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## **Simplifying differential diagnoses of orofacial conditions – a guide to surgical sieves and red-flags.**

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### **Abstract** (106 words)

Formulation of a differential diagnosis with appropriate diagnostic tests is critical in day to day clinical practice. Many specialists or hospital-based practitioners in specialties such as oral medicine and oral surgery will be familiar with the use of surgical sieves and the term red-flags in their practice. However, it is the authors' experience that General Dental Practitioners may not be as familiar with such tools. Primary care practitioners are often the first port of call for patients with uncommon symptoms it is essential therefore that appropriate and timely referrals are made. The use of a surgical sieve and heightened awareness of 'red-flags' will assist practitioners significantly.

### **Keywords** (2-6)

Surgical sieve  
Differential diagnosis  
Diagnosis  
Red flags  
Dentistry

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## **Introduction**

During undergraduate training, dental students develop their abilities to elicit concise and appropriate histories from patients encompassing all relevant information. Following this, students learn to process this information, together with their clinical findings to form a differential diagnosis, arrange further investigations and then confirm the diagnosis and formulate a management plan.

When General Dental Practitioners (GDPs) identify an unusual lesion of uncertain significance or a pathological entity that fulfils referral criteria, specialist input should be sought. Studies have demonstrated limited adherence to referral criteria and a lack of key information in patient referrals including medical history and clinical diagnosis (1, 2). The greater the depth of information provided in the referral letter, the more appropriate the outcome of the triage will be. This includes more accurate triage of the initial referral, identification of relevant special tests and potential causative agents which merit further investigation.

A methodical approach is required for both medical and dental conditions that ensures consistency and minimises the risks of missing out important information. The systematic assessment and consideration of a range of differential diagnoses requires experience, practice and consistency, and ideally, such an approach should be taught to dental students at undergraduate level. Medical students learn the concept of the 'surgical sieve' at an early stage of their learning and practice it throughout their undergraduate training. It is the authors' experience however, that not all dental students gain familiarity in the technique as teaching of surgical sieves is not embedded into undergraduate curricula across UK dental schools.

Irrespective of their ultimate career pathway, it is critical (both from a patient safety and medico-legal perspective) that dental undergraduates and GDPs have a method which allows them to formulate a differential diagnosis for a multitude of conditions which patients may present with. We have an ageing population with multiple co-morbidities. Such patients present to the dental practitioner with more complex medical issues and it is important that practitioners are able to appropriately diagnose and manage or refer these patients.

The two-week wait (TWW) referral system allows practitioners to recognise common signs of malignant disease, ensuring the patient is seen promptly and that appropriate diagnostic tests are completed.

Failure to provide a structured, comprehensive and sequential treatment plan risks fragmenting the patients' care and may impact on their general health(3). There is a substantial difference between medicine and dentistry, particularly in primary care, whereby patients often only see their physician when they develop symptoms. Conversely, in general dental practice, a high proportion of patients are seen at regular intervals even in the absence of any symptoms. Therefore, dentists are important gatekeepers in terms of recognising early signs or symptoms of both systemic and local disease(4).

Diagnosis is often poorly documented, and there seems to be a lack of appreciation of its importance. Incorrect diagnoses can impact adversely on care leading to invasive and irreversible treatments e.g. tooth extraction for non-odontogenic pain (5, 6).

Students should be taught a "systematic approach to diagnosis that is simple enough to learn yet, so rational as to be difficult to forget"(7). Accurate history taking, investigation and diagnosis will reduce errors which ensure that we maintain a risk averse environment. Diagnostic errors are not subject to the same scrutiny, despite the emphasis placed on clinical acumen in the training of primary and secondary care doctors and dentists (8). There have been two descriptions of approaches to clinical decision making which inform teaching methods (9): Type 1 is fast, intuitive and vulnerable, and is reliant on pattern recognition based on past experience. Type 2 is an effortful, systematic and analytical approach, requiring more time, concentration and attention to detail. Type 2 thinkers will be more suited to 'surgical sieves' which provide a framework, allowing the individual to consider questions relating to the underlying clinical problem and associated pathological conditions.

### **The Surgical Sieve**

The surgical sieve in table 1 illustrates a mnemonic that facilitates a structured analytical approach allowing clinicians to consider a range of differential diagnoses. However, there is limited literature for its direct application to dentistry despite recommendations for its adaptation for dental conditions (10).

The aim of this article is therefore to adapt the surgical sieve (table 1), as a tool which dental clinicians and students can implement to simplify differential diagnoses and assist their clinical decision making with regards to management and/or referral of patients

**Table 1 - A common mnemonic of the surgical sieve is "vitaminsCDE"**

V	Vascular
I	Infective
T	Trauma
A	Autoimmune
M	Metabolic
I	Idiopathic/Iatrogenic
N	Neoplasia
S	Social Factors
C	Congenital problems
D	Degenerative/Drug related
E	Endo/exocrine

### **Application of the surgical sieve to orofacial conditions:**

#### Vascular

Haemangiomas are benign lesions often found at birth and can appear as red or bluish soft masses which can be smooth or lobulated and sessile or pedunculated. They can present in the superficial dermis in the head and neck however are rarely seen in the oral cavity. Careful assessment should be undertaken, including imaging and a biopsy to rule out other diagnoses (11, 12). Vascular malformations are congenital lesions that are detectable later in life as they slowly enlarge through ectasia (13). A key difference is that it does not involute and regress whereas this is well documented to occur in haemangiomas. One third of patients can have osseous involvement and they can be low flow (capillary, venous, lymphatic) or high flow (arterio-venous) whereas haemangiomas are low flow. (14)

#### Infective

The cardinal signs of inflammation were described by Celsus (30 BC to AD 38) in Latin as *rubor, calor, tumor and dolor* which translates to redness, heat, swelling and pain respectively.

Clinical presentation of odontogenic infections can be variable, depending on the origin of infection, however the cardinal signs described above are likely to be present in any inflammatory process. Odontogenic infections have a variety of causes, and some may initially present with pulpitis-like symptoms. Lymphadenopathy and systemic signs (e.g. tachycardia and pyrexia) suggest systemic involvement and spreading infection. Patients with evidence of

dysphagia, trismus, elevated floor or mouth/tongue and suspicion of airway compromise must be referred as a matter of urgency to ensure rapid assessment and management. Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection. Odontogenic infections have the potential to lead to sepsis, and therefore clinicians need to be able to recognise the hallmark signs which require urgent intervention.

It is essential to distinguish between pulpitis, whether reversible or irreversible, and identify the spread of infectious material (purulent exudate formed inside the dental pulp) beyond the peri-apical soft tissues. This can manifest as either an acute apical abscess or the infectious material can infiltrate medullary bone, collecting within soft tissues and resulting in pressure to surrounding structures with potentially serious complications. Periapical abscesses are often described as periapical infections or periapical/apical periodontitis. These are commonly a sequelae from a necrotic pulp. Radiographs may reveal an apical radiolucency, although sometimes changes are insignificant depending on the timing.

Maxillary sinus infections may present to the dental practitioner and it is important that an odontogenic cause is either confirmed or excluded. At present, rhinosinusitis is the accepted term used to refer to sinusitis (15) and diagnosis is by the presence of two or more persistent symptoms for at least 12 weeks, one of which should be nasal obstruction and/or nasal discharge, and/or facial pain/pressure or anosmia(16). Acute sinusitis is characterised by a moderate to severe constant pain over the antrum/cheek area which can be mistaken for dental pain (17).

### Trauma

A mucocele or mucous extravasation cyst is the result of saliva from a ruptured minor salivary gland accumulating in the surrounding soft tissues. Trauma to the ducts of the sublingual (or less commonly the submandibular salivary glands) can result in a mucous extravasation cyst in the floor of the mouth, termed a Ranula (18).

Fibrous polyps are common and usually present in the buccal mucosa, lateral border of the tongue and lips, often as a result of trauma. They are firm and painless with mucosal covering of normal appearance. Often patients are unaware of these and if monitored may remain unchanged. If there is any doubt of the clinical diagnosis, histological analysis should be carried out.

### Autoimmune

Pemphigus Vulgaris is a rare chronic mucocutaneous disease that predominantly affects adults. It is the most common variant of the Pemphigus group of autoimmune diseases and is characterised by the blistering of cutaneous and/or mucosal surfaces. The condition has been noted to manifest in regions of the oral mucosa subject to frictional trauma and as such, the most common site of involvement is the buccal cavity followed by the palatal and lingual mucosa (19). Gingival involvement can be local or widespread as desquamative gingivitis (20). Oral manifestations tend to precede skin lesions however may be the first indicator of the disease. Mucous Membrane Pemphigoid (MMP) is an autoimmune subepidermal blistering disorder caused by autoantibodies against the basement membrane zone components. Oral manifestations include subepidermal bullae formation, which burst and heal with ulceration or scarring. Gingival involvement presents as desquamative gingivitis. The most severe complication is involvement of the eyes which causes conjunctival erosions and scarring leading to blindness. Other complications involve anogenital, oesophageal, laryngeal and pharyngeal involvement (21, 22). Oral ulcerations and erosions should always be carefully inspected, and a threshold of suspicion held for recurrent ulcers, which merit further investigations. Often for the aforementioned autoimmune conditions, the oral cavity can be the first site for presentation of symptoms.

### Metabolic

There are seldom few metabolic disorders which present in the oral cavity. Hyperparathyroidism is an endocrine disorder characterised by hypercalcaemia and elevated parathyroid hormone (PTH) (23). There are several clinical manifestations in the oral and maxillofacial regions; of note is brown's tumour and peripheral giant cell granuloma.

Brown's tumour (also known as osteitis fibrosa) is a giant cell lesion of the bone which represents an inflammatory rather than a neoplastic process. Hallmark features include a progressively enlarging asymptomatic mass displacing teeth in either the mandible or maxilla. Radiographically, it appears as a unilocular radiolucency resorbing adjacent teeth roots (24, 25). Bilateral presentations have also been reported (26, 27).

Peripheral giant cell granulomas (or epulis if situated on the gingivae) are commonly seen in the interdental papilla or edentulous alveolar margins and can be a response to local irritation (28). Resorption of alveolar bone has been associated with this lesion. It is distinguished from a peripheral ossifying fibroma and pyogenic granuloma on histology (29). In rare cases, they have been identified as an oral manifestation of hyperparathyroidism.

### Idiopathic

The most common diagnoses for dental idiopathic conditions are encompassed within the umbrella of idiopathic orofacial pain (30). Often they are described as “unilateral or bilateral intraoral or facial pain in the distribution(s) of one or more branches of the trigeminal nerve(s) for which the aetiology is unknown. The pain is usually persistent, of moderate intensity, poorly localized and described as dull, pressing or of burning character.”(30)

The most commonly described idiopathic orofacial pains are atypical facial pain (now persistent idiopathic orofacial pain), burning mouth syndrome and atypical odontalgia (now persistent idiopathic dento-alveolar pain). These diagnoses are reached after local causes have been excluded and clinical and radiological findings are normal.

It is important to note that some neuralgias can also be idiopathic and the most recent ICOP classification(30) includes these within idiopathic orofacial pains: (idiopathic trigeminal neuralgia, idiopathic trigeminal neuropathic pain, idiopathic glossopharyngeal neuralgia, idiopathic glossopharyngeal neuropathic pain). More recently added within this classification and although rare, is constant unilateral facial pain with additional attacks (CUFPA), described as an idiopathic orofacial pain that is “constant (unremitting) dull unilateral facial pain of mild to moderate intensity, accompanied by distinct attacks of moderate to severe pain in the same location lasting 10–30 minutes. There are no typical autonomic and/or migrainoid features accompanying either the constant pain or the additional pain attacks”. However, the clinical picture is often not so clear-cut and many of these idiopathic pains can overlap within the orofacial region and also with other chronic pain conditions like fibromyalgia, irritable bowel syndrome and chronic fatigue with additional psychosocial comorbidities (31). The pain is often described as dull, nagging and aching(32) and it is important to undertake appropriate psychosocial assessment in addition to a pain history (33).

### Iatrogenic

Causes of iatrogenic dental injuries include that of damage to vital anatomical structures such as the inferior alveolar nerve. Iatrogenic injuries to the third division of the trigeminal nerve remain a common and complex clinical problem (34). Such injuries are avoidable with accurate surgical planning including the use of advanced imaging such as cone beam CT scanning. Fracture of dental instruments is rare, but if not recognised can lead to a local nidus of infection or long term sequelae. In addition, other iatrogenic causes include damage to adjacent teeth during exodontia, thermal injuries and laceration injuries to soft tissues.

### Neoplasia



Presentation can vary, but the classic description of an oral malignancy includes an intraoral ulcer which is raised with exophytic margins and has failed to heal or improve after 3 weeks. However, dysplasia may present in other disguises such as erythematous lesions, mixed red and white lesions, indurated lumps or lesions similar to that of erosive lichen planus. High risk areas, although not exclusive, are the anterior floor of mouth, lateral borders of tongue and retromolar area extending onto the soft palate/pillar of fauces. Patients who have a suspicious lesion which is thought to be dysplastic or malignant should be referred on the two-week wait head and neck cancer pathway. There may be associated lymphadenopathy or systemic signs such as weight loss, dysphagia or loss of appetite. Oral potentially malignant disorders (OPMDs) include oral leukoplakia, erythroplakia, oral submucous fibrosis, palatal lesions in reverse smokers, oral lichen planus and lichenoid reactions, graft-versus-host disease, oral lupus erythematosus and some hereditary conditions such as dykskeratosis congenita and epidolysis bullosa(35). Additionally, it should be noted that actinic cheilitis on the lower lip is associated with lip malignancy.

#### Socio-cultural factors:

The consumption of Paan, is a common cultural practice in Southeast Asia and the Indian subcontinent (36). This can cause oral submucous fibrosis which causes trismus. Clinical presentation includes blanching or a marble like appearance on the buccal mucosa which can extend to involve the lips and also impair tongue movement(37). In advanced disease, vertical fibrous bands develop in the buccal mucosa that is firm to palpation (36, 38). Tobacco smoking can cause smoker's keratosis which is a classic white patch with red spots on the palatal mucosa, however, can occur in any part of the oral mucosa. The lesion can regress with smoking cessation (39).

#### Congenital

Bony exostoses are bony outgrowths of unknown aetiology, and of benign nature. Within the jaws they are commonly found lingually in mandible and in the palate. Providing there are no suspicious findings these should be monitored, and no treatment is required.

#### Degenerative or drug related

Oral lichenoid reactions (OLR) are inflammatory processes seen in the oral mucosa. They share some clinical and histologic features consistent with lichen planus (40). Clinical presentation can be white (reticular, papular or plaque like) or red (erosive, atrophic or bullous) forms. Often OLR presents unilaterally as opposed to lichen planus which more often presents bilaterally(41). OLR has been associated with a variety of restorative materials and

medications (including non-steroidal anti-inflammatories, anti-hypertensives and some antimicrobials).

### Endocrine or exocrine

Diabetes is a common condition and rarely presents with oral symptoms and signs, however one should be alert to the fact that such patients are predisposed to infection, may suffer from angular stomatitis and infections should be treated aggressively. A rare but important sign is that of peri-oral anaesthesia which should alert to the risk of hypoglycaemia.

Pleomorphic adenoma is the most common benign salivary gland tumour, especially in the parotid gland, and may present with a discrete swelling which progressively enlarges over time. It is rare for the facial nerve to be involved with a benign exocrine tumour of the salivary gland.

### **Red Flags**

In addition to non-healing ulcers and OPMDs, there are a number of other signs and symptoms which would constitute red flag conditions(42). A 'red flag', in the context of dentistry or medicine, is 'an alarm symptom, warning sign or near patient diagnostic test' (43) which might indicate a serious pathological condition. The term has been around since the mid 1980's and there are many publications outlining lists of 'red flags' for all aspects of medical diagnostics. In the current context, a red flag would constitute an oral or head and neck sign or symptom which might indicate a serious systemic condition(44).

### Bleeding

Whilst bleeding in the oral cavity is not an infrequent complaint from patients attending a dental appointment, the context and history of that bleeding is important. Where there is evidence of periodontal disease with associated bleeding on probing, a complaint of bleeding on brushing is common. However, spontaneous bleeding should prompt the practitioner to take a clinical history (including a drug history) and record the responses accurately. Warfarin (where the patient's INR is measured regularly) is no longer the drug of choice in almost all situations requiring anticoagulation, and the use of direct oral anticoagulant (DOAC) medications are increasing. A history of spontaneous bleeding should prompt the clinician to perform a full periodontal assessment (with radiological examination as necessary) in order to ascertain cause. Examination of the soft tissues is necessary to determine whether there is a specific 'point' (a small vascular abnormality for example). Whilst rare, spontaneous oral bleeding can be a presenting feature of haematological malignancy, and clinicians should make enquiry about general health in addition (weight loss, cough, fever for example).

### Numbness

Patients infrequently complain of numbness, and the onset, duration, location and chronology of numbness needs to be recorded carefully. If there is no clear cause for the change in sensation (local odontogenic pathosis or direct nerve injury) then it should be treated as a suspicious cause until proven otherwise. Causes of numbness can include neoplasia of the head and neck and intracranial lesions(45, 46). Such patients, once odontogenic causes have been excluded, should be referred on a TWW pathway.

### Trismus

A thorough history and clinical examination is necessary in patients presenting with trismus and the chronology of symptoms and any associated factors is important. Trismus following traumatic or repeated inferior dental block local anaesthesia will have a relevant timeline, whereas patients presenting with spontaneous trismus may have more serious underlying disease. Whilst a TMJ disorder may be the most likely scenario, tonsillar malignancy may give rise to unilateral facial pain and restriction in opening(47), and an infective cause should also be considered (48). Urgent referral of patients with trismus should be considered when the history and clinical findings are unusual, and symptoms do not resolve.

### Neck lumps

A thorough history and clinical examination is essential in any patient presenting with a neck lump, and there are resources available to assist the practitioner in establishing a differential diagnosis and making an onward referral(49). That said, the authors would regard a neck lump as a 'red flag' symptom which should heighten the index of suspicion of a serious cause and the patient should be referred onwards without delay.

Below is a worked example of a surgical sieve with examples of three signs/symptoms (not exhaustive) which students and clinicians can use to adapt to their clinical specialty / environment.

	Bleeding	Numbness	Lump
Vascular	Haemangioma	Haemangioma Malignant cell infiltrate	Haemangioma
Infective	Infection from tooth Periodontal disease	Infection tooth in mandible	Dental infection (abscess)

	Acute necrotising ulcerative gingivitis		
Trauma	Sharp trauma	Fractured Mandible	Healed fracture Fibroepithelial polyp Mucocele
Auto-immune	Pemphigus Systemic lupus erythematosus	Multiple sclerosis	Lymphadenopathy Sjogrens Syndrome
Metabolic	Epulis Peripheral Giant Cell Granuloma		Peripheral Giant Cell Granuloma Epulis
Idiopathic	Surgery	Endodontic treatment Mandibular third molar surgery Implant treatment Fractured instrument	Healing wound E.g. post lip biopsy
Neoplastic	Tumour Haematological	Tumour Metastatic deposit Cyst	Enlarged lymph node Salivary gland lesion
Social	Post-piercing	Trauma	Self-harm
Congenital	Arteriovenous malformation	Familial trigeminal anaesthesia	Hygroma Branchial cyst Thyroid
Degenerative	Periodontal disease	Neck arthritis	
Endo/exocrine	Diabetes	Hypoglycaemia	Browns 'tumour'

### Discussion

The use of a surgical sieve and awareness of red flags symptoms is of paramount importance in dentistry however this sieve is not designed to diagnose dental disease as such, but more as an aid for practitioners to establish differential diagnoses with regards to uncommon presentations of orofacial conditions in clinical practice. We have highlighted the importance

of the use of such a tool with an example of its application in clinical practice. The tool is flexible and can be adapted by dental practitioners to their clinical specialty. Further research is needed to explore whether implementation of the sieve can improve patient safety by accurate diagnosis and timely management and referral.

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