

# Orthodontics in patients with significant medical comorbidities

## **ABSTRACT:**

A wide variety of patients with medical comorbidities may present to general orthodontic practice. It behoves the treating clinician to have a general understanding of key medical conditions which may impact upon their treatment options. This clinical review provides a treatment-focused summative update for the orthodontist regarding significant medical comorbidities, their general prevalence and an exploration of potential impacts upon orthodontic treatment. This review also discusses the significance of key medications and provides suggestions as to safe provision of orthodontic treatment.

Key words: orthodontics, medical disorders, medication, medically compromised

# INTRODUCTION

A small but significant proportion of the population undergoing orthodontic treatment have medical and surgical comorbidities which have direct bearing upon the choice, duration and complications of orthodontic treatment. A close collaborative working relationship with the patient's medical team is necessary to facilitate the best possible outcome. It behoves the orthodontist to have a general understanding of such conditions, together with how they might affect the patient and their treatment. Here, we review key aspects of orthodontics in the "medically compromised" patient and highlight aspects of their conditions and management most relevant to the orthodontist.

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# CARDIOVASCULAR SYSTEM

The most common cardiovascular conditions relevant to the younger age groups which predominate in orthodontics, include congenital heart disease, infective endocarditis, cardiomyopathies and dysrhythmias.

## Congenital Heart Disease:

- Overall live birth prevalence of 700-1,200/100,000 in Western populations.(Geva et al., 2014)
- The majority resolve spontaneously in early childhood without sequelae.
- Subtypes of CHD are myriad. The more common or significant types are outlined in Table 1.
- Most haemodynamically significant cardiac defects are corrected surgically, early in infancy or childhood
- More complex structural defects, notably those which involve a combination of aortic or pulmonary root developmental abnormalities with ventricular septal defects, such as Tetralogy of Fallot, will likely require follow up from cardiovascular specialists into adulthood.
- Valvular disease may require surgical repair or replacement, with either biological or metallic valves.
- Metallic heart valves predominate in young age group due to durability, but they require lifelong therapeutic-level anticoagulation, using warfarin or Low Molecular Weight Heparin (LMWH).(Harris et al., 2015)
- CHD which remains uncorrected or resistant to treatment may lead to signs and symptoms of Heart Failure (reduced exercise tolerance, shortness of breath, together with both peripheral and pulmonary oedema).

Most CHD is unlikely to be of direct relevance to the orthodontist. The exception to this is potentially delayed tooth eruption and enamel defects if ameloblasts are affected during tooth formation, which can lead to the formation of a thinner and/or softer enamel tissue.

As a result, these teeth are more risk of caries and are more difficult to restore.(Nosrati et al., 2013; Babaji, 2018) Patients are also likely to be more susceptible to gingival tissue problems when orthodontic appliances are placed.(Gaidry et al., 1985) CHD treated with prosthetic devices, or which cause cyanosis, render patients at higher risk of infective endocarditis with associated considerations for antibiotic prophylaxis (Garrocho-Rangel et al., 2017) although NICE guidelines published in 2008 and most recently revised in 2016 do not recommend this at present.(NICE, 2008)

### Infective Endocarditis:

Infective endocarditis (IE) is a rare but life-threatening infection of the endocardium, particularly affecting the heart valves. It can be difficult to diagnose and, with case fatality rates at approximately 30% (Lalani et al., 2013), it is associated with significant mortality and morbidity. Approximately 50% of IE patients require corrective cardiac surgery, depending on the organism responsible and the heart valve involved. (Lalani et al., 2013; Selton-Suty et al., 2012)

It has an incidence rate of <10 per 100,000.(DeSimone et al., 2015; Selton-Suty et al., 2012; Thornhill et al., 2018)

Patients at increased risk of developing infective endocarditis include those with:

- Acquired valvular heart disease - stenosis or regurgitation;
- Hypertrophic cardiomyopathy;
- Previous infective endocarditis;
- Structural congenital heart disease, including surgically corrected or palliated structural conditions, but excluding isolated atrial septal defect, fully repaired ventricular septal defect or fully repaired patent ductus arteriosus, and endothelialised closure devices;
- Valve replacement;(SDCEP, 2019; NICE, 2008)
- Intravenous drug abuse;(Miro et al., 2003)
- Indwelling central venous catheters and other prosthetic devices e.g. pacemakers.(Kale and Raghavan, 2013; Habib et al., 2015a)

A direct link between orthodontic treatment and IE has never been proven. Orthodontics has been implicated in four patients who suffered from IE but was not proven to be a causative factor. (Biancaniello and Romero, 1991; Dajani, 1991; Hobson and Clark, 1993) Given that bacteraemia is present after toothbrushing in approximately 10% of patients, (Maharaj et al., 2012) antibiotic prophylaxis is no longer routinely recommended by National Institute for Health and Care Excellence (NICE) for invasive dental procedures such as extractions (NICE, 2008) Supra-gingival orthodontic bands and separators and the placement or adjustment of orthodontic appliances are considered non-invasive dental procedures. However, although it has been suggested that orthodontic separators are the most likely orthodontic intervention to cause a bacteraemia, a study by Lucas and colleagues did not identify any significant increase in bacteraemia with separators compared to bands. (Lucas et al., 2002) Moreover, although there appears to be a difference in the incidence of pre- (3%) and post (13%) debonding bacteraemia, (Burden et al., 2004) the same has been demonstrated with pre- and post-interproximal reduction. (Yagci et al., 2013). Ultimately, however, all patients at significant risk of infective endocarditis should be informed of the importance of oral hygiene and that poor oral hygiene may increase their risk of transient bacteraemia after toothbrushing. Where more invasive treatment, such as orthognathic surgery, is warranted, patients at significant risk of IE require counselling about the benefit and risks of antibiotic prophylaxis, as well as "safety-net" advice regarding the signs and symptoms of IE. These may comprise a combination of: flu-like symptoms, unexplained fever, rigors, reduced exercise tolerance, weight loss, fatigue, muscle, joint or back pain, though the individual may remain asymptomatic. (Habib et al., 2015b) If suspected, or further advice is required, early liaison with local cardiology services is recommended.

### **Cardiac arrhythmias:**

Cardiac arrhythmias are common at all ages, ranging from the



benign sinus arrhythmia to supraventricular tachycardia and ventricular fibrillation. They are usually caused by an error in the conductive pathways of the heart and can be induced through a variety of situations, including excess caffeine, drugs e.g. alcohol or cocaine, blood electrolyte abnormalities, medication and stress. The presence of conditions such as CHD or the cardiomyopathies, where the heart muscle is dysfunctional, may exacerbate the risk of dangerous arrhythmias.

- Key symptoms include palpitations, shortness of breath, chest tightness/pain, lightheadedness and syncope.
- Syncope (loss of consciousness) is potentially the most severe warning sign, though Sudden Cardiac Death may also occur.
- Treatment can be pharmacological and/or interventional, including the use of pacemakers and implantable defibrillator devices (see Table 2).(Hessling, 2016)
- Resuscitation Council (UK) BLS, ILS and ALS protocols provide a guide as to how to approach and manage dangerous arrhythmias in the emergency setting, however urgent medical assistance should be sought. (Resuscitation Council UK, 2015) (Chaudhry et al., 2016)

\*Local measures(SDCEP, 2015) when treating patients and wishing to avoid excessive bleeding include:

1. The use of oxidised cellulose ('Surgicel') or collagen sponges and sutures
2. 5% tranexamic acid mouthwashes used four times a day for 2 days although this is not readily available in the primary care dental setting in the UK, as it is not on the Dental Practitioners' Formulary in the BNF.
3. Nerve blocks may need to be avoided and care taken to avoid haematoma formation.(Piot et al., 2002)

# SKELETAL SYSTEM

Juvenile idiopathic arthritis:

Juvenile idiopathic arthritis (JIA) is a broad term that describes a clinically heterogeneous group of inflammatory arthropathies of unknown cause, which begins before 16 years of age.(Patel et al., 2009; Giancane et al., 2016) It may cause similar effects to the temporomandibular joints as rheumatoid arthritis.(Sasaguri et al., 2009; Ringold et al., 2012) including pain, stiffness, locking and joint damage.

Prevalence is 100 per 100,000 children in the UK.(Manners and Bower, 2002)

- JIA can be of varying severity with localized and/or systemic complications, including functional impairment of the affected joints.
- NSAIDs are used in the early stages in the management of the condition.
- More severe cases are prescribed a variety of medicaments such as corticosteroids, methotrexate, anti-TNF $\alpha$  biologics and antimalarial drugs.(Giancane et al., 2016) (Patel et al., 2009)

JIA may result in disturbances in growth and developmental anomalies. The temporomandibular joint (TMJ) is affected in 45% of cases with JIA,(Twilt et al., 2004) with progressive joint damage similar to that found in Rheumatoid Arthritis,(Sasaguri et al., 2009) and it may be managed by intracapsular steroid injections. Some patients may develop condylar hypoplasia, resulting in a downwards and backwards growth rotation. On occasion this can cause significant pain, and some may require TMJ replacements, with the potential for a concurrent osteotomy to correct the mandibular retrognathia. JIA patients commonly present with skeletal Class II and open bite malocclusions,(Sidiropoulou-Chatzigianni et al., 2001) while mandibular asymmetry is seen in cases with unilateral TMJ involvement.(Patel et al., 2009) The prevalence of dental caries and

periodontal disease is higher in adolescents with JIA cases. This may be due to difficulties in performing optimal oral hygiene, poor diet or the side effects from the long-term administration of medication. (Welbury et al., 2003)

It is essential to assess the TMJ when examining the patient and to repeat the review at regular intervals throughout treatment (Müller et al., 2009). Modified toothbrush handles and electrical toothbrushes can be recommended to rheumatology patients in the case of significant destructive joint pathology, (Greenwood and Meechan, 2003; Treister and Glick, 1999) however this is extremely rare under current medical regimens in young people. A bite splint may be provided to unload the joint during any acute periods of inflammation, however the use of functional appliances in patients is a controversial area. It has been argued that functional appliances and class II elastics put increased stress on the TMJ and should be avoided, yet it has also been suggested that functional appliances protect the joints by potentially moving the mandible into the normal anterior growth rotational pattern therefore potentially improving the skeletal relationship.(Kjellberg et al., 1995; Patel et al., 2009) Liaison with the associated specialist medical team is recommended.

### **Ankylosing spondylitis**

Ankylosing spondylitis (AS) is a debilitating autoimmune disease affecting the sacroiliac joints, spine, and entheses.(Sieper et al., 2002; McVeigh and Cairns, 2006; Tudsri et al., 1997; Arora et al., 2013)

Prevalence of symptomatic AS is 660/100,000 in the UK.(Hamilton et al., 2015)

- Human Leucocyte Antigen (HLA)-B27 is present.(Sieper et al., 2002; Moon and Kim, 2014)
- Severe and progressive morning stiffness, back pain, enthesitis and fatigue symptoms are common unless treatment is adequate. (Tudsri et al., 1997; Mehdizadeh and Mir, 2012)

- Multidisciplinary management of AS includes appropriate exercise, physiotherapy and non-steroidal anti-inflammatory drugs as a first line to control symptoms.(Mehdizadeh and Mir, 2012; Arora et al., 2013)
- Biological agents e.g. anti-TNF- $\alpha$  therapies, such as infliximab(Braun et al., 2002; van der Heijde et al., 2005) and etanercept (Gorman et al., 2002), target the specific inflammatory processes of the disease, and is effective at controlling disease progression.(Zochling et al., 2006; Arora et al., 2013)
- Corticosteroids may also be used in those intolerant of NSAIDs. (Sieper et al., 2002; McVeigh and Cairns, 2006; Moon and Kim, 2014)
- Bisphosphonates are frequently prescribed in this group due to inflammatory bone density loss.

Temporomandibular joint dysfunction can develop, which includes clicking and impaired mouth opening, although this is usually present in the advanced stages of the disease(Mehdizadeh and Mir, 2012; Arora et al., 2013), with limited movement of these joints occurring in 10% of those patients.(Tudsri et al., 1997; Arora et al., 2013) Spinal stiffness or deformities may make it uncomfortable, or even painful, to sit in the dental chair for extended periods of time. (Mehdizadeh and Mir, 2012) Extremes of neck extension and flexion should be avoided during positioning of the head and oral cavity, including during anaesthetic induction,(Tudsri et al., 1997; Arora et al., 2013) due to restricted range of movement. The risk of periodontal disease is also found to be increased in this cohort and specialist input is recommended.(Keller et al., 2013) This may be related to a compromised inflammatory response against oral infections which has been suggested by some authors.(Mehdizadeh and Mir, 2012)

### **Medication-related osteonecrosis of the jaws**

Medication-related osteonecrosis (MRONJ) of the jaw is a severe adverse drug reaction, consisting of progressive bone destruction in the maxillofacial region, that has persisted for more than eight weeks, where there has been no history of radiation exposure or obvious

metastatic disease affecting the jaws.(Ruggiero et al., 2014a; Rosella et al., 2016)

The estimated incidence of MRONJ in cancer patients treated with anti-resorptive or anti-angiogenic drugs is 1,000 per 100,000 individuals, while in osteoporosis patients the incidence lies at approximately 10-100 per 100,000 individuals.(SDCEP, 2017)

Those at high risk for MRONJ include:

- Cancer patients (especially breast cancer, prostate cancer, multiple myeloma and other blood cancers)
- Previous history of MRONJ
- >5 years bisphosphonate use (see table 3)
- concomitant use of bisphosphonates with systemic glucocorticoids.(SDCEP, 2017)
- The risk of MRONJ in patients receiving intravenous bisphosphonates appears to be no greater than those taking oral bisphosphonates.(SDCEP, 2017)
- Mucosal trauma from orthodontic appliances, either fixed or removable, is considered a risk factor and should be minimised.
- Dental trauma, extractions or any oral surgery procedures that may impact on bone should be avoided where possible.

There is no evidence that MRONJ risk will be reduced if the patient temporarily, or even permanently, stops taking bisphosphonate drugs prior to invasive dental procedures since the drugs may persist in the skeletal tissue for years.(SDCEP, 2017) Bisphosphonate use is associated with an increased duration of orthodontic treatment, as they result in reduction in speed of tooth movement due to the interference with osteoclastic resorption,(Krishnan et al., 2015) while non-extraction treatment plans may be preferred. The role of temporary anchorage devices is controversial and the associated risk is unknown.(Ruggiero et al., 2014b) As yet, orthodontic tooth movement has not been associated with any reported cases of MRONJ. (Di Fede et al., 2018)

# CONNECTIVE TISSUE

## **Ehlers-Danlos Syndrome:**

Ehlers-Danlos Syndrome (EDS) is a group of inherited conditions that affect the structure and function of collagen proteins, which may be functionally weaker or produced in a lesser amount. Typical features include stretchy skin, hypermobile joints and fragile bony tissues, though a myriad of systemic symptoms such as intestinal dysmotility may also be associated. The syndrome was reclassified recently and there are thirteen different subsets.(Malfait et al., 2017)

The prevalence of classic Ehlers-Danlos Syndrome is 5/100,000. (Malfait et al., 2010)

Relevant dental characteristics include; joint hypermobility, dystrophic scars, poor wound healing and a tendency to bleed excessively.(Porter, 2016) In those patients where the TMJ is prominently affected, more brief appointments with frequent rests and regular clinical assessment of the TMJ may be warranted. Patients with certain forms of EDS will be more susceptible to periodontal problems (Kapferer-Seebacher et al., 2016; Porter, 2016) and caries due to tooth morphology.(De Coster et al., 2005) Extractions, periodontal treatment and orthognathic treatment may be compromised by poor healing and increased bleeding tendency (Porter, 2016). This may also affect the mechanism of local anaesthetic administration, for example inferior dental blocks may lead to haematoma. In certain subgroups of EDS local anaesthetic is less efficient. When performing orthodontic treatment teeth are likely to move quickly due to problems with patients' collagen.(Porter, 2016) There is an increased risk of damage to the fragile periodontal ligament so light forces should be used. There is also a high orthodontic relapse potential, so the use of both bonded and removable retainers should be considered. The buccal mucosa is prone to trauma so self-ligating brackets and plastic aligners may be considered. Excessive root resorption is not thought to be a concern. (Norton, 1984)

# NERVOUS SYSTEM

## Epilepsy:

Epilepsy is a chronic condition characterised by recurring seizures; paroxysms of cerebral electrical activity caused by sudden, disorderly and excessive neuronal discharge.

The prevalence of epilepsy is 760 per 100,000.(Fiest et al., 2017)

- Treatment usually involves antiepileptic drugs including phenytoin, carbamazepine, sodium valproate, lamotrigine and levetiracetam (see Table 4).(Joshi et al., 2013)
- NICE guidelines recommend carbamazepine or lamotrigine as first-line treatment to children, young people and adults with newly diagnosed focal seizures, whereas sodium valproate should be offered for generalised or absence seizures.(Excellence, 2018) Levetiracetam is being used with increasing frequency for refractory epilepsy presenting to secondary and tertiary care services.
- Phenytoin is generally reserved for the most resistant cases, such as Status Epilepticus. It is associated with significant side effects, including gingival hyperplasia which may require periodontal input.(Sanders et al., 1995)
- Antifungal agents (such as fluconazole) and antibiotics (such as erythromycin or metronidazole) may interfere with the metabolism of certain antiepileptic drugs, which themselves are often notable inducers or inhibitors of hepatic cytochrome complexes and which therefore may affect the efficacy of other medications.
- An MRI scan of the brain is a very commonly used modality in the investigation of seizures and the diagnosis of epilepsy.

Generalised “tonic–clonic” seizures frequently cause oral injury, such as tongue biting, dental trauma and, in some cases maxillofacial damage.(Sheller, 2004) Protective mouthguards are recommended to mitigate these risks.(Fiske and Boyle, 2002) Most well-controlled epileptic patients may undertake fixed appliance treatment, however

such patients should be consented for the risks of soft tissue and dental injury. Removable appliances should be used with caution as they may become dislodged, causing further trauma and posing an aspiration risk. If removable appliances cannot be avoided, they should be designed for maximum retention and high impact acrylic should be used.(Fiske and Boyle, 2002)

When using MRIs to investigate seizure activity, there may be potential artefacts caused by stainless steel orthodontic appliances which may degrade image quality. Measures such as the use of ceramic or titanium brackets or software modification, may mitigate this effect. The removal of stainless steel orthodontic appliances may be necessary in some cases prior to imaging.(Poorsattar-Bejeh Mir and Rahmati-Kamel, 2016) however bonded retainers generally only need to be removed if the oral cavity itself is under investigation. (Beau et al., 2015) Discussion with the patient's radiologist is recommended as there can be differences in opinion between radiologists depending on the area to be scanned and the radiological equipment and protocol used.

### **Multiple Sclerosis (MS):**

MS is a chronic, inflammatory, demyelinating disease of the central nervous system.

The prevalence in the UK is 203.4 per 100,000.(Mackenzie et al., 2014)

- Symptoms such as tremor, weakness and paraesthesia may vary in severity, location and duration and affect the limbs, trunk, head, jaw, lips, tongue and speech, both at rest or during purposeful movement.
- Multiple sclerosis (MS) symptoms tends to be aggravated by emotions, stress and fatigue.(Goldenberg, 2012)
- Diagnosis is made on the basis of clinical findings and supporting evidence from MRI of the brain and spinal cord, together with the identification of oligoclonal bands in cerebrospinal fluid.(Link and Huang, 2006)



- The use of MRI has orthodontic implications similar to those in the epilepsy section.(Goldenberg, 2012)
- 4 subtypes of MS exist, of which the most common is the “Relapsing-remitting” form. This accounts for 85% of patients and is marked by flare-ups (relapses or exacerbations) of symptoms followed by periods of remission.(Goldenberg, 2012)

Patients often experience pain and numbness in the face and mouth as part of their condition. Significant tremor and loss of co-ordination may compromise oral hygiene. Custom-made toothbrush handles and electric toothbrushes are recommended to assist in self-care. (Fiske et al., 2002) MS-associated disability may also affect orthodontic treatment; for example, the patient may need someone else to change their intermaxillary elastics and assist them with oral hygiene. Transient spasticity may also be a feature of MS, leading to lack of co-ordination, muscle spasm and pain and, potentially, compromising the safe provision of orthodontic treatment. Treatment should therefore be delayed until the patient is in a remission phase. Depression and fatigue are common in people with chronic, progressive medical conditions, such as MS. This can decrease motivation for overall dental care and the effects of dental pathology may be compounded by the xerostomic effects of antidepressant drugs or supplements with a high sugar content.(Talic, 2011) Treatment objectives should be tailored to the individual patient and a compromised outcome may be acceptable.

### **Autism Spectrum Disorder (ASD):**

This refers to a group of neurodevelopmental disabilities with a core set of defining criteria that comprise impaired social interaction, communication, and restricted or repetitive behavioural stereotypes. The spectrum consists of Autism, Asperger Syndrome, and Pervasive Developmental Disorder-Not Otherwise Specified, which differ in the number and severity of diagnostic features. The aetiology of ASD is likely to be related to both genetic and environmental factors.(Faras et al., 2010) A full assessment of the patient is essential if orthodontic

treatment is to be successful. Depending on the severity of the condition the treatment plan may need to be altered, i.e. the use of fixed or removable appliances, extractions etc. It may be useful to begin with a functional or removable appliance or a sectional fixed appliance prior to any extractions and assess patient cooperation. The views of the patient regarding possible treatment must not be ignored.

The prevalence of ASD is 1,100/100,000 in the UK.(2012)

- Dyspraxia, anxiety, depression, epilepsy or a strong gag reflex are often associated with ASD.(Dziuk et al., 2007; Gandhi and Klein, 2014)
- Information should be sought regarding any repetitive behaviours, such as chewing material.
- Hyper- or hypo-sensitivity to sensory stimuli such as light, sound, pain or touch is a notable aspect of the condition and information on this should also be sought from the patient or carer so that sensory overload might be avoided. A “flight or fight” response to a new or overwhelming environment may be precipitated, as may a “melt down” or “shut down”, where the patient is unable to communicate. (Gough, 2012; McGuire et al., 2016)

A study comparing adults with ASD and unaffected pairs found an increased frequency of anterior open bites and dental crowding in the adults with ASD, compared to unaffected pairs. Likewise, spacing, reverse overjet and Class II molar relationship tendencies were higher in autistic patients evaluated by orthodontists. (Luppanapornlarp et al., 2010) Orthodontics is not contraindicated in this group of patients, but a tailored treatment plan, perhaps with some compromise regarding the final outcome, may be accepted and planning often requires a degree of conforming to the patient’s behaviour.(Rada et al., 2015) Appropriate behaviour management is essential, for example via the use of “Tell-show-do”, social stories or Makaton (Short and Calder, 2013) and using precise clear instructions. Maintaining consistency between appointments is also important. For example, attendance at the same appointment time, in the same

surgery, with the same staff members and ideally avoiding keeping the patient waiting.(Delli et al., 2013)

### **Downs Syndrome:**

This is a genetic trait of trisomy 21, where the individual develops characteristic facies and frequently exhibits delayed physical growth and mild to moderate learning difficulties, among other associations.

The prevalence is 66/100,000 in the UK.(Wu and Morris, 2013)

- 40-50% of babies with Downs syndrome are born with some type of cardiac abnormality, mostly corrected in early childhood, although some may exhibit residual intra-cardiac shunts.
- Immune compromise due to decreased T cell numbers.
- Increased risk of acute lymphoblastic/myeloid leukaemia. (Xavier and Taub, 2010)
- Predisposition to early dementia.
- Dentally, soft tissue manifestations include macroglossia, tongue fissuring, thick/dry/fissured lips and cheilitis.(Shukla et al., 2014)
- Hard tissue features include midface hypoplasia (CIII anterior open bite, posterior crossbite), hypodontia, microdontia, delayed eruption and enamel anomalies.(Fiske and Shafik, 2001)
- There is an increased incidence of severe early periodontal disease yet low incidence of caries present in this patient group. (Fiske and Shafik, 2001)

Orthodontic treatment plans should be tailored to the patient and a less complex treatment plan, which still addressed patient concerns, may be appropriate. There are a number of alterations to treatment which may it easier for the patient to cope with treatment, for example quick set impression material, self-ligating brackets to allow easier activation and the use of tubes rather than bands. (Musich, 2006).

# RESPIRATORY SYSTEM

## **Asthma:**

Asthma is a chronic disease that affects the bronchioles, characterised by recurrent and reversible airflow limitation due to an underlying inflammatory process. Asthma is one of the most common causes of death in young people.(Gullach et al., 2015)

The incidence rate of asthma is 520/100,000 in the UK.(Simpson and Sheikh, 2010)

- Signs and symptoms of asthma include intermittent wheezing, coughing, dyspnoea, and chest tightness.
- Severity ranges from the relatively mild to severe.
- Severely affected patients may have growth restriction due to recurrent steroid use.(Doull, 2004)
- Inhaled short-acting and long-acting beta adrenoceptor agonists (bronchodilators), together with inhaled corticosteroids (anti-inflammatory) provide the mainstay of treatment.
- Up to 10,000 per 100,000 of adult asthmatic patients have an allergy to aspirin and other nonsteroidal anti-inflammatory agents, leading to bronchoconstriction. This is not a concern for children.

Oral manifestations of asthma include candidiasis, decreased salivary flow, increased calculus, increased gingivitis, and increased periodontal disease.(Patel et al., 2009) A tenuous link between external root resorption in posterior teeth and orthodontic treatment in asthmatics has been reported. However, this resorption was mild and similar amounts of moderate and severe root resorption was seen in both asthmatic and healthy control patients. It may be prudent to advise patients of this risk.(McNab et al., 1999; Patel et al., 2009) When treating patients care should be taken in the positioning of suction tips as they may elicit a cough reflex.(Maheshwari et al., 2012) The orthodontist should ensure the patient has their inhaler nearby in case of sudden onset wheeze,(Maheshwari et al., 2012) though in severe attacks, medical on-call assistance or urgent transfer to an emergency department should be considered. Cystic Fibrosis:

## **Cystic Fibrosis:**

Cystic fibrosis (CF) is an autosomal recessive disease involving epithelial sodium and chloride transport systems and principally affects lungs, liver, pancreas, intestines and male infertility. It is of equal prevalence in males and females (Slutsky and Greenberg, 2011) and is the most common life limiting inherited condition affecting Caucasians with a median survival of less than 60 years in the UK. (Hurley et al., 2014)

The incidence rate is 40/100,000 births in the UK. (Taylor-Robinson et al., 2018)

- The British Thoracic Society have produced NICE guidelines in relation to CF. (Society, 2018)
- Recurrent and persistent chest infections, with progressive pulmonary damage and bronchiectasis are common.
- Chronic sinusitis may manifest as facial pain, nasal congestion and the inability to breathe through the nose. (Harrington et al., 2016)
- Malabsorption of fat-soluble vitamins A, D, E, and K are common due to a combination of pancreatic and biliary disease with gut dysmotility. (Slutsky and Greenberg, 2011)
- Pancreatitis and liver cirrhosis are notable features of the later stages of the condition. (Slutsky and Greenberg, 2011)
- Osteopenia and osteoporosis can occur secondary to malnutrition, vitamin D deficiency and the use of systemic glucocorticoids. (Harrington et al., 2016)
- Life expectancy has increased considerably over the past 20 years and it is likely with future abnormal chloride channel-modifying small molecules therapies, the median life expectancy of CF patients will continue to increase.

Dentally, oral antibiotics have been associated with the development of black hairy tongue. Although xerostomia is common in the CF patient, reduced caries risks have been attributed to altered oral microflora due to the long term antibiotic treatments for CF patients. (Harrington et al., 2016) Often these patients have delayed dental eruption. General anaesthetic for extractions should be

avoided due to frequent poor lung function. Two CF patients should not be seen in clinic consecutively in order to reduce the risk of spreading resistant pulmonary infections between individuals. These patients have a restricted adult life expectancy. Thus, the aims of orthodontic treatment may need to be modified to account for the patient's need to avoid infection and regular other healthcare appointments.

## **HAEMATOLOGY**

### **Haemophilia:**

Haemophilia is the most common group of severe inherited anticoagulant disorders. Haemophilia A is an X-linked disorder caused by genetic deficiency in clotting factor VIII. Other similar bleeding disorders include haemophilia B, (Christmas disease, factor IX deficiency) and von Willebrand's disease (defects of von Willebrand's factor).(Patel et al., 2009)

The prevalence of haemophilia A is 20/100,000 males. The prevalence of haemophilia B is 3.3/100,000 males.(Fijnvandraat et al., 2012)

If extractions or surgery cannot be avoided, management relies on careful surgical technique, including an attempt at primary wound closure. A haematologist may be able to advise:

- increasing Factor VIII production with 1-desamino-8-D-arginine vasopressin (DDAVP)
- to replace missing Factor VIII with cryoprecipitate, Factor VIII, fresh frozen plasma or purified forms of Factor VIII (although this is less commonly practiced nowadays)
- antifibrinolytic therapy with tranexamic acid or epsilon-amino caproic acid (EACA)(Gupta et al., 2007; Patel et al., 2009)

Orthodontic treatment is not contraindicated in patients with bleeding disorders, however it is essential that excellent oral hygiene is maintained. The duration of treatment should be given careful consideration as a longer treatment duration will increase the potential for complications. Fixed appliances are preferable to removable appliances as the latter can cause gingival irritation.

Self-ligating brackets are preferable to conventional brackets as they may help to reduce trauma.(Maheshwari et al., 2012) Conventional modules should be tied in with elastomeric modules rather than wire ligatures. As always care should be taken when inserting and removing arch-wires and care should be taken to avoid long wire ends distally. Pain relief should avoid drugs which may cause bleeding i.e. aspirin and NSAIDs. No evidence on the use of TADs available, theoretically these are transmucosal, so their placement should not cause significant issues, however local blood vessels will still be affected so again good communication with the patient's treating physician is essential. Nerve-block anaesthetic injections require cover to prevent the risk of a haematoma forming. (Piot et al., 2002) It is important to liaise with the patient's haematologist before moderate/major surgery.

### **Sickle Cell Anaemia:**

This genetic disorder is characterized by a HbS haemoglobin gene mutation. Deoxygenation induces the red cells to deform into a sickle shape, which restricts their movement through blood capillaries. Tissue hypoxia may cause end-organ damage and severe pain. (Patel et al., 2009)

The prevalence is 21.7/100,000 in the UK.(Dormandy et al., 2018)

- The most characteristic manifestations of SCD is the sickle cell crisis. It consists of an episode of severe pain of 1 to 2 weeks duration, often accompanied by a low-grade fever and leucocytosis.
- A crisis may be precipitated by infection, dehydration or acidosis, amongst other causes,(Acharya, 2015; Amoah et al., 2015) including physical and psychological stress.(Buck and Davies, 2005; Amoah et al., 2015)
- Splenic infarction is common in HbS-affected individuals, leading to increased susceptibility to infection from encapsulated organisms such as *Streptococcus pneumoniae* and *Haemophilus influenzae*. Penicillin-based prophylaxis is frequently used post-splenectomy.

Orthodontically, it is advisable to avoid dental extractions where possible to reduce the risk of osteomyelitis.(Alves et al., 2006; Amoah et al., 2015) If extractions are necessary they should be carried out in a hospital setting ideally using local anaesthetic, rather than a general anaesthetic, to avoid hypoxia.(Alves et al., 2006) The potential for orthognathic surgery is understandably limited. Oral manifestations of SCD include enamel hypoplasia and dentinal hypomineralisation, which could compromise orthodontic bracket/ band bonding onto dentition.(Michaelson and Bhola, 2004) When moving teeth there is a risk of pulpal necrosis and it is recommended that forces should be reduced, and breaks given between activation to allow healing of regional microvasculature. and excessive forces to maintain regional microcirculation(Alves et al., 2006). Close liaison with GP/haematology is recommended.(Killick et al., 2016)

### **Leukaemia:**

Leukaemia is a malignant disease of the blood, where the uncontrolled proliferation of immature blood cells occurs. Eventually these aberrant cells compete with normal cells for space in the bone marrow, causing bone marrow failure and death. There are four main types of leukaemia; (1) acute lymphocytic, (2) acute myeloid, (3) chronic lymphocytic, and (4) chronic myeloid.(Zimmermann et al., 2015b)

The incidence rate is 11.25/100,000 births in the UK.(Bhayat et al., 2009)

- In general, the recommended treatment is chemotherapy +/- bone marrow transplantation, depending upon the type of leukaemia.
- It is unlikely that orthodontic therapy will be indicated in patients with active leukaemia, however given recovery rates from childhood leukaemia, the orthodontist may need to be mindful of the long-term effects of the condition and its treatment. (Zimmermann et al., 2015b)



In terms of orthodontics the effects are two-fold, those problems which are present at time of treatment and those which manifest in disturbances in growth and development. In acute leukaemia, gingival hyperplasia is generally observed. A patient with good oral hygiene whose gums bleed spontaneously should be referred urgently to their GP. In chronic leukaemia, pallor of the mucosa and soft tissue infections can often be observed. Opportunistic candida and herpes infections are common.(Zimmermann et al., 2015a) Any patient who is planned for chemotherapy or radiotherapy should have their appliances removed. Continuation of orthodontic treatment may be considered later.

Children who have had radiotherapy or chemotherapy are likely to experience a range of oral complications including arrested root development, microdontia, hypodontia, mucosal damage, xerostomia and altered craniofacial growth.(Nasman et al., 1997; Padmini and Bai, 2014) Efforts should be made to use light forces and appliances that will minimise the risk of root resorption. Treatment should be kept as short as possible, perhaps accepting a compromised result and using the simplest treatment method.(Dahllof et al., 2001) If possible treatment in the lower arch should be avoided along with extraction and orthognathic surgery as there is a risk of osteonecrosis. If elective orthodontic extractions are to be performed they should be delayed until the patient completes their antineoplastic treatment successfully, at least two years after bone marrow transplant and are considered to be in remission by their haematologist. (Zimmermann et al., 2015a) It is also important that the patient is aware of the risk of osteonecrosis. As total body irradiation can suppress general growth, the prognosis for growth modification in skeletal Class II malocclusions is guarded. (Dahllöf and Huggare, 2004)

# ENDOCRINOLOGY

## **Hypo/hyperthyroidism:**

Thyroid dysfunction is the second most common glandular disorder of the endocrine system and is increasing, predominantly amongst women.(Chandna and Bathla, 2011) Hypothyroidism is defined by an increase in thyroid stimulating hormone (TSH) and thyroxine production. Hyperthyroidism, by contrast, is a condition caused by excessive production of thyroid hormones.

In Europe, the prevalence of hyperthyroidism is 750 per 100,000 population, while the prevalence of hypothyroidism is 3,000 per 100,000.(Garmendia Madariaga et al., 2014)

- Hypothyroidism may be caused by autoimmune thyroiditis (Hashimoto's disease), radioactive iodine, peri-thyroid surgery, nutritional iodine deficiency and pharmacological agents such as lithium or amiodarone.
- Insufficient levels of thyroid hormone cause symptoms such as slower metabolic rate, slow heart rate, weight gain, lethargy, intolerance to cold, dry and cool skin, and puffiness of the face and eyelids.(Chandna and Bathla, 2011)
- Dental aspects of hypothyroidism manifest as thick lips, large protruding tongue (macroglossia), impacted mandibular second molars and delayed eruption of teeth.(Young, 1989)
- Primary causes of Hyperthyroidism include Grave's disease and functional nodular goitres. Secondary causes include high levels of human chorionic gonadotrophin, functional pituitary adenomata (excess TSH production) and medication such as amiodarone.
- Clinical manifestations include tremor, anxiety, intolerance to heat, sinus tachycardia, increased cardiac output (increased susceptibility to congestive heart failure), systolic heart murmur, hypertension, increased appetite and weight loss.(Chandna and Bathla, 2011) Grave's Disease presents with a combination of hyperthyroidism, pretibial swelling (myxoedema) and exophthalmos.

- Dental aspects of hyperthyroidism include increased susceptibility to caries, periodontal disease, enlargement of extra-glandular thyroid tissue (mainly in the lateral posterior tongue), maxillary or mandibular osteoporosis, accelerated dental eruption (Poumpros et al., 1994) and burning mouth syndrome. (Pinto and Glick, 2002)

### **Diabetes mellitus:**

Diabetes mellitus (DM) represents a group of metabolic diseases that are characterised by hyperglycaemia due to a total, or relative, lack of insulin secretion and insulin resistance or both. (Al-Maskari et al., 2011)

The prevalence of Type 1 DM is 187.7 per 100,000. (Chaugule et al., 2017) The prevalence of Type 2 DM is 5260 per 100,000. (Zghebi et al., 2017)

Current classifications describe four sub-types of DM:

- Type 1 DM is also known “insulin-dependent” DM, (Al-Maskari et al., 2011) because of an absolute requirement for exogenous insulin supplementation. This is most common amongst children and young adults, with first presentation commonly below the age of 20 years; though it can occur as late as the fourth decade of life. Type 1 DM results from the autoimmune destruction of pancreatic  $\beta$ -cells, resulting in the inability of the body to produce insulin in response to glycaemic stimuli. Insufficient insulin administration can lead to potentially fatal diabetic ketoacidosis. (2014; Al-Maskari et al., 2011)
- Type 2 DM is also known as “non-insulin-dependent” DM, though some individuals may be dependent upon insulin for therapy due to suboptimal response to other treatments. Type 2 DM commonly starts insidiously, frequently in those over the age of 40 years and is caused by a combination of insulin resistance and inadequate insulin secretion from pancreatic  $\beta$ -cells. (Al-Maskari et al., 2011; Pfeffer et al., 2015)

- Type 3 DM occurs due to pancreatic  $\beta$ -cell destruction, frequently because of disease processes such as chronic pancreatitis or pancreatic surgery. This results in an overall reduction in the capacity for insulin production, often together with a degree of insulin resistance.(Hart et al., 2016)
- Gestational diabetes is defined as significantly impaired glucose tolerance, in the diabetic range, related to the pregnant state and usually resolves post-partum. Females who are genetically predisposed to diabetes can develop DM during pregnancy as a result of the physiological and hormonal changes associated with the gravid state.(Al-Maskari et al., 2011) A diagnosis of gestational diabetes is associated with increased risk of developing Type 2 Diabetes in later life.

DM may cause significant mortality and morbidity through microvascular and macrovascular damage. This is often progressive dependent upon glycaemic control, duration of the condition or the sub-type of diabetes. Microvascular damage frequently leads to a greater morbidity, with associated peripheral and autonomic neuropathy, nephropathy, retinopathy and cataracts. Macrovascular damage is the main driver of increased mortality with higher risk of atherosclerotic and thrombotic pathology such as myocardial infarcts, peripheral vascular disease and stroke. Wound healing may be significantly impaired and infection rates increased in the diabetic patient with microvascular disease or poor glycaemic control. (Leite et al., 2013) Oral complications include: xerostomia, burning mouth and/or tongue, candida infection, altered taste, progressive periodontal disease, dental caries, acetone breath, oral neuropathies, parotid enlargement, sialosis and delayed wound healing. These complications can occur even when the blood glucose is well controlled due to impaired neutrophil function but are all more severe in uncontrolled DM. (Patel et al., 2009; Leite et al., 2013; Al-Maskari et al., 2011; Almadih et al., 2018)

Well-controlled DM is not a contraindication for orthodontic treatment(Patel et al., 2009), however, orthodontic treatment should

be avoided in patients with poorly controlled DM as they are more likely to suffer from periodontal involvement(Almadih et al., 2018). If in doubt, the orthodontist should liaise with patient and their diabetologist in the provision of care. Diabetic-related microangiopathy can affect the peripheral vascular supply, resulting in unexplained toothache, tenderness to percussion or potentially loss of vitality.(Bensch et al., 2003) It has also been suggested that the diabetic state up-regulates osteoclast migration and activity and down-regulates osteoblast differentiation, resulting in greater orthodontic tooth movement.(Braga et al., 2011) This is why light orthodontic forces has been suggested for the diabetic patient. (Bensch et al., 2003) Light physiological forces should be used in all patients to avoid overloading the teeth.(Patel et al., 2009) Patients should be advised to eat a usual meal and take their medication as usual prior to their appointments and the practitioner should always be vigilant to hypoglycaemic medical emergencies and respond appropriately. It is particularly important that patients with Type 1 Diabetes, or whom take insulin, are aware of the need to eat regularly, despite any orthodontic related discomfort, to avoid hypoglycaemia and rebound hyperglycaemia.

### **Addison's Disease:**

Addison's disease involves adrenal suppression from a variety of causes, including the regular and protracted intake of exogenous corticosteroids (Iatrogenic Addison's).

Addison's disease has a prevalence of 9.3-14/100,000.(Vaidya et al., 2009)

- Supplemental steroids should be considered in any patient on long term steroids during times of physiological stress(Sarkar et al., 2012) to counteract the risk of acute adrenal crisis, leading to hypotension and collapse.(Patel et al., 2009)

A suitable regimen for corticosteroid replacement, in patients who have taken more than 10 mg prednisolone daily (or equivalent) within 3 months of surgery, is:

- Minor surgery under general anaesthesia—usual oral corticosteroid dose on the morning of surgery or hydrocortisone (usually as sodium succinate) intravenously at induction, the usual oral corticosteroid dose is recommenced after surgery.
- Moderate or major surgery—usual oral corticosteroid dose on the morning of surgery and hydrocortisone intravenously at induction, followed by hydrocortisone 3 times a day by intravenous injection for 24 hours after moderate surgery or for 48–72 hours after major surgery, the usual pre-operative oral corticosteroid dose is recommenced on stopping hydrocortisone injections. (NICE, 2018b)

General dental procedures (including orthodontics) for patients receiving long-term steroid medication do not warrant supplementation with additional glucocorticoids. (Gibson and Ferguson, 2004) Patients on long-term corticosteroid treatment should carry a steroid treatment card which gives guidance on minimising risk and provides details of prescriber, drug, dosage and duration of treatment. (NICE, 2018b) Should unexplained peri-operative hypotension or typical electrolyte imbalance occur, adrenal insufficiency should be suspected and appropriate supplemental steroid should be administered by the medical team. Close liaison and follow up with an endocrinologist is warranted. (Gibson and Ferguson, 2004) It is reported that corticosteroids administration on rats resulted in a lower amount of rat tooth movement. (Bhanot and Mago, 2016; Kalia et al., 2004) Therefore, it may be wise to postpone orthodontic treatment on patients on acute doses and that orthodontic forces should be reduced and checked more frequently in patients on chronic steroid treatment. (Kalia et al., 2004)

# GASTROENTEROLOGY

## **Inflammatory Bowel Disease:**

Inflammatory Bowel Disease (IBD) comprise a series of autoimmune conditions which result in acute, chronic and recurring inflammation of the gastrointestinal tract.(Satsangi et al., 2006) Crohn's Disease and Ulcerative Colitis are the two main subtypes.

## **Crohn's Disease:**

Crohn's disease (CD) mainly involves the terminal ileum and colon but may affect any part of the gastrointestinal tract including the oral cavity, such as orofacial granulomatosis or recurrent aphthous ulceration.(Tan et al., 2016)

The prevalence of Crohn's disease is 10.6 per 100,000 in the UK. (Molodecky et al., 2012)

- CD results from an inappropriate gut-focused inflammatory response in a genetically susceptible host.(Gamez-Valero et al., 2015)
- Clinical symptoms include abdominal pain, diarrhoea, rectal blood loss, decreased appetite, weight loss, fever and growth failure in children.(Dignass et al., 2010b) Extra-intestinal manifestations include uveitis and episcleritis, arthropathy, skin rashes such as Erythema Nodosum and recurrent peri-anal fistulae and abscesses.
- Malabsorption of essential micronutrients and vitamins may be observed.
- The TMJ may be involved as part of the disease process or with associated arthropathy.
- The main drugs used in therapy are corticosteroids e.g. prednisolone and hydrocortisone, immunomodulators e.g. azathioprine and methotrexate and biologics, mostly comprising anti-Tissue Necrosis Factor  $\alpha$  monoclonal antibodies. Antibiotics such as Ciprofloxacin and Metronidazole are also frequently prescribed to treat infective complications.
- Corticosteroids and some antibiotics are prescribed to induce a

remission, though biologics such as infliximab, can also be used in this fashion as well as to maintain disease control.(Satsangi et al., 2006)

- Thiopurines, methotrexate and biologics are primarily used as maintenance immunosuppressive therapy and

To relieve the pain of aphthous ulcerations, topical agents such as lidocaine and/or topical steroids such as triamcinolone 0.1% can be used, though appropriate treatment of the underlying IBD is crucial. (Rowland et al., 2010; Lankarani et al., 2013) If orthodontic treatment is being provided it is essential to minimise trauma. Retention regimes may need to be altered if the patient is unable to cope with a vacuum formed retainer, bonded retainers may be a viable alternative.

Oral manifestations include diffuse labial and buccal swellings and cobblestones, mucosal tags, deep linear ulcerations, mucogingivitis, granulomatous cheilitis. Other findings include aphthous ulcerations, pyostomatitis vegetans, dental caries, gingivitis and periodontitis, angular cheilitis, glossitis, gingival hyperplasia, altered taste perception and candidiasis.(Tan et al., 2016; Johannsen et al., 2015)

### **Ulcerative colitis:**

Ulcerative colitis (UC) is characterised by deep mucosal inflammation of the colon.(Langan et al., 2007; Lemberg and Day, 2015) The rectum is always involved but UC may extend proximally in a contiguous pattern up to the entire colon (pancolitis)(Feuerstein and Cheifetz, 2014; Langan et al., 2007) 89

The prevalence of UC in the UK is 243 per 100,000.(Soubières and Poullis, 2017)

- The first line therapy in mild to moderate disease activity is administration of 5-aminosalicylic acid (5-ASA), which can be given orally, locally by suppository or enema or ideally in combination. (Marshall et al., 2010) For patients who do not respond or cannot tolerate 5-ASA, oral and topical steroid therapy can be considered. (Regueiro et al., 2006)



- Corticosteroids are frequently prescribed to induce remission and bridge to maintenance therapy with thiopurines or biologics. (Chapman et al., 1986; Rutgeerts et al., 2005; Dignass et al., 2010a)
- A colectomy may be required in extreme circumstances such as acute severe UC which does not respond to high dose IV steroid and infliximab rescue therapy, (Oresland et al., 2015) leaving an end stoma of ileal bowel protruding from the abdominal wall.
- Extra-intestinal manifestations may include uveitis or episcleritis, arthropathy, Erythema nodosum/Pyoderma gangrenosum and Primary sclerosing cholangitis.

Oral associations with UC include pyostomatitis vegetans, aphthous ulcerations, candidiasis, gingivitis and periodontitis while symptoms include halitosis, acidic taste and taste change, which also may be related to use of medication. (Tan et al., 2017) A study shows UC patients had a significantly higher mean Decayed-Missing-Filled-Teeth (DMFT) index and more frequently periodontitis, deeper pocket depths and fewer teeth in patients with UC compared to controls. (Brito et al., 2008) This should be taken into account when planning for orthodontic treatment. Care also needs to be taken to avoid further trauma from the orthodontic appliance and retainers.

### **Coeliac disease:**

Coeliac disease is a chronic autoimmune-mediated enteropathy of the small bowel, caused by the dietary intake of gluten in genetically predisposed individuals. (Ludvigsson et al., 2013)

The prevalence of coeliac disease in Europe is 1000 per 100,000. (Gujral et al., 2012)

- Coeliac disease creates an epithelial lymphocytosis and subtotal villous atrophy due to a hypersensitivity reaction to the gliadin fragment of gluten. This results in functionally decreased absorptive surface of the duodenum and varying degrees of malabsorption. (van Gils et al., 2017)
- Symptoms may be related to malabsorption, including chronic diarrhoea, weight loss, and abdominal distension.

- Other manifestations include iron deficiency, with or without
- anaemia, reduced bone mineral density, aphthous stomatitis, short stature, elevated aminotransferase levels, dermatitis herpetiformis and chronic fatigue.(van Gils et al., 2017)
- The only recognised and accepted treatment of coeliac disease is a life-long gluten-free diet, i.e., foods that contain wheat, barley, rye, spelt or kamut.(van Gils et al., 2017)

Oral manifestations in coeliac disease include enamel defects, recurrent aphthous stomatitis, delayed tooth eruption, elevated risk of dental caries, microdontia, angular cheilitis, oral lichen planus, atrophic glossitis, burning feeling of the tongue and geographic tongue.(Maloney et al., 2014; Bramanti et al., 2014; Rashid et al., 2011)

## **INFECTIOUS DISEASES**

### **Blood borne viruses:**

The most common blood borne viruses in the UK are Hepatitis C virus (HCV) which has a prevalence of 500-1000 per 100,000(2019b), followed by Hepatitis B virus (HBV) which has a prevalence of 100-500 per 100,000(2019a) and Human immunodeficiency virus (HIV) which has a prevalence of 130 per 100,000(2019c). After occupational exposure to an HIV infected blood percutaneously, the approximate risk of viral transmission of HIV is 300 per 100,000. The approximate risk of viral transmission of HCV is 500 per 100,000 while the risk of HBV transmission following percutaneous exposure to HBsAg/ HBeAg-positive blood is 30,000 per 100,000. (Laheij et al., 2012) The risk of transmission from saliva is minimal in most cases, unless contaminated with blood. All viruses may cause serious and life threatening diseases, especially if diagnosed late or if untreated (Lala et al., 2018), although with modern treatments, patients can lead a relatively normal life and cure rates now approach 95% with the latest Hepatitis C treatments.(Pau and George, 2014)

For the orthodontic practice, preventive measures include universal cross-infection precautions, HBV immunisation for the dental team

including post vaccination blood tests to verify adequate immunisation, implementing a robust sharps protocol and an infection control policy aligned with the Department of Health best practice guidance *Health Technical Memorandum 01-05: Decontamination in primary care dental practice.*(Sultan et al., 2014) Notable drug-drug interactions exist between ante-retroviral therapy and prescribed medications. The website: <https://www.hiv-druginteractions.org/checker> can be used to check upon particular drug.(Sultan et al., 2014)

## Allergies

### Nickel:

Patients can be sensitised by nickel containing body piercings and jewelry. Nickel sensitivity is also higher in asthmatics. It is estimated that 11,000 per 100,000 of all women and 2,000 per 100,000 of all males have a sensitivity to nickel.(Nielsen and Menne, 1993) It is estimated that the occurrence of a harmful intraoral response by orthodontic patients to nickel is 100-200 per 100,000. (Menne, 1994)

Most patients who have a skin nickel sensitivity can wear orthodontic appliances without difficulty. Usually intraoral stainless-steel components are safe to use in nickel sensitive patients due to the molecular structure of the stainless steel which prevents nickel release. It may, on occasion, be necessary to place a sectional appliance with a NiTi archwire initially to monitor the patient's response, however intraoral responses are rare, even in those patients with known skin sensitivity. If there is still doubt after placement of the sectional appliance the patient can be referred to the dermatologist for patch testing and further advice. If a patient is shown to have an intraoral reaction to nickel there are several treatment options, including using stainless steel with a lower nickel content. Other options include nickel free brackets such as ceramic, polycarbonate, titanium or gold. Nickel free archwires include titanium molybdenum alloy (TMA), fiber-reinforced composite,

titanium and gold plated. Plastic aligners may also be considered. If extraoral orthodontic appliances such as headgears containing nickel causes hypersensitivity of the skin(Burden and Eedy, 1991) alternatives could be considered such as covering the metal components or other orthodontic devices such as the use of TADs. The response by the immune system to nickel is usually a Type IV cell-mediated delayed hypersensitivity reaction, known as allergic contact dermatitis. It is mediated by T-cells and monocytes/macrophages rather than antibodies.(Uzzaman and Cho, 2012)

### **Latex:**

Allergy to natural rubber latex (NRL) increased dramatically in the 1980s-90s. The most common type of reaction is contact dermatitis. However, almost half of those who are allergic to NRL demonstrate associated hypersensitivity to certain fruits e.g. kiwi, chestnut, avocado, peach.(Wagner and Breiteneder, 2002).

The prevalence of latex allergy in the general population is approximately 4,300 per 100,000. The prevalence of latex allergy in healthcare workers is 9,700 per 100,000.(Wu et al., 2016)

In terms of the orthodontic management of these patients they should be seen early in the morning in a latex free environment. Latex free materials should be stored away from those containing latex. All material and equipment should be latex free, including: gloves, inter-maxillary elastics, Kesling springs rather than separators, and latex free headgear components and band removers. Brackets should be self-ligating or secured using metal ligatures rather than elastomeric modules. All members of the orthodontic team should be educated recognising and dealing with medical emergencies such as anaphylaxis.

## **CONCLUSION**

A variety of medically compromised patients will present to the orthodontist. It is important that all healthcare professionals continuously update their knowledge and it is worthwhile being aware of medical disorders that may have significant implications for their treatment planning. For consent to be informed and valid, it is also important to ensure the patient is informed of the potential consequences which their medical background may have on their orthodontic management as far as possible. A good medical history and clinical assessment is imperative to assess the significance of any medical background. Liaison with the relevant medical or surgical teams and clear communication can permit a safe and a successful management of the patient.

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Table 1: Types, incidence and potential consequences of CHD

Type of CHD	Nature	Incidence at birth	Consequences
Structural heart disease e.g. Atrial or Ventricular Septal defects	Defects in septal wall leading to intra-cardiac shunts and/or murmurs.	800-1,200/100,000 live births.(Hoffman, 2013)	Few if small or corrected. If significant and untreated may lead to right to left shunt (cyanotic heart disease) which may be fatal. Increased risk of IE with closure prostheses. Increased risk of paradoxical thromboembolism from venous to arterial systems.
Bicuspid Aortic valve	Two rather than three leaflets to the valve	1,000-1,200/100,000 live births.(Hoffman, 2013)	Early valvular degeneration and increased risk of Infective Endocarditis
Patent Ductus Arteriosus	Persistence of the fetal shunt between the aorta and pulmonary artery(Brickner et al., 2000)	50/100,000 live births.(Dice and Bhatia, 2007)	If untreated, may lead to right to left shunt and pulmonary hypertension, which may require heart/lung transplant.
Pulmonary Stenosis	Obstructed flow from right ventricle to the Pulmonary artery.	50/100,000 live births.(Cuypers et al., 2013)	If severe may lead to right ventricular hypertrophy and heart failure.
Tetralogy of Fallot (FitzGerald et al., 2010; Barron, 2013)	A combination of Pulmonary Stenosis, an over-arching aorta, a Ventricular Septal Defect and Right Ventricular Hypertrophy	19-26/100,000 live births.(Bailliard and Anderson, 2009)	Increased risk of sudden cardiac death and heart failure over lifetime. Approximately 21% with Tetralogy have an associated syndrome such as Down's Syndrome, Noonan Syndrome, Branchial Arch Syndrome and Chromosome 22q11 Microdeletion.(Sivertsen et al., 2016)



Table 2: Key medications in the treatment of cardiovascular concerns and special considerations:

<p>Warfarin(Perry et al., 2007; Baglin et al., 2006; SDCEP, 2015) (anticoagulant)</p>	<ul style="list-style-type: none"> <li>• Effects can last 3-5 days.</li> <li>• Reversal agents available for use in acute haemorrhage (Vitamin K and Prothrombin Complex Concentrate/octaplex)</li> <li>• Do not stop warfarin when performing minor dental surgery i.e. extracting teeth, use local measures*. INR check 72 hours prior to surgery is recommended to ensure warfarin is within the therapeutic range (usually INR 3-4 in metallic heart valves, 2-3 in Atrial Fibrillation).</li> <li>• Patients taking warfarin should only be prescribed aspirin, NSAIDs and COX-2 inhibitors with caution, due to their antiplatelet action and increased risk of significant haemorrhage.</li> <li>• Patients with an unstable INR should be discussed with their anticoagulant management team.</li> </ul>
<p>Low Molecular Weight Heparin(SDCEP, 2015) (anticoagulant)</p>	<ul style="list-style-type: none"> <li>• Effects last approximately 24 hours. Similar risk of bleeding to warfarin. Often used for Pulmonary Embolism or Deep Vein Thrombosis treatment in all age-groups. Discuss with the GP/haematologist prior to any invasive therapy as there is limited evidence as to its use or interaction with dental therapies.</li> <li>• Drug activity can be monitored via measurement of Factor Xa levels.</li> </ul>
<p>Direct Oral Anticoagulants (DOACs/NOACs) (SDCEP, 2015)</p>	<ul style="list-style-type: none"> <li>• INR is inaccurate in measuring anticoagulant effects of these drugs. No accurate measurement of anticoagulant effect is currently available.</li> <li>• Only dabigatran has a commercially available reversal agent at the current time.</li> <li>• On the day of dental surgery, patients can miss apixaban or dabigatran and delay rivaroxaban morning dose. (SDCEP, 2015)</li> <li>• Patients should be treated early in the day with the use of local measures. *</li> <li>• Effects can last up to 48 hours.</li> </ul>
<p>Anti-platelet/anti-inflammatory medications e.g. Aspirin, Clopidogrel, NSAIDs (SDCEP, 2015)</p>	<ul style="list-style-type: none"> <li>• Use local measures when performing surgery. *</li> <li>• Aspirin is to be avoided in children due to risk of Reye’s syndrome. (Hall, 1986)</li> </ul>

Table 3: Skeletal system medications and their uses:

<p>Antiresorptive Drugs e.g. Bisphosphonates (e.g. alendronic acid)(SDCEP, 2017)</p>	<ul style="list-style-type: none"> <li>• Used in the management of osteoporosis and a variety of other non-malignant and malignant conditions.</li> <li>• Risk of oesophagitis and ulceration with bisphosphonates.</li> </ul>
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Table 4: Antiepileptics and notable side-effects:

Sodium Valproate (Aragon and Burneo, 2007)	<ul style="list-style-type: none"> <li>Decreased platelet count- direct bone marrow suppression, which can impair wound healing and increase postoperative bleeding and infections.</li> <li>Hepatic enzyme inhibitor</li> </ul>
Carbamazepine (Aragon and Burneo, 2007)	<ul style="list-style-type: none"> <li>Xerostomia, stomatitis, glossitis and oral ulceration.</li> <li>Interacts with clarithromycin.</li> <li>Risk of osteopenia and osteomalacia.</li> <li>Hepatic enzyme inducer</li> </ul>
Phenytoin (Aragon and Burneo, 2007)	<ul style="list-style-type: none"> <li>About 50% of patients will develop gingival hyperplasia within 12–24 months of initiation of treatment.</li> <li>Risk of osteopenia and osteomalacia.</li> <li>Hepatic enzyme inducer</li> </ul>
Levetiracetam (Carreno, 2007)	<ul style="list-style-type: none"> <li>Behavioural changes (hostility and aggression), anxiety, depression.</li> </ul>

Table 5: Key medications in the management of multiple sclerosis and their side-effects:

Monoclonal Antibodies e.g. Natalizumab(Fischer et al., 2009)	<ul style="list-style-type: none"> <li>Notable side-effects include an increased risk of progressive multifocal leukoencephalopathy (viral opportunistic infection), hepatotoxicity, arthralgia, headache, depression, an increased risk of systemic and/or oral opportunistic infection, mucositis and ulcerative stomatitis.</li> </ul>
Steroids e.g. Prednisolone (Gibson and Ferguson, 2004; Fischer et al., 2009)	<ul style="list-style-type: none"> <li>Short term side-effects include acne, psychosis and candida, hypokalaemia, muscle wasting and proximal myopathy, diabetes, pancreatitis, hypertension.</li> <li>Long term side-effects can induce osteoporosis, adrenal insufficiency, risk of glaucoma/cataracts and growth suppression.</li> <li>Less frequently used than in previous years.</li> </ul>

Table 6: Key medications used in the autistic spectrum disorder patient and their side-effects:

Anticonvulsants/ Antiepileptics e.g. Carbamazepine(Friedlander et al., 2006)	<ul style="list-style-type: none"> <li>Long term side-effects can result in decreased white blood cell and platelet counts.</li> <li>Drugs such as Erythromycin, Clarithromycin and Propoxyphene may inhibit the metabolism of carbamazepine and increase the risk of side effects.</li> </ul>
SSRI Antidepressants e.g. Fluoxetine(Friedlander et al., 2006)	<ul style="list-style-type: none"> <li>Side-effects include diarrhoea, nausea, somnolence and dizziness.</li> <li>Occasionally, it causes an increase in bleeding time, increases CNS depression and may inhibit the metabolism of codeine (and therefore its analgesic effect).</li> <li>Some benzodiazepines, erythromycin and clarithromycin may inhibit metabolism of fluoxetine.</li> </ul>

Stimulant Medications e.g. Methylphenidate (Friedlander et al., 2006)	<ul style="list-style-type: none"> <li>• May rarely cause thrombocytopenia, leukopenia and anaemia, anorexia and reduced weight gain in children with long-term use.</li> <li>• Vasoconstrictors should be used with caution.</li> </ul>
SSRI Antidepressants e.g. Sertraline (Friedlander et al., 2006)	<ul style="list-style-type: none"> <li>• Side-effects include diarrhoea, nausea, somnolence and dizziness</li> <li>• Occasionally increased bleeding time, increases CNS depression.</li> <li>• It may inhibit the metabolism of codeine (and, therefore, its analgesic effect).</li> <li>• Erythromycin and clarithromycin may inhibit the metabolism of sertraline.</li> </ul>
Hormone Medications e.g. Melatonin (Andersen et al., 2016)	<ul style="list-style-type: none"> <li>• Side-effects include dizziness, headache, nausea and sleepiness.</li> </ul>

Table 7: Key medications in the management of asthma and their side-effects:

B2 Agonists e.g. Salbutamol (Buchman, 2001; NICE, 2018b; Gibson and Ferguson, 2004)	<ul style="list-style-type: none"> <li>• Oral side-effects include xerostomia, sialorrhea, sialadenitis, stomatitis, gingival enlargement, oedema and discoloration of the tongue.</li> <li>• Temporary hypokalaemia and tachycardia may be associated, especially when given in nebulized forms.</li> </ul>
Leukotriene Receptor Antagonists e.g. Montelukast (Paggiaro and Bacci, 2011)	<ul style="list-style-type: none"> <li>• Side-effects include diarrhoea, fever, gastric discomfort, headache, nausea, upper respiratory tract infection and dry mouth.</li> </ul>
Inhaled corticosteroids e.g. Beclomethasone (Buchman, 2001; NICE, 2018b; Gibson and Ferguson, 2004). Orally-administered systemic steroids e.g. Prednisone (Shefrin and Goldman, 2009; Richards, 2008)	<ul style="list-style-type: none"> <li>• See section on steroids below.</li> </ul>

Table 8: Iron as the treatment for sickle cell anaemia and their oral side-effects:

Iron (Killick et al., 2016)	<ul style="list-style-type: none"> <li>• Side-effects include constipation, diarrhoea, nausea, vomiting, gastric reflux and dark coloured stools/urine.</li> <li>• Oral side-effect includes temporary staining of teeth.</li> </ul>
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	<ul style="list-style-type: none"> <li>• Side effects are frequently proportional to the weight of elemental iron within the preparation.</li> </ul>
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Table 9: Key endocrine medications and their implications:

Levothyroxine(Chandna and Bathla, 2011)	<ul style="list-style-type: none"> <li>• Side-effects are rare with this drug and it can be difficult to differentiate between the clinical evidence of systemic excess or a dearth of the drug.</li> <li>• Levothyroxine is metabolised more swiftly when co-administered with hepatic enzyme inducers such as Phenytoin, Rifampicin and Carbamazepine.</li> <li>• Levothyroxine may increase the effects of Warfarin.</li> </ul>
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Table 10: Common corticosteroids and their side-effects:

Steroids e.g. Prednisolone / Hydrocortisone / Dexamethasone/ Methylprednisolone(Gibson and Ferguson, 2004)	<ul style="list-style-type: none"> <li>• Short term side effects of the medication include acne, psychosis, candida, hypokalaemia, muscle wasting and proximal myopathy, diabetes, pancreatitis and hypertension.</li> <li>• Long term use can induce osteoporosis, adrenal insufficiency, risk of glaucoma/cataracts and growth suppression.</li> </ul>
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Table 11: Key medications in gastroenterology and their side-effects and implications:

Steroids e.g. Prednisolone / Hydrocortisone / Dexamethasone/ Methylprednisolone(Gibson and Ferguson, 2004)	<ul style="list-style-type: none"> <li>• Short term side effects of the medication include acne, psychosis and candida, hypokalaemia, muscle wasting and proximal myopathy, diabetes, pancreatitis and hypertension.</li> <li>• Medium term to long term use – obesity with peripheral muscle wasting due to excess systemic glucocorticoids (Cushing’s Disease). Increased risk of osteoporosis, adrenal insufficiency at times of stress (Addison’s Disease), glaucoma/cataracts, type 2 diabetes and growth suppression in children.</li> </ul>
Immunosuppressants e.g. Methotrexate(Patel and Patel, 2018; Cooper and Brown, 2015)	<ul style="list-style-type: none"> <li>• Side-effects include bone marrow suppression, most notable leucopenia and anaemia, nephrotoxicity, hepatotoxicity, pulmonary fibrosis, nausea and increased risk of infection.</li> <li>• Oral side-effects include MRONJ and oral mucositis.</li> </ul>

<p>Immunomodulators e.g. azathioprine, 6-mercaptopurine</p>	<ul style="list-style-type: none"> <li>• Main side effects are nausea – usually dose dependent.</li> <li>• Bone marrow suppression, notably neutropenia, anaemia and thrombocytopenia are the main reasons for stopping the drug.</li> </ul>
<p>5-Aminosalicylic Acid e.g. Sulfasalazine(NICE, 2018a)</p>	<ul style="list-style-type: none"> <li>• Generally, well tolerated with minimal side effects. Headache, abdominal pain and diarrhea are most common.</li> </ul>
<p>Anti-Tissue Necrosis Factor -<math>\alpha</math> monoclonal antibodies e.g. Infliximab(SDCEP, 2015)</p>	<ul style="list-style-type: none"> <li>• Main risks include increased risk of opportunistic infections and infusion-related reactions such as transient pyrexia.</li> <li>• Patients require monitoring for hypersensitivity reactions and non-melanoma skin cancers.</li> </ul>

Table 12: Nickel in Orthodontics and side-effects and implications:

<p>Metals e.g. Nickel(Shelley, 1981; Lamster et al., 1987; Cohen and Cohen, 1998; Janson et al., 1998)</p>	<ul style="list-style-type: none"> <li>• a burning sensation, gingival hyperplasia, alveolar bone loss, labial desquamation, angular cheilitis, erythema multiforme, oral stomatitis</li> </ul>
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# APPENDIX 1 MEDICAL HISTORY FORM

## MEDICAL HISTORY FORM

We need to ask patients about their general health so that we can treat them safely. Please write the PATIENT'S details below and then answer the health questions about the PATIENT. All information will remain confidential.

Mr. Mrs. Ms. Miss. Mx. Other.....

Surname.....

First Names.....

Gender..... Date of Birth .....

Address .....

.....

.....Postcode.....

Tel. home..... Tel. work.....

Tel. mobile..... E-mail address.....

School/Occupation .....

Doctor's Name & Address.....

.....

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<b>IS THE PATIENT</b> (please tick the appropriate column)	<b>Yes</b>	<b>No</b>	<b>Please give details below</b>
Receiving treatment from a doctor, hospital or clinic?			
Taking steroids (now or in the last 2 years)?			
Taking bisphosphonates (now or at any time in the past)?			
Taking any other medicines or drugs e.g. tablets, creams, injections or inhalers?			
Allergic to any medicines, foods or materials e.g. latex?			
A smoker/vaper (now or at any time in the past), if so how many were smoked per day?			
<b>DOES THE PATIENT</b> (please tick the appropriate column)	<b>Yes</b>	<b>No</b>	<b>Please give details below</b>
Have any heart problems?			
Have any chest problems e.g. asthma, bronchitis, TB?			
Have fits, fainting attacks or blackouts?			
Have diabetes?			
Have a bleeding disorder e.g. haemophilia, Von Willebrand disease, sickle cell anaemia?			
Have kidney disease?			
Have liver disease?			
Carry a medical warning card, bracelet or warning token?			
Drink alcohol, if so how many units are consumed per week?			
<b>HAS THE PATIENT EVER</b> (please tick the appropriate column)	<b>Yes</b>	<b>No</b>	<b>Please give details below</b>
Had rheumatic fever or infective endocarditis?			
Had any mental health issues?			
Had jaundice e.g. hepatitis?			
Had any other serious illnesses?			

Been admitted to hospital for any operations? (if yes, what for and when?)			
Had a bad reaction to a local anaesthetic?			
Bled excessively following an injury, surgery or a tooth extraction (or has anyone in the family)?			
Is there anything else about the patient's health or activities that you think the orthodontist should know about?			
<b>DENTAL QUESTIONS</b> (please tick the appropriate column)	<b>Yes</b>	<b>No</b>	<b>Please give details below</b>
Has the patient worn a brace before?			
If yes, what kind of brace was this?			
If yes, who provided the treatment?			
Has the patient ever injured his/her teeth or face?			
If yes, please describe the dental or facial injury			

**Who completed this Questionnaire?**

Print name .....

Relationship to the patient .....

Signature .....

Date .....

Please make sure that any changes to the patient's medical history are reported to the orthodontist straight away.





**Reviewed and updated by the Clinical Governance Directorate of the British Orthodontic Society, 2021**