

Loss of smell and COVID-19: Anatomical and physiological considerations

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Abstract— *There are numerous conflicting discussions about the outbreak of the new coronavirus (COVID-19). This letter to the editor presents some anatomical and physiological considerations regarding one of the symptoms reported by patients: the loss or reduction of smell, based on recent descriptions and studies, and aims to stimulate knowledge and debate on this topic.*

Keywords— *Coronavirus covid-19, covid-19, loss smell, olfactory nerve, covid-19 pandemic.*

In December 2019 it was observed the emergence of a new disease in Wuan (China) that is related to the development of pneumonia and in more severe cases it can lead to death. Since then, the international scientific community has been mobilizing to describe this pathology in terms of how it is contagious, how to prevent it and what are the possible treatments (GUO et al., 2020). All of this aroused more interest as of January 30, 2020, a date that the World Health Organization (WHO) officially declared the epidemic COVID-19 as a public health emergency of international interest. Following the increase in the number of cases and the spread to several continents, on 11 March 2020, WHO declared the Covid-19 pandemic (JIANG et al., 2020).

At that time, due to the transmission between people, there was an increase in the rate of spread of the virus and half of the affected countries recorded the first cases of Covid-19 in the ten days prior to that date. In the past two weeks, according to WHO, the number of cases outside China has increased 13 times and the number of affected countries has tripled. There were already more than 118,000 cases worldwide and 4,291 deaths (WU et al., 2020).

3,917,366 cases of COVID-19 and 274,361 deaths were confirmed worldwide until May 10, 2020. The ways of protection are the same as those used to prevent common respiratory diseases, such as seeking medical attention in case of fever, cough and difficulty breathing; describe travel history and contact with others in recent days; wash hands frequently with soap and water or 70% V / V alcohol-based hand sanitizers; cover the mouth when sneezing or coughing and always with elbow flexed. (LIVINGSTON; BUCHER; REKITO, 2020).

SARS-CoV-2 (virus that causes COVID-19 disease), can be transmitted from one sick person to another or by close contact through an aerosol caused by sneezing, interpersonal touches such as handshaking, saliva, aerosol caused by coughing, phlegm or touching contaminated objects or surfaces (door handles, handrails, cell phones and others) (GUO et al., 2020; LAI et al., 2020).

Early diagnosis is one of the ways to prevent dissemination. Germany, through early detection with an increase in the number of COVID-19 tests to 500,000 per week, helped to keep the number of deaths relatively low (LESCURE et al., 2020). This fact can be explained by the

performance of many laboratory diagnoses, such as molecular biology exams (real-time RT-PCR) used to diagnose COVID-19, Influenza or the presence of Respiratory Syncytial Virus (RSV), and the immunological (rapid test), which detects the presence of antibodies or not (HELMY et al., 2020; LESCURE et al., 2020).

One of the first reported symptoms is the reduction or loss of smell. Smell is a type of special sensitivity captured by nerve endings of the olfactory nerve, the first cranial nerve pair, which originates in numerous small nerve bundles located in the upper third of the nasal cavity and upper third of the nasal septum (olfactory type mucosa) (DOTY et al., 2004; BUCHAIM; ISSA, 2018). The primary neurons (neuron I) are the olfactory cells themselves, bipolar neurons located in the olfactory mucosa of the nasal cavity, whose small peripheral extensions end in dilations called olfactory vesicles. The central prolongations, which are of the unmyelinated type, form filaments consisting of a cluster of olfactory bundles, which together constitute the olfactory nerve (MACHADO; HAERTEL, 2013).

Primary olfactory neurons are stimulated by odorants, that is, chemicals from the air that are transformed into action potentials (JOHN H. MARTIN, 2013). After this stimulus is received, the special visceral afferent fibers that make up the olfactory nerve pass through several foramina called cribriforms that form the cribriform lamina of the ethmoid bone (BUCHAIM; ISSA, 2018). In this way they gain access to the anterior cavity of the skull where they synapse with the secondary neuron (neuron II), which are called mitral cells, whose branched dendrites synapse with the also branched central extensions of neuron I, constituting their shape called the glomerulus olfactory (WILLIAMS et al., 1995).

At this synapse site, an enlargement of the olfactory nerve called the olfactory bulb is formed. The projections of these secondary neurons (mitral cells) are myelinated axons that pass through the olfactory tract, gaining the lateral and medial olfactory streaks directly to the primitive allocortex on the anterior face of the cerebral hemispheres. The conscious olfactory nerve impulses end in the uncus (primary cortical projection area), corresponding to the piriform cortex. From there, it projects into the thalamus, which then goes on to the straight and olfactory gyres (orbitofrontal). Smells that can be associated with emotions such as aversion or pleasure are projected into the limbic system (WILLIAMS et al., 1995; JOHN H. MARTIN, 2013; MACHADO; HAERTEL, 2013; BUCHAIM; ISSA, 2018).

Olfactory sensitivity has some peculiarities, such as: having only two neurons from reception to cortical projection; the primary neuron is not located in a ganglion, but in the upper third of the nasal cavity; be homolateral for projection; nerve impulses go directly to the cortex without first passing through the thalamus; projection towards the allocortex instead of the isocortex, as occurs in other ways (MACHADO; HAERTEL, 2013).

The anatomical description can help to understand the path of the SARS-CoV-2 virus and the development of anosmia, a technical term used for the loss or absence of smell, also present in craniocerebral trauma with ethmoid fracture. Could this be the way of the virus to neuronal destruction in the Central Nervous System? It is estimated that 30% of those people infected with the new coronavirus have neurological manifestations such as loss of taste and smell, mental confusion, stroke and muscle pain unrelated to any muscle injury (MAO et al., 2020; RAMOS et al., 2020; SHEEHY, 2020).

The advancement of clinical and experimental research may answer even more questions such as: how often is this symptom? What is the recovery time for smell? With the partial loss of smell should the person be in social isolation? What is the action of retrovirals such as Valacyclovir, an antiviral medication used to treat infections caused by the herpes simplex virus and the varicella-zoster virus, such as herpes zoster and genital herpes (CHEEMA et al., 2020)? Physical therapies by photobiomodulation are effective in nerve repair and could accelerate recovery (BUCHAIM et al., 2015, 2016, 2017; DE OLIVEIRA ROSSO et al., 2017; ROSSO et al., 2017, 2018)?

COVID-19 is perhaps the biggest confrontation of world science in the last 100 years since the Spanish flu. At this moment, many questions are still unanswered or there are prospects for an answer soon. We hope that this challenge will be overcome, mainly with the discovery of vaccines (many are already in laboratory tests or are already being tested in humans). May science win!

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