The pathophysiology and management of taste changes in Chronic Kidney Disease.

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One of the most disabling, yet neglected, symptoms of patients with chronic kidney disease is alteration in taste.
Food, drink and their enjoyment are significant nutritional, cultural and social phenomena.
Oysters

by Seamus Heaney
Our shells clacked on the plates,
My tongue was a filling estuary,
My palate hung with starlight...

From *Oysters* by Seamus Heaney
Lack of taste or alteration in taste can be frustrating, debilitating and have a profound impact on interest in food, nutritional status, mood and the quality of life.
1. Basic anatomy and physiology of taste

2. Epidemiology

3. Pathophysiology of taste changes in CKD

4. Management strategies
The anatomy and physiology of taste
Taste is a sensation.

Indeed, it has been described as “a chemosensory event.”
The primary tastes are:
salt, sweet, savoury (umami), sour and bitter.
The human tongue
Anatomically, the human tongue is divided into the anterior two thirds and the posterior one third.
The anterior two thirds of the tongue has four types of surface papillae.

Filiform and fungiform papillae are scattered on the tip and lateral borders of the tongue and circumvallate and foliate papillae lie on the lateral borders.
The posterior third of the tongue has surface foliate and circumvallate papillae.
With the exception of filiform, all other papillae have taste buds.

On the taste buds are a group of chemoreceptive taste receptor cells.
There are three main taste cells.

In broad terms:

Type I cells detect salt taste

Type II cells detect sweet, bitter and umami tastes

Type III cells detect sour and, in certain circumstances, salt tastes.
Taste Cells and their tastants

Salt

Type I Cell

Sweet/ Bitter/ Umami

Type II Receptor Cell

Sour/ Salt

Type III Presynaptic Receptor Cell
<table>
<thead>
<tr>
<th>Classic stimulant</th>
<th>Taste sensation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkali metal (e.g. Na+)</td>
<td>Salt</td>
</tr>
<tr>
<td>Glucose</td>
<td>Sweet</td>
</tr>
<tr>
<td>Meat, Glutamate</td>
<td>Savoury</td>
</tr>
<tr>
<td>Caffeine; Urea</td>
<td>Bitter</td>
</tr>
<tr>
<td>Acids</td>
<td>Sour</td>
</tr>
</tbody>
</table>
Salt taste
The transmission of a salty taste occurs through sodium channels on the membranes of the taste bud.

When alkali metals, such as sodium, enters the taste bud, saltiness is perceived.

A salty taste is detected only when it is above the background concentration of salivary NaCl to which the taste receptors are adapted.

Salty taste mainly involves Type 1 cells but, if sodium is in high concentration, a salty taste can also be transmitted by Type III presynaptic receptor cells.

Sweet, bitter and umami tastes
Type II receptor cells detect sweet, bitter or umami tastes.

Each of these tastes is transduced by its own Type II receptor cells depending on the taste receptor proteins expressed.
The transmission of these tastes is linked with G-protein coupled receptors.

There are seven transmembrane proteins of primarily two classes: Taste family Type 1 and 2 receptors (T1Rs and T2Rs).
Sweet taste
Carbohydrates, such as sugar, are a common stimulant of sweet taste cells.
Sweet-sensitive Type II receptor cells express T1R2/T1R3 heterodimers.

Sweet taste is the strongest suppressor of other tastes.

It is also the most resistant to being suppressed itself.
It is postulated that the ability to perceive sweet carbohydrates in food, a vital source of energy, provides a clear adaptive advantage.

Similarly, the resistance of sweetness to suppression by other tastes, contributes to this advantage.
Bitter taste
Humans have a natural aversion to substances with a bitter taste.
Bitterness acts as a warning of the potential presence of exogenous and dietary toxins.
This fact indicates the evolutionary importance nature places on this warning system.

Bitter taste is detected by Type II receptor cells with Taste family Type 2 receptors [T2Rs].

Relevant to this topic, urea causes a bitter taste.
Remarkably, while the other tastes have one type of receptor each, there are at least 25 different bitter receptors.

Umami taste
Umami taste is detected by Type II receptor cells. Umami –sensitive Type II receptor cells express T1R1/T1R3 heterodimers.

A common example of the umami tastant is glutamate that is found in meat and mature cheese.

Sour taste
Type III presynaptic receptor cells detect sourness and respond to acidic stimuli. Sourness is perceived when hydrogen ions cross hydrogen channels on taste buds.

Examples are citric acid in fruits, acetic acid (vinegar)

Human saliva
Normal saliva is critical to oral health and taste stimulation.

Approximately 99 % of its composition is water and the remainder a combination of electrolytes and proteins.

Normal saliva is hypotonic, high in potassium and phosphorus and low in sodium and urea.
Saliva assists in the perception of taste by the transportation of taste substances, the solubilisation of these substances and the protection of taste receptors from damage caused by dryness, disuse atrophy or infection.

Zinc
Zinc plays an important role in the maturation, maintenance and repair of taste buds.


Cell-to-cell transmission
There is a close interaction between taste cells. This interaction has an important role in the taste that is ultimately perceived.
Taste Cells and their interactions

Salt
Type I Cell
ATP degraded by surface ATPase
K^+

Sweet/Bitter/Umami
Type II Receptor Cell
ATP

Sour/Salt
Type III Presynaptic Receptor Cell
5HT
NE

Stimulatory
Inhibitory
Afferent nerve fibres
Afferent nerve
The interaction of individual tastes
In addition to activating individual taste receptor cells, stimuli have an effect on other tastes. For instance, as stated above, sweetness stimuli is the most suppressive of other tastes and resistant to suppression itself.

Clinically, this is significant.

The response of taste detection to specific taste stimuli

<table>
<thead>
<tr>
<th>Stimuli</th>
<th>Salt</th>
<th>Sweet</th>
<th>Umami</th>
<th>Bitter</th>
<th>Sour</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salt</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sweet</td>
<td></td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Umami</td>
<td></td>
<td></td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bitter</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Sour</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>+</td>
</tr>
</tbody>
</table>
Genetics and taste
The perception of taste is affected by genetics.
For instance, with bitter tastants, genetic variability dictates an individual’s taste response.

Individuals have been classified as non-tasters, medium tasters and supertasters according to their perception of bitter compounds.

For example, urea is especially bitter to persons who are genetically sensitive to the taste of thiourea.

According to genetic variability, some people (the supertasters) have a heightened perception of bitter taste and others will be not perceive the bitterness.

There may be similar genetic variations in the other taste receptors.

Lugaz and colleagues reported a substantial variation in umami taste sensitivity. They found that humans can be classified into tasters, reduced tasters (hypoguesia) and non-tasters.

The clinical implication of this evidence is that when assessing taste abnormalities in a patient with CKD it is prudent to examine whether these taste patterns are long standing (genetic) or new (due to CKD).

Taste, flavour and chemesthesis
Taste is a single, albeit extraordinarily complex, sensation.
Flavour is a constellation of sensations – a combination of taste, smell and the sensations of temperature and texture.

It is estimated that approximately 75 % of the flavour sensation is produced by odorants.

When one ingests food and drink, aromas are released that enter the nose through a retronasal passage connecting the roof of the mouth with the nose.

Nerve endings in the olfactory bulb in the nose transmit these smell stimuli to the brain. It is this aroma, when combined with the stimuli of taste, temperature and texture that gives food its flavour.
Whilst the sensations of taste and smell are distinct, their signals are integrated in the orbitofrontal and other areas of the cerebral cortex to generate flavours.

The practical implications for patient care is that an alteration in taste results from a change in perception of the five taste qualities. An alteration in flavour may occur from an alteration in multiple sensations, taste, smell and the temperature and texture of food.
A wide variety of chemical compounds act on the mucous membranes in the mouth to trigger senses such as heat, cold, pungency and irritation. This is called chemesthesis.
Examples within the oral cavity include the heat of chilli, the irritation of wasabi, the cooling of menthol and the astringency of tannins in tea. The most important channels detecting these sensations are the Transient Receptor Potential (TRP) channels.

The language of taste alteration
There are four main descriptors of taste alteration:

• Absence of taste (aguesia)
• Reduced taste (hypoguesia)
• Taste disturbance (dysguesia). Here food is described as bitter or unpleasant, “like cardboard” or “like metal”.
• Exaggerated taste (hyperguesia).
Patients may have these taste alterations in isolation or in combination.

For instance, a patient may describe hypoguesia for some foods and dysguesia for other foods.
Chronic Kidney Disease and taste alteration
Epidemiology
Taste alterations are common in patients with CKD.


One of the greatest challenges in synthesising the literature in this area is the significant diversity of individual responses to an enquiry about taste and any alteration experienced.
When asked to characterise the type of taste alteration experienced, patients report various responses including metallic, acidic or bitter taste, a mixture of tastes or no taste. They also reported malodour.

Some patients report food aversion; others, food cravings.
In addition to taste alterations, the most striking feature of these studies is the high proportion of patients reporting xerostomia.
# The prevalence and characteristics of oral and taste changes in CKD

<table>
<thead>
<tr>
<th>Study</th>
<th>Manley 2014</th>
<th>Manley 2017</th>
<th>Kaushik</th>
<th>Kho</th>
<th>Konstantinova</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CKD stage</strong></td>
<td>CKD 4-5</td>
<td>CKD 4-5</td>
<td>HD</td>
<td>HD</td>
<td>Dialysis</td>
</tr>
<tr>
<td><strong>Number of patients</strong></td>
<td>30</td>
<td>42</td>
<td>100</td>
<td>22</td>
<td>70</td>
</tr>
<tr>
<td><strong>Dry mouth</strong></td>
<td>63%</td>
<td>90%</td>
<td>40%</td>
<td>32.9%</td>
<td></td>
</tr>
<tr>
<td><strong>Metallic taste</strong></td>
<td>33%</td>
<td>43%</td>
<td></td>
<td></td>
<td>31.4%</td>
</tr>
<tr>
<td><strong>Acidic taste</strong></td>
<td>23%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Bitter taste</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Mixture of tastes</strong></td>
<td></td>
<td></td>
<td>14%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>No taste</strong></td>
<td>13%</td>
<td>12%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Loss of taste</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>41%</td>
</tr>
<tr>
<td><strong>Taste change</strong></td>
<td></td>
<td></td>
<td>36%</td>
<td>31.7%</td>
<td>38.5%</td>
</tr>
<tr>
<td><strong>Malodour</strong></td>
<td></td>
<td></td>
<td>43%</td>
<td>34.1%</td>
<td></td>
</tr>
<tr>
<td><strong>Food aversion</strong></td>
<td>36%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Food cravings</strong></td>
<td>33%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Taste assessment tools
For the general population there are several methods of assessing taste.

Firstly, there are self-reporting questionnaires and Visual Analogue Scales.
In the general symptom assessment instruments commonly used in CKD, taste alteration does not appear as a symptom.

The IPOS-Renal instrument includes ‘dry or sore mouth’,

Dialysis Symptom Index includes ‘dry mouth’

Edmonton Symptom Assessment System (ESAS) (renal modified) does not refer to taste.
Karen Manley devised a Taste Questionnaire.

Impact of taste alteration in CKD patients
Whilst articles on the topic of CKD and taste frequently state that taste alterations can lead to an effect on quality of life, there is a dearth of literature in this area.
In terms of the effect of taste alterations on the nutritional status of patients with CKD, the main study found that taste alterations are independently associated with:

1. poorer indices of nutritional status and
2. increased all-cause mortality.

There is also a complex interaction between taste alterations and upper gastrointestinal symptoms such as anorexia, nausea, vomiting, early satiety and weight loss.

Manley KJ. Saliva Composition and Upper Gastrointestinal Symptoms in Chronic Kidney Disease. 
*J Renal Care* 2014; 40(3): 172-179.
The pathophysiology of taste changes in CKD
While an understanding of the pathophysiology of taste alteration in chronic kidney disease remains incomplete, several facts are known. Each of these phenomena contribute to taste alterations.
1. Changes in salivary flow
The literature on the rate of salivary flow in CKD is divided.

In a series of studies, patients with ESKD were found to have a reduced flow of saliva. Other investigators found no reduction in flow.


Patients with CKD may be susceptible to fluid overload or dehydration secondary to fluid restrictions and frequent use of diuretics. When body water content is reduced by 8% (about 3.5L for an average 70kg man), salivary flow decreases almost to zero.

This is particularly relevant for those treated with dialysis as this treatment results in substantial body fluid level fluctuations. The level of hydration is directly related to salivary secretion: dehydration leads to reduced salivary secretion and higher concentrations of salivary solutes.
2. Changes in salivary pH
Normal saline is slightly acidic.

Studies have consistently found that the saliva of patients with ESKD is more alkaline than people with normal renal function.

There are several reasons.

Firstly, the concentration of salivary urea is increased in CKD. Urea is broken down by oral bacterial ureases into ammonia, an alkali, and carbon dioxide.
Bacterial ureases

Urea + H₂O \rightarrow 2\text{NH}_3 (\text{Ammonia}) + \text{CO}_2
Another factor is the interface of urea and glucose metabolism.
In a fasting state, the metabolism of urea to ammonia elevates the salivary pH.

Once ingested, carbohydrates are metabolised, producing hydrogen ions leading to a fall in pH.

Initially, therefore, carbohydrate intake results in a decrease in pH. That pH shift is counteracted by the metabolism of urea into ammonia.

*In vitro* studies show that a small increase in urea results in a significant decrease in acidification by cells co-metabolising urea and glucose.

In the context of CKD, there is a significant increase in salivary urea levels. It is estimated that the production of hydrogen ions falls by up to 10 fold in patients in CKD.

3. Changes in salivary composition
<table>
<thead>
<tr>
<th></th>
<th>CKD saliva</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Na+</strong></td>
<td>Increased</td>
</tr>
<tr>
<td><strong>K+</strong></td>
<td>Increased</td>
</tr>
<tr>
<td><strong>Bicarbonate</strong></td>
<td>Increased</td>
</tr>
<tr>
<td><strong>Zinc</strong></td>
<td>No difference</td>
</tr>
<tr>
<td><strong>Urea</strong></td>
<td>Increased</td>
</tr>
</tbody>
</table>
The effect of salivary changes on specific tastes
<table>
<thead>
<tr>
<th></th>
<th>CKD saliva</th>
<th>Known changes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Na+</strong></td>
<td>Increased</td>
<td>Salty taste; in high levels reduces sweet taste.</td>
</tr>
<tr>
<td><strong>K+</strong></td>
<td>Increased</td>
<td>Metallic taste</td>
</tr>
<tr>
<td><strong>Bicarbonate</strong></td>
<td>Increased</td>
<td>Loss of sour and umami taste</td>
</tr>
<tr>
<td><strong>Zinc</strong></td>
<td>No difference</td>
<td></td>
</tr>
<tr>
<td><strong>Urea</strong></td>
<td>Increased</td>
<td>Spectrum from bitter taste to no taste. May also cause metallic taste.</td>
</tr>
</tbody>
</table>
High concentration of salivary bicarbonate

The level of salivary bicarbonate is inversely related to the intensity of umami (savoury) taste.


The combination of this and the elevation of salivary urea may explain the frequently observed lack of interest in meat by many CKD patients.
High concentration of salivary urea

The effect of high concentrations of salivary urea on taste is complex. In essence two observations have been made:
(a) a high concentration of salivary urea is associated with a bitter taste;
(b) the higher the concentration of salivary urea, the lower the perceived intensity of bitter taste.

Why is there such a spectrum of response?
First, high salivary urea stimulates the bitter-specific Type II receptor cells. The degree of sensitivity to bitter substances, such as urea, varies greatly. Most of the bitter taste receptors have genetic variations that increase or decrease the sensitivity of an individual to bitter compounds.

According to genetic variability, some people (the supertasters) have a heightened perception of bitter taste and others will be not perceive the bitterness.

Logically, therefore, within the CKD population there will be variations in sensitivity to elevated levels of salivary urea.
Another explanation may be that there is a biphasic response to urea.

Initially, there is a strong response to raised urea by the bitter-specific Type II cells that are genetically sensitive. These cells release ATP that stimulate, in turn, Type III cells which release 5HT that has an inhibitory effect on Type II cells, including bitter-specific cells.
Taste Cells and their interactions

Salt
Type I Cell

ATP degraded by surface ATPase

K^+

Sweet/ Bitter/ Umami
Type II Receptor Cell

ATP

Sour/ Salt
Type III Presynaptic Receptor Cell

5HT

NE

--- Stimulatory
----- Inhibitory

Afferent nerve fibres

Afferent nerve
Meat aversion
It has been observed that in patients with ESKD dietary protein intake spontaneously decreases. Many CKD patients describe an aversion to meat.

In a survey of patients with an eGFR < 25, 36 % reported that they avoided specific food, especially meat.
In a study by Bossola et al, the patients who reported a food aversion universally reported an aversion to meat.

The inability to identify umami (savoury) taste can explain this.

There are several possible reasons this may occur.
1. Glutamate has a major role in signalling protein-rich food. The concentration of salivary bicarbonate is inversely related to the ability to detect glutamate intensity and the liking of glutamate.

2. Salivary bicarbonate removes sodium ions. A reduction of sodium ion concentration decreases umami (savoury) perception.
3. The genetic variation in the perception of taste, including savoury taste.

4. Age, also may play a role; some elderly patients suffer from a specific loss of umami taste with preservation of the other tastes.
Summary of salivary changes in CKD

1. Changes in salivary flow.

2. Changes in salivary pH.

Management of taste alterations in CKD
The overall level of evidence of management strategies for taste alteration in CKD is low.

A recent Cochrane review of interventions for taste disturbance, including those secondary to CKD, concluded that there was a “very low – quality evidence” of all the interventions examined.

The only intervention that has been subject to randomised trials for CKD-induced taste disturbances is zinc.
In ESKD there is a lower concentration of serum zinc than normal controls.

One study found the prevalence of serum zinc level deficiency in haemodialysis patients was 40%.

One reason is a high removal in haemodialysis.

Zinc is important in the maturation, maintenance and repair of taste buds.

Theoretically, therefore, zinc deficiency may lead to a global diminution of taste.

However, the level of *salivary* zinc in CKD is not statistically different from controls.

The zinc studies

Two cross-over and one parallel arm trial studied the effects of zinc sulphate on taste disorders in CKD. Two parallel arm trials studied the effects of zinc acetate.

The authors of the Cochrane review of these studies concluded that, overall, there was “limited evidence” on the primary outcomes of taste acuity and discrimination and “is not conclusive in demonstrating improvement in taste perception.”

Mouth washes
Will mouth wash solutions of water, salt, sodium bicarbonate or citric acid improve upper GIT symptoms in CKD?

Manley K. *Nephrology* 2017; 22: 213-219
An interventional cross over study of CKD patients with an upper GIT symptom.

93 % reported taste changes.

Water; salt; Sodium bicarbonate; citric acid mouth washes were given to all patients in a randomised order.
Sodium bicarbonate produced the greatest improvement in taste and upper GIT symptoms.
In the absence of a significant body of literature two phenomena have quietly unfolded.
A. Based on observations over time, various remedies or interventions have been recommended by Renal Dieticians to manage taste changes.

These remedies have been largely empirical.
Sodium Bicarbonate mouth wash

1 teaspoon sodium bicarbonate mixed in 500 ml water

Rinse mouth out regularly throughout the day.
B. Patients and families have independently gravitated away from and towards certain foods and drinks.
Patients with taste alterations naturally shift their taste preferences.

Examples include the person with a bitter taste gravitating to sweet foods and drinks; the person with a salty taste avoiding salty foods; the person with an absence of taste preferring foods that stimulate some taste response, such as chilli or spices.
Whether based on professional advice or naturally reached, do these empirical approaches have a basis in the underlying pathophysiology?
For if they do
future management strategies
may not be simply waiting for
pharmacological interventions
but carefully adapting the diet according to mechanism.
The keyboard of taste
A significant challenge to a coherent approach to the management of taste alterations in CKD is the sheer heterogeneity of self-reported changes. It may be useful to think of tastes as keys on a piano. When a key is struck discordantly another key can be introduced to counteract or moderate the original sound.
A good example is bitterness. A bitter taste activated by raised salivary urea is highly discordant. Invariably patients avoid bitter tastants that enhance that note and gravitate to other keys, such as sweetness or sour. Sweetness, in particular, can completely suppress the bitter note.
Another example is taste absence. Here all major tastes keys appear to be inactivated.

People are drawn to minor keys, other channels of sensation, including chilli/spices activating the TRPV1 channel or cold activating the TRPM8 channel or may respond to stronger stimuli of one major key such as acidic foods, drinks and condiments activating sour taste.
We know, through the formal testing of taste perception in patients with CKD that, compared to controls, they have a poorer ability to perceive sour, umami (savoury), salty and bitter tastes.

In taste absence it may still be worthwhile giving a sweet tastant a trial.
Apart from sugar itself, what foods naturally contain carbohydrates that will trigger the sweet taste cell?
• Tomatoes (4% carbohydrate)
• Pumpkin (7%)
• Beetroot (10 %),
• Carrot (10%)
• Sweet potato (20%).
Another non-pharmacological approach...
It has been found that umami taste is enhanced by active tongue and pharyngeal movements (touching the tongue to the hard palate; swallowing), suggesting that there may be a central interaction between the taste afferent and tactile, kinaesthetic systems.

Summary of taste changes, proposed pathophysiological mechanism and empirical management in patients with CKD
<table>
<thead>
<tr>
<th>Taste change</th>
<th>Proposed Mechanism</th>
<th>Empirical management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salty taste</td>
<td>High concentration of salivary sodium stimulates Type I cells.</td>
<td>Salt restriction to change threshold. Sweet: in addition to classic sweet tastants consider foods containing carbohydrates.</td>
</tr>
</tbody>
</table>
Loss of taste
May be a complete loss of taste (aguesia) or the loss of individual taste(s).
Aguesia may be due to a mechanism affecting all taste buds or the suppression of all tastes by individual mechanisms.

<table>
<thead>
<tr>
<th>Attempt to enhance taste by:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Add herbs and spices, including chilli and pepper.</td>
</tr>
<tr>
<td>Activate sweet-specific Type II cells - cook with honey, tomatoes, fruit juices.</td>
</tr>
<tr>
<td>Activate Type III cells by</td>
</tr>
<tr>
<td><strong>Acidic foods</strong></td>
</tr>
<tr>
<td>Grains</td>
</tr>
<tr>
<td>Lentils</td>
</tr>
<tr>
<td>Kiwi fruit</td>
</tr>
<tr>
<td>Blueberries</td>
</tr>
</tbody>
</table>

Example: marinating meats, chicken or fish with spices or lemon juice.

Trial of zinc supplementation

Reduce sodium intake.
| Metallic taste | High concentration of potassium  
High concentration of urea.  
Urea converted, by bacterial ureases, into ammonia and CO2. | Avoid metallic cutlery.  
Sodium bicarbonate mouth washes.  
Prior to meals - menthol (mints), ginger beer, fruit juices, tea. |
| Bitter taste | High concentration of urea activates bitter-specific Type II cells. Note the genetic variability in sensitivity to urea. | *Avoid bitter tastants eg. coffee, chocolate, beer.*  
*The activation of sweet-sensitive Type II cells shuts down bitter taste. Increase sweet/carbohydrates in diet (cook with honey, fruit juices, tomatoes, beetroot, carrot).*  
*Activate Type III cells by acidic foods and drinks. Acidity enhances sour taste, counteracting bitter taste.* |
<table>
<thead>
<tr>
<th><strong>Loss of umami taste</strong></th>
<th><strong>High concentration of salivary bicarbonate (eg. cannot taste meat).</strong></th>
<th><strong>Acidic foods/ drinks (as above). Tongue movements</strong></th>
</tr>
</thead>
</table>

To what extent do these taste changes in CKD contribute to upper gastrointestinal symptoms?
In addition to the transmission of sensation of taste, taste buds initiate physiological reflexes that prepare the gastrointestinal system for absorption (releasing digestive enzymes, initiating peristalsis and increasing mesenteric blood flow) and other organs for metabolic activity, insulin release, and the sympathetic activation of brown adipose tissue.
Collectively these reflexes that are triggered by the sensations of taste, smell and sight of food are termed *cephalic reflexes*. 
There is also a complex interaction between taste alterations and upper gastrointestinal symptoms such as anorexia, nausea, vomiting, early satiety and weight loss.

Bitter tastes can precipitate nausea, vomiting and dry retching.

The perception of bitterness has a genetic basis and the subsequent upper GIT symptoms flow from that initial perception.

Bitter tastes can cause early satiety secondary to gastroparesis.

Nausea, vomiting and dry retching are not precipitated by sweet, sour or umami tastes.
Nausea can be precipitated by significantly raised salivary sodium and a significantly raised salivary Na+/K+ ratio.

Patients with markedly elevated salivary bicarbonate levels reported less dry retching and xerostomia.

Manley explained this by a reduction in taste sensitivity.

Anorexia is a complex symptom.

Lynch et al found a “strong association” between altered taste perception and decreased appetite.

Taste alterations in CKD patients are associated with poorer indices of nutritional status including protein energy malnutrition.

This, in turn, is associated with increased mortality.


So, while taste alterations are not the *only* cause for upper GIT symptoms, they do, when present, contribute to these symptoms.
Taste alteration

Anorexia

Nausea

Early satiety

Weight loss/malnutrition
Given:

• The close association of taste changes with upper GIT symptoms and
• The emerging understanding of the basic mechanisms of taste changes in CKD, it may be that basic interventions may not only improve taste perception but also upper GIT symptoms.
Conclusion

Over time, the understanding of the complex pathophysiology of human taste has matured considerably.

In contrast, the literature on the pathophysiology and management of taste alteration is more limited.
There are clear gaps in the literature generally, and in the specific context of CKD
Currently, this symptom does not appear in the commonly used symptom inventories for CKD patients, may be neglected by clinicians and, if addressed, is treated empirically.
Apart from zinc there is an absence of randomised trials of interventions.
Nevertheless, even in the absence of studies, patients and their families naturally gravitate away from vexatious tastes and towards food or drink that is more pleasant or, in the case of aguesia, more stimulatory.
Indeed, unlike other symptoms, the answer to the challenge of taste alterations in CKD patients may be based largely, if not solely, on a natural, rather than pharmacological, approach.
That is, an approach that involves a careful adjustment of diet based on a mechanistic understanding of the pathophysiology of individual and collective taste changes, taking advantage of the array of tastes and their interaction.
The primary clinical challenge for the discipline of nephrology is giving taste alteration a greater focus.
The primary research priority is the development and evaluation of strategies addressing this unpleasant and difficult symptom.