EluMed
YOUR DENTAL MEDICAL INFORMATION SUPPLEMENT
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Editorial

What a wonderful specialty is the Oral Surgery? What do you think should be the future of the oral surgery?

We train our students in Oral Surgery at the University/Hospital centers to allow them to manage several pathological conditions: extraction of impacted or non-restorable teeth; placement of dental implant in pristine bone; reconstruction of deficient bone and gum tissues before dental implant placement; treatment of tumors and pathologies of the oral mucosa and bone; infections of the oral cavity (teeth, gum and bone), salivary glands, and jaws; management of facial trauma sequelae such as intra-oral mucosal lacerations, fractured alveolar bones and traumatized teeth. All these treatments make the Oral Surgery a quite wide and never boring practice.

If we look at the daily professional life of an oral surgeon we could recognize a sort of dichotomy between what we are trained for and what we actually do in practice. If we think that our future relies on wisdom teeth and implants we would ignore the inevitable and tragic outcome. It might seem comfortable and remunerative for now, but would be that attractive for our students? The future of Oral Surgery will depend on one side from the remunerative profit and on the other side from our ability to project toward the expectations of our patients in terms of cooperation with the other medical branches.

That means that we as oral surgeons should be able to improve our knowledge and skills in treating medically compromised patients and to manage clinically demanding situations through an active and symbiotic relationship with all the medical fields.

We should never forget that the future relies on what we would be able to do now!!!

When the Editor of EluMed asked me to write an editorial on the dry mouth syndrome, I believed that this would be an ideal opportunity to provide an example of that. The dry mouth syndrome is caused by a reduction of salivary flow. The reduction of salivary flow could be associated to several diseases such as Sjögren's syndrome, HIV/AIDS and diabetes. Moreover, several drugs could cause a reduction of salivary flow, which has been also associated to radiotherapy and chemotherapy in patients affected by cancer. The clinician - who takes care of patients affected by dry mouth syndrome- should be tailored toward a robust knowledge of several medical conditions and drugs which could cause the reduction of salivary flow as well as an ability to interact with experts of several medical branches.

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Dry mouth

Xerostomia or dry mouth is not generally considered to be at the heart of dental surgery practice.

However, this symptom is gradually becoming a new challenge for health professionals. It affects approximately 20% of the general population and incidence is increasing in women and the elderly.

The accompanying change to quality of life (feeling of discomfort whilst chewing, swallowing and speech) emphasizes the importance of and the need for treatment. Furthermore, chronic forms can result in oral dental diseases developing, particularly an increased risk of dental decay, infections and changes to oral mucosa, especially candidiasis.

Given the social and demographic context (development of chronic diseases, ageing population, multi-medication etc.), dentists are, and will be in the future, increasingly confronted with this symptom and its treatment.

Xerostomia, a subjective symptom, must be well differentiated from true decreased salivary flow, which is objective. Making the difference lies in listening to and careful questioning of a patient preceding an appropriate clinical examination, supplemented if required with paraclinical examinations. It is his/her responsibility to identify this symptom and document associated decreased salivary flow.

Symptomatic treatments are available to treat dry mouth. Patients should be informed about rigorous dental hygiene and multi-annual regular monitoring by a practitioner.

Post-radiation xerostomia
(Dr D Gauzeran's collection)

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World Workshop on Oral Medicine VI: a systematic review of medication-induced salivary gland dysfunction: prevalence, diagnosis, and treatment.

SALIVA

1 PRIMARY CHARACTERISTICS

• **Biological, viscous liquid,** colourless. Its pH is either neutral or slightly alkaline, depending on secretion flow.

• **Hypoosmolar:** Osmolarity varies according to secretion flow; it is relatively low at baseline (30 mosm/L) and can increase up to 300 mosm/L.

• **Saliva production is ensured from the eight month in the womb**, by a set of salivary glands.

• **Primary saliva** whose ionic composition is similar to that of hypertonic plasma.

• **Definitive saliva** develops in excretory canals where active reabsorption of sodium and chloride occurs, and active secretion of bicarbonates and potassium.

Excretory canals are not very water permeable and ionic exchanges (active reabsorption of sodium) result in the formation of **a hypotonic liquid** in relation to plasma.

2 COMPOSITION

• **Composed of approximately 99.5% water** and 0.5% proteins, electrolytes, various bactericides and anti-microbial substances.

Electrolyte concentrations differ depending on salivary flow and hydration of the body and are essential for maintaining oral dental health and numerous oral functions (chewing, tasting, digestion, speech, etc.).

A. ORGANIC SUBSTANCES

Salivary amylase, is a glycoprotein that alters alpha1-4 glucosidic binding of starch with neutral pH, which releases maltose and glucosidic oligomers (dextrins). It is inhibited by gastric acid; salivary amylase represents 30% of salivary proteins.

It is mainly secreted by parotid glands, approximately 20% by submandibular glands and in very low quantities by sublingual and accessory glands.

Lysozyme, a minor glycolytic protein, is also a salivary enzyme with an antiseptic role. It represents 10% of total salivary proteins.

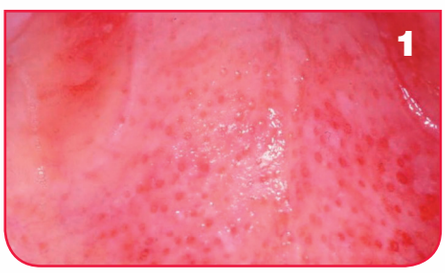
It inhibits the aggregation of mutant streptococcus and the fermentation of glucose.

Other salivary enzymes: kallikreins, collagenase of tissue origin, gelatinase, peroxidase, elastase, protease, lipase, cholinesterase and ribonuclease.

They can break down fat, carbon hydrates or proteins. In addition, some of them have anti-bacterial power.

Salivary mucins

These are large molecules which make saliva viscous. They are glycoproteins made from a set of proteins and carbon hydrates which are secreted mainly by sublingual and parotid glands.


1

They are involved in the formation of an acquired exogenous film and give saliva its lubricating capacity.

Plasmatic immunoglobulins (IgA, IgG and IgM)

are found in saliva by diffusion but they also contain secretory A immunoglobulins which have a fundamental role in antibacterial defences in the digestive tract

B. INORGANIC SUBSTANCES

These are sodium ions (Na^+), potassium (K^+), calcium (Ca^{2+}), hydrogen (H^+), chlorides (Cl^-), phosphates, bicarbonates, thiocyanates, halogens (iodine, fluoride) and metals (copper and iron). Only traces of copper, iron and fluoride are found. H^+ ions are responsible for salivary pH, and bicarbonate ions buffer it.

C. SEROUS SECRETION

It contains bactericide substances (thiocyanate), proteolytic enzymes (lysozymes), antibodies (IgA) and enzymes acting on starch (amylase).

D. MUCOUS SECRETION

It contains water and mucin. It lubricates and hydrates mucous, speech, swallowing, chewing and perception of taste.

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*Dans un souci didactique, la forme est adaptée à la ligne éditoriale de la revue, le fond étant scrupuleusement respecté.

E. SALIVARY FLOW

Normal salivary flow is 0.6 L/day, 90% secreted by the primary salivary glands, accessory glands, dispersed in oral mucosa, by providing 10%. Variation in flow occurs according to a circadian cycle, with a peak in late afternoon. Resting flow is 0.3-0.4 mL/minute and stimulated flow is 1.5 to 2 mL/minute.

Sub-mandibular glands produce 60% of resting saliva. Parotid glands produce serous saliva, which is rich in amylase and proteins rich in proline, whereas other glands produce saliva rich in mucins, which are more visco-elastic.

Image 1
Orifices for accessory palate salivary glands
(Dr D Gauzeran's collection)

Image 2
Lobules for accessory labial salivary glands
(Dr D Gauzeran's collection)

Points to remember...

- Saliva is made up of 99.5% water and its pH is either neutral or slightly alkaline.
- **Primary saliva** is defined as hypertonic and **definitive saliva** as hypotonic liquid.
- 30% of salivary proteins are **salivary amylase** and 10% are **lysozymes** which contribute to the antibacterial role of saliva.
- **Salivary mucins** give viscosity and lubricating capacity to saliva.
- **Normal salivary flow** is 0.6 L/day, 90% secreted by the primary salivary glands, accessory glands, dispersed in oral mucosa, by providing 10%. Variation in flow occurs according to a circadian cycle, with a peak in late afternoon. Resting flow is 0.3-0.4mL/minute and stimulated flow is 1.5 to 2 mL/minute.

XEROSTOMIA

1 PRIMARY CHARACTERISTICS

Salivary secretory malfunctions are defined as quantitative or qualitative changes to salivary secretion.

Xerostomia, a subjective feeling of a dry mouth felt by a patient is often correlated with a secretory malfunction (decreased salivary flow).

However, a decreased salivary flow is not always found in patients complaining of xerostomia, and conversely, some patients with severe decreased salivary flow do not complain of a dry mouth. Xerostomia is common in elderly subjects, and often remains untreated

Stress, depression and anxiety are often related to xerostomia.

Multi-medication often causes a reduction in salivary secretion, probably via a reduction in resting flow.

2 EPIDEMIOLOGY

Decreased salivary flow affects 5 to 40% of patients and its incidence tends to increase with age.

Multi-medicated patients are statistically significantly more affected than non-multi-medicated patients.

The increase in drug prescriptions encourages the prevalence of decreased salivary flow.

It is associated with several drug families: neuroleptic agents, antidepressants, anticholinergic agents, antihypertensives and serotonin reuptake inhibits, anti-Parkinson agents, oral antidiabetic agents, calcium channel inhibitors, NSAIDs, opioids, etc.

3 DIAGNOSIS

• Diagnosis is based on careful clinical assessment.

Questioning reveals dry mouth, problems swallowing or talking, hypersensitivity to acidic or spicy foods, dysgeusia, denture adaptation problems, etc. These symptoms can appear shortly after starting a new drug treatment or the opposite, can increase gradually with the taking of long-term medications.

• Xerostomia evaluation questionnaires exist

- → *Does the amount of saliva in your mouth seem insufficient, excessive or do you not notice it?*
- → *Do you have problems swallowing?*
- → *Does your mouth seem dry when you eat?*
- → *Do you have to drink a little water to help you swallow certain foods?*

Patients can also be asked about dryness of the throat, tongue, the level of thirst that is felt.

• Medical-surgical anamnesis and more specifically the taking of certain medications must be seriously raised. The existence of a systemic disease at the root of decreased salivary flow (Gougerot-Sjôgren syndrome, amyloidosis, sarcoidosis) or a therapy (history of cervico-facial radiation) must be reported.

• The extra and intra-oral examination includes:

the palpation of primary salivary glands, with the expulsion of saliva from primary excretory canals, the examination of mucosa and of teeth.

No clinical signs exist that can determine the causes of decreased salivary flow. However, a clear response to a stimulus means no irreversible effect on secretory potential and can be in favour of a diagnosis of a malfunction induced by medications.

• An oral dryness score can be established, depending on the existence/absence of the following clinical signs:

- → *mirror stuck to oral mucosa in examination*
- → *the mirror sticks to the tongue*
- → *foamy saliva*
- → *absence of saliva on floor of mouth*
- → *bald tongue*
- → *the gum has lost its "orange peel" appearance and is altered*
- → *mucosa appears smooth and glossy*
- → *the tongue is lobulated or cracked*
- → *cervical decay on more than 2 teeth*
- → *existence of mucosa deposits on the palate (in the absence of an adjoining maxillary denture).*

4 SUPPLEMENTARY CLINICAL EXAMINATIONS

A- MEASUREMENT OF SALIVARY FLOW (SIALOMETRY)

In general, with decreased salivary flow induced by medications, the total resting flow is reduced whereas stimulated flow is unchanged.

However, some anticholinergic or central analgesic agents cause a reduction in saliva, both resting and stimulated.

1 COLLECTION METHODS FOR TOTAL SALIVA

Non-painful and not invasive.

Saliva is generally collected in the morning, over 5 minutes.

Too short a period (< 1 minute) or too long a period (>15 minutes) does not enable good reproducibility.

Patients must abstain from drinking, eating or smoking two hours before the examination.

Measurement of total non-stimulated salivary flow

1st method:
The patient is always in a seated position. Either the patient spits out instead of swallowing saliva that he/she excretes, or a suction system takes saliva from the floor of the mouth.

The quantity of saliva is measured in a graduated tube. Non stimulated salivary flow less than 1.5mL/15min is considered to be pathological.

2nd method:
The other technique involves placing cotton buds or compresses in the mouth; these are weighed before and then after

5 minutes, with the salivary volume secreted being obtained by converting the weight unit into a unit of capacity.
A mass gain less than 2.5 g means insufficient salivary flow (Saxon method).

Measurement of total stimulated salivary flow

The patient has to chew a piece of paraffin or unscented chewing gum, in a calibrated way (for example 70 cycles per minute).

Saliva is collected at fixed intervals in a graduated cylinder.
Regarding stimulated salivary flow, this is considered to be pathological if flow is less than 3,5mL/15min.

Stimulated salivary flow can also be obtained by using a 2% citric acid solution applied to the edges of the tongue every 30 seconds.

The sugar test involves allowing a lump of sugar n°4 to dissolve. The result must normally be obtained in less than 3 minutes. This indicative test is not painful and is easy to perform but does not measure resting salivary flow, in fact the sugar triggers a gustatory stimulation.

SELECTIVE MEASUREMENT OF FLOW

is generally reserved for clinical studies or specialised salivary disease consultations.

It can demonstrate hypo-functioning of a salivary gland in particular.

Saliva collection is done by positioning small specific cups in the orifices of excretory canals (Lashley cups). These cups are connected to a suction system.

2 ANALYSIS OF SALIVARY COMPOSITION

Its constituents vary according to the nycto-hemeral period and the stimulation or non-stimulation of salivary glands.

Similarly, variations in salivary composition can reflect electrolytic disturbances in the acinus, protein or aqueous secretion disorders or excretory canal malfunctions.

The influence of medications on salivary composition has been poorly documented, except for chemotherapy where it has been shown that it causes an increase in salivary levels of sodium and chloride and a reduction in inorganic phosphates. This would tend to demonstrate that acinus and ductal cells are affected by chemotherapy.

Antihistamines, antidepressants and beta-blockers seem to affect salivary composition.

B- OTHER EXAMINATIONS

Ultrasound (anatomical and functional imaging). It assesses the size of salivary glands and the homogeneity of tissue.

Sialography and scintigraphy of salivary glands. They assess the functioning of salivary glands.

Biopsy of accessory salivary glands remains a highly specific test for the diagnosis of Gougerot-Sjôgren syndrome.

5 THERAPEUTIC STRATEGY

It is recommended testing for decreased salivary flow and proposing symptomatic or curative treatments for this debilitating disease and informing patients about regular multi-annual checks.

- **Adaptation of drug treatment responsible for decreased salivary flow**, if possible, must occur. This can involve a dose adaptation (dose reduction), reduction in the number of medicines taken by a patient or changes to the drug pharmaceutical form (particularly for medicines where a sustained release form exists). It has been shown that above 2 to 3 medicines that the risk of developing decreased salivary flow is significantly increased.

- **Parasympathomimetics** are the most common medicines to stimulate salivary glands. Stimulation requires a residual secretory potential, with functional glandular tissue.

The usual dose is 5mg up to 3 times a day and for at least 3 months, before the effect of treatment can be evaluated. Possible side effects are nausea, vomiting, diarrhoea, increased sweating, bronchoconstriction, cutaneous vasodilation, bradycardia, hypotension and visual accommodation disorders.

Prescribing these to asthmatic patients or patients with a cardiovascular or chronic pulmonary disease must be done with care. Before prescribing parasympathomimetics, the absence of a contra-indication should be checked with the treating physician and the persistence of secretory potential should be evaluated (chewing gum).

- **Several topical treatments exist** (salivary substitutes) on the market. These are very useful palliative methods because these substitutes help to humidify and lubricate the oral sphere by imitating saliva.

They contain agents that increase viscosity, such as hydroxyethyl cellulose or carboxymethyl cellulose, mucins or xanthan gum, minerals (calcium, phosphate ions and fluorides), preservatives and flavourings.

Several studies have demonstrated a significant difference between mucin sprays and a placebo in the treatment of xerostomia.

These substitutes are very widely used, including in patients with a significant change to their general condition.

Homoeopathy and phytotherapy treatments exist but are controversial because they are difficult to evaluate.

- **The following can also be recommended and/or envisaged:**

hydration, bicarbonate hydration, dietary adaptation, use of sialogogues, use of lubricants/salivary substitutes, improved oral hygiene and prevention of dental decay.

- **Prevention of dental decay involves:**

→ *strict control of dietary and oral hygiene, bicarbonate mouth washes,*

→ *the use of a high fluoride content toothpaste,*

→ *fluorination.*

- **Therapeutic strategy: points to remember...**

→ adaptation of drug treatment responsible for decreased salivary flow (if possible)

→ use of sialogogues and/or lubricants/salivary substitutes

→ adaptation of dietary hygiene (bicarbonate hydration);

→ strict oral dental hygiene combined with the prevention of dental decay

(high fluoride content toothpaste and/or fluorination).

Extracted from **"Management of hyposalivation and xerostomia:** criteria for treatment strategies."

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1 BIOLOGICAL FUNCTIONS OF SALIVA:

ON AN INTRAORAL LEVEL:

- Humidification of oral surfaces, cleaning, bolus training
- Lubrication (mucins): speech, swallowing, prosthetic functionalities
- Natural barrier (mucins, humidification)
- Protection of mucosa (mucins): growth factors, hydration; ease of tissue repair
- Anti-microbial effect: limits bacterial adherence, existence of antibodies
- Protection of hard tissue: pH, remineralisation, cleaning.

OTHER FUNCTIONS:

- Initiates digestion; social role; elimination of certain medicines
- Subjective functions: comfort, regulation of feeling of thirst, tasting…

2 SPECIFICATIONS FOR A SALIVARY SUBSTITUTE:

- **Rapid relief**
- **Lasting effect**
- **Continuous application system**
- **Improved secretion**
- **Pleasant**
- **Non-irritating**
- **Non-allergenic**
- **Alcohol free**
- **Non-sensitizing**
- **Moderate taste**
- **No risk of infection**
- **No systemic side effects**
- **Practical (packaging, storage, transport)**
- **Low cost**
- **Accessible.**

Extracted from **"Systematic literature review:** xerostomia in advanced cancer patients."

S. **HANCHANALE,** L. **ADKINSON,** S. **DANIEL,** M. **FLEMING,** S.G. **OXBERRY**

Support Care Cancer (2015) 23:881–888

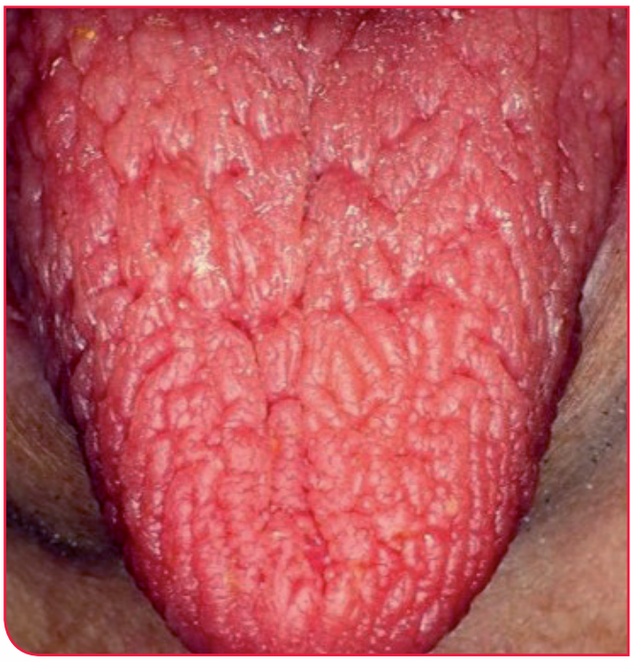
Decreased salivary flow is the **second major complaint** (after chronic fatigue) in patients treated with radiotherapy for cancer in the upper digestive tract (UDT) due to its impact on quality of life. Various therapies can be proposed, but the specific context and the aetiology of decreased salivary flow modify efficacy.

A visual analogue scale evaluated improvements made by these therapies.

"Artificial" saliva or salivary substitute versus parasympathomimetics:
The efficacy of parasympathomimetics seemed better, however accessibility (pharmaceutical form, no additional tablets taken) made "artificial" saliva interesting.

The various treatments proposed have variable efficacy, and the patient profile as well as his/her choice must be taken into account in the therapeutic proposition.

Decreased salivary flow of drug origin
(Dr D. Gauzeran's collection)



Xerostomia due to systemic disease: a review of 20 conditions and mechanisms.

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1 MECHANISMS OF XEROSTOMIA RELATED TO SYSTEMIC DISEASES

MECHANISM	DISEASE
Neuropathic	Diabetes Parkinson's disease
Immune and inflammatory -mediated	Viral infections HIV EBV CMV HTLV-1 GVHD Rheumatoid arthritis Primary biliary cirrhosis SLE Scleroderma Autoimmune thyroid diseases
Granulomatous reaction	Tuberculosis Sarcoidosis
Storage of substances	Hemochromatosis Amyloidosis
Dehydratation	ESRD Diabetes
Alteration in salivary gland structure	Scleroderma Hemochromatosis Amyloidosis Actinomycosis GVHD CMV infection
Genetic disorder	Ectodermal dysplasia

NA: Not assigned,
SLE: Systemic lupus erythematosus,
GVHD: Graft-versus-host disease,
ESRD: End stage renal disease,
HIV: Human immunodeficiency virus,
HCV: Hepatitis C virus,
EBV: Epstein-Barr virus,
CMV: Cytomegalovirus,
HTLV-1: Human T-lymphotropic virus type 1

2 INCIDENCE OR PREVALENCE OF XEROSTOMIA DUE TO SYSTEMIC DISEASES

SYSTEMIC DISEASE	PREVALENCE OR INCIDENCE OF RELATED XEROSTOMIA
Diabetes type 1	38.5-53
Diabetes type 2	14-62
Viral infections	
HIV	1.2-40
HCV	5-55
EBV	NA
CMV	NA
HTLV-1	3.8-36.7
Autoimmune thyroid disease	NA
ESRD	28-59
Rheumatoid arthritis	NA
Primary biliary cirrhosis	47-73
Ectodermal dysplasia	33,3
GVHD	16-59
Hemochromatosis	NA
Parkinson's disease	NA
Sarcoidosis	6
Tuberculosis	NA
SLE	75
Amyloidosis	NA
Actinomycosis	NA

Demineralisation in a context of decreased salivary flow
(Dr D Gamm's collection)

Opinion

We are not sufficiently aware of it but our daily well-being also depends on satisfactory quantitative and qualitative salivary secretion, which is essential to daily activities. Whether related to old age, a disease or the consequences of various therapies, the absence or reduction in salivary flow is rapidly a source of major discomfort and oral dental problems for patients.

Xerostomia is experienced as a feeling of a dry mouth. In most cases, but not always, it is accompanied by true decreased salivary flow (reduction in salivary flow). It is estimated that at least 10 to 15% of the population is affected by xerostomia, with most being women.

The impact is major in terms of quality of life, particularly as the pathway for these patients is complex. They complain of pain, tingling or burning of oral mucosa and even bad breath. These patients come to see us regularly after having consulted with several colleagues who, given the absence of clear symptoms and the difficulty of diagnosis, sometimes only advise psychological care.

This is often poorly accepted by patients, although not lacking in sleep, therefore chronic fatigue, speech and swallowing difficulties. Therefore, patients frequently develop an avoidance strategy during meals (elimination of certain foods, refusal to go to restaurants, etc.), thereby compromising their social life. The comprehension of the aetiology and the physical and psychological impact of decreased salivary flow can propose a solution or customized therapeutic assistance. With decreased salivary flow due to Gougerot-Sjogren syndrome, the use of targeted therapies (monoclonal antibodies) seems to significantly improve oro-salivary parameters for these patients but this remains to be confirmed. Stem cell research may also provide a decisive advance but in the not too distant future.

In the interim, a treatment strategy for patients with xerostomia lies in early testing, information and therapeutic education for patients and the use of preventive or palliative therapies faced with predictable consequences of true decreased salivary flow.

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