the nose and the paranasal sinuses.

In this review, we aim to synthesize narratively evidence from the relevant literature and introduce a practice-oriented diagnostic and treatment algorithm of the NSNS.

METHODS

This study was designed as a narrative review informed by a structured database search and did not adhere to the formal methodological frameworks of either a systematic review or a scoping review. An unrestricted electronic search of PubMed and Scopus was performed using the following keywords: (anterior ethmoid* nerve syndrome), ("sinus headache"), ("sinonasal headache) until 30/11/2025. English-, French- and German-language original research, reviews, or clinical trials addressing the clinical entity of the anterior ethmoidal nerve syndrome were included, in an effort to review and critically assess the existing evidence. A thorough review of the references in the articles of interest along with website search were also conducted, leading to the inclusion of additional articles. Studies with a full text in another language as well as conference abstracts were excluded.

A formal assessment of study quality or risk of bias was not undertaken, given the narrative design of the review and the fact that the available

literature consists predominantly of case series and historical reports. ❑

RESULTS

Following a literature search on two databases, we retrieved a total number of 580 studies. Subsequently, 130 duplicate records were removed. We performed title and abstract screening in the remaining 450 studies. Four hundred thirty-one records were excluded, resulting in a total of 19 articles. After full-text assessment, we excluded 13 more articles. The manual search of the references section of retrieved articles resulted in 19 additional articles (1, 3, 4-20), while website searching resulted in three more included studies (21, 26, 27). Overall, 28 studies were included in this comprehensive review. The study selection process is depicted in the flowchart (Figure 1).

Overall, 11 studies were included that reported case reports or case-series. A great variety of interventions, either medical, or surgical, were reported in the different studies. The adopted terminology, interventions utilized in different studies and patient outcomes are showcased in Table 1. ❑

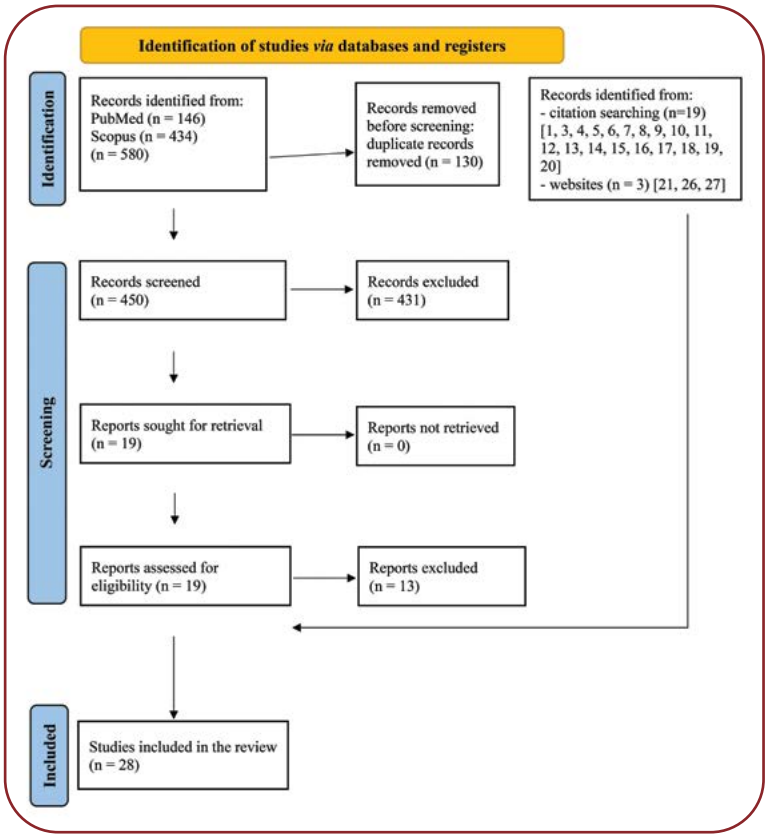

FIGURE 1. Flowchart of the study selection process

DISCUSSION

First mentions

In 1908, Greenfield Sluder described the 'lower half headache' of nasal origin, which was initially linked to the pterygopalatine (or Meckel's) ganglion. The syndrome was originally attributed to lesions peripheral to the ganglion, which would correspond to cocaine treatment of the ganglionic area (7). Later, lesions lying centrally to the ganglion and being non-responsive to neuronic desensitization were outlined (9).

Later, in 1928, G. Sluder presented the first description of the anterior ethmoidal nerve syndrome in his book *Nasal Neurology, Headaches and Eye Disorders* (8). Specifically, he reported a symptom constellation regarding varieties of nasal disease with the following characteristics: headache; possible presence of other ophthalmic disorders; and neurological symptoms that are either clearly attributed to nasal disorders or responsive to nasal therapy, which could be as follows: non-suppurative obstruction of the frontal sinuses, anterior ethmoidal neuralgia of the nasociliary nerve, nasal ganglion neurosis syndrome, hyperplastic inflammation of the posterior ethmoids and sphenoid sinuses, orbital phlegmon and neurological symptoms that are amenable to nasal treatment, but with no apparent nasal source.

Confirmation of the diagnosis was achieved by the amelioration of pain following cocainization at the region of the pterygopalatine ganglion. Nevertheless, the author stated that inflammatory conditions of the nasal sinuses could be the origin of this type of headache, and these should be diagnosed and treated by the otolaryngologist- although it could be difficult at the time (8).

Charlin described nasociliary neuralgia in 1931, with a case-series of 14 patients. The related symptoms he reported were as follows: unilateral acute rhinitis with nasal discharge; significant pain of the oculo-orbital region; inflammatory signs of the cornea with possible keratitis and corneal ulcers; and pain obliteration by cocaine application on the anterior ethmoidal area (10).

TABLE 1. Studies reporting case reports or series, with the adopted terminology, interventions and outcomes

Authors	Study design	Diagnostic basis	Major limitations	Terminology adopted	No. of patients	Intervention	Outcomes
Sluder, 1908 (7)	Narrative clinical essay with an embedded case-series	Clinical criteria, topical cocaine test	Small sample (n=10), no formal patient selection, variable response of topical cocaine test, historical era (1908), conflation with other headache entities, no standardized outcome measures	Lower half headache of nasal origin	10	Application of a silver 2% or formaldehyde 0.5% solution on the sphenopalatine ganglion	Complete symptom resolution to treatment failure
Charlin, 1931 (10)	Case-series	Clinical criteria, topical cocaine test	Small sample (n=14), historical era (1931), no standardized outcome measures	Syndrome of the nasociliary nerve	14	Cocainization of the anterior ethmoidal region	Cure of the pain in a few days
Littell, 1946 (13)	Narrative literature review, pathological/ anatomical thesis, case-series	Clinical criteria, anterior rhinoscopy, sinus X-ray, topical cocaine test, air current demonstration with Sulfadiazine powder, surgical nerve division as diagnostic confirmation	Small sample (n=2), historical era (1944-1946), no standardized outcome measures, olfactory fissure pathology not visible by standard examination, confounding by multiple surgical procedures	Syndrome of the olfactory fissure	2	Anterior ethmoidal nerve segmentation	Pain resolution
McNeill, 1963 (4)	Prospective case-series	Clinical criteria with common trauma history, sinus X-ray, topical anesthetic test	Small sample (n=12), no control group, variable F/U duration, historical era (1963), no standardized outcome measures	Traumatic nasal neuralgia	12	Application of a 4% lignocaine and 1:1000 adrenaline solution against the lateral nasal wall, followed by the injection of 2 mL of a 2% lignocaine solution over the lateral nasal nerve	Pain relief after one or two injections
Shalom, 1963 (2)	Narrative literature review with an embedded prospective case series	Clinical criteria, physical examination, sinus X-ray, mechanical probing test, topical cocaine test	Small sample (n=5), historical era (1959-1963), no standardized outcome measures, variable F/U duration, informal control probing procedure, cases partially attributed to other clinicians	Anterior ethmoidal nerve syndrome	5	Middle turbinate fracture or resection with or without submucous septum resection	Pain relief
Burnham, 1949 (24)	Case report	Clinical criteria, physical examination, topical anesthetic test	Small sample (n=1), lack of generalizability, lack of causality, historical era (1949)	Anterior ethmoidal nerve syndrome	1	Anterior ethmoidal nerve segmentation	Pain resolution
Rozen, 2009 (23)	Case report series, brief communication	Clinical criteria, physical examination, CT/MRI scan, topical anesthetic test, psychological evaluation	Small sample (n=4), selection bias, no standardized treatment protocol, no standardized outcome measures, variable F/U duration	Post-traumatic external nasal pain syndrome	4	Chronic pain medication, multiple nerve blocks, surgical removal of intranasal contact point, pulsed radiofrequency procedure of different nerves, botulinum toxin injections, topical ketorolac and intranasal lidocaine spray	Different combinations of the treatment modalities led to pain resolution
Dragovich, 1961 (22)	Expert opinion with an embedded retrospective case-series	Clinical criteria, topical cocaine test	No formal methodology, no outcome report, no control group, historical era (before 1961), diagnostic validity concerns	Anterior ethmoidal nerve syndrome	172	Submucous septum resection with pressure relief on the anterior area of the middle turbinate	Overall good results
Morgenstein, 1980 (17)	Retrospective case-series with an expert opinion component	Clinical criteria, anterior rhinoscopy, topical anesthetic test	Small sample (n=36), no control group, no formal exclusion criteria, historical era (1962-1980), variable F/U duration, no standardized outcome measures, selection bias, complications underreported	Middle turbinate syndromes: pain and obstruction	19 patients with headache and 18 with obstruction	Middle turbinectomy	17/19 patients in the headache group and 16/18 patients in the obstruction group had good results
Anselmo-Lima, 1997 (25)	Prospective case-series	Anterior rhinoscopy (with a microscope), CT scan, topical lidocaine test	Small sample (n=5), no control group, historical era (1994), variable F/U duration, selection bias, no standardized outcome measures, homogeneous etiology (concha bullosa)	Middle turbinate headache syndrome	5	Septoplasty and partial middle turbinectomy	Pain resolution in four patients, occasional headaches in one patient
Yadav, 2022 (21)	Retrospective case-series	Clinical criteria, nasal endoscopy, CT scan, diagnostic local anesthetic test	Small sample (n=30), no control group, retrospective design, no long-term F/U, heterogeneous etiologies grouped together	Anterior ethmoidal nerve syndrome	30	Chronic pain medical treatment, surgical treatment based on the specific pathology	26 patients improved with surgical and two with medical management

CT: computed tomography; F/U: follow-up; MRI: magnetic resonance imaging

At about the same time, Burnham reported this type of pain as originating from the anterior ethmoidal nerve on the lateral nasal wall, without other signs of sinonasal disease. He correlated the neuralgia episodes with alterations in temperature and humidity, and highlighted nasal discharge as the initiating factor (11).

In 1946, Littell conducted a study in which he referred to this type of headache as the syndrome of the olfactory fissure, attributing the fol-

lowing characteristics to it: unilateral nasal congestion; persistent dull pain in the supply area of the ophthalmic nerve; postnasal drip; and clinical state of systemic entry of toxins. Treatment with anterior ethmoidal nerve segmentation led to pain resolution (13).

It is obvious that, throughout the above-mentioned descriptions, the pain attributed to the anterior ethmoidal nerve syndrome can be localized from a circumscribed area above the medial canthus relieved by cocainization of the nerve to an expanded distribution affecting the head area and even the neck (22).

Of course, in these first reports of the disorder, major headache syndromes which are well-defined today, such as cluster headache (14), chronic paroxysmal hemicrania and the SUNCT syndrome, were not known (15). This could explain both the varying descriptions provided by different authors and the reduction in relative study publication during the next decades. Notably, a significant part of a study carried out by Shalom in 1963 is devoted to distinguishing the anterior ethmoidal nerve syndrome from Charlin's syndrome, nasociliary neuralgia, the olfactory fissure syndrome and sphenopalatine neuralgia (2). Certain limitations have also been recognized across the included reports and are presented in Table 1.

The foregoing discussion highlights that the diagnostic boundaries between these entities have remained controversial and poorly defined for many decades. This lack of consensus regarding the precise nature of the underlying condition is reflected throughout the historical literature and continues to complicate interpretation of published reports. Even today, distinguishing between these clinical entities can be challenging because of their overlapping symptomatology. In an effort to facilitate interpretation, we provide a comparative overview of these syndromes, summarizing their historical nomenclature, key clinical features and relevant differential diagnoses (Table 2). Because the proposed pathophysiological mechanisms underlying these syndromes appear to overlap substantially, we did not attempt to differentiate them as distinct entities in the present review.

The body of literature examining the anterior ethmoidal nerve syndrome and related rhinogenic headache syndromes spans over a century, from Sluder's foundational 1908 description of sphenopalatine ganglion neuralgia through to contemporary case-series, yet remarkably little has changed in its methodological character across this period. Every included publication, without exception, is a case-series, case report, narrative review, or expert opinion. Sample sizes range from two to 172 patients and no study includes a control group, randomization, blinding, or validated pain outcome measures.

The diagnostic cornerstone across all studies has been topical anaesthetic application to the suspected contact point with subsequent pain relief, a test that has remained essentially unchanged from Sluder's cotton-tipped cocaine applicator in 1908 (7) to the lidocaine-soaked pledget of contemporary practice (21, 25). The limitations of this test are well recognized and include susceptibility to placebo response

TABLE 2. Comparative overview of entities within the umbrella of nose- and sinus-related neuralgia syndromes (NSNS)

	Anterior ethmoidal nerve syndrome	Nasociliary neuralgia	Contact-point headache	Post-traumatic external nasal pain syndrome
Historical terms	Anterior ethmoidal neuralgia; Sluder's neuralgia; olfactory fissure syndrome; five-finger headache	Charlin's syndrome	Middle turbinate headache; rhinogenic headache	Traumatic nasal causalgia
Key symptoms	Unilateral, persistent, dull periorbital and frontal pain; nasal congestion	Unilateral acute rhinitis; severe oculo-orbital neuralgia; possible keratitis	Periorbital pain at medial canthus or temporo-zygomatic region; intermittent; modulated by nasal cycle; gravity-dependent; nasal congestion	Persistent or paroxysmal burning or aching pain over external nose; hyperalgesia on palpation; autonomic symptoms
Modern differential diagnosis	Migraine; tension-type headache; cluster headache; trigeminal neuralgia; sinusitis; persistent idiopathic facial pain	Cluster headache; acute sinusitis; eye disorders; trigeminal neuralgia	Migraine; tension-type headache; acute sinusitis; persistent idiopathic facial pain; trigeminal neuralgia	Trigeminal neuralgia; persistent idiopathic facial pain; post-traumatic headache

(13, 17), the confounding vasoconstrictor effects of the anaesthetic agent (2, 17) and the absence of any standardized threshold defining a positive result. Furthermore, the specificity of this test has never been formally established against a blinded control, meaning its diagnostic value remains incompletely validated. Notwithstanding these limitations, the addition of coronal computed tomography (CT) and nasal endoscopy in the modern era has meaningfully advanced the anatomical characterization of sinonasal contact points and improved patient selection, representing the most substantive diagnostic evolution in the field over the past century.

Anatomy

The outer surface of the nose possesses a broad and intricate sensory innervation. Sensory supply originates from branches of both the ophthalmic and maxillary divisions of the trigeminal nerve. The nasociliary nerve, a principal branch of the ophthalmic division, provides sensation to the nasal tip. It further divides terminally into the anterior ethmoidal nerve, which conveys sensation from the mid-dorsum of the nose to the tip, and the infratrochlear nerve, which serves the superior nasal sidewall (23).

The anterior ethmoidal nerve exits the orbit via the anterior ethmoidal foramen and transverses into the anterior cranial fossa. It then courses anteriorly between the dura mater and the bone before passing through an opening adjacent to the crista galli to enter the nasal cavity. Within the nose, it issues nasal branches to the septum and the anterior aspects of the superior and middle turbinates, as well as the lateral nasal wall anterior to these structures (2). To be noted, the nerve supply of the rest of the middle turbinate originates from the sphenopalatine ganglion and its branches (16).

The nerve branches of the anterior ethmoidal nerve traverse narrow osseous channels, accompanied by their corresponding vessels, in the area of the middle turbinates and nasal bones (12). Eventually, the nerve courses along a groove on the inner surface of the nasal bone and ultimately emerges as the external nasal nerve between the nasal bone and the upper nasal cartilage, enervating the lateral surface of the nasal pyramid (2).

Additionally, the infraorbital nerve, which is derived from the maxillary division, contributes

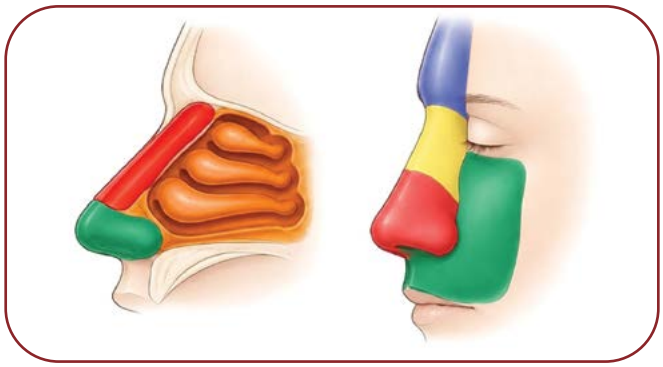

FIGURE 2. A) Innervation of the lateral nasal wall; **B)** innervation of the skin of the nasal pyramid (green: infraorbital nerve; red: anterior ethmoidal nerve; yellow: infratrochlear nerve; blue: supratrochlear nerve; orange: branches of the sphenopalatine ganglion)

sensory input to the lateral nasal region. Since these neural pathways travel in close anatomical proximity, trauma or injury to any nasal portion may simultaneously damage several branches. Such lesions of trigeminal sensory fibers innervating the external nose are considered the probable etiology of post-traumatic external nasal pain syndrome (23). The innervation of the lateral nasal wall and the nasal pyramid can be observed in Figure 2A and B.

Proposed mechanisms

Anatomical studies have shown that stimulation or pressure on different intranasal areas can produce facial pain radiating along the pathways of the trigeminal nerve. Intranasal stimulation elicits pain along the distribution of the anterior ethmoidal, infratrochlear and supratrochlear nerves – branches of the ophthalmic division of the trigeminal nerve – manifesting in the medial canthus and supraorbital areas (18, 19).

Intranasal structures that come into contact are likely linked to localized reflex vascular congestion and the release of vasoactive amines, which can either trigger pain or lower the pain threshold. Contact of the mucosa could activate specific receptors that cause the release of substance P and probably other neuropeptides, resulting in local vasodilation, hypersecretion and implication in the sensation of facial pain. Central or regional peripheral orthodromic pathways could be involved (20).

An early theory formulated by Littell, supported the origin of the disorder from the retro-tubercular space. This is a highly-vascular

rich-in-cavernous-tissue region giving rise to the internal nasal branches of the anterior ethmoidal nerve. The area is located anteriorly and posteriorly the nasal tubercle, which can be found at the junction of the perpendicular plate of the ethmoidal bone and the septal cartilage and between the middle turbinate and the nasal septum. The septal thickness is maximal at the area of the tubercle. The peculiarity of the retro-tubercular space is that it is covered by a highly sensitive mucosa layer and that it may become isolated with suppuration, leading to symptomatology (13).

The hypothesis of the purulent infection was never confirmed. On the other hand, Thomas formulated the theory that a non-purulent infection of the nasal cavities and sinuses by *Staphylococcus* and *Streptococcus* species could the triggering factor of the syndrome (2).

According to McNeill, the chronic nasal pain would most commonly occur following nasal trauma and more specifically after fractures of the nasal pyramid. The onset of pain could be directly after the injury or even several months after it (4). The pain was primarily located at the mucosal area between the nasal bone and the upper lateral cartilage of the nose, but it would often extend outside the nerve's area of innervation. It is also considered to deteriorate during winter months (4).

An incomplete lesion of a nerve can lead to a burning sensation, which is described as causalgia. Several theories have been proposed to establish the underlying factor of pain (4). Granit *et al* attributed the pain to a possible diversion of efferent sympathetic neurons into sensory somatic fibers at the site of neuronic injury. The rearrangement of myelin along the affected fibers could be the culprit of this pain sensation (5). Earlier, Spurling *et al* had attributed this to phenomena of hyperemia or ischemia (6). Nevertheless, it appears that pain symptomatology is not confined to the involved nerve region. Psychogenic factors are also believed to contribute substantially to causalgia (4).

According to Burnham, the syndrome could arise from the branches of the anterior ethmoidal nerve, which, as already mentioned, alongside their accompanying vessels, course through narrow bony passages situated in the middle turbinates and nasal bones. Bacterial by-products, along with temperature and humidity alterations, could affect the small vessels, leading to dilation, which, in turn, could exert pressure and result in hypersensitivity of the neighboring sensory nerve endings. Neuralgia only provoked by mild stimulation and to 'tender spots' upon pressure on the areas innervated by the nerve could be the final outcome (11, 12).

Furthermore, Burnham stated that the migrainous character of the syndrome could be attributable to this anatomical feature of the nerve. Impaired or compressed axons following nasal trauma could lead to defective reinnervation, and finally excitability of other branches of the ophthalmic nerve, or even the rest of the trigeminal nerve upon applying pressure on the hypersensitive area (24).

Towards a modern characterization of the syndrome and comparison to common headache disorders

In a case-series study published in 1961, Albert Shalom reported on five patients whom he diagnosed with the anterior ethmoidal nerve syndrome; none of them showed clinical or imaging signs of sinonasal disease, while the diagnosis was established by evoking frontal pain after exerting pressure with a probe between the nasal septum and the head of the middle turbinate. Interestingly, the same procedure did not stimulate frontal pain in control subjects (2).

Thus, probing of the area between the septum and the anterior end of the middle turbinate, with subsequent frontal pain elicitation, could be a logical first step in the diagnosis of the syndrome. Alternatively, anesthetization of the area with resulting pain alleviation could be performed. These can assist in the differential diagnosis of the disorder from other migrainous syndromes, trigeminal neuralgia and other secondary headaches. In any case, benign or malignant sinonasal pathologies should be initially excluded with a thorough otolaryngological examination and possibly with a paranasal sinus CT scan.

In an influential study conducted by Morgenstein and Krieger in 1980, the role and efficacy of middle turbinectomy is discussed, citing the two opposing schools of middle turbinate preservation and sacrifice and recognizes two middle turbinate syndromes, including obstruction (or crowded nose) and headache. The first disorder can occur in conditions where the middle turbinate is enlarged enough to hinder

the normal air flow over the middle turbinate (17), while the second one could arise from compression between the middle turbinate and the bulla ethmoidalis, the nasal septum or the uncinate process; the result is periodic and shifting headache around the supraorbital or infraorbital region, the medical canthus and the orbit, arising from changes in the congestion status of the nasal mucosa. Bilateral contact can lead to centralized pain around these areas, characterized as the 'four-finger' headache (17).

In an effort to characterize NSNS, the pain is typically situated in the periorbital region, particularly the medial canthus, the supraorbital, or the temporo-zygomatic area. It is usually single-sided, reflecting the higher incidence of unilateral mucosal engorgement and contact, though bilateral pain can also occur. The pain is intermittent, corresponding to normal fluctuations in mucosal edema during the nasal cycle, and may be accompanied by a feeling of nasal congestion. Episodes generally last for several hours and show a high recurrence rate (25).

This is in agreement with a study by Anselmo-Lima *et al*. Specifically, headache associated with middle turbinate variations is localised to the medial canthus or the temporozygomatic region. The pain is intermittent and follows the variations of mucosal thickening. The pain is gravity-dependent, therefore it decreases when the patient is in a vertical position or in the supine position with the affected side downward (25).

Currently, no specific subcategory for contact-point headache without active sinonasal disease exists. The clinical characterization of NSNS shares several superficial features with established primary headache disorders as defined by the International Classification of Headache Disorders, third edition (ICHD-3), yet differs in important and diagnostically decisive ways across pain location, character, associated features and modifying factors (26).

Among the primary headache disorders, NSNS and migraine share several clinical features, including unilateral presentation, recurrent episodes and severe pain intensity, which may contribute to an initial misdiagnosis of migraine, as reported by multiple authors (2, 21, 25). However, characteristic migraine-associated features such as pulsating pain quality, nausea and vomiting, photophobia, phonophobia and responsiveness to triptans help distinguish migraine from NSNS. In contrast, tension-type headache is generally easier to differentiate from NSNS because it typically presents with bilateral pain, pericranial tenderness on palpation, and a strong association with musculoskeletal factors and psychological stress.

Trigeminal autonomic cephalalgias, encompassing cluster headache, paroxysmal hemicrania, SUNCT/SUNA and hemicrania continua, share with NSNS the features of strictly unilateral pain in the periorbital or temporal region and, in some cases, associated nasal symptoms. Cluster headache in particular presents with severe unilateral orbital, supraorbital, or temporal pain lasting up to three hours, accompanied by ipsilateral autonomic features including lacrimation, rhinorrhoea, nasal congestion, miosis, ptosis and eyelid oedema. The nasal congestion seen in cluster headache can closely mimic the nasal symptoms occasionally reported in NSNS (17, 22). However, trigeminal autonomic cephalalgias are distinguished by the excruciating and paroxysmal pain characteristics, the autonomic features and the circadian and circannual periodicity (27).

The differential diagnosis of NSNS must also encompass secondary headache disorders. Intracranial pathology, including space-occupying lesions, increased/decreased intracranial pressure (headache attributed to non-vascular intracranial disorder) and vascular disorders (headache attributed to cranial or cervical vascular disorder) must be actively excluded before attributing headache to an intranasal contact point, and neuroimaging and appropriate laboratory investigations should therefore precede any rhinological diagnostic workup where clinical suspicion exists. Headache attributed to trauma or injury to the head and/or neck represents a particularly relevant differential in patients with a history of head/nasal injury, as the temporal relationship to trauma and possible perinasal localization are shared with post-traumatic NSNS. According to ICHD-3, headache or facial pain attributed to disorder of the nose and paranasal sinuses addresses headache attributed to disorders of the nose and paranasal sinuses.

Moreover, trigeminal neuralgia may be confused with NSNS given the shared trigeminal distribution and unilaterality. However, trigeminal neuralgia produces brief, lancinating, paroxysmal pain triggered by innocuous stimuli rather

	Headache types
Primary headaches	Migraine
	Tension-type headache
	Trigeminal autonomic cephalalgias
	Other primary headache disorders
Secondary headaches	Headache attributed to trauma or injury to the head and/or neck
	Headache attributed to cranial or cervical vascular disorder
	Headache attributed to non-vascular intracranial disorder
	Headache attributed to infection
	Headache or facial pain attributed to disorder of the cranium, neck, eyes, ears, nose, sinuses, teeth, mouth or other facial or cervical structure
	Trigeminal neuralgia
	Persistent idiopathic facial pain

TABLE 3. Major headache categories

than the dull, continuous and intranasally-triggered pain of NSNS. Intranasal anaesthetic application has no therapeutic effect in trigeminal neuralgia. Finally, persistent idiopathic facial pain is a diagnosis of exclusion that should not be applied before identifiable structural causes are investigated.

According to ICHD-3, ciliary neuralgia, Sluder's neuralgia, sphenopalatine neuralgia and vidian neuralgia are terms previously used for trigeminal autonomic cephalalgias and, more specifically, for cluster headache. Sinus headache has been used in the past to describe headache attributed to disorder of the nose or paranasal sinuses, while anterior ethmoidal nerve syndrome is not reported in ICHD-3 (26). The major headache categories associated with NSNS, as defined by the ICHD-3, are summarized in Table 3.

Post-traumatic external nasal pain syndrome

This clinical entity can be described as a subclass of the anterior ethmoidal neuralgia. Rozen described four cases of this novel type of trigeminal pain. The anatomy of the trigeminal branches on the nasal pyramid and, more specifically, the close proximity of the nerves, can explain the clinical presentation. Trauma to any portion of the nose can injure multiple nerves. According to the author, the best therapy appears to be direct anaesthesiologic blockade of the responsible branches. This can be achieved following successful confirmation of the suspected cause with application of short-acting anaesthetic block (23).

This study has also suggested eight diagnostic criteria for the post-traumatic external nasal pain syndrome, including: pain localized to the external portion of the nose; pain occurring after external nose trauma can be immediate or delayed; pain can be daily persistent or be paroxysmal attacks of pain lasting from a fraction of a second to two minutes, with persistence of aching between paroxysms; pain can be mild, moderate, or severe in intensity; autonomic symptoms may occur including swelling of the nose, while migrainous symptoms are less prevalent; external nose is painful to palpation; complete or partial pain alleviation of external nose pain (duration of response variable) with anaesthetic blockade of any of the following: nasociliary nerve, infratrochlear nerve, anterior ethmoidal nerve, external nasal nerve, infraorbital nerve, or sphenopalatine ganglion; and may have normal nose and sinus imaging.

Diagnostic approach

A significant proportion of patients with undiagnosed cause are referred to ENT clinics as 'sinus headache'. The diagnosis is generally achieved after ruling out other causes of headache. Focused history of headaches, including the frequency, intensity, region, type and radiation is essential. Moreover, the patient should be fully assessed for possible sinonasal pathology. In this respect, a thorough nasal endoscopy together with CT scan and/or magnetic resonance imaging (MRI) constitutes an essential part of the diagnostic evaluation.

Diagnosis can also be ascertained by placing a pledget soaked with local anaesthetic in the ethmoidal cleft. This leads to immediate relief if the suspected diagnosis is accurate. Differential diagnosis includes sinonasal diseases, various types of migraine, trigeminal neuralgia, cluster headache and dental problems (21).

It must be emphasised that the diagnosis of NSNS is fundamentally one of exclusion, and no

single clinical feature, imaging finding, or diagnostic test is sufficiently specific to establish the diagnosis in isolation. Before an intranasal contact point can be accepted as the causative factor of a patient's pain, a systematic and thorough exclusion of more common and potentially serious alternative diagnoses is mandatory. These include migraine and tension-type headache, cluster headache and other trigeminal autonomic cephalalgias, trigeminal neuralgia, headache or facial pain attributed to disorder of the nose and paranasal sinuses and intracranial pathology.

Treatment

It is evident that no uniform treatment approach has been established for NSNS. On the contrary, authors have chosen different treatment modalities based on the different mechanisms they used to describe the disorder. Thus, these strategies have traditionally aimed to either reduce the pressure phenomena inside the nasal cavities, or to directly dissect the nerve endings.

Saline irrigation does not appear to result in pain relief (4). However, topical anesthetics (ephedrine, 2% lignocaine) on the nasal mucosa had a positive impact on the pain symptoms, designating local infiltration of the middle turbinate, and the neighboring lateral nasal wall, along with the anterior ethmoidal fissure as a first-line treatment in cases of chronic nasal pain. Pain control can be achieved over a period of at least one year (2, 4).

A treatment method aiming to reduce the intranasal pressure on the area of interest was proposed by Shalom, who performed fracture or resection of the head of the middle turbinate with or without submucous nasal septum resection (2).

In recalcitrant debilitating cases of patients with sinus-type chronic pain that did not respond to topical anesthetics, neurectomy of the two anterior ethmoidal nerves from the orbital side has been practiced in the past with significant symptom control over the following months (11). Burnham advanced this technique by plugging the anterior ethmoidal foramen with a periosteum graft, after dissection of the anterior ethmoidal nerves and vessels at their insertion into the foramen, so that a reinnervation would be avoided (24).

Another surgical strategy includes middle turbinectomy under local or general anesthesia. This can have significant symptom relief in cases of 'four-finger' headache, or nasal obstruction as a result of an enlarged middle turbinate, or compression of the middle meatus complex structures, the lateral nasal wall and/or the septum. The procedure can be combined with a septoplasty, when indicated. Interestingly, the symptoms seem to significantly ameliorate in a great

TABLE 4. Diagnostic and therapeutic algorithm of the nose- and sinus-related neuralgia syndromes (NSNS)

majority of patients, following the procedure, while no crusting, atrophic rhinitis, or drying is related to it (17).

Furthermore, Senocak *et al* studied 204 patients who underwent sinonasal surgery with various indications but common symptom their chronic headache. Surgery that resulted in removal of lesion, trigger and anatomical obstruction led to 85% improvement of headaches (28).

Based on the above, we propose the following algorithm of the NSNS (Table 4). It should be noted that this is a practice-oriented proposal based on limited evidence and it has not been prospectively validated in a controlled clinical setting. Moreover, interpretation of the findings should be undertaken with caution, as the available evidence is derived primarily from small observational studies and case reports, with substantial methodological and clinical heterogeneity across publications. Thus, further studies are required to solidify an evidence-based diagnostic approach and treatment strategies. ❑

CONCLUSIONS

Nose- and sinus-related neuralgia syndromes have been described in the medical literature for more than a century, yet the entire evidence base continues to rely on uncontrolled case reports, case series and expert opinion, with heterogeneous diagnostic criteria and non-standardized outcome measures. Despite this long-standing recognition, NSNS remain a rare and frequently under-diagnosed presentation, requiring prompt identification, specialist assessment and targeted management. Their clinical heterogeneity and overlap with primary and secondary headache disorders make them a considerable diagnostic challenge, and multidisciplinary collaboration between the ENT surgeon, neurologist and pain specialist is therefore essential to ensure accurate diagnosis and appropriate treatment. In this review, we synthesize the available evidence and propose a practice-oriented diagnostic and therapeutic algorithm to guide the clinical management of NSNS. Prospective studies with validated diagnostic protocols, blinded outcome assessment and adequate long-term follow-up are nonetheless needed before definitive recommendations regarding diagnosis and surgical management can be established. ❑

Data availability: All data generated or analyzed during this study are included in this published article (and its supplementary information files).

Conflicts of interest: none declared.

Financial support: none declared.

References

1. **Moskowitz MA.** The neurobiology of vascular head pain. *Ann Neurol* 1984;16:157-168.
2. **SHALOM AS.** The anterior ethmoid nerve syndrome. *J Laryngol Otol* 1963;77:315-325.
3. **Finnerup NB, Kuner R, Jensen TS.** Neuropathic Pain: From Mechanisms to Treatment. *Physiol Rev* 2021;101:259-301.
4. **McNeill RA.** Traumatic Nasal Neuralgia and Its Treatment. *Br Med J* 1963;2:536-537.
5. **Granit R, Leksell L, Skoglund CR.** Fibre Interaction in Injured or Compressed Region of Nerve. *Brain* 1944;67:125.
6. **Spurling RG.** Causalgia of the Upper Extremity: Treatment by Dorsal Sympathetic Ganglionectomy. *Arch NeurPsych* 1930;23:784-788.
7. **Sluder G.** The role of the sphenopalatine (or Meckel's) ganglion in nasal headaches. *N Y Med J* 1908;87:989-990.
8. Nasal Neurology. Headaches and Eye Disorders. *Arch Otolaryngol* 1928;7:96-97.
9. **Sluder G.** "Lower Half Headache" (Neuralgic) of Nasal Origin: Glossodynia, Otalgia, Nausea, Parageusia, Vertigo, Scotoma, Photophobia, Rhinorrhea and Asthma as Isolated Related Phenomena. *JAMA* 1922;79:1898-1899.
10. **Charlin C.** Le syndrome du nerf nasal. *Ann Ocul* 1931;168:86-102.
11. **Burnham HH.** Headache from the Nasal Wall. *Ann Otol Rhin Laryng* 1937;46:69.
12. **Burnham HH.** An Anatomical Investigation of Blood Vessels of the Lateral Nasal Wall and Their Relation to Turbinates and Sinuses. *J Laryng Otol* 1935;2:569.
13. **Littell JJ.** Disturbances of the ethmoid branches of the ophthalmic nerve, with description of a syndrome associated with chronic suppuration of the olfactory fissure. *Arch Otolaryngol* (1925) 1946;43:481-499.
14. **Horton BT.** The Use of Histamine in the Treatment of Specific Types of Headaches. *JAMA* 1941;116:377-383.
15. **Pareja JA, Pareja J, Yangüela J.** Nummular headache, trochleitis, supraorbital neuralgia, and other

epicranial headaches and neuralgias: the epicranias.
J Headache Pain 2003;4:125-131.
16. **Becker SP.** Anatomy for endoscopic sinus surgery.
Otolaryngol Clin North Am 1989;22:677-682.
17. **Morgenstein KM, Krieger MK.** Experiences in middle turbinectomy.
Laryngoscope 1980;90(10 Pt 1):1596-603.
18. **Wolff HG.** The nasal, paranasal, and aural structures as sources of headache and other pain. In: Wolff HG, ed.
Headache and Other Head Pain.
New York: Oxford University Press; 1948, pp 532-560.
19. **Wolf G, Saria A, Gamse R.** Neue Aspekte zur autonomen Innervation der menschlichen Nasenschleimhaut (New aspects of the autonomic innervation of human nasal mucosa).
Laryngol Rhinol Otol (Stuttg) 1987;66:149-151. German.
20. **Stammberger H, Wolf G.** Headaches and sinus disease: the endoscopic approach.
Ann Otol Rhinol Laryngol Suppl 1988;97(suppl 134):3-23.
21. **Yadav R, Chakraborty P, Saini R, et al.** Anterior Ethmoidal Nerve Syndrome-An Under-diagnosed Cause of Headache. Bengal
Journal of Otolaryngology and Head Neck Surgery 2022;30:35-40.
22. **Dragovich JJ.** Anterior ethmoid nerve syndrome.
Northwest Med 1961;60:290.
23. **Rozen T.** Post-traumatic external nasal pain syndrome (a trigeminal based pain disorder).
Headache 2009;49:1223-1228.
24. **Burnham HH.** The anterior ethmoidal nerve syndrome; referred pain and headache from the lateral nasal wall.
Arch Otolaryngol (1925) 1949;50:640-646, illust.
25. **Anselmo-Lima WT, de Oliveira JA, Speciali JG, Bordini C, et al.** Middle turbinate headache syndrome.
Headache 1997;37:102-106.
26. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition.
Cephalalgia 2018;38:1-211.
27. **Lambru G, Matharu MS**. Trigeminal autonomic cephalalgias: A review of recent diagnostic, therapeutic and pathophysiological developments.
Ann Indian Acad Neurol 2012;15(Suppl 1):S51-S61.
28. **Senocak D, Senocak M.** Sinonasal pathology and headaches.
Rhinology 20041;42:8-14.