



# Dentistry for Patients with Noncommunicable Chronic Diseases

Systemic Arterial Hypertension  
Diabetes Mellitus  
Chronic Kidney Disease

## Organizers

Ana Emilia Figueiredo de Oliveira  
Ana Estela Haddad







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São Luís



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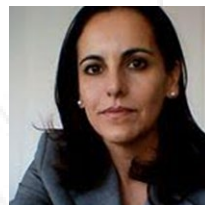


<sup>1</sup> A lecturer [livre-docente] is an academic degree granted by some universities in Brazil to researchers who hold a P.hD degree and have passed through a civil service exam.

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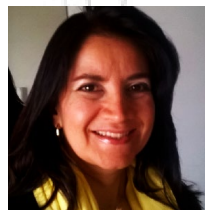
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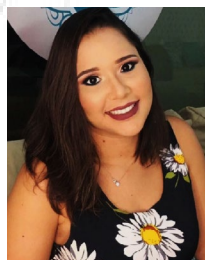
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# PREFACE

Everyday technology gains more space in our daily routine where computers, smartphones, tablets and many others electronic devices present us to information that will surely change the way we relate to each other and to our tasks. Reading habits in digital media still have a timid expression in Brazil, but it is already possible to identify the advantages that most certainly will disclose this environment. The convenience of acquiring digital books, the fact that they do not take up space, are sustainable, easy to transport and facilitate research and hyperlinks are certainly appealing to many people.

This digital book, specially directed to dentistry professionals, gather information on noncommunicable chronic diseases (NCDs), such as chronic kidney disease, diabetes and hypertension, which are becoming more frequent among the Brazilian and world population. Since treatment has proved to be very expensive for the government, preventive actions are crucial in order to avoid an epidemic growth and its drastic consequences on people's quality of life.

Dentists are health professionals with great potential to identify those diseases and to educate their patients on eating habits, smoking consequences and physical exercise. To endorse the oral health care of these patients, dentists must know all consequences caused by systemic alterations possibly interfering with dental care. They must also predict the possible effects of dental care considering the patient's systemic condition.

By knowing the dental patient's underlying disease and performing the appropriate oral treatment, dentists go even further: not only they endorse oral health care but they also strongly contribute to the well-being and general balance of people with NCDs, improving their quality of life.

This e-book gathers the main aspects of chronical kidney disease, diabetes and hypertension by pointing out the impact of those diseases to the patient's oral health and dental care. By considering those aspects, these health professionals are better equipped to face the challenge of treating dental patients who need special attention due to NCDs.

**Ph. D Prof. Marina Gallottini**

Full professor of the Oral Pathology discipline at FOU SP.

# 1 INTRODUCTION

Since the 1960's many countries are going through a process of epidemiological, demographic and nutritional transition. Such alterations in the population's profile caused changes to the pattern of illness among people by decreasing the frequency of infectious diseases and increasing the prevalence of noncommunicable chronic diseases (NCDs).

NCDs are long term multifactorial diseases developed through the course of life. They are responsible for approximately 70% of death worldwide. Among the NCDs are the cerebrovascular accident, myocardial infarction, hypertension, diabetes, cancer, respiratory diseases and chronic kidney disease<sup>1</sup>.

Such diseases have in common their modifiable risk factors: smoking, unhealthy diet, physical inactivity and harmful consumption of alcohol. In 2011, the United Nations - UN<sup>2</sup> acknowledged that oral diseases along with eye and kidney diseases are public health issues and defined that coping and prevention actions set with NCDs may bring benefits since they present the same risk factors<sup>3,4</sup>.

Considering the increase of prevalence in chronic diseases, their complexity and relation to oral conditions, it is crucial that the dental surgeons treating patients in these conditions seek knowledge concerning the subject so that they are capable of assisting the patient's needs with responsibility while assessing the systemic conditions identified in each case so to personalize the service and offer full care.

As health professionals, dentists have an important role in identifying those chronic conditions and are responsible for the task of instructing their patients on the importance of good eating habits, giving up smoking and the practice of physical exercises for a healthier life. Thus, knowledge sharing, while aiming to improve the quality of dental care to patients and consequently their life quality, becomes fundamental.

This book will address dental care for patients with three prevalent chronic diseases: systemic arterial hypertension, diabetes

mellitus and chronic kidney disease. Themes related to dental care for chronic disease patients will also be discussed here, approaching aspects such as epidemiological disease, diagnosis, treatment and dental care.

**Ph. D Prof. Ana Lidia Ciamponi**

Associate professor of the pediatric dentistry discipline at FOUSP.

## 2 SYSTEMIC ARTERIAL HYPERTENSION

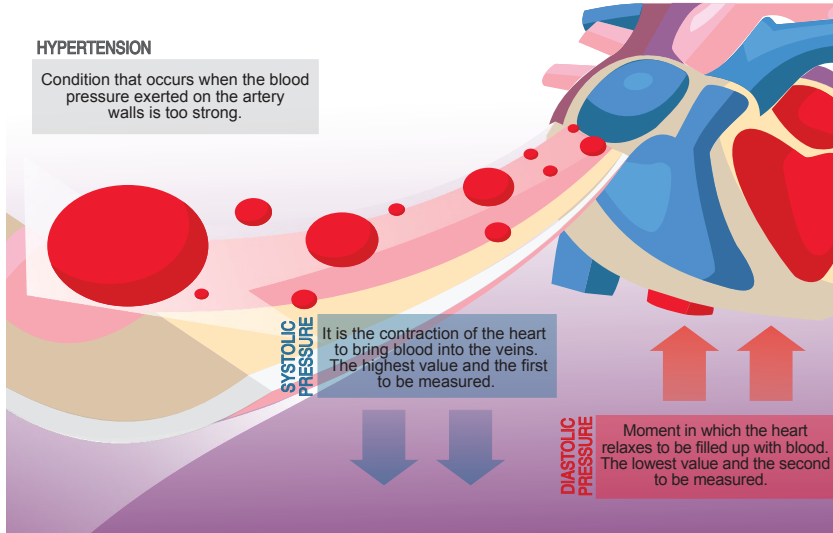
Systemic arterial hypertension is a high prevalence disease that represents an important risk factor for cardiovascular complications, cerebrovascular accident and coronary, kidney and peripheral vascular diseases. Systemic arterial hypertension is also associated with other chronic diseases and conditions, such as chronic kidney disease and diabetes. Such evidences suggest even greater consequences to this illness due to the worsening of the patient's health conditions which contributes to the loss of life quality, early lethality, and high costs with health system and social life. In this chapter we will discuss clinical aspects related to the dental care of the individual with systemic arterial hypertension<sup>5</sup>.

### 2.1 Definition

According to the American Heart Association<sup>6</sup>, arterial pressure is the pressure made by the blood to the artery walls during circulation, being measured in millimeters of mercury (mm Hg).

The maintenance of blood circulation and blood pressure (BP) is made by the heart through the movements of systole and diastole. Alterations in the pressure exerted during these two movements is what can lead to hypertension. In Figure 1 we can take a better look at these definitions:

Figure 1 – Movement of blood flow.



Source: Adapted from: Sociedade Brasileira de Hipertensão<sup>7</sup>.

Systemic arterial hypertension, or just arterial hypertension (AH), is a multifactorial clinical condition characterized by elevated and sustained BP levels. It is a world public health problem often associated with functional and/or structural changes in target organs (heart, brain, kidneys and blood vessels). Metabolic changes have been considered as the main risk factor for cardiovascular diseases. In a meta-analysis report involving 61 studies with more than one million hypertensive participants it was observed that the reduction of both systolic and diastolic pressures reduced cardiovascular complications<sup>8</sup>.

## 2.2 Epidemiological aspects

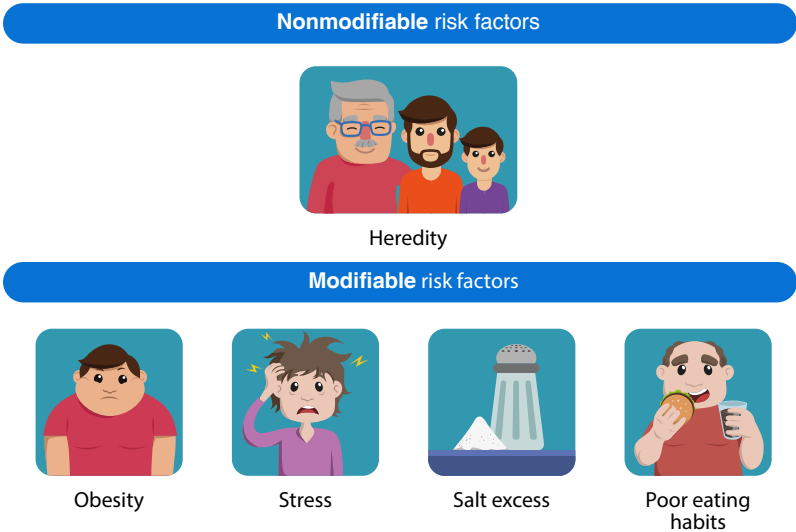
The number of adults with hypertension in the world has doubled over the past 40 years, going from 594 million in 1975 to 1.13 billion in 2015. This increase was noted mainly in countries of low and middle income<sup>9</sup>.

Arterial hypertension is more prevalent in the male population up to the age of 50 years. The global prevalence in 2015 was standardized

by the age of 24.1% in men and 20.1% in women<sup>9</sup>. After this age range the numbers begin to reverse, revealing a higher prevalence in women. However, the numbers increase with advancing age in both sexes<sup>10</sup>.

Among the most well-known risk factors for AH are age, gender and ethnicity, salt intake, alcohol intake, sedentary lifestyle, socioeconomic factors, among others.

Figure 2- Nonmodifiable and modifiable risk factors for systemic arterial hypertension.



Source: Adapted from: SBC. SBH. SBN<sup>11</sup>.

### 2.3 Diagnosis and treatment

AH is diagnosed by the detection of elevated and sustained BP levels in at least two measurements, on two different occasions<sup>10</sup>. Blood pressure measurement can be done by doctors and health professionals such as dentists<sup>12</sup>.

The values that define and classify BP levels are arbitrary, but necessary to guide the diagnosis, treatment and especially the prevention of systemic arterial hypertension. According to the American Heart Association and American College of Cardiology guidelines<sup>10,13</sup>, it is accepted as normal, for adult individuals (older than 18 years old),



numbers below 120 mmHg for systolic blood pressure (SBP), and below 80 mmHg for diastolic blood pressure (DBP). Values greater than 120 mmHg for SBP with DBP <80 mmHg already characterize a status of high BP. Chart 1 summarizes the BP classification for individuals over 18 years old according to these guidelines.

Chart 1- Classification of BP in adults (> 18 years).

BP Category	SBP		DBP
Normal	<120 mm Hg	and	<80 mm Hg
Elevated	120-129 mm Hg	and	<80 mm Hg
<b>Hypertension</b>			
Stage 1	130-139 mm Hg	or	80-89 mm Hg
Stage 2	≥140 mm Hg	or	≥90 mm Hg

\*Individuals with SBP and DBP in 2 categories should be designated to the higher BP category.

BP indicates blood pressure (based on an average of ≥2 careful readings obtained on ≥2 occasions, as detailed in Section 4); DBP, diastolic blood pressure; and SBP systolic blood pressure.

Source: Whelton PK, Carey RM, Aronow WS, Casey DE Jr, Collins KJ, Dennison Himmelfarb C, DePalma SM, Gidding S, Jamerson KA, Jones DW, MacLaughlin EJ, Muntner P, Ovbigele B, Smith SC Jr, Spencer CC, Stafford RS, Taler SJ, Thomas RJ, Williams KA Sr, Williamson JD, Wright JT Jr<sup>10</sup>.

The change in the AH classification performed by the American Heart Association and American College of Cardiology in 2017 was based on the observation of randomized controlled trials and meta-analyses that showed an association between hypertension and cardiovascular diseases (CVDs). At the time, it was observed that BP values lower than 120/80 mmHg were associated with a lower occurrence of coronary diseases and myocardial infarction when compared to higher BP values. Thus, the classification with the desired values of lower BP seeks a more efficient prevention of CVDs<sup>10</sup>.

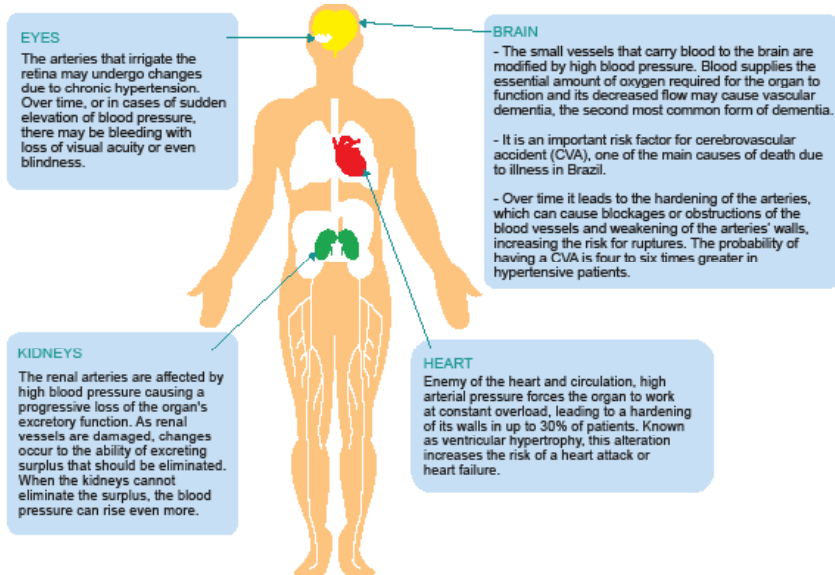
Proper and priority handling of arterial hypertension requires jointed actions in three axes: the surveillance of hypertension,

comorbidities and their determinants; integrality of care; and health promotion. Behavioral strategies focused on lifestyle change should be the focus of actions for social mobilization. Encouragement of healthy habits and self-care whether through educational actions or government investments that favor access to a healthier diet and physical activities are fundamental for controlling AH<sup>10, 14</sup>.

Many people with hypertension present other risk factors for obesity, diabetes mellitus, chronic kidney disease (CKD) and other noncommunicable chronic diseases. Considering this, the screening and management of modifiable risk factors for all adults diagnosed with hypertension should be performed to prevent the individual from suffering from other chronic diseases<sup>10</sup>.

AH can cause damage to other organs, which is why they are called target organs. Take a look at Figure 3:

Figure 3- Target organs of blood pressure increase.



Source: Adapted from: Cruz<sup>15</sup>.

Medication strategies for controlling arterial pressure should be considered according to individual factors, taking into account the person's degree of motivation for lifestyle changes, in addition to BP levels and cardiovascular risk. Antihypertensive drugs are usually well tolerated, presenting few adverse effects during treatment. However, a frequent complaint among the medication users is dizziness, attributed to the excess of the hypotensive effect<sup>16</sup>. The abrupt drop in BP and the orthostatic hypotension that can affect individuals who use antihypertensives (especially those with a vasodilatory effect) may also lead to syncope<sup>17</sup>.

## 2.4 Oral manifestations

Systemic arterial hypertension by itself does not cause direct oral manifestations, however secondary manifestations may appear due to the use of drugs for blood pressure control. The use of antihypertensive drugs, especially diuretics, can cause oral dryness. Other possible oral changes are summarized below in chart 2.

Chart 2- Main oral manifestations associated with the use of medications by hypertensive patients.

Medication group	Oral changes
Diuretics	Dry mouth, lichenoid reactions
Beta blockers	Taste changes, lichenoid reactions
$\alpha$ and $\beta$ associated blockers	Taste changes
Angiotensin-converting enzyme (ACE) inhibitors	Angioedema of lips, face, and tongue, taste changes
Angiotensin receptor blockers (ARBs)	Angioedema of lips, face and tongue
Calcium channel blockers	Gingival enlargement
$\alpha$ -blockers	Dry mouth, taste changes
central $\alpha$ -agonists and other drugs of central action	Dry mouth, taste changes
Direct vasodilators	Oral and cutaneous lesions similar to lupus <sup>18</sup>

## 2.5 Dental treatment guidelines

The main concern of a dentist who is treating hypertensive patients involves the maintenance of their hemodynamics. Regarding this aspect, the risk for fast and symptomatic increase of arterial pressure must be minimized, considering a potential risk of target organ deterioration or, in rare and extreme cases, with immediate risk of life. The sudden drop in AH and orthostatic hypotension should also be minimizing, being a condition that can occur accompanied by syncope, affecting those individuals who use antihypertensive drugs, especially those with a vasodilatory effect<sup>19</sup>.

It is recommended that the dental surgeon who will assist the patient diagnosed with AH know the patient's previous and current medical history, medicines that he/she are/were on and its adherence to the proposed medical treatment. Therefore, anamnesis should include questions about the date of the hypertension diagnosis, form of treatment, identification of antihypertensive drugs, patient's adherence to the medical therapeutic diet, presence of symptoms associated with hypertension, ascertainment of repercussions on the target organs affected by hypertension and the level of stability and control of the disease<sup>18</sup>.

Considering the high prevalence of hypertension, it is recommended that the dentistry professionals measure all new patients' blood pressure at their first consultation, even those without an AH diagnosis. Hence, if any BP alteration is identified, the dental surgeon must refer the patient to a general practitioner or cardiologist for the establishment of appropriate treatment in case of confirmed AH diagnosis.

When outpatient dental care is required for individuals with hypertension, the ideal is that the treatment does not interfere with the patient's hemodynamics. Alterations in the blood pressure, heart rate and demand for myocardial oxygen, for example, should be avoided. These alterations may be triggered by emotional stress, usually present in situations involving dental care. For that reason, the dentist should minimize this stress by scheduling the patient's

appointment to a moment of greater comfort for them, conducting short consultations, properly controlling intraoperative pain and, if needed, prescribing an anxiolytic drug before treatment.

There are no exact guidelines regarding the pressure limits that restrict or allow outpatient dental care. However, BP rate above 180x120 mmHg is considered as a medical emergency, prevailing over dental urgency. The need of dental care in patients with uncontrolled AH should be analyzed individually at the time of the consultation, considering the procedure to be performed, the patient's stress and his/her clinical condition.

We should not forget that pain contributes to the elevation of arterial pressure, hence the answer to why it must be treated with surgical procedures or drug prescription.

When treating a patient with systemic arterial hypertension, the use of local anesthetics is a common concern among dental surgeons. Many studies have shown no alteration in the hemodynamic conditions of patients receiving local anesthetic with vasoconstrictor, which leads to the indication of its use, considering that the control of pain and emotional stress are very important to the patient's condition since they increase the release of endogenous catecholamines<sup>20, 21, 22</sup>. To reduce the emotional stress of hypertensive patients, the inhaled sedation with nitrous oxide/oxygen may be a useful option<sup>14</sup>.

The use of two 2% lidocaine tubes with 1: 100,000 epinephrine is well tolerated by hypertensive individuals considering that this vasoconstrictor's use has more benefits than risks. However, the use of an aspirating syringe should be done with caution in order to prevent injection into the vessel, as well as not to perform intraligamentary anesthesia. Studies have shown that the use of felypressin (0.03 IU/ml) as a vasoconstrictor is also safe since it is non-adrenergic, does not increase BP, heart rate or respiratory rate. The dose of the anesthetic is conditioned to the vasoconstrictor's type and concentration and there is no consensus on the use of anesthetics with vasoconstrictors.

The maximum dose of felypressin recommended for hypertensive patients should not exceed 0.27 IU, which corresponds to five tubes

of 1.8 ml, while 1: 100,000 or 1: 200,000 epinephrine may also be used in small doses; the ideal is not to exceed the limit of two tubes per session when treating a controlled hypertensive person<sup>14</sup>.

Although there are no records in academic literature concerning hypertensive complications in the dental office (level C of evidence), a possible complication is the hypertensive crisis, a generic term that describes a fast and symptomatic elevation of BP normally accompanied by high levels of diastolic blood pressure (DBP) that exceeds 120 mmHg, with potential risk for deterioration of target organ or immediate life risk.

Another practice that inspires caution is the prescription of non-steroidal anti-inflammatory drugs (NSAIDs), which may affect the action mechanism of antihypertensive drugs such as  $\beta$ -blockers, ACE inhibitors and diuretics and, therefore, should be preferably prescribed for shorter periods no longer than four days<sup>8,14</sup>.

Other possible complications include syncope, abrupt drop in BP and orthostatic hypotension, more frequent in those individuals taking antihypertensives, especially those with a vasodilatory effect.

AH is often accompanied by functional and/or structural alterations in what are known as target organs (heart, encephalon, kidneys and blood vessels) and metabolic alterations, with a consequent increase in the risk of fatal and non-fatal cardiovascular events. Acute myocardial infarction ("heart attack") and cerebrovascular accident ("stroke") are the two acute manifestations capable of occurring to hypertensive patients in any stage of their lives, regardless of dental treatment.

Short service sessions should be scheduled preferably in the second part of the morning. Blood pressure should be monitored before, during and after the entire intervention, depending on the patient's stage of hypertension<sup>23</sup>.

Clinical practices empirically adopt BP values lower than 180/120 mmHg as limit values for the performance of a dental procedure, although academic literature still does not clearly establish which BP value is safe for performing an elective or urgency procedure.

The dentist must also instruct the patient on the AH's risk

factors, such as obesity, sedentary lifestyle, diet, smoking habits and alcohol consumption, emphasizing that a change in these behaviors are crucial for a better quality of life and prevention of other NCDs<sup>14</sup>.

### 3 DIABETES MELLITUS

Diabetes mellitus is considered one of the greatest health challenges of the world in the 21st century. It is estimated that by 2040 the disease reaches 640 million adults worldwide with a 60% rate of increase in Central and South America<sup>24</sup>. Factors such as the aging of the population, dietary changes, smoking habits, obesity, sedentary lifestyle, among others, contribute to the enhance of type 2 diabetes prevalence<sup>25</sup>. In this chapter we will discuss the clinical aspects of diabetes mellitus and its possible implications during dental care.

#### 3.1 Definition and classification

According to the *American Diabetes Association*, diabetes mellitus (DM) is a heterogeneous group formed by metabolic disorders that have in common the following health conditions: hyperglycemia, as a result of defects in insulin action, insulin secretion or both<sup>26</sup>.

Diabetes is classified as diabetes mellitus type 1 and type 2, gestational diabetes and other specific types of diabetes<sup>27</sup>:

##### Type 1 DM:

Accountable for 5% to 10% of the diabetes cases. It is characterized by an absolute deficiency in insulin production. It is caused predominantly by the autoimmune destruction of the pancreas beta cells, but it can also be caused by cystic fibrosis, loss of pancreatic tissue, or surgical removal of the pancreas.

##### Type 2 DM:

It is the most common form of diabetes, accounting for 90% to 95% of the cases, being characterized by the decrease in tissue response to normal levels of circulating insulin or by insufficient insulin production. It is associated with obesity and sedentary lifestyle.



### Gestational DM:

It is defined as any degree of reduction in glucose tolerance, which begins or is commonly detected during pregnancy. In Brazil, it affects about 7% of all pregnant women and implies an increased risk of diabetes development for the mother (after birth) and for the baby.

### Other specific types of DM:

This category embraces the less common forms of DM, such as drug-induced DM, DM associated with genetic syndromes, DM associated with endocrinopathies or DM associated with pancreatic exocrine dysfunction.

Besides this classification there are also two specific situations known as "pre-diabetes", considered to be an increased risk for the development of DM: **impaired fasting glucose** and **impaired glucose tolerance**. Impaired fasting glucose is related to the fasting glucose concentrations that are lower than the diagnostic criterion for DM, but still higher than the normal reference value. Decreased glucose tolerance represents an abnormality in the regulation of glucose in post-overload, diagnosed by the oral glucose tolerance test (OGTT)<sup>27</sup>.

## 3.2 Epidemiological aspects

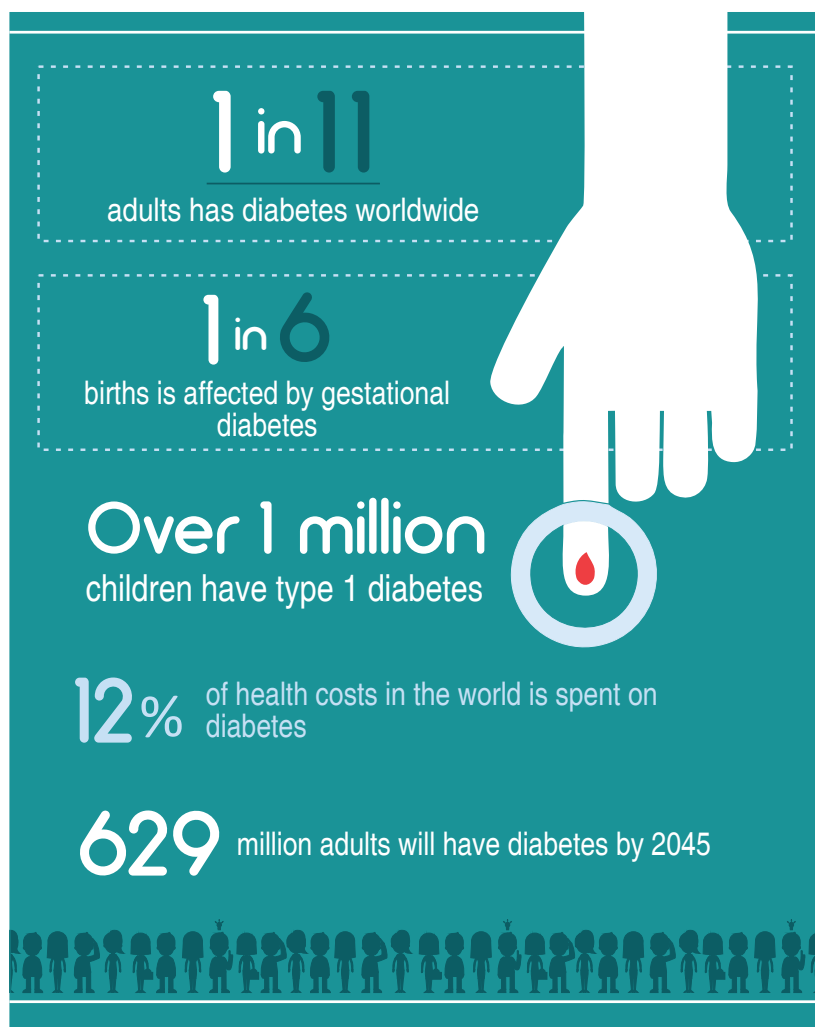
Diabetes is a public health issue that carries a significant morbidity rate due to acute and chronic complications accompanied by a high percentage of hospitalizations and mortality. The number of cases and their prevalence have increased over the last decades. Among the factors related to this increase are the aging of the population, urbanization, sedentary lifestyle, obesity and the increased longevity of people with DM<sup>28</sup>.

In 2016, the World Health Organization (WHO) estimated that the number of people with diabetes in the world has grown from 108 million in 1980 to 422 million in 2014. The global prevalence among adults jumped from 4.7% in 1980 to 8.5% in 2014<sup>25</sup>.

Type 1 diabetes mellitus is responsible for 90% of the diabetes cases among children; although the diagnosis before the age of 15 years occurs in only 50% of the cases<sup>27</sup>.

Figure 4 shows some data regarding the epidemiology of diabetes in the world:

Figure 4- Data on the epidemiology of diabetes in the world.



Source: International Diabetes Federation<sup>29</sup>.

The disease affects the quality of life and produces economic and social impact for individuals, society and countries. Aiming to face these challenges, the World Health Organization has been recommending that countries implement integrated health care systems that effectively address the population's health needs<sup>30</sup>.

### 3.3 Diagnosis and treatment

The diagnosis for DM can be established by fasting glucose (8 hours), random blood glucose, oral glucose tolerance, and glycated hemoglobin, which cutoff values - determined in the last consensus of the American Diabetes Association- are described in Chart 3<sup>27</sup>.

Chart 3- Criteria for DM diagnosis.

TEST	Pre-diabetes	Diabetes
Fasting glucose	100-125 mg/dl	≥ 126 mg/dl
Random glucose	--	≥ 200 mg/dl + classic symptoms
Oral glucose tolerance	140-199 mg/dl	≥ 200 mg/dl
Glycated hemoglobin	5.7%-6.4%	≥ 6.5%

Treatment for diabetes is based on the control of blood glucose levels in order to prevent acute and chronic complications. According to the Brazilian Society of Diabetes [*Sociedade Brasileira de Diabetes - SBD*], changes in lifestyle and eating habits, practice of physical activity, restructure of eating habits and use of medications and/or insulin, when necessary, are the main resource for the treatment of an individual with diabetes.

Drug therapy varies according to the type of diabetes and clinical aspects.

The treatment for **type 1 diabetes** is carried out with exogenous

insulin since the pancreas does not produce this hormone. There are several types of insulin on the market today with different times of action. Treatment, either with multiple doses or with a continuous insulin infusion system, requires intensive monitoring of the patient through tests of capillary blood glucose throughout the day<sup>27</sup>.

Metabolic control of **type 2 diabetes** includes, besides the strategies for lifestyle change and diet reorganization, the use of oral hypoglycemic agents and even exogenous insulin for cases in which the pancreas loses the capacity of hormone secretion. Among the modifiable habits that may contribute to the control of type 2 diabetes are: proper eating, optimal body weight maintenance and exercising<sup>27</sup>.

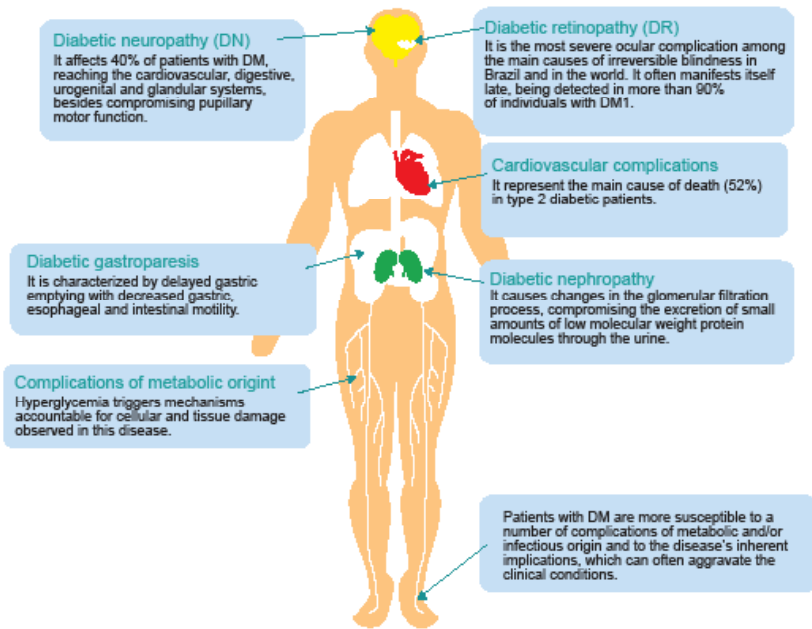
### 3.4 Acute and chronic complications

Type 2 diabetes mellitus (DM2) is asymptomatic in most people, which explains why 50% of individuals with diabetes have no idea they have the disease, that often remains undiagnosed until it develops complications. Sometimes, symptoms similar to type 1 diabetes can be observed, but with less intensity. The most common symptoms are: polyuria, polyphagia, weight loss, fatigue and vision alterations<sup>25</sup>.

Type 2 DM is asymptomatic at its beginning. If there is no adequate follow-up, high blood glucose rates can favor chronic complications such as microangiopathy, which aggravations include retinopathy, nephropathy, and neuropathy; and macroangiopathy, which includes cardiovascular diseases such as myocardial infarction, peripheral vascular disease and poor blood circulation in the legs (WEINERT et al., 2011). These changes occur depending on the duration of diabetes, its metabolic control, hypertension's presence and control and genetic susceptibility<sup>31</sup>.

See below, in Figure 5, some examples of chronic complications related to diabetes and the organs affected by it:

Figure 5- Chronic complications related to diabetes and the organs affected by it.



Source: Pessoa<sup>32</sup>.

Regarding the cases of type 1 DM, the first clinical manifestations are evident and acute, appearing in less than one week after the disease onset, accompanied by ketoacidosis<sup>31, 33</sup>. The complications previously mentioned for type 2 diabetes can also establish themselves in type 1 DM cases, depending on the control of the disease over the years.

Acute complications can occur in all types of diabetes, resulting from hypoglycemia and hyperglycemia. Hypoglycemia is characterized by blood glucose levels below 70 mg/dL or 60 mg/dL. It may be asymptomatic or manifest symptoms that include (Figure 6):

Figure 6 – Symptoms of diabetes mellitus.



Source: adapted from: Selwitz, Pihlstrom<sup>31</sup>.

Untreated hypoglycemia can progress to syncope, seizure, coma and death<sup>31</sup>. The acute complications related to hyperglycemia are: diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS). The most usual precipitating factors of DKA and HHS are infections, especially the upper respiratory tract infections and pneumonia and urinary tract infections. DKA and HHS treatments are similar and should be conducted in an intensive care unit<sup>31</sup>.

### 3.5 Oral manifestations

There are no specific oral manifestations of diabetes, but some alterations seem to be related to its presence and to the quality of glycemic control.

Some studies have shown a higher prevalence and severity of periodontal disease (PD) in individuals with diabetes when compared to others without the disease. Some data suggest that the severity of PD is related to the degree of metabolic control, the duration of diabetes and the presence of comorbidities<sup>26, 28</sup>. Periodontitis has a significant impact on the control of diabetes and patients with periodontitis present more complications related to DM<sup>34</sup>.

Xerostomia and decreased salivary flow may occur due to glycemic decompensation and arise from dehydration or be associated with the use of salivary flow-reducing medications, such as hypotensives, which are often taken by people with diabetes. Dry mouth causes discomfort and increases susceptibility to opportunistic fungal infections, especially candidiasis. Treatment for candidiasis will vary according to the extent and severity of the infection in topical or systemic treatment<sup>35</sup>.

Topical antifungal medications	Systemic antifungal medicines
<ul style="list-style-type: none"><li>- Nystatin</li><li>- Miconazole (gel)</li></ul>	<ul style="list-style-type: none"><li>- Fluconazole 100 mg/day</li><li>- Ketoconazole 200 mg/day</li><li>- Itraconazole 200 mg/day</li></ul>

Measures like the use of salivary stimulants, artificial salivary replacements, fluoridated mouthwashes and good oral hygiene habits can help patients with diabetes and reduction of salivary flow. Burning mouth syndrome, defined as pain or intense burning sensation in the oral mucosa, with no identified etiology, may be secondary to diabetes, hormonal alterations, nutritional deficiencies, among other conditions<sup>27</sup>.

### 3.6 Dental treatment guidelines

Anamnesis of the dental patient with diabetes must be detailed and evaluate their general conditions. Primary attention should be given to the recent levels of fasting glucose and glycated hemoglobin, type and dosage of antidiabetogenic drugs and comorbidities present<sup>36, 37, 38</sup>.

Before the dental consultation begins, even though the procedures

to be performed are non-invasive, it is prudent to check the capillary blood glucose, always considering the patient's information about the time and dose of medicine ingested and the time of the last food intake<sup>36, 37, 38</sup>.

Blood pressure must be read in patients with diabetes. Whether it is for the screening of systemic arterial hypertension or for its control, if the patient is already diagnosed with AH. The frequency of blood readings at dental consultations varies with the classification of hypertension. Therefore, it is recommended that patients with systolic blood pressure between 160 and 179 and diastolic blood pressure between 100 and 109 have their BP checked in all dental appointments<sup>36, 37, 38</sup>.

The dental surgeon must not perform procedures on hypoglycemic patients, who generally have capillary glucose levels below **70 mg/dl**, in order to prevent acute hypoglycemic crisis. In these cases, the patient should eat first and then start the treatment<sup>36, 37, 38</sup>.

There are no defined hyperglycemic values that restrict outpatient dental care. When glycemia levels are above 250 mg/dl and there are signs and symptoms such as nausea, lethargy, abdominal pain, dyspnea, vision disturbances, drowsiness, irritability, tachycardia, orthostatic hypotension, dehydration, hypothermia, Kussmaul breathing, and breath acetone, the consultation should be postponed and the patient referred for prompt care, since he/she is likely to have ketoacidosis. However, if the patient is clinically well, although presenting values above 250 mg/dl, dental interventions, especially the ones set to minimizing pain and infection, can be performed<sup>36,37,38</sup>.

#### IMPORTANT!

“Individuals with diabetes mellitus should be questioned about previous episodes of symptomatic or asymptomatic hypoglycemia at each consultation. If the patient presents a drop in glucose levels (<70 mg/dL) during dental consultations, the dental surgeon must immediately discontinue treatment and indicate the intake of food rich in carbohydrate, such as juices/soft drinks (120 ml) or skim milk (240 ml).



Pure glucose (15g – 20g) is the ideal treatment at those conditions, but any form of carbohydrate that contains glucose will increase glycemic levels. After the intake, read the glucose levels again in 15 minutes. If the hypoglycemia persists, the treatment with glucose should be repeated. Once the glycemic levels return to normal, the patient should have a meal or snack to avoid another episode of such crisis<sup>39</sup>.

Monitoring of blood pressure in patients with systemic arterial hypertension at the time of consultation allows the dentist to better understand the risk of cardiovascular complications such as angina, acute myocardial infarction and cerebrovascular accident, resulting from a possible increase in BP during operative dental procedures<sup>40,41,42</sup>.

The use of anesthetic with vasoconstrictors for patients with DM is recommended. Anesthesia is indicated with epinephrine 1:100,000 obeying the maximum recommended doses. Felypressin is a vasoconstrictor that can also be safely used in patients with DM, since it does not alter glycemia, heart rate or blood pressure<sup>40,41,42</sup>.

Chronic renal failure is a comorbidity that affects approximately 30% to 40% of patients with DM. When dealing with those patients, we should avoid the long-term prescription of non-steroidal anti-inflammatory drugs, which are drugs metabolized in the kidneys<sup>38</sup>.

There is no scientific evidence to support the use of the prophylactic antibiotic before invasive dental procedures simply because the patient has diabetes. Moreover, some recent studies have shown that although patients with DM may present some delay in alveolar epithelialization, the frequency of infection or postoperative complication in patients submitted to simple exodontia is not higher in people with diabetes than in those without diabetes<sup>40, 41,42</sup>.

These studies encourage the presumption that patients with diabetes do not need to be treated with antibiotic prophylaxis before simple exodontia exclusively due to the fact of having diabetes. Studies have shown that even patients who have poor glycemic control, but

are clinically well, and whose hemogram shows no change, especially in the white series, do not exhibit rates of post-exodontic complications higher than expected for the normoreactive population<sup>40,41,42</sup>. In case of post-exodontic infectious complication, such as alveolitis, then this complication can be conventionally treated with local curettage and antibiotic therapy.

It is important to emphasize that patients should be fully evaluated avoiding care fragmentation. Regarding this scenario, oral health preventive and curative actions have a fundamental importance for the care of patients with DM. Oral health actions should be fully integrated among dentists and other professionals responsible for health assistance, allowing the maintenance of the patients' health and better quality of life<sup>43</sup>.

## 4 CHRONIC KIDNEY DISEASE

Chronic kidney disease (CKD) is characterized by a progressive and irreversible decline in renal clearance, which compromises the maintenance of the organism internal homeostasis. Some of the causes of the disease in adults are: systemic arterial hypertension, diabetes mellitus, glomerulopathies, polycystic kidney disease, among others. CKD is a disease with high morbidity, mortality and disability which makes primary prevention strategies key to reducing its incidence. Considering this context, we will discuss in this chapter some epidemiological and clinical aspects, relating them to oral health care for individuals with CKD.

### 4.1 Definition

Kidney failure or renal disease is the loss of renal function due to vascular disorders of the glomeruli, tubules, renal interstitium or lower urinary tract, which may be acute or chronic (LUKE, 2001). Chronic kidney disease (CKD) is defined, according to the National Kidney Foundation, as renal damage or reduced renal function with a duration of over three months, regardless of the cause<sup>44</sup>.

Although there has been substantial improvement in dialysis therapies over the recent years, CKD is associated with a significant impact on life quality and high morbidity and mortality. In general, patients who undergo kidney transplantation have a higher survival rate over the years. However, the indication of the best treatment strategy should be personalized for each case.

### 4.2 Epidemiological aspects

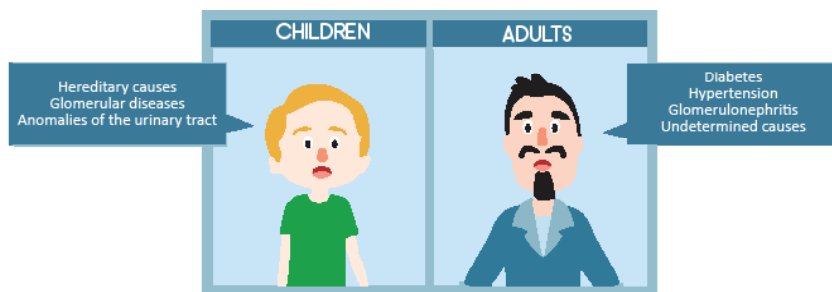
The prevalence of CKD ranges from 11% to 13% considering the different stages of the disease<sup>45</sup>. However, the number of individuals with CKD is estimated to be greater than the currently available data, given the difficulty of diagnosis on initial stages which compromises

epidemiological measurement. Most epidemiological studies are developed from data collected at dialysis centers that treat patients in advanced stages whenever renal replacement therapy (RRT) is required<sup>46, 47</sup>.

In several countries, the available data show an increase in the prevalence of chronic end-stage renal disease (CKD) in both adults and children, although the causes for such increase are different<sup>48</sup>. The higher prevalence in adults occurs mainly due to the aging of the population and the greater number of individuals affected by hypertension and diabetes mellitus, that are the main causes of CKD in adults<sup>47,49</sup>.

Figure 7 presents the main causes of CKD in children and adults.

Figure 7- Causes of CKD in children and adults.



Source: KDIGO <sup>50</sup>. Harambat J, van Stralen KJ, Kim JJ, Tizard EJ <sup>51</sup>.

Causes of CKD in adults include hypertension, diabetes mellitus, glomerulonephritis and indeterminate causes. In children, the causes usually involve genetically inherited conditions, glomerular diseases, and malformations of the urinary tract<sup>51</sup>.

Though the number of affected people under 20 years old is significantly lower when compared to the number of adults, CKD is devastating in children and adolescents<sup>51</sup>. Unlike adults, who have complete physical, intellectual and psychological maturity, children who are affected by CKD are particularly vulnerable to the adverse effects of the disease. They often present growth impairment as well as problems in their physical, sexual and mental development<sup>51</sup>.

### 4.3 Diagnosis and treatment

CKD's early stages are commonly asymptomatic, which hinders its early detection. The patient often discovers the disease in advanced stages, when one or more complications have already developed. To determine the cause, it is essential to evaluate the previous and family medical history, environmental and social factors, medications, and physical, laboratory, imaging and histopathological examinations.

As of 2013, the guideline for Kidney Disease: Improving Global Outcomes (KDIGO) included proteinuria or albuminuria, which are markers of renal damage, to the staging system, given the importance of these factors in disease outcomes and treatment choice<sup>50</sup>.

See below a brief summary of the CKD pathophysiology.

Figure 8- Pathophysiology of CKD progression- simplified model.









Source: Adapted from: Remuzzi G, Pisoni R, Schieppati A<sup>52</sup>.

CKD is classified into five progressive stages according to the intensity of renal function loss (Figure 9). The damage in stages 1 and 2 are reversible, however, from stage 3, the damage is permanent

and will be progressive until stage 5, which will be fatal if there is no possibility of dialysis or transplantation<sup>44</sup>.

The level of renal function reduction is determined by the glomerular filtration rate (GFR) that measures the kidney’s ability to depurate a substance from the blood. In individuals with normal renal function the GFR is approximately 120 mL/min/1.73 m<sup>2</sup>. Renal function is considered to be decreased when GFR is <60 mL/min/1.73 m<sup>2</sup>.

Figure 9 – CKD stages.

CHRONIC KIDNEY DISEASE STAGES		GFR	% OF OPERATION OF THE KIDNEY
PHASE 1	Renal injury – Normal or enhanced kidney function	≥ 90	
PHASE 2	Mild loss of kidney function	60 - 89	
PHASE 3 A	Mild to moderate loss of kidney function	45 - 59	
PHASE 3 B	Moderate to severe loss of kidney function	30 - 44	
PHASE 4	Severe loss of kidney function	15 - 29	
PHASE 5	Kidney failure	<15	

Source: Adapted from: KDIGO<sup>50</sup>.

According to the K/DOQI guidelines, CKD treatment should be personalized, based on the patient’s diagnosis, disease stage and clinical status while aiming to prevent and delay the loss of renal function, control hypertension, anemia, cardiovascular diseases and other risk

factors. In children, attention should also be directed to problems of growth and development<sup>44, 53</sup>.

At the more advanced stage, the patient is prepared for renal replacement therapy (RRT) that includes peritoneal dialysis, hemodialysis and/or renal transplantation<sup>44, 53</sup>.

Dialysis removes metabolites from the blood and it is the most commonly used treatment for end-stage CKD, followed by renal transplantation.

A study published by Parekh<sup>54</sup> estimates that the number of people around the world, among adults and children, receiving RRT will have its number doubled in 2030 (5,439 million) compared to the numbers in 2010 (2,618 million). Only half of all patients requiring RRTs, or less than the half, were able to receive the treatment in 2010, which means that at least 2,284 million people may have died prematurely due to lack of treatment that year.

#### **4.4 Clinical aspects and complications of CKD**

Chronic kidney disease is a general term for several disorders affecting the kidney's structure and function, however, its clinical manifestations vary depending on the cause, severity, and rate of the disease progression<sup>53</sup>.

The level of renal function and the signs and symptoms of uremia show variability in CKD patients. Decreased glomerular filtration rate (GFR) is associated with a wide range of complications due to changes in other systems in the body. The main symptoms of CKD are leg swelling, lack of appetite, skin paleness, fatigue, increased blood pressure and changes in urinary habits<sup>53, 55</sup>.

Reduction of kidney capacity causes retention of numerous substances stemming from protein metabolism, changes in blood pressure and hematocrit, besides from causing potassium, sodium, water and acid-base imbalance<sup>56</sup>.

Hospitalizations are frequent in the advanced stages and there is a significant increase in morbidity and mortality, notably due to

cardiovascular problems. The two most common causes of death among children and adults with CKD are heart disease and infections<sup>53</sup>.

The cardiovascular system is one of the most affected in people with CKD, presenting a high risk for atherosclerosis and coronary lesions<sup>57, 54</sup>. The main and most well-known risk factors are hypertension, diabetes, hyperuricemia and dyslipidemia. The exact mechanisms of deaths from cardiac problems or risk factors still remain unclear<sup>58</sup>.

Chronic kidney disease is multifarious and its complexity requires multiple approaches. Nutritional counseling, care in medication prescriptions -with special attention to renal metabolism-, glycemic and blood pressure control, physical rehabilitation, psychological support and oral health maintenance involve an attention that must be coordinated and interdisciplinary. Although we do not know exactly which actions generate better outcomes, the interactions between well-informed patients and proactive interdisciplinary teams that offer a pre-planned treatment can benefit patients by improving health outcomes<sup>49, 58</sup>.

#### **4.5 Oral manifestations in patients with CKD**

Literature relates CKD to the alterations detected in the hard and soft tissues of the mouth of both adults and children. Some manifestations are associated with the underlying disease; others to the drugs used<sup>59, 60</sup>.

Among soft tissue alterations, conditions like the paleness of the oral mucosa, petechiae and ecchymoses, and uremic stomatitis deserves attention<sup>65</sup>. Uremic stomatitis is a rare and debilitating painful condition, probably caused by the accumulation of nitrogenous substances in the blood which may occur in the advanced stages of CKD. The presence of gingival bleeding, infections and immune suppression may represent supporting factors to the development of this stomatitis. Such condition may present itself as an ulcerated and hemorrhagic lesion, in pseudomembranous or hyperkeratotic form<sup>61</sup>.

Alterations in calcium metabolism and the occurrence of



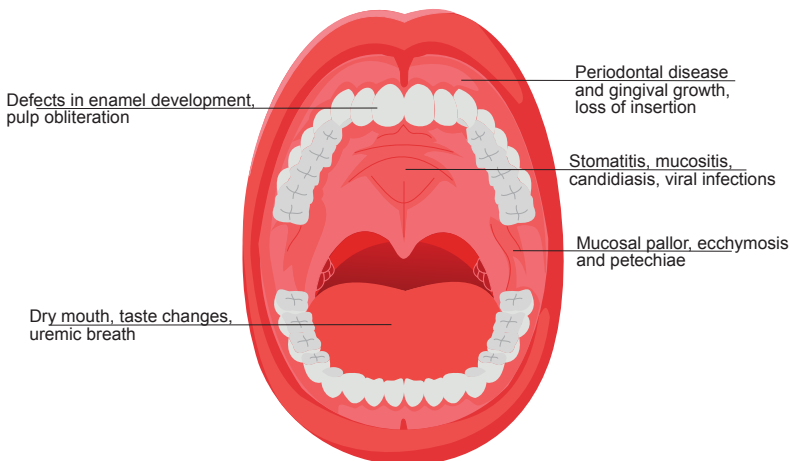
hyperparathyroidism in CKD patients can lead to bone and dental abnormalities such as bone demineralization, enamel hypoplasia, calcification and pulpal narrowing, and delays in tooth eruption. Common complaints involve taste changes, reduced salivary flow accompanied by dry mouth sensation, and uremic breath<sup>59, 60</sup>.

Despite the common insufficiency of oral hygiene care, accompanied by a diet rich in carbohydrates (necessary to reduce renal work), high rates of enamel hypoplasia, continuous use of medications and low salivary flow, some studies show that the prevalence of dental caries in CKD patients is low<sup>62, 63, 64</sup>. According to some studies, salivary changes may explain the low incidence of caries in these patients<sup>62, 63, 65</sup>.

According to different studies, gingivitis and periodontitis have been observed in various levels of prevalence<sup>67, 68, 69</sup>. Preliminary results from a cohort study conducted by Sharma, Mucino, and Ronco<sup>66</sup> have shown that pre-dialysis CKD patients at high risk for cardiovascular events presented high prevalence, severity and extent of periodontal disease.

Figure 10 shows some of the innumerable oral manifestations found in CKD patients.

Figure 10- Oral manifestations in patients with CKD.



Source: Davidovich, Schwarz, Davidovitch, Eidelman, Bimstein<sup>70</sup>.

### 4.6 Dental treatment guidelines

Regardless of the level of health care, dental treatment should address the humanized care for the patient with CKD.

The main strategies to be considered in each stage of dental assistance, from a perspective of integral care, are shown below in Chart 4. For the delineation of those outlines, it is essential to recognize the importance of the joint action between the multidisciplinary team and the oral health professionals in the promotion of integral care to the patient with CKD, regardless of the disease stage.

Chart 4- Main strategies to be considered for dental management from an integral care perspective.

Recommended guidelines
To provide a humanized care while establishing a relationship of trust with the patient.
To establish contact with the nephrologist physician in order to obtain information about the case and set an appropriate guideline focused on the patient's condition.
To know the cause of chronic kidney disease in order to recognize the aspects acting upon the patient's health and to ensure that the patient is receiving the most appropriate dental treatment.
To know the patient's hematological parameters and urea levels in order to plan invasive dental procedures that can prevent problems with hemostasis.
To evaluate the patient's blood pressure, since dental procedures can cause alterations in the renal patient's BP levels and worsen the disease. Changes in treatment planning may be required.
For patients undergoing dialysis, do not use the arm with the arteriovenous fistula for measuring blood pressure and administrating medication.
To know the patient's dialysis routine so to properly plan the dental treatment (days of the week, frequency, medications used, intercurrents).
To investigate the presence of signs and symptoms of uremia such as pallor of the buccal mucosa, uremic breath, metallic taste, fatigue, nausea, lethargy, vomiting, among others.
Dose adjustments or changes in dosing frequency of some medications may be necessary due to possible alterations in the absorption, distribution, metabolism and excretion of certain drugs in patients with renal disease.
To establish treatment for elimination of infectious processes and a routine of clinical reviews for the early identification of oral complications.

To promote educational measures that encourage the patients to improve their self-care concerning oral health.

Source: Adapted from: Proctor, Kumar, Stein, Moles, Porter<sup>60</sup>, Brockmann, Badr<sup>71</sup> Jover, Bagán, Jiménez, Poveda<sup>72</sup>.

Although there are some factors related to the complex systemic condition of renal disease capable of influencing on the occurrence of the oral issues found in these patients, whether adults or children, we cannot forget the etiological role of plaque accumulation in the process of periodontal disease.

Poor oral hygiene is a frequent condition in chronic renal patients, which aggravates the oral condition<sup>59, 67, 73</sup>. In addition, researches show a low demand for dental care, although patients with CKD are affected by oral problems and suffer from local and systemic disorders<sup>60, 73</sup>.

Some studies suggest that bad oral health conditions in people with CKD may contribute to increased morbidity and mortality when associated with systemic manifestations of the disease, such as inflammation, infections, energy-protein losses, atherosclerotic and hematologic complications<sup>73</sup>. Cohort studies conducted since 2010 in Europe, engaging 4,500 patients of CKD going through dialysis, found that poorer oral health conditions were associated with early death, while preventive oral health practices were associated with increased patient survival<sup>74</sup>.

The clinical management of people with CKD can represent a challenge for the dental surgeon, especially when there is a need to perform invasive dental procedures<sup>74</sup>. Some authors describe concerns such as altered metabolism due to drug use, immune response and bone metabolism, and increased risk of bleeding. The enhanced risk for bacterial endocarditis is mentioned by some authors, however, there are still no scientific evidences to support the use of prophylactic antibiotics prior to invasive dental procedures<sup>60, 72, 74, 75</sup>. Cases of infective endocarditis are more often associated with bacteria that colonize the skin.

Regarding hemostasis care and medication prescription, the interdisciplinary attention with the nephrologist represents an important

part of treatment. During anamnesis, it is essential that the physician collects information regarding the patient's systemic condition and have the examinations for blood, coagulation, creatinine and urea requested.

Ideally, patients going through hemodialysis should be seen by the doctor on the day after dialysis, since the attention after dialysis exposes them to increased bleeding risk. Even so, it is not uncommon for patients with advanced CKD to present platelet dysfunction. This condition requires the recommendation of local hemostatics if a greater bleeding is observed after exodontia.

When there is a need for drug prescription, the dentist should consider the CKD stage in which the patient is, the GFR from that moment and the mechanism of drug excretion. Some drugs, such as non-steroidal anti-inflammatory drugs, should be avoided. On the other hand, the use of hepatic metabolizing analgesics is preferable for these patients<sup>72,76</sup>. The prescription of amoxicillin for an adult with CKD may include doses of 500 mg every 8 hours for those with GFR greater than 50 mm/min, for example, whereas those which present GFR between 10 and 50 ml/min or lower than 10 ml/min should receive one dose every 12 and 24 hours respectively<sup>71</sup>.

The following table provides a summary of the most commonly prescribed antibiotics in dental practice for patients with CKD.

Table 1 - Dosage and dose adjustments of some of the most commonly prescribed antibiotics in dental practice for patients with CKD.

DRUG	Usual dosage	Dose adjustment according to GFR *		
		>50 mL per min/1.73 m <sup>2</sup>	10-50 mL per min/1.73 m <sup>2</sup>	<10 mL per min/1.73 m <sup>2</sup>
Decreased dosage				
Metronidazole	200-500 mg every 8 hours	100%	100%	50% (reduction not necessary for shorter periods)

Increasing dosage interval				
Amoxicillin	200-500 mg every 8 hours 500-875 mg every 12 hours	Unaltered	Every 8 to 12 hours if GFR <30mL/min (do not use 875 mg)	Every 24 hours
No dosage adjustment is required				
Clindamycin	300 mg three times per day		Not applicable	
Erythromycin	250-500 every 6 hours		Not applicable	

\*GFR: Glomerular Filtration Rate

Source: Adapted from: Brockmann, Badr<sup>71</sup>.

A better understanding of the CKD pathophysiology, as well as the related oral alterations, enables dentists to perform a more effective dental treatment, always adapted to individual needs so to prevent oral issues. With the development and enhanced availability of dialysis and renal transplantation, some oral manifestations, especially those related to uremia, became less frequently observed. However, it is notable that the dental surgeon plays an important role in diagnosing the alterations, planning and applying treatment and guiding these patients.

## 6 FINAL CONSIDERATIONS

In the course of this e-book we addressed the general and dental aspects of three of the major chronic diseases that increasingly affect the population around the world.

In the long run, we hope that the content here presented may have contributed to increase your knowledge and provide subsidies for an appropriate dental care to patients with chronic kidney disease, diabetes and hypertension.

We hope that this work's greatest impact will concern the improvement of oral health care by providing better outcomes in general health and a better quality of life for patients with systemic impairment.

## REFERENCES

1. WHO. Noncommunicable Diseases Progress Monitor. Geneva: World Health Organization [Internet]; 2017 [accessed in 2018 apr 30]. Available at: <http://apps.who.int/iris/bitstream/handle/10665/258940/9789241513029-eng.pdf;jsessionid=AE1A41248348FECFC13BD9AC7729B599?sequence=1>.
2. UN General Assembly. Political Declaration of the High-level Meeting of the General Assembly on the Prevention and Control of Non-communicable Diseases [Internet]; 2012 [accessed in 2018 apr 30]. Available at: [http://www.who.int/nmh/events/un\\_ncd\\_summit2011/political\\_declaration\\_en.pdf?ua=1](http://www.who.int/nmh/events/un_ncd_summit2011/political_declaration_en.pdf?ua=1).
3. WHO. Global action plan for the prevention and control of noncommunicable diseases 2013-2020 [Internet]. World Health Organ; 2013 [accessed in 2018 apr 30]. Available at: [http://apps.who.int/iris/bitstream/10665/94384/1/9789241506236\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/94384/1/9789241506236_eng.pdf).
4. WHO. Global status report on noncommunicable diseases 2014: Attaining the nine global noncommunicable diseases targets; a shared responsibility. Geneva: Who Press; 2014.
5. Ministério da Saúde (Brasil), Secretaria de Vigilância em Saúde, Departamento de Análise de Situação de Saúde. Plano de ações estratégicas para o enfrentamento das doenças crônicas não transmissíveis (DCNT) no Brasil 2011-2022 [Internet]. Brasília, DF: Ministério da Saúde; 2011 [accessed in 2018 apr 30]:160 p. (Série B. Textos Básicos de Saúde). Available at: [http://bvsms.saude.gov.br/bvs/publicacoes/plano\\_acoes\\_enfrent\\_dcnt\\_2011.pdf](http://bvsms.saude.gov.br/bvs/publicacoes/plano_acoes_enfrent_dcnt_2011.pdf).
6. American Heart Association. What is High Blood Pressure? [internet]. 2018 [accessed in 2018 aug 7]. Available at: <https://www.heart.org/en/health-topics/high-blood-pressure/the-facts-about-high-blood-pressure/what-is-high-blood-pressure>

7. Sociedade Brasileira de Hipertensão. O que é hipertensão [Internet]. São Paulo; 2016 [accessed in 2018 jun 20]. Available at: <http://www.sbh.org.br/geral/oque-e-hipertensao.asp>.
8. Turnbull F, Neal B, Algert C, Chalmers J, Chapman N, Cutler J, Woodward M, MacMahon S. Effects of different blood pressure-lowering regimens on major cardiovascular events in individuals with and without diabetes mellitus: results of prospectively designed overviews of randomized trials. *Arch Intern Med*. [Internet]. Jun. 2005 [accessed in 2016 nov 8]; 165 (12): 1410-9. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/15983291>.
9. Zhou B, Bentham J, Di Cesare M, Bixby H, Danaei G, Cowan MJ, Paciorek CJ, Singh G, Hajifathalian K, Bennett JE, Taddei C, Bilano V, Carrillo-Larco RM, Djalalinia S, Khatibzadeh S, Lugero C, Peykari N, Zhang WZ, Lu Y, Stevens GA, Riley LM, Collaborators'. Worldwide trends in blood pressure from 1975 to 2015: a pooled analysis of 1479 population-based measurement studies with 19.1 million participants. *Lancet*. 2017 Jan 7;389 (10064): 37-55.
10. Whelton PK, Carey RM, Aronow WS, Casey DE Jr, Collins KJ, Dennison Himmelfarb C, DePalma SM, Gidding S, Jamerson KA, Jones DW, MacLaughlin EJ, Muntner P, Ovbiagele B, Smith SC Jr, Spencer CC, Stafford RS, Taler SJ, Thomas RJ, Williams KA Sr, Williamson JD, Wright JT Jr. High Blood Pressure Clinical Practice Guideline: Executive Summary [Internet]. 2017 [accessed in 2018 apr 30]. Available at: <http://hyper.ahajournals.org/content/hypertensionaha/early/2017/11/10/HYP.0000000000000066.full.pdf>.
11. SBC. SBH. SBN. VI Diretrizes Brasileiras de Hipertensão. *Arq Bras Cardiol* [Internet]. 2010 [accessed in 2018 jul 28]; 95 (supl. 1):1-51. Available at: [http://publicacoes.cardiol.br/consenso/2010/Diretriz\\_hipertensao\\_associados.pdf](http://publicacoes.cardiol.br/consenso/2010/Diretriz_hipertensao_associados.pdf).



12. James PA, Suzanne O, Barry L. Carter, et al. Evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). JAMA [Internet]. 2014 [accessed in 2016 nov 8]. Available at: <http://jama.jamanetwork.com/journal.aspx>.
13. American Heart Association, American Stroke Association. AHA/ASA Journals [internet]. 2018. [accessed in 2016 nov 8]. Available at: <https://www.ahajournals.org/>
14. Ministério da Saúde (Brasil), Secretaria de Vigilância em Saúde. Estratégias para o cuidado da pessoa com doença crônica: hipertensão arterial sistêmica [Internet]. Brasília, DF: Ministério da Saúde; 2013 [accessed in 2016 nov 7]: 128 p. (Cadernos de Atenção Básica, n. 37). Available at: [http://189.28.128.100/dab/docs/portaldab/publicacoes/caderno\\_37.pdf](http://189.28.128.100/dab/docs/portaldab/publicacoes/caderno_37.pdf).
15. Cruz MM. Inimiga do coração: hipertensão atinge um a cada quatro adultos: médicos tentam combater e alertar a população sobre a doença [Internet]. 2015 [accessed in 2018 jul 28]. Available at: <http://www.uai.com.br/app/noticia/saude/2015/04/26/noticias-saude,187728/inimiga-do-coracao-hipertensao-atinge-um-a-cada-quatro-adultos.shtml>
16. Ministério da Saúde (Brasil), Secretaria de Atenção à Saúde, Departamento de Atenção Básica. Estratégias para o cuidado da pessoa com doença crônica: hipertensão arterial sistêmica [Internet]. Brasília: Ministério da Saúde, 2014 [accessed in 2016 nov 7]: 128 p. (Cadernos de Atenção Básica, n. 37). Available at: [http://bvsms.saude.gov.br/bvs/publicacoes/hipertensao\\_arterial\\_sistemica\\_cab37.pdf](http://bvsms.saude.gov.br/bvs/publicacoes/hipertensao_arterial_sistemica_cab37.pdf).

17. SBC, SBH, SBN. VI Diretrizes Brasileiras de Hipertensão. Arq Bras Cardiol. [Internet].2010 [accessed in 2016 nov 8]; 95 (Supl. 1): 1-51, 2010. Available at: [http://publicacoes.cardiol.br/consenso/2010/Diretriz\\_hipertensao\\_associados.pdf](http://publicacoes.cardiol.br/consenso/2010/Diretriz_hipertensao_associados.pdf).
18. Fonseca FAH, Fenelon GD. (Coord.). I Manual SOCESP de condutas multidisciplinares no paciente grave. Rev Soc Cardiol do Estado de São Paulo. [Internet]. São Paulo. 2015 abr./ jun. [accessed in 2017 nov 7]; 25 (2, supl A): 13-58. Available at: <http://www.socesp.org.br/upload/suplemento/2015/SUPLEMENTO-DA-REVISTA-SOCESP-V25-N2A-DIRETRIZ.pdf>.
19. Rosário TM, Scalai LCN, França GVA, Pereira MRG, Jardim PCBV. Prevalência, controle e tratamento da hipertensão arterial sistêmica em Nobres, MT. Arq. Bras. Cardiol. [Internet]. São Paulo. 2009 Dec. [accessed in 2016 nov 8]; 93 (6): 672–678. Available at: [http://www.scielo.br/scielo.php?script=sci\\_arttext&pid=S0066-782X2009001200018](http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0066-782X2009001200018).
20. Silvestre FJ, Salvador-Martínez I, Bautista D, Silvestre-Rangil J. Clinical study of hemodynamic changes during extraction in controlled hypertensive patients. Med Oral Patol Oral Cir Bucal. 2011; 16 (3):354- 358.
21. Laragnoit AB, Neves RS, Neves IL, Vieira JE.. Locoregional anesthesia for dental treatment in cardiac patients: a comparative study of 2% plain lidocaine and 2% lidocaine with epinephrine (1:100,000). Clinics (Sao Paulo). 2009; 64(3):177-82.
22. Neves RS, Neves ILI, Giorgi DMA; Grupi CJ; César LAM, Hueb, M Grinberg. Effects of epinephrine in local dental anesthesia in patients with coronary artery disease. Arq Bras Cardiol. [Internet]. São Paulo. 2007 Mayo [accessed in 2016 nov 8]; 88 (5): 545-51. Available at: [http://www.scielo.br/scielo.php?pid=S0066-782x2007000500008&script=sci\\_arttext&lng=en](http://www.scielo.br/scielo.php?pid=S0066-782x2007000500008&script=sci_arttext&lng=en).

23. Rajeev G, Soneil G. Strategies for initial management of hypertension. Indian J Med Res. [Internet]. 2010 Nov. [accessed in 2016 nov 8]; 132: 531-542. Available at: <http://medind.nic.in/ibyt/t10/i11/ibyt10i11p531.pdf>.
24. International Diabetes Federation. Annual Report: 2015 [Internet] 2015 [accessed in 2016 out 27]. Available at: [http://www.idf.org/sites/default/files/IDF\\_AnnualReport\\_2015\\_WEB.pdf](http://www.idf.org/sites/default/files/IDF_AnnualReport_2015_WEB.pdf).
25. WHO. Global report on diabetes [Internet]. Geneva: Who Press; 2016 [accessed in 2016 out 27]. Available at: [http://apps.who.int/iris/bitstream/10665/204871/1/9789241565257\\_eng.pdf?ua=1](http://apps.who.int/iris/bitstream/10665/204871/1/9789241565257_eng.pdf?ua=1)
26. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2015; 38: S8-S16.
27. Milech A, Angelucci AP, Golbert A, Matheus A, Carrilho AJF, Ramalho AC, Aguiar ACB, Cardoso AMC, Seyffarth AS, Sachs A, Camargo AP, Lerario AC, Pires AC, Ferreira AR, Chacra AR, Pimazoni Netto A, Tschiedel B, Pereira BG, Wajchenberg BG, Astiarraga B, Geloneze B, Barcia C, Negrato CA, Couri CEB et al. Diretrizes da Sociedade Brasileira de Diabetes (2015-2016) [Internet]. São Paulo: Sociedade Brasileira de Diabetes; 2016 [accessed in 2016 out 27]: 348 p. Available at: <http://www.diabetes.org.br/sbdonline/images/docs/DIRETRIZES-SBD-2015-2016.pdf>.
28. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care. 2004 mayo; 27 (5):1047-53.
29. International Diabetes Federation. Diabetes Atlas - 8 th Edition [Internet]. 2017 [accessed in 2018 jun 30]. Disponível em: <http://diabetesatlas.org/resources/2017-atlas.html>.

30. WHO. Global Strategy on People-centred and Integrated Health Services [Internet]. Geneva: Who Press, 2015 [accessed in 2016 out 27]. Available at: <http://www.who.int/servicedeliverysafety/areas/people-centred-care/global-strategy/en/>.
31. Selwitz RH, Pihlstrom BL. How to lower risk of developing diabetes and its complications: recommendations for the patient. J Am Dent Assoc. 2003 oct; 134.
32. Pessoa FS, organizador. Redes de atenção à saúde: rede de atenção às condições crônicas. São Luís: UNA-SUS; 2015.
33. Weinert LS, Silveiro SP, Oppermann ML, Salazar CC, Simionato BM, Siebeneichler A, Reichelt AJ. Gestational diabetes management: a multidisciplinary treatment algorithm. Arq Bras Endocrinol Metabol. 2011 oct; 55 (7): 435-45.
34. Graziani F, Gennai S, Solini A, Petrini M. A systematic review and meta-analysis of epidemiologic observational evidence on the effect of periodontitis on diabetes An update of the EFP-AAP review. Journal of clinical periodontology [Internet]. 2018 [accessed in 2016 out 27]; 45 (2): 167-187. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29277926>.
35. Garcia-Cuesta C, Sarrion-Perez M, Bagan J. Current treatment of oral candidiasis: A literature review. J Clin Exp Dent [Internet]. 2014 [accessed in 2018 abr 30]; 6(5): e576–82. Available at: <http://www.medicinaoral.com/odo/volumenes/v6i5/jcedv6i5p576.pdf>.
36. Kidambi S, Patel SB. Diabetes mellitus: considerations for dentistry. J Am Dent Assoc. 2008 oct; 139.
37. Miley DD, Terezhalmay GT. The patient with diabetes mellitus: etiology, epidemiology, principles of medical management, oral disease burden, and principles of dental management. Quintessence Int. 2005 nov./dec; 36 (10): 779-95.

38. Ship JA. Diabetes and oral health: an overview. J Am Dent Assoc. 2003 oct; 134, v. 134, oct. 2003.
39. American Diabetes Association. 6. Glycemic targets: Standards of Medical Care in Diabetes - 2018. Diabetes Care. [Internet]. 2018 [accessed in 2018 abr 30];41(Suppl. 1):S55–S64. Available at: [http://care.diabetesjournals.org/content/41/Supplement\\_1/S55.full-text.pdf](http://care.diabetesjournals.org/content/41/Supplement_1/S55.full-text.pdf).
40. Fernandes KS, Glick M, de Souza MS, Kokron CM, Gallottini M. Association between immunologic parameters, glycemic control, and postextraction complications in patients with type 2 diabetes. J Am Dent Assoc. 2015 Aug;146(8):592-599.
41. Aronovich S, Skope LW, Kelly JP, Kyriakides TC. The relationship of glycemic control to the outcomes of dental extractions. J Oral Maxillofac Surg. 2010; 68 (12): 2955-2961.
42. Huang S, Dang H, Huynh W, Sambrook PJ, Goss AN. The healing of dental extraction sockets in patients with Type 2 diabetes on oral hypoglycaemics: a prospective cohort. Aust Dent J. 2013; 58 (1): 89-93.
43. Ministério da Saúde (Brasil). Estratégias para o cuidado da pessoa com doença crônica: Diabetes Mellitus [Internet]. Brasília: Ministério da Saúde; 2013 [accessed in 2016 out 27]; 36: 162. (Cadernos de Atenção Básica, n. 35). Disponível: [http://189.28.128.100/dab/docs/portaldab/publicacoes/caderno\\_36.pdf](http://189.28.128.100/dab/docs/portaldab/publicacoes/caderno_36.pdf).
44. Hogg RJ, Furth S, Lemley KV, Portman R, Schwartz GJ, Coresh J, Balk E, Lau J, Levin A, Kausz AT, Eknoyan G, Levey AS. National Kidney Foundation's Kidney Disease Outcomes Quality Initiative clinical practice guidelines for chronic kidney disease in children and adolescents: evaluation, classification, and stratification. Pediatrics. 2013; 111 (1):1416 -21.

45. Hill NR, Fatoba ST, Oke JL, Hirst JA, O'Callaghan CA, Daniel S, Lasserson, F. D. Richard Hobbs. Global Prevalence of Chronic Kidney Disease – A Systematic Review and Meta-Analysis. PLoS One [Internet]. 2016 [accessed in 2018 jul 30]; 11(7): e0158765. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4934905/>.
46. Louvisonl MCP, Cecilio MAP, Osianol VLLPR, Portas SLC, Sesso R. Prevalência de pacientes em terapia renal substitutiva no Estado de São Paulo. Bepa. 2011; 8 (95): 23–42.
47. Sesso CS, Lopes AA, Thomé FS, Lugon JR, Watanabe Y, Santos DR. Relatório do censo brasileiro de diálise crônica 2012. Jornal Brasileiro de Nefrologia [Internet]. 2014 jan./mar. [accessed in 2018 abr. 30]; 36 (1): 48-53. Available at: <http://www.scielo.br/pdf/jbn/v36n1/0101-2800-jbn-36-01-0048.pdf>
48. Saran R, Li Y, Robinson B, Ayanian J, Balkrishnan R, Bragg-Gresham J, Chen JT, Cope E, Gipson D, He K, Herman W, Heung M, Hirth RA, Jacobsen SS, Kalantar-Zadeh K, Kovesdy CP, Leichtman AB, Lu Y, Molnar MZ, Morgenstern H, Nallamothu B, O'Hare AM, Pisoni R, Plattner B, Port FK, Rao P, Rhee CM, Schaubel DE, Selewski DT, Shahinian V, Sim JJ, Song P, Streja E, Kurella Tamura M, Tentori F, Eggers PW, Agodoa LY, Abbott KC. US Renal Data System 2014 Annual Data Report: Epidemiology of Kidney Disease in the United States. Am J Kidney Dis. 2015; 65.
49. Bastos MG, Kirsztajn GM. Doença renal crônica: importância do diagnóstico precoce, encaminhamento imediato e abordagem interdisciplinar estruturada para melhora do desfecho em pacientes ainda não submetidos à diálise. J Bras Nefrol. 2010; 33 (1): 384-4.
50. KDIGO, International Society of Nephrology. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int Suppl. 2013;3(1):1–150.

51. Harambat J, van Stralen KJ, Kim JJ, Tizard EJ. Epidemiology of chronic kidney disease in children. *Pediatr Nephrol* [Internet]. 2012 Mar 29 [accessed in 2016 out 27]; 27(3):363–73. Available from: <http://link.springer.com/10.1007/s00467-011-1939-1>.

52. Remuzzi G, Pisoni R, Schieppati A. Pathophysiology of chronic kidney disease-in. 5. ed. National Kidney Foundation, 2009: 422-35.

53. National Kidney Foundation. K/DOQI Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification and Stratification. *American Journal of Kidney Diseases*. 2002; 39: S1–266.

54. Parekh RS, Carroll CE, Wolfe RA, Port FK.. Cardiovascular mortality in children and young adults with end-stage kidney disease. *J Pediatr*. 2002 aug; 141 (2): 191-7.

55. Riyuzo MC, Macedo CS, Assao AE, Fekete SMW, Amélia A T, Bastos THD. Insuficiência renal crônica na criança: aspectos clínicos, achados laboratoriais e evolução. *J Bras Nefrol*. 2003; 25 (4): 200-8.

56. Luke RG. Insuficiência renal crônica. In: Goldman L, Bennet JC. *Tratado de medicina interna*. 21. ed. Rio de Janeiro: Guanabara Koogan; 2001. p. 632–40.

57. Gansevoort RT, Correa-Rotter R, Hemmelgarn BR, Jafar TH, Heerspink HJ, Mann JF, Matsushita K, Wen CP. Chronic kidney disease and cardiovascular risk: Epidemiology, mechanisms, and prevention. *Lancet*. 2013; 382 (9889): 3329-52.

58. Remuzzi G, Benigni A, Finkelstein FO, Grunfeld JP, Joly D, Katz I, Liu ZH, Miyata T, Perico N, Rodriguez-Iturbe B, Antiga L, Schaefer F, Schieppati A, Schrier RW, Tonelli M. Kidney failure: aims for the next 10 years and barriers to success. *Lancet*. 2013; 9889 (382): 353-62.

59. Ruospo M, Palmer SC, Craig JC, Gentile G, Johnson DW, Ford PJ, Tonelli M, Petruzzi M, De Benedittis M, Strippoli GF. Prevalence and severity of oral disease in adults with chronic kidney disease: a systematic review of observational studies. *Nephrol Dial Transplant*. 2014; 29 (2): 364-75.
60. Proctor R, Kumar N, Stein A, Moles D, Porter S. Oral and dental aspects of chronic renal failure. *J Dent Res*. 2005; 84 (3): 199-208.
61. Sudarshan S, Annigeri RG, Mamatha GP, Vijayabala GS. Uremic stomatitis. *Contemp Clin Dent*. [Internet] 2012 [accessed in 2016 out 27]; 3 (1) :113, 2012 . Available at: <http://www.contempclindent.org>.
62. Seraj B, Ahmadi R, Ramezani N, Mashayekhi A, Ahmadi M. Oro-dental health status and salivary characteristics in children with chronic renal failure. *J. Dent*. 2011; 8 (3): 146-51.
63. 56Anuradha BR, Katta S, Kode VS, Praveena C, Sathe N, Sandeep N, Penumarty S. Oral and salivary changes in patients with chronic kidney disease: A clinical and biochemical study. *J Indian Soc Periodontol*. 2015; 19 (3): 297.
64. Reyes E, Martin J, Moncada G, Neira M, Palma P, Gordan V, Oyarzo JF, Yevenes I. Caries-free subjects have high levels of urease and arginine deiminase activity. *J Appl Oral Sci*. 2014; 22 (3): 235-40.
65. Kho HS, Lee SW, Chung SC, Kim YK. Oral manifestations and salivary flow rate, pH, and buffer capacity in patients with end-stage renal disease undergoing hemodialysis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1999; 88 (3): 316-9.
66. Sharma A, Mucino MJ, Ronco C. Renal functional reserve and renal recovery after acute kidney injury. *Nephron Clin Pract*. 2014; 127: 94–100.



67. Palmer SC, Ruospo M, Wong G, Craig JC, Petruzzi M, De Benedittis M, Ford P, Johnson DW, Tonelli M, Natale P, Saglimbene V, Pellegrini F, Celia E, Gelfman R9, Leal MR, Torok M, Stroumza P, Bednarek-Skublewska A, Dulawa J, Frantzen L, Ferrari JN, Del Castillo D, Bernat AG, Hegbrant J, Wollheim C, Gargano L, Bots CP, Strippoli GF. Dental health and mortality in people with end-stage kidney disease treated with hemodialysis: a multinational cohort study. *Am J Kidney Dis*. 2015; 66 (4): 666-76.
68. Hajishengallis G. Periodontitis: from microbial immune subversion to systemic inflammation. *Nat Publ Gr*. 2015; 15 (1): 30-44.
69. Fisher MA, Taylor GW, Shelton BJ, Jamerson KA, Rahman M, Ojo AO, Sehgal AR. Periodontal disease and other nontraditional risk factors for CKD. *Am J Kidney Dis*. 2008; 51 (1):45-52.
70. Davidovich E, Schwarz Z, Davidovitch M, Eidelman E, Bimstein E. Oral findings and periodontal status in children, adolescents and young adults suffering from renal failure. *J Clin Periodontol*. 2005 oct; 32 (10): 1076–82.
71. Brockmann W, Badr M. Chronic kidney disease: pharmacological considerations for the dentist. *J Am Dent Assoc*. 2010; 141: 1330-9.
72. Jover CA, Bagán JV, Jiménez SY, Poveda RR. Dental management in renal failure: patients on dialysis. *Med oral, Patol oral y cirugía bucal*. 2008 jul; 13 (7): 419-26.
73. Akar H, Akar GC, Carrero JJ, Stenvinkel P, Lindholm B. Systemic consequences of poor oral health in chronic kidney disease patients. *Clin J Am Soc Nephrol*. 2011; 6 (1): 218-26.
74. Gupta M, Gupta M. Oral conditions in renal disorders and treatment considerations - a review for pediatric dentist. *Saudi Dent J*. 2015; 27 (3):113-9.

75. Werner CW, Saad TF. Prophylactic antibiotic therapy prior treatment for patients with end-stage renal disease. Spec Care in Dentist. 1999; 19 (3): 106-111.

76. Prado Fc, Ramos Já, Valle JR. Atualização terapêutica. 20. ed. São Paulo: Artes Médicas; 2001.

