# CLINICAL RESEARCH PROTOCOL TO EVALUATE THE EFFECTIVENESS AND SAFETY OF INDIVIDUALIZED HOMEOPATHIC MEDICINE IN THE TREATMENT AND PREVENTION OF THE COVID-19 EPIDEMIC

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**Clinical research protocol to evaluate the effectiveness and safety of individualized homeopathic medicine in the treatment and prevention of the COVID-19 epidemic.**


## Abstract

In addition to the recognized application in chronic diseases, individualized homeopathy can also act in a resolutive or complementary way in acute cases, including epidemic diseases. However, to achieve this intent, it presents a specific semiologic and therapeutic methodology that must be followed and respected, with the risk of not presenting the desired efficacy and safety. In the case of epidemic diseases, which due to the virulence of their agents causes a common symptomatological picture in most susceptible individuals, the individualized homeopathic medicine *(homeopathic medicine of the epidemic genius)* should present similarity with the set of characteristic symptoms and signs of the patients affected in the different stages of each epidemic outbreak. Studies show the efficacy and safety of this prophylactic and/or therapeutic practice in several epidemics of the past. Therefore, after the survey of possible homeopathic drugs individualized from the epidemic genius of each epidemic, its prophylactic and/or large-scale therapeutic application should be supported by previous clinical trials that demonstrate its efficacy and safety, in line with the ethical and bioethical aspects of research involving human beings. Fulfilling these premises of good clinical practice, we developed the current protocol with the objective of investigating, in a randomized, double-blind and placebo-controlled clinical trial, the effectiveness and safety of possible individualized homeopathic drugs of epidemic genius of COVID-19, in adjuvant and complementary treatment of patients affected by the disease. If effectiveness and safety are confirmed, and only in this condition, the medicine may be used in a generalized and collective manner in the treatment and prevention of the current epidemic.



**Keywords:** Homeopathy; Epidemics; Epidemic genius; Ethics in research; Randomised controlled clinical trial; COVID-19.

## SUMMARY

# I. INTRODUCTION

Coronavirus is a family of viruses that can cause damage to animals and humans. In humans, it can result in respiratory infections ranging from a cold to severe acute respiratory syndromes. The new coronavirus (SARS-Cov-2 or 2019-nCoV) produces the disease classified as COVID-19, which started in the city of Wuhan (China) in December 2019.

In the clinical management of cases of human infection by SARS-CoV-2, there are still no effective therapeutic measures, and many details remain to be clarified. However, it is known that the virus has high transmissibility and can cause acute respiratory syndrome ranging from asymptomatic or mild cases (around 80%) to very severe cases with respiratory failure (around 5% to 10%). Its lethality varies, mainly, according to the age group and associated comorbidities.

As there is currently no vaccine for COVID-19 prophylaxis, the best form of prevention is to avoid exposure to coronavirus through hygienic-prophylactic measures (constant hand washing, avoiding contact with infected people and agglomerations, among others).

In view of this lack of specific treatment and / or vaccine that can be used to control and / or prevent the current epidemic, respectively, the search for other therapeutic and preventive approaches is necessary, in order to minimize the harmful consequences of this pandemic outbreak that plagues humanity. Therefore, homeopathy can be a complementary and adjuvant alternative to existing hygienic-prophylactic measures and to the existing therapeutic arsenal, and can be used as a measure to promote the health of the population, provided that the safety and effectiveness of its proposals are scientifically validated.

Medical specialty recognized by the Federal Council of Medicine (CFM) of Brasil since 1980, homeopathy is taught to doctors in the form of post-graduation lato sensu and, since 2004, medical residency. With established scientific assumptions (principle of therapeutic similarity, homeopathic pathogenetic experimentation and use of individualized and potentized medicines) and broad and secular application, it presents a growing body of

evidence in the field of basic and clinical research (Teixeira, 2011a, 2018, 2019; Cremesp, 2017a, 2017b, 2017c).

Using an integrative approach in the diagnosis and treatment of organic disorders (mental, general and private), homeopathy can act preventively in most of the acute or chronic diseases, ahead of the process of their installation. To accomplish this goal, the homeopathic medicine must stimulate a systemic and homeostatic reaction of the organism against the various susceptibilities that predisposes to illness, being essential to select an individualized medicine according to the totality of signs and symptoms characteristic of each sick individual.

In addition to its recognized application in chronic diseases, individualized homeopathy can also act in a resolutive or complementary manner in acute cases, including epidemic diseases. However, to achieve this goal, it presents a specific semiological and therapeutic methodology that must be followed and respected, with the risk of not presenting the desired efficacy and safety.

In the case of epidemic diseases, which, due to the virulence of their agents, causes a common symptom picture in most susceptible individuals, the individualized homeopathic medicine (homeopathic medicine of the epidemic genius) must show similarity with the set of signs and symptoms of patients affected at different stages. or phases of each epidemic outbreak. Studies show the effectiveness and safety of this prophylactic and / or therapeutic practice in several past epidemics (Teixeira 2009a, 2010a, 2013a, 2014, 2015a, 2015b).

Therefore, after surveying the possible individualized homeopathic medicines of the epidemic genius of each epidemic, their prophylactic and / or therapeutic application on a large scale must be supported by previous clinical trials that demonstrate their efficacy and safety (Dantas et al., 2008), in line with the ethical and bioethical aspects of research involving human beings (Brasil, 2012).

Fulfilling these premises of good clinical practice, the current protocol aims to investigate, in a randomized, double-blind, placebo-controlled clinical trial, the gold standard of clinical epidemiology (Oliveira et al., 2015), the efficacy and safety of possible individualized homeopathic medicines of the epidemic genius of COVID-19, indicated for adjuvant and complementary treatment of patients affected by the disease.

If the hypothesis is confirmed, and only in this condition, the medicine can be used in a generalized and collective way in the treatment and prevention of the current epidemic (Brasil, 2012).

On the other hand, in order for us to execute this and other research protocols, necessary for the scientific basis of the assumptions and proposals for homeopathic treatment, an impartial posture on the part of doctors, researchers and teachers is necessary, allowing rational and scientific space to propose, discuss and apply its projects in research institutions and health services.

# II. LITERATURE REVISION

## II.1. COVID-19 epidemic

Coronaviruses cause respiratory and intestinal infections in humans and animals; being that the majority of coronavirus infections in humans are caused by species of low pathogenicity, leading to the development of mild respiratory symptoms; however, they can eventually cause serious infections in high-risk groups, the elderly and children.

Prior to 2019, two highly pathogenic and animal-derived coronavirus species (SARS-CoV and MERS-CoV) were responsible for outbreaks of severe acute respiratory syndromes. In the current human infection with the new coronavirus (SARS-Cov-2 or 2019-nCoV), the clinical spectrum is not completely described, as well as its pattern of infectivity, transmissibility, morbidity and mortality, is not known. There is still no vaccine or specific drugs available and, currently, the treatment is basic and non-specific support (Brazil, 2020).

Analogously to what has been happening in dozens of other countries, in several continents, the sustained spread from person to person (community) is occurring in Brazil, transmitted through respiratory droplets of infected people, similar to the way influenza and other respiratory pathogens spread. Analogously to the SARS-CoV and MERS-CoV outbreaks of the past, health professionals have represented a significant portion of the number of cases infected by SARS-Cov-2, acting as possible vectors in the spread and amplification of this epidemic.

The average incubation period for SARS-Cov-2 infection is 5-6 days, with an interval that can reach up to 14 days. In turn, the average transmission period for infected patients is seven days after the onset of symptoms; however, infected and asymptomatic individuals can also transmit the virus (Brasil, 2020).

The clinical spectrum of coronavirus infection is very broad, ranging from a simple cold to severe and fatal pneumonia. As we will see below, knowledge of the signs and symptoms of each epidemic is indispensable for choosing the respective individualized homeopathic medicine of the epidemic genius.

In general, the clinical signs and symptoms referred are mainly respiratory (fever, cough and difficulty breathing). The evaluation of dozens of patients with

pneumonia and laboratory diagnosis of SARS-Cov-2 infection admitted to the Wuhan Jin Yin-tan Hospital (Wuhan, China) points to a higher rate of hospitalization in male patients over 50 years. The main symptoms observed were fever, cough, shortness of breath, muscle pain, mental confusion, headache, sore throat, rhinorrhea, chest pain, diarrhea, nausea and vomiting. Imaging tests showed that most patients had bilateral pneumonia (Chen et al., 2020).

According to a report by the joint WHO-China mission on COVID-19 (WHO, 2020) released in February/2020, based on tens of thousands of cases with laboratory confirmation, typical signs and symptoms included fever, dry cough, fatigue, production phlegm, shortness of breath, sore throat, headache, myalgia, arthralgia, chills, nausea, vomiting, nasal congestion, diarrhea, hemoptysis and conjunctival congestion.

That report showed that the majority of people infected with the SARS-Cov-2 virus developed mild illness and recovered. Around 80% of infected patients had mild to moderate disease, including cases with and without pneumonia, 13.8% had severe disease and 6.1% reached critical and fatal states. Among the individuals most at risk of developing severe cases were the elderly (over 60 years old) and those with chronic diseases, such as hypertension, diabetes, cardiovascular diseases, chronic respiratory diseases and cancer. (WHO, 2020)

In this retrospective study, the gross mortality rate (CFR) was 3.8%, varying with the location and intensity of transmission (ie 5.8% in Wuhan vs. 0.7% in other areas in China) . The CFR was higher in the early stages of the outbreak, halving after one month of the disease. (WHO, 2020)

As prevention and control measures, in view of the absence of a vaccine or other treatment, the Ministry of Health (Brasil, 2020) recommends daily preventive actions that can assist in the prophylaxis of the spread of respiratory viruses in general, such as: frequent hygiene of hands with soap and water or alcoholic preparation; avoid touching eyes, nose and mouth without proper hand hygiene; avoid close contact with sick people; cover your mouth and nose when coughing or sneezing; stay at home and avoid contact with people when you are sick; clean and disinfect frequently touched objects and surfaces, among others.

It is worth mentioning that the economic and social impacts caused by COVID-19 will be of great magnitude and directly proportional to the duration of the epidemic, given that social isolation is the only preventive measure to control the spread of the virus. Therefore, proposals that have the potential to assist in the prophylaxis and / or treatment of SARS-Cov-2 infection should be tried, as long as they are easy to implement and do not cause risks to the population. Homeopathy fits this profile.

## II.2. Homeopathy

### II.2.1. Introduction

Homeopathy is a therapeutic model employed worldwide and that has awakened in recent decades, along with other approaches to integrative medicine, the growing interest of users, medical students and physicians (Teixeira et al., 2004, 2005; Teixeira and Lin, 2013), in order to be a safe and efficient medical practice, proposing to understand and treat the disease-patient binomial according to a vitalistic, globalizing and humanistic anthropological approach (Teixeira, 2009b, 2017a), valuing the various aspects of sick individuality.

Founded by the German physician Samuel Hahnemann in 1796, homeopathy is a medical specialty recognized by the Federal Council of Medicine (CFM) of Brazil since 1980 (Resolution CFM Nº 1000/1980), with the title of specialist conferred by the Brazilian Medical Association (AMB) since 1990 (Resolution CFM Nº 2.068/2013). (Teixeira, 2019)

Developing its activities in parallel to conventional and hegemonic medicine, it disseminates its theoretical, practical and scientific rationality in lato sensu postgraduate courses, taught by training entities linked to the Brazilian Homeopathic Medical Association (AMHB). In 2004, after Resolution CFM nº 1634/2002, was offered in the medical residency program of the Federal University of the State of Rio de Janeiro (UNIRIO - University Hospital Gaffrée e Guinle). Currently, two more medical residency programs offer homeopathy as a service training option (Regional Public Hospital of Betim, Minas Gerais, since 2014; Federal University of Mato Grosso do Sul, since 2015). (Teixeira, 2019)

Although it has existed for more than two centuries as a therapeutic option in several countries, homeopathy remains marginalized in the face of modern scientific rationality, because it is based on unorthodox concepts that challenge the dominant biomedical thought.

The homeopathic treatment model employs the principle of cure by similarity, administering infinitesimal doses of single and individualized medications that, having been previously tried in healthy individuals, caused symptoms similar to those of sick individuals. To become a homeopathic medicine, the substance must undergo pathogenetic experimentation protocols in humans and have its primary effects described in Homeopathic Materia Medica. (Teixeira, 2011a, 2013e, 2019)

In short, homeopathic scientific rationality is based on four pillars or epistemological premises: (1) principle of therapeutic similarity, (2) homeopathic pathogenetic trial or experimentation, (3) dynamized or potentized medicine (ultra-high dilutions) and (4) individualised medicine according to symptomatic totality (therapeutic individualization).

### II.2.2. Epistemological premises of the homeopathic model

#### *II.2.2.1. Principle of therapeutic similarity*

Based on the study of the pharmacological properties of dozens of drugs of his time, in which he observed a secondary reaction (indirect effect) of the organism after the primary action (direct effect) of several classes of drugs, Hahnemann reported an aphorism for the action of drugs in the human constitution.

> "Every agent that acts upon the vitality, every medicine, deranges more or less the vital force, and causes a certain alteration in the health of the individual for a longer or a shorter period. This is termed *primary action*. […]. To its action our vital force endeavors to oppose its own energy. This resistant action is a property, is indeed an automatic action of our life-preserving power, which goes by the name of *secondary action* or counteraction." (Hahnemann, 1995, § 63)

Illustrating this phenomenon or natural law, Hahnemann describes the 'primary action' of the drugs of his time, promoting changes in the various physiological systems, and the consequent 'secondary action' of the organism (vital reaction or life-preserving power), which manifests itself in order to neutralize the

primary disorders promoted by drugs, seeking to return to homeostatic balance prior to drug intervention.

> "[...] Excessive vivacity follows the use of strong coffee (primary action), but sluggishness and drowsiness remain for a long time afterwards (reaction, secondary action), if this be not always again removed for a short time by imbibing fresh supplies of coffee (palliative). After the profound stupefied sleep caused by opium (primary action), the following night will be all the more sleepless (reaction, secondary action). After the constipation produced by opium (primary action), diarrhea ensues (secondary action); and after purgation with medicines that irritate the bowels, constipation of several days' duration ensues (secondary action). And in like manner it always happens, after the primary action of a medicine that produces in large doses a great change in the health of a healthy person, that its exact opposite, when, as has been observed, there is actually such a thing, is produced in the secondary action by our vital force." (Hahnemann, 1995, § 65).

By administering to sick individuals the simple substances that have aroused similar symptoms in healthy experimenters *(similia similibus curentur),* the principle of therapeutic similarity aims to stimulate a reaction of the body against their own disorders or diseases, inducing a curative homeostatic response.

Cited since Hippocrates, the principle of similarity (vital or homeostatic reaction) finds its scientific basis in the 'rebound effect' of modern drugs (paradoxical reaction of the organism), being described after discontinuation or change in doses of numerous classes of medicines that act palliatively (contrary or antagonistic) to the symptoms of diseases, aggravating the initially suppressed symptoms. The rebound effect is confirmed in hundreds of clinical and experimental pharmacology studies (Teixeira, 1998, 1999, 2006, 2007a, 2007b, 2009c, 2010b, 2011b, 2012a, 2012b, 2013b, 2013c, 2016).

Despite the idiosyncratic character of this rebound phenomenon, which manifests itself in a small proportion of individuals, scientific evidence warns of the occurrence of severe and fatal iatrogenic events due to this paradoxical reaction of great intensity, after the administration of modern drugs: anti-inflammatory drugs (selective and non-selective of cyclooxygenases) causing thrombotic events (AMI and stroke), secondarily to the primary antithrombotic action; long-term bronchodilators causing irreversible bronchospasms; antidepressants serotonin reuptake inhibitors exacerbating depression and suicidal ideations; immunobiological drugs triggering severe forms of multiple

sclerosis and psoriasis; among other classes of drugs (Teixeira, 2006, 2007a, 2007b, 2009c, 2010b, 2011b, 2012a, 2012b, 2013b, 2013c, 2016).

When used according to the principle of therapeutic similarity, the great magnitude of this rebound effect can also awaken proportional curative responses. Therefore, since 2003, we have been proposing a systematization for the use of the curative rebound effect of 1,250 modern drugs, administered to sick individuals, at infinitesimal doses (dynamized, potentized or ultradiluted medicine), the same drugs that cause similar adverse events, in order to stimulate a homeostatic or paradoxical reaction of the body against its own disorders (Teixeira, 2003, 2005, 2010c, 2011c, 2011d, 2013d).

In a postdoctoral project completed in 2017, we evidenced the efficacy and safety of this proposal in the use of potentized estrogen (17-beta estradiol) in homeopathic treatment of chronic pelvic pain in patients with endometriosis refractory to conventional hormone treatments, through a randomized, double-blind and placebo-controlled clinical trial (Teixeira, 2017b; Teixeira et al., 2016, 2017a, 2017b). This was made possible by the fact that endometriosis is an estrogen-dependent syndrome and 17-beta estradiol presents as pathogenetic effects (adverse events) a set of signs and symptoms very similar to endometriosis syndrome (anxiety, depression, insomnia, migraine, abdominal pain, dysmenorrhoea, dyspareunia and endometrial hyperplasia, among others) (The United States Pharmacopeial Convention, 2004).

*II.2.2.2. Homeopathic pathogenetic trial or experimentation*

To acquire knowledge of the healing properties of substances that allow the application of the principle of therapeutic similarity, homeopathy uses homeopathic pathogenetic trial or experimentation as a model of pharmacological clinical research (similar to preclinical phase 1 trial), valuing all classes of symptomatic manifestations (mental, general and paticular) aroused by medicines in humans, called by modern pharmacology as adverse or side effects of drugs.

> “The whole pathogenetic effect of the several medicines must be known; that is to say, all the morbid symptoms and alterations in the health that each of them is specially capable of developing in the healthy individual must first have been observed as far as possible, before we can hope to be able to find among them, and

> to select, suitable homoeopathic remedies for most of the natural disease." (Hahnemann, 1995, § 106)

Following the premises stipulated by Hahnemann (Hahnemann, 1995, § 105-145), around 3,000 substances were experimented with following several experimental protocols (Teixeira, 2013e), with the aim of getting to know and catalog "the pathogenetic power of the medicines, in order, when called on to cure, to be able to select from among them one, from the list of whose symptoms an artificial disease may be constructed, as similar as possible to the totality of the principal symptoms of the natural disease sought to be cured".

All signs and symptoms observed in the various pathogenetic trials of homeopathic drugs were compiled for Homeopathic Materia Medica, following an anatomical-functional systematization.

In clinical practice, the homeopathic physician also uses the Repertory of Homeopathic Symptoms, in which all homeopathic medicines that aroused the same symptom in trials are grouped in the same 'rubric', facilitating the selection of the homeopathic drug that encompasses the characteristic totality of signs and symptoms of the individual.

*II.2.2.3. Dynamized or potentized medicine (ultra-high dilutions)*

Contrary to the biochemical and dose-dependent pharmacological model, the biomedical reasoning is surprising to the fact that ultradiluted substances (dynamized or potentized) at concentrations lower than the Avogadro constant ($6.02 \times 10^{23}$ $mol^{-1}$) may arouse some response in biological systems or living beings, which is the main target of criticism of the homeopathic model.

With the initial objective of avoiding the poisonings and symptomatic aggravations that the principle of therapeutic similarity could cause in patients, Hahnemann proposed a pharmacotechnique for the preparation of homeopathic drugs (dynamization or potentization), in which the substances are diluted and agitated successively in order to reduce the primary pathogenetic effect. A posteriori, he observed that these infinitesimal and imponderable preparations mobilized biological activity in spheres of individuality not affected by weight doses, such as psychoemotional dynamics (Hahnemann, 1995, § 269).

In a simplified way, the pharmacotechnical method of dynamization or potentization described in the Brazilian Homeopathic Pharmacopoeia (2011),

consists of centesimal and successive dilutions of the matrix substance, accompanied by 100 vigorous agitations (succussions) per passage (centesimal hahnemannian or cH).

Above the 12th potency or dynamization, these ultra-high dilutions present concentrations lower than the Avogadro constant ($6.02 \times 10^{23}$ $mol^{-1}$), in which there is no grass molecule of the substance of origin in the final solution, making them free of toxicity and/or adverse events (Dantas, 2017; Dantas and Rampes, 2000), as demonstrated by bisecular homeopathic treatment with toxic substances of high pathogenetic power (*Arsenicum album, Atropa belladonna, Cuprum metallicum, Lachesis muta, Phosphorus* and *Rhus toxicodendron,* among others).

In the classic homeopathic treatment, these ultra-high dilutions are administered in potencies 12cH, 30cH, 200cH and 1000cH, among others, in single monthly doses or repeated daily, according to the clinical indication (chronic or acute diseases, respectively).

The ability of this drug 'information' (contained in the infinitesimal doses of ultradiluted substances) to promote changes in physiological systems, analogous to weight doses, has been studied in scientific studies employing physicochemical or biological models of research.

Some hypotheses based on experimental physicochemical models seek a scientific explanation for the phenomenon of transmission of 'information' of the primary effects of substances in homeopathic ultra-dilutions. Among them, we mention the researches that study the electromagnetic changes of water according to quantum electrodynamics, in which the aqueous solution would not represent an inert cluster of molecules but rather a dynamic medium, capable of selecting and catalyzing molecular reactions according to the various electromagnetic fields of the solute dissolved inside it. Through mathematical and experimental models, they infer that the electromagnetic field of a solute can generate certain domains of stable coherence in the solvent (with specific structures and vibrations), producing 'clusters' of water molecules (with specific sizes, shapes and properties), such as an electromagnetic signature of the solute in water ('water memory'). Thus, the organization of water would be a coherent process, reproducible and associated with long-range electromagnetic interactions and very low intensity, transmitting the 'electromagnetic information

of the solute' initially diluted and agitated by the process of dynamization (Homeopathy, 2007).

In biological models of research, numerous experimental studies in the various areas of scientific knowledge and research models (*in vitro,* plants and animals), support the assumption that infinitesimal doses can awaken biological phenomena similar to those obtained with weighted doses of the same substances, validating the use of ultra-high diluted drugs by homeopathic therapy (Homeopathy, 2009, 2010).

*II.2.2.4. Individualized medicine (therapeutic individualization)*

According to Hahnemann, the doctor who is called a "legitimate artist of healing" should be able to recognize what should be cured in each case individually and understand the curative element of medicines, adapting them in quality and quantity to the needs of the sick, according to the principle of therapeutic similarity.

Understanding the process of illness as a weakening of the physiological mechanisms of adaptation and compensation, Hahnemann correlated any physiological imbalance with the corresponding symptomatic manifestations presented by the individual, using the set of signs and symptoms (symptomatic totality) as the main reference for diagnosing "affection of the vital force" (individual predisposition, morbid susceptibility or homeostatic imbalance) and to prescribe the homeopathic medicine more similar to the sick individuality.

> "[...] the totality of these its symptoms, of *this outwardly reflected picture of the internal essence of the disease, that is, of the affection of the vital force,* must be the principal, or the sole means, whereby the disease can make known what remedy it requires - the only thing that can determine the choice of the most appropriate remedy - and thus, in a word, the *totality of the symptoms* must be the principal, indeed the only thing the physician has to take note of in every case of disease and *to remove* by means of his art, in order that it shall be cured and transformed into health." (Hahnemann, 1995, § 7)

In the set of manifest signs and symptoms, homeopathic semiology selects "the *more striking, singular, uncommon and peculiar*" in each case, disregarding the common, general and undefined symptoms due to the inherent absence of individualizing power (idiosyncratic) in them.

> "In this search for a homoeopathic specific remedy, that is to say, in this comparison of the collective symptoms of the natural disease with the list of symptoms of known medicines, in order to find among these an artificial morbific agent corresponding by similarity to the disease to be cured, the *more striking, singular, uncommon and peculiar* (characteristic) signs and symptoms of the case of disease are chiefly and most solely to be kept in view; for it *is more particularly these that very similar ones in the list of symptoms of the selected medicine must correspond to*, in order to constitute it the most suitable for effecting the cure. The more general and undefined symptoms: loss of appetite, headache, debility, restless sleep, discomfort, and so forth, demand but little attention when of that vague and indefinite character, if they cannot be more accurately described, as symptoms of such a general nature are." (Hahnemann, 1995, § 153)

Associating drug individualization with the prescription of "*a single, simple medicine at one time*", it is strongly opposed to the simultaneous use of more than one homeopathic drug (mixture of medicines or homeopathic complexes), because homeopathic pathogenetic experimentation, a reference for the correct and safe therapeutic prescription, was performed with simple and unique substances.

> "In no case under treatment *is it necessary and therefore not permissible* to administer to a patient more than *one single, simple medicinal substance* at one time. It is inconceivable how the slightest doubt could exist as to whether it was more consistent with nature and more rational to prescribe *a single, simple medicine at one time* in a disease or a mixture of several differently acting drugs. It is absolutely not allowed in homoeopathy, the one true, simple and natural art of healing, to give the patient *at one time* two different medicinal substances." (Hahnemann, 1995, § 273)

Therefore, adequate homeopathic treatment should prioritize the individualization of the single medicine according to the most peculiar and characteristic signs and symptoms of each patient, in its various constitutional aspects (mental, general and particular), allowing, for the same disease, each individual can receive different unique medications, according to their own susceptibilities (physical, psychic, emotional, food and climatic , among others).

Several randomized clinical trials (RCT) that disrespected this drug individualization, administering the same medicine to several individuals with the same disease (exemplified in the indiscriminate use of *Arnica montana* for

inflammatory processes in general; Ernst and Pittler, 1998), showed no significant results compared to placebo, because they hurt the scientific rationality of the homeopathic model. The same occurred with meta-analyses and systematic reviews that grouped RCTs with non-individualized homeopathic medicines (Shang et al., 2005; Mathie et al., 2017; Homeopathy Research Institute), unlike those who valued individualizing therapy (Mathie et al., 2014; Vithoulkas, 2017).

It is noteworthy that this process of drug individualization requires a regular and variable follow-up period, in which the responses to the various drug hypotheses (individualized single medicines) are evaluated successively, adjusting the medications, doses and homeopathic potencies to the various susceptibilities of each patient. (Teixeira, 2009d)

In addition to these brief citations used to exemplify the scientific basis of each homeopathic epistemological premise, homeopathic assumptions are based on hundreds of studies in several contemporary lines of research (Teixeira, 2011a, 2018, 2019; Cremesp, 2017a, 2017b, 2017c), contrary to prejudice propagated indistinctly that 'there is no scientific evidence in homeopathy'.

For the finding of our statement, we indicate the reading of the "Special Dossier: Scientific Evidence for Homeopathy", prepared by the Technical Chamber of Homeopathy of Regional Council of Medicine of the State of São Paulo (Cremesp) in 2017.

### II.2.3. Guidelines for homeopathic treatment in epidemic diseases

#### *II.2.3.1. Samuel Hahnemann*

In a similar way to acute and chronic diseases, Hahnemann provides individualizing semiological and therapeutic guidelines in the approach of epidemic diseases (Teixeira 2009a, 2010a, 2013a, 2014, 2015a, 2015b).

Just as each patient presents a set of characteristic signs and symptoms that differs from other individuals affected by the same acute or chronic disease, each epidemic disease "respects a phenomenon of a unique character, differing vastly from all previous epidemics is a phenomenon with its own characteristics". With this warning, Hahnemann criticizes the application of the knowledge obtained in previous epidemics in new outbreaks of the same

disease, without conducting a meticulous examination of the pure picture of the current disease.

> "In investigating the totality of the symptoms of epidemic and sporadic diseases it is quite immaterial whether or not something similar has ever appeared in the world before under the same or any other name. The novelty or peculiarity of a disease of that kind makes no difference either in the mode of examining or of treating it, as the physician must any way regard to pure picture of every prevailing disease as if it were something new and unknown, and investigate it thoroughly for itself, if he desire to practice medicine in a real and radical manner, never substituting conjecture for actual observation, never taking for granted that the case of disease before him is already wholly or partially known, but always carefully examining it in all its phases; and this mode of procedure is all the more requisite in such cases, as a careful examination will show that every prevailing disease is in many respects a phenomenon of a unique character, differing vastly from all previous epidemics [...]." (Hahnemann, 1995, § 100)

As the image of the pathological picture of collective diseases appears only after the observation of a number of patients considered, Hahnemann suggests the observation of several cases to form the "complete picture of the disease", based on the characteristic set of its symptoms and signs, according to homeopathic semiology.

> "It may easily happen that in the first case of an epidemic disease that presents itself to the physician's notice he does not at once obtain a knowledge of its complete picture, as it is only by a close observation of several cases of every such collective disease that he can become conversant with the totality of its signs and symptoms. The carefully observing physician can, however, from the examination of even the first and second patients, often arrive so nearly at a knowledge of the true state as to have in his mind a characteristic portrait of it, and even to succeed in finding a suitable, homoeopathically adapted remedy for it." (Hahnemann, 1995, § 101)

In the search for the 'essence' or 'genius' of the epidemic (epidemic genius), which will make it possible by similarity to identify among the various substances tested the most appropriate medicine, the 'characteristic picture of the epidemic' will be formed by the 'totality of the most characteristic signs and symptoms'. This individualized medicine can be applied therapeutically to patients affected by the same outbreak of the disease.

> "In the course of writing down the symptoms of several cases of this kind the sketch of the disease picture becomes ever more and more complete, not more spun out and verbose, but more significant (more characteristic), and including more of the peculiarities of this collective disease; on the one hand, the general symptoms (e.g., loss of appetite, sleeplessness, etc.) become precisely defined as to their peculiarities; and on the other, the more marked and special symptoms which are peculiar to but few diseases and of rarer occurrence, at least in the same combination, become prominent and constitute what is characteristic of this malady. All those affected with the disease prevailing at a given time have certainly contracted it from one and the same source and hence are suffering from the same disease; but the whole extent of such an epidemic disease and the totality of its symptoms (the knowledge whereof, which is essential for enabling us to choose the most suitable homoeopathic remedy for this array of symptoms, is obtained by a complete survey of the morbid picture) cannot be learned from one single patient, but is only to be perfectly deduced (abstracted) and ascertained from the sufferings of several patients of different constitutions." (Hahnemann, 1995, § 102)

Discussing the nature and treatment of intermittent fever epidemics, Hahnemann reiterates the need to individualize the "specific homeopathic remedy" for the treatment of the epidemic manifestation, according to the characteristic set of symptoms common to all patients. Maintaining its reasoning coherence, he emphasizes the epistemological premise of using simple and unique substances, avoiding complex means, in the individualization of the homeopathic medicine.

> "Epidemics of intermittent fever, in situations where none are endemic, are of the nature of chronic diseases, composed of single acute paroxysms; each single epidemic is of a peculiar, uniform character common to all the individuals attacked, and when this character is found in the totality of the symptoms common to all, it guides us to the discovery of the homeopathic (specific) remedy suitable for all the cases, which is almost universally serviceable in those patients who enjoyed tolerable health before the occurrence of the epidemic, that is to say, who were not chronic sufferers from developed psora." (Hahnemann, 1995, § 241)

In addition to indicating the homeopathic medicine as a therapeutic measure in the manifest cases of the epidemic disease, Hahnemann also describes the use of individualized homeopathy as a prophylactic practice.

> "A striking fact in corroboration of this is, that whilst previously to the year 1801, when the smooth scarlatina of Sydenham still occasionally prevailed epidemically

> among children, it attacked without exception all children who had escaped it in a former epidemic; in a similar epidemic which I witnessed in Konigslutter, on the contrary, all the children who took in time a very small dose of belladonna remained unaffected by this highly infectious infantile disease. If medicines can protect from a disease that is raging around, they must possess a vastly superior power of affecting our vital force." (Hahnemann, 1995, footnote to § 33)
>
> "Subsequently to the year 1801 a kind of *purpura miliaris* (roodvonk), which came from the West, was by physicians confounded with the scarlet fever, notwithstanding that they exhibited totally different symptoms, that the latter found its prophylatic and curative remedy in belladonna, the former in aconite, and that the former was generally merely sporadic, while the latter was invariable epidemic. Of late years it seems as if the two occasionally joined to form an eruptive fever of a peculiar kind, for which neither the one nor the other remedy, alone, will be found to be exactly homoeopathic." (Hahnemann, 1995, footnote to § 73)

Despite recognizing the benefits of the antiviral vaccine, introduced by his contemporary Edward Jenner in 1796 (following observation and detailed description of a series of 27 immunized cases), Hahnemann criticizes the indiscriminate use of ultra-dilutions of disease by-products or the pathogen (nosodes or biotherapics) as a prophylactic method or isopathic treatment (principle of identity; *aequalia aequalibus curentur*), without the pathogenetic experimentation of the by-product in healthy people and the application of individualizing similarity.

> "A third mode of employing medicines in diseases has been attempted to be created by means of Isopathy, as it is called - that is to say, a method of curing a given disease by the same contagious principle that produces it. But even granting this could be done, yet, after all, seeing that the virus is given to the patient highly potentized, and consequently, in an altered condition, the cure is effected only by opposing a 'simillimum' to a 'simillimum'. To attempt to cure by means of the very same morbific potency (per Idem) contradicts all normal human understanding and hence all experience. Those who first brought Isopathy to notice, probably thought of the benefit which mankind received from cowpox vaccination by which the vaccinated individual is protected against future cowpox infection and as it were cured in advance. But both, cowpox and smallpox are only similar, in no way the same disease. In many respects they differ, namely in the more rapid course and mildness of cowpox and especially in this, that is never contagious to man by more nearness. Universal vaccination put an end to all epidemics of that deadly fearful

> smallpox to such an extent that the present generation does no longer possess a clear conception of the former frightful smallpox plague. Moreover, in this way, undoubtedly, certain diseases peculiar to animals may give us remedies and thus happily enlarge our stock of homoeopathic remedies. But to use a human morbific matter (a Psorin taken from the itch in man) as a remedy for the same itch or for evils arisen therefrom is - ? Nothing can result from this but trouble and aggravation of the disease." (Hahnemann, 1995, footnote to § 56)

Remember that to be considered a homeopathic medicine and to be able to be used therapeutically and/or prophylactically in a safe and effective way according to the principle of similarity, any substance (simple or complex), regardless of its origin, needs to be subjected to experimentation in human individuals, so that its pathogenic symptoms are known and described. In this way, any animal by-product (nosodes or biotherapics) can be used homeopathically, as long as it is subjected to previous pathogenetic experimentation and is prescribed according to the similarity of characteristic signs and symptoms with the sick individuality.

Therefore, it is worth mentioning that the isopathic medicine or isotherapeutic treatment (used according to the principle of identity and disregarding previous pathogenetic experimentation, similar to modern oral immunotherapy) does not match the homeopathic episteme and cannot be considered "homeopathic". (Teixeira, 2014, 2015a, 2015b)

*II.2.3.2. James Tyler Kent*

In his work *Lectures on homeopathic philosophy,* Lesson III, Kent (1998) describes a semiological protocol for diagnosing the group of medicines of the 'epidemic genius', based on the hahnemannian premises mentioned above.

He suggests the careful observation of 20 patients affected by the disease in question, recording all the symptoms present in a schematic way (repertorial classification), which when considered collectively ill present an image, "as if a single man had expressed all the symptoms". Putting in front of each symptom the number of patients who manifested it, the homeopathic doctor will discover "the essential traits of the epidemic" (nature of the disease) through the common symptomatic totality (pathognomonic signs and symptoms) and characteristic (peculiar signs and symptoms). Using a repertory of symptoms,

he will select six or seven drugs that cover the symptomatic totality of that epidemic (group of individualized homeopathic medicines of epidemic genius), fixing the individual pictures of each drug in the study of homeopathic materia medica.

Then proceeding from general to particular, for “there is no other way to proceed in homeopathy”, the homeopathic physician will adapt the characteristics of each patient to the particularities of each selected drug (therapeutic individualization), because even in individuals of the same family will be observed “a small difference in each case”. If none of the selected medications are useful, the doctor should return to his or her original anamnesis to see which of the other medicines is appropriate. Kent points out that the application of epidemic genius in the selection of homeopathic medicines is hard work, but brings spectacular results.

> “[...] Every remedy has in itself a certain state of peculiarities that identifies it as an individual remedy, and the patient has also a certain state of peculiarities that identifies him as an individual patient, and so the remedy is fitted to the patient. No remedy must be given because it is in the list, for the list has only been made as a means of facilitating the study of that epidemic. Things can only be made easy by an immense amount of hard work, and if you do the drudgery in the beginning of an epidemic, the prescribing for your cases will be rapid, and you will find your remedies abort cases of sickness, make malignant cases simple, so simplify scarlet fever that classification would be impossible, stop the course of typhoids in a week, and cure remittent fevers in a day.” (Kent, 1998, Lição III)

### II.2.4. Evidence of the effectiveness of homeopathy in epidemic diseases

Several initiatives employing homeopathic medicines in the treatment and prophylaxis of epidemic diseases are described in the literature, most of them as reports of cured or immunized cases in which medicines of the epidemic genius were used (Shepherd, 1996; Hoover, 2001; Shalts, 2005; Bradford, 2007).

In the shorter writing “Some types of continuous and remitting fevers”, published in 1798 in Hufeland’s Journal der practischen Arzneykunde, Hahnemann (2006a) describes the use of *Ignatia amara* in the treatment of a continuous and sporadic fever that affected children in January 1797, which had the following

characteristic symptoms: instead of skin heat, continued chills and great laxity; forehead covered with cold sweat; memory weakness; excessively short and spasmodic breathing. After two months, another fever of the same character, but with different characteristic symptoms (immobility of the pupil, pressure pain around the navel, stupor, decreased strength, relief from sweating, etc.), returned to affect children, finding its curative medicine. In the following month, he describes the use of *Camphora* in an influenza epidemic aggravated by the use of *Opium*, in order to present a distinct set of peculiar symptoms. With these examples, Hahnemann emphasizes the importance of individualizing the medicine according to the characteristic symptoms of each epidemic (or stage) of a similar character.

In another shorter writing entitled “Cure and prevention of scarlet fever”, Hahnemann (2006b) describes the use of *Atropa belladonna* in the prophylaxis and treatment of the initial phase of the scarlet fever epidemic that occurred in the vicinity of Helmstädt to Königslutter in 1799, a medicine chosen according to the epidemic genius of the initial phase of the disease: “a medicine that is capable of quickly blocking a disease in its beginnings should also be your best preventive”. He also describes the use of *Opium* and *Ipeca* in the treatment of two morbid conditions of the fully developed disease, administering these drugs in isolation or alternating, according to the assessment of each patient and the set of signs and symptoms of each episode: “From me, when called upon for cases of fully developed disease (where it was not a matter of prevention or preventing its onset), I realized that I had to combat two different states of the body that sometimes quickly alternated, each of which was composed of a convolute of symptoms”. He also mentions the use of *Matricaria chamomilla* for the skin disorder called “insane skin” and for the characteristic suffocating cough that could come on the disease.

**It is worth mentioning that Hahnemann, in the treatment of any epidemic disease, prescribed the different medicines individually and at different times (different stages of the disease), without ever mixing the drugs in the same prescription (homeopathic complexes).**

Other doctors described the high levels of protection that *belladonna* gave children exposed to the same type of scarlet fever epidemic in the 1820s:

Dudgeon (2002) reports that ten allopaths (Bloch, Cramer, Gelnecki, Wolf, Ibrelisle, Velsen, Berndt, Schenk, Behr and Zeuch) used *belladonna* prophylactically in 1646 children, observing the manifestation of symptoms in only 123 cases (7.5%), a high degree of protection in an epidemic that affected 90% of those exposed at the time.

A review of these results of the prophylactic use of *belladonna* in scarlet fever, published in the Hufeland's Journal in 1826 (Hufeland, 1826), made the Prussian government mandatory to use it during the 1838 epidemic (Dunham, 1994). These data show the use of *belladonna* as a "specific" prophylactic of scarlet fever by allopathic doctors of the time.

In the shorter writing "Cure and prevention of Asian cholera", Hahnemann (2006c) describes the use of *Camphora, Cuprum metallicum* and *Veratrum album* as homeopathic medicines to the epidemic genius of the successive stages of the disease (prescribed individually, according to the similarity with the symptoms each stage of the disease), to prevent and treat Asian cholera during the 1831 epidemic in Germany. Preferably, he used *Cuprum* as a prophylactic against cholera, *Camphora* for the treatment of the initial phase of the disease, and *Cuprum* or *Veratrum* in the later phase (alone or alternately, as the symptoms indicated). In his historical review, Shalts (2005) states that during this epidemic (1831-1832) the mortality rates of European homeopathic hospitals were 7-10%, while with conventional treatments they reached 40-80%.

Studying in a systematic way the symptoms that affected patients during the cholera epidemic of 1849 in Europe, Von Böeninghausen (2005), in August of the same year, proposed the administration of *Camphora* by non-doctors as an individualized medicine of the epidemic genius for the treatment of patients affected by the disease: "Only the use of this remedy can and should be entrusted to the hands of a non-physician". During this epidemic, according to Shepherd (1996) and Hoover (2001), the mortality rate of patients undergoing homeopathic treatment was 5-16%, while those receiving conventional treatments showed 54-90%. Homeopathy was also used in the cholera epidemic of 1854 in London (Leary, 1994, 1997), significantly reducing mortality.

In the *Lectures on homeopathic philosophy,* Lesson XI, Kent (1998) describes the treatment of some cases of the same epidemic of childhood diarrhea with

the 30th potency of the medicine *Podophyllum peltatum,* which had in its pathogenesis symptoms similar to those observed in sick patients (epidemic genius), reporting that “the cures were almost instantaneous, it seemed as if there were no more stools after the first dose of the drug”, although not always using a single dose.

Meta-analysis of three randomized homeopathic clinical trials (Jacobs et al., 2003) showed that individualized homeopathic treatment was significantly more effective than placebo in childhood diarrhea epidemics. However, another randomized clinical trial conducted by the same authors (Jacobs et al., 2006) showed that non-individualized homeopathic treatment (complex or mixture of five homeopathic medicines commonly indicated in the treatment of childhood diarrhea), which disregarded the individualizing guidelines for the homeopathic medicine of the epidemic genius, did not present a significant response to the placebo.

In the shorter writing “Treatment of typhus or hospital fever that currently predominates”, Hahnemann (2006d) describes the use of *Bryonia alba, Hyosciamus niger* and *Rhus toxicodendron* as homeopathic medicines to the typhus epidemic genius (prescribed in a single or alternate way, according to similarity of symptoms between the patient and each stage of the disease), in the treatment of the epidemic that affected Germany in 1813: “Of the 183 patients I treated with this condition in Leipizig, I did not lose one, which caused a great sensation among the members of the Russian Government that then occupied Dresden, but no news was given by the medical authorities”. (Hahnemann, 1994).

A severe diphtheria epidemic has also been effectively treated by individualized homeopathy: in the three-year (1862-4) historical records of the disease in Broome County (New York, USA), there are reports of an 84% mortality rate with conventional treatments and a rate of only 16% with homeopathic treatment (Shalts, 2005).

In 1918, at the beginning of the Spanish flu pandemic that infected 20% of the world population and killed around 30 million people, homeopathic doctors met at the British Homeopathic Society (London) to discuss the probable drugs of the epidemic genius, through the report of a series of cases and their characteristic symptoms. The discussions and the results of this meeting were

published in a scientific periodical (British Homoeopathic Society, 1918), guiding the individualized treatment of epidemic outbreaks in different regions and countries.

Several homeopathic medicines were used to treat this epidemic outbreak (*Arsenicum album, Bryonia alba, Baptisia tinctoria, Eupatorium perfoliatum* and *Gelsemium sempervirens,* among others), according to the epidemic genius observed in the different stages of the disease, times and regions (Hoover, 2001; Shalts , 2005; Baker, 1920). In estimates published in the Journal of the American Institute of Homeopathy (Dewey, 1921), McCann referred that 26,000 cases of flu treated homeopathically in Ohio had a 1% mortality rate, contrasting with the rate of 28% in 24,000 cases allopathically treated. In Philadelphia, Pearson reported similar rates in 26,795 cases of flu treated homeopathically.

Recent reviews analyzed the results at the time and described the benefits of homeopathic treatment in this influenza (Spanish flu) pandemic that devastated humanity in the early 20th century (1918-1920). (The Canadian Academy of Homeopathy, 2013; Jahn, 2014)

Systematic review of three placebo-controlled clinical trials (n = 2265) that used the biotherapic *Oscillococcinum* (prepared with autolysate from the heart and liver of an infected wild duck, a vector of the avian influenza virus) as a “specific” preventive of influenza syndromes (ignoring the individualizing guidelines cited above), there was no significant effect of this nosode on placebo. (Vichers and Smith, 2006)

During a conjunctivitis epidemic in Pittsburgh (USA), a placebo-controlled clinical trial was conducted to evaluate the effectiveness of *Euphrasia officinalis* 30cH (chosen according to the epidemic genius of previous years’ epidemics) in preventing the disease, neglecting the entire symptomatic characteristic of the current epidemic. The treatment group consisted of 658 students, who received the homeopathic medicine for three consecutive days; the control group was composed of 648 students, who received placebo in the same dosage. There was no statistically significant difference in the incidence and severity of the disease between the groups. (Mokkapatti, 1992)

In another epidemic of keratoconjunctivitis that occurred in Cuba, 108 patients were randomly assigned for homeopathic (n = 58) and allopathic (n = 50) treatment, using *Pulsatilla nigricans* 6cH as an individualized homeopathic

medicine of the epidemic genius of that epidemic. Homeopathic treatment was significantly more effective than allopathic treatment in improving symptoms in less than 72 hours. (Varela et al., 1995)

In Brazil, Marino (2006, 2008) evaluated the action of the individualized homeopathic medicine *Eupatorium perfoliatum* in the prophylaxis of dengue during the 2001 epidemic in São José do Rio Preto (SP), showing that the homeopathic intervention showed a significant decrease in the incidence of the disease before the control group.

## II.3. Study of the epidemic genius of the current COVID-19 pandemic

Following the assumptions stipulated by Hahnemann and Kent, previously described, using the reports and studies that described the signs and symptoms common to several patients affected by COVID-19 in other countries, we can raise some possible individualized homeopathic medicines for the epidemic genius of the current pandemic, in its different stages.

Retrospective observational study with 99 cases infected with SARS-Cov-2 and admitted to the Wuhan Jin Yin-tan Hospital (Wuhan, China) showed that the set of signs and symptoms presented were: fever (83%), cough (82%), dyspnea (31%), muscle pain (11%), mental confusion (9%), headache (8%), sore throat (5%), rhinorrhea (4%), chest pain (2%), diarrhea (2%) and nausea and vomiting (1%). According to imaging studies, 75% had bilateral pneumonia, 14% had multiple spots and ground-glass opacity (interstitial thickening or partial alveolar collapse) and 1% evolved with pneumothorax. 17% of patients developed acute respiratory distress syndrome (ARDS) and, among them, 11% worsened in a short period of time, dying from multiple organ failure: acute renal failure (ARF, 3%), acute respiratory failure (8%) and septic shock (4%). Elderly and comorbid patients progressed more easily to severe and fatal respiratory diseases. (Chen et al., 2020)

According to a report from the joint WHO-China mission, based on 55924 cases infected with SARS-Cov-2, typical signs and symptoms included: fever (87.9%), dry cough (67.7%), fatigue (38, 1%), phlegm production (33.4%), dyspnea (18.6%), sore throat (13.9%), headache (13.6%), myalgia or arthralgia (14.8%),

chills (11.4%), nausea or vomiting (5.0%), nasal congestion (4.8%), diarrhea (3.7%), hemoptysis (0.9%) and conjunctival congestion (0.8%). In general, the 'clinical picture' started with fever and mild respiratory symptoms (dry cough), 5-6 days after infection. 13.8% of patients had severe pneumonia, with dyspnea, respiratory rate ≥30 / minute, blood oxygen saturation ≤93%, PaO2/FiO2 ratio < 300 and / or pulmonary infiltrates > 50% of the pulmonary field, in 24 to 48 hours. 6.1% of the patients had critical conditions, with respiratory failure, septic shock and/or multiple organ dysfunction. Individuals with a higher risk of serious illness were elderly and with chronic diseases. (WHO, 2020)

Retrospective observational study of 52 seriously ill adult patients with SARS-CoV-2 pneumonia, admitted to the ICU of the Wuhan Jin Yin-tan Hospital (Wuhan, China) between December 2019 and January 2020, showed that the set of signs and symptoms presented were: fever (98%), cough (77%), dyspnea (63.5%), myalgia or arthralgia (11.5%), malaise (35%), rhinorrhea (6%), and chest pain (2%). The mean age of the patients was 59.7 years (with more severe conditions progressing with age) and 40% had associated chronic diseases. The majority of patients had insufficiency in any organ: ARDS (67%), acute renal failure (29%), heart failure (23%), liver failure (29%) and pneumothorax (2%). 71% of patients required mechanical ventilation (respiratory failure). Patients who died were older. (Yang et al., 2020)

Retrospective observational study of 81 patients admitted with COVID-19 pneumonia between December 2019 and January 2020 described the radiological findings (chest CT). The most common initial symptoms were fever (73%) and dry cough (59%). Other non-specific symptoms included dizziness (2%), diarrhea (4%), vomiting (5%), headache (6%) and generalized weakness (9%). In pulmonary images, 79% had bilateral pulmonary involvement, 54% with peripheral distribution and 44% with diffuse distribution, involving mainly the right lower lobes (27%). The predominant pattern of abnormalities observed was ground-glass opacity (65%), ill-defined margins (81%), smooth or irregular interlobular septal thickening (35%), air bronchogram (47%) and adjacent pleura thickening (32%). COVID-19 pneumonia manifested itself with radiological abnormalities even in asymptomatic patients (preclinical phase), with rapid evolution from opaque unilateral ground glass to diffuse bilateral, transforming into consolidations over three weeks. (Shi et al., 2020)

Using the data from these studies and following Kent's guidelines (Lesson III, 1998), initially, we must register "the symptoms present in a schematic way (repertory classification), placing in front of each symptom the number of patients (%) who manifested it, discovering the essential features of the epidemic through the common symptomatic totality (pathognomonic signs and symptoms) and characteristic (peculiar signs and symptoms)". (Table 1)

**Table 1. Total signs and symptoms of COVID-19**

| Total signs and symptoms | **Chen et al., 2020 (n=99)** | **WHO, 2020 (n=55924)** | **Yang et al., 2020 (n=52)** | **Shi et al., 2020 (n=81)** |
|---|---|---|---|---|
| Fever | 83% | 87.9% | 98% | 73% |
| Chills | | 11.4% | | |
| Dry cough | 82% | 67.7% | 77% | 59% |
| Dyspnea | 31% | 18.6% | 63.5% | unreported |
| Fatigue / Weakness | | 38.1% | | 9% |
| Malaise | | | 35% | |
| Dizziness | | | | 2% |
| Phlegm production | | 33.4% | | |
| Myalgia or arthralgia | 11% | 14.8% | 11.5% | |
| Mental confusion | 9% | | | |
| Headache | 8% | 13.6% | | 6% |
| Sore throat | 5% | 13.9% | | |
| Rhinorrhea | 4% | | 6% | |
| Nasal congestion | | 4.8% | | |
| Hemoptysis | | 0.9% | | |
| Conjunctival congestion | | 0.8% | | |
| Chest pain | 2% | | 2% | |
| Diarrhea | 2% | 3.7% | | 4% |
| Nausea and vomiting | 1% | 5.0% | | 5% |
| Respiratory failure (acute) / ARDS | acute (8%) / 17% (ARDS) | acute (6.1%) | 71% / 67% (SDRA) | unreported |
| Pneumonia (higher risk in the elderly and patients with chronic diseases) | unreported | severe (13.8%) | severe (100%) | severe (100%) |
| | bilateral (75%) | | unreported | bilateral (79%) |
| | | | | peripheral (54%) |
| | | | | diffuse (44%) |
| | | | | right lower lobe (27%) |
| Ground-glass opacity | 14% | | | 65% |
| Poorly defined margins | | | | 81% |
| Septal thickening | | | | 35% |
| Pleural thickening | | | | 32% |
| Air bronchogram | | | | 47% |
| Pneumothorax | 1% | | 2% | |
| Multiple organ failure / sepsis | ARF (3%) / septic shock (4%) | 6.1% | ARF (29%), IC (23%), IH (29%) | unreported |

Note: 'not reported' refers to the unquestionable existence of the sign/symptom, although it has not been quantified and computed.

Despite the absence of scientific studies to substantiate the occurrence of anosmia in this epidemic, doctors from several countries (China, South Korea, Italy, England, Germany, France, the United States and Iran, among others) have reported loss of smell (and the consequent loss of taste) in a large percentage of patients affected by COVID-19, suggesting that the presence of sudden anosmia (associated or not with respiratory symptoms) may indicate SARS-Cov-2 infection, as has been observed in other viruses (Suzuki et al., 2007).

Another epidemiological data related to climatic factors, an aspect highly valued by individualizing homeopathy as a general symptom (climatic susceptibility), it is worth mentioning that this pandemic, as well as other epidemics caused by respiratory viruses (influenza serotypes), is spreading in the spring seasons (Northern Hemisphere) and autumn (Southern Hemisphere), in which cold and dry weather predominates.

With the description of this set of signs and symptoms, observed in hundreds to thousands of patients, we must select the most frequent and peculiar ones, in order to have the 'epidemic genius' of COVID-19. Then, it is necessary to transform the 'common' language of these signs and symptoms into a 'repertory' language ("repertoire classification" of signs and symptoms, according to the "repertoire homeopathic rubrics" described in the Homeopathic Symptom Repertory) (Ribeiro Filho, 1998) (Tables 2 and 3).

We will add to this set of repertoire homeopathic rubrics the one that groups the homeopathic medicines that have shown clinical efficacy in other respiratory virus epidemics (influenza) in the past, as described in the aforementioned history (II.4. Evidence of the effectiveness of homeopathy in epidemic diseases).

**Table 2. Overall symptomatic totality of COVID-19**

| **Signs and symptoms in common language** | **Signs and symptoms in repertory language** (repertoire homeopathic rubrics) |
|---|---|
| Fever + dry cough (onset of the picture in general) | COUGH - DRY - Fever, during |
| Dyspnea | RESPIRATION - DIFFICULT |
| Myalgia + Arthralgia | GENERALITIES – PAIN - Muscles, of<br>GENERALITIES – PAIN - Joints, of |
| Respiratory failure (acute) / Acute respiratory distress syndrome (ARDS) | RESPIRATION – IMPEDED, obstructed<br>RESPIRATION – ANXIOUS |
| Pneumonia: in the elderly, bilateral, | CHEST – INFLAMMATION, Lungs |

| | |
|---|---|
| peripheral (pleuropneumonia), diffuse and in the right lower lobe<br><br>Radiological changes: ground-glass opacity (interstitial thickening or alveolar collapse); septal and pleural thickening (infiltration or fibrosis) | CHEST – INFLAMMATION, Lungs, old people<br>CHEST – INFLAMMATION, Lungs, right<br>CHEST – INFLAMMATION, Lungs, right, lower lobe<br>CHEST – INFLAMMATION, Lungs, pleura-pneumonia<br>CHEST – INFLAMMATION, Pleura |
| Multiple organ failure / sepsis | KIDNEYS – SUPPRESSION of urine (anuria)<br>GENERALITIES – SEPTICEMIA, blood poisoning |
| Anosmia | NOSE AND SMELL – SMELL, wanting, lost |
| Cold and dry weather worsens (autumn and spring seasons) | GENERALITIES – SEASONS, autumn, inn, agg.<br>GENERALITIES – SEASONS, spring, in, agg.<br>GENERALITIES – WEATHER, cold dry weather, agg. |
| Homeopathic medicines used in influenza epidemics in the past | GENERALITIES - INFLUENZA |

**Table 3. General symptomatic totality of COVID-19 in repertory language**

| Sint. | Selec | Diret | S1 | S2 | S3 | |
|---|---|---|---|---|---|---|
| 1 | X | | | | | NOSE AND SMELL -> SMELL -> wanting, lost |
| 2 | X | | | | | KIDNEYS -> SUPPRESSION of urine (anuria) |
| 3 | X | | | | | RESPIRATION -> ANXIOUS |
| 4 | X | | | | | RESPIRATION -> DIFFICULT |
| 5 | X | | | | | RESPIRATION -> IMPEDED, obstructed |
| 6 | X | | | | | COUGH -> DRY -> fever -> during |
| 7 | X | | | | | CHEST -> INFLAMMATION -> Pleura |
| 8 | X | | | | | CHEST -> INFLAMMATION -> Lungs |
| 9 | X | | | | | CHEST -> INFLAMMATION -> Lungs -> right |
| 10 | X | | | | | CHEST -> INFLAMMATION -> Lungs -> right -> Lower lobe |
| 11 | X | | | | | CHEST -> INFLAMMATION -> Lungs -> pleura-pneumonia |
| 12 | X | | | | | CHEST -> INFLAMMATION -> Lungs -> old people |
| 13 | X | | | | | GENERALITIES -> PAIN -> Joints, of |
| 14 | X | | | | | GENERALITIES -> PAIN -> Muscles, of |
| 15 | X | | | | | GENERALITIES -> SEASONS -> autumn, in -> agg. |
| 16 | X | | | | | GENERALITIES -> SEASONS -> spring, in -> agg. |
| 17 | X | | | | | GENERALITIES -> INFLUENZA |
| 18 | X | | | | | GENERALITIES -> SEPTICEMIA, blood poisoning |
| 19 | X | | | | | GENERALITIES -> WEATHER -> cold dry weather -> agg. |

Then (Kent, Lesson III, 1998), “using a repertoire of symptoms, the homeopathic doctor will select six or seven drugs that cover the entire symptomatic of that epidemic (group of individualized drugs of the epidemic genius of COVID-19), fixing the tables of each medicine in the study of Homeopathic Materia Medica”.

Performing the repertorization of the overall symptomatic totality of COVID-19 (Table 4), there are several possibilities for individualized homeopathic

medicines of the epidemic genius to be used in this epidemic, such as: *Bryonia Alba, Phosphorus, Rhus toxicodendron* and *Arsenicum album,* among others.

**Table 4. Repertorization of the overall symptomatic totality of COVID-19**

| Sin. | Med./Rem. | Cobert. | Pts. | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | BRY | 17 | 38 | 2 | | 1 | 3 | 2 | 3 | 3 | 3 | 3 | | 3 | 2 | 3 | 2 | 1 | 2 | 1 | 2 | 2 |
| 2 | PHOS | 14 | 32 | 3 | 2 | 3 | 3 | 1 | 3 | 2 | 3 | 2 | 2 | 3 | | 2 | | | | | 2 | 1 |
| 3 | RHUS-T | 14 | 28 | 2 | | 2 | 2 | | 1 | 1 | 3 | | | 2 | | 3 | 2 | 3 | 2 | 2 | 2 | 1 |
| 4 | BELL | 14 | 25 | 3 | 2 | 2 | 2 | 1 | 1 | 2 | 2 | 2 | | | | 2 | 1 | | 3 | | 1 | 1 |
| 5 | CALC | 14 | 24 | 3 | 1 | 1 | 2 | 1 | 1 | 2 | 2 | | | 2 | | 2 | | 2 | 3 | | 1 | 1 |
| 6 | PULS | 13 | 26 | 3 | 1 | 3 | 3 | 1 | 1 | 1 | 3 | | | | | 3 | 1 | | 2 | | 2 | 2 |
| 7 | MERC | 13 | 25 | 3 | 1 | | 2 | 2 | | 2 | 3 | 2 | 2 | | | 2 | 1 | 2 | | 1 | 2 | |
| 8 | ARS | 12 | 28 | 2 | 3 | 3 | 3 | 2 | 2 | 2 | 3 | | | | | 2 | 1 | | | | 3 | 2 |
| 9 | ACON | 12 | 27 | | 3 | 3 | 2 | 1 | 3 | 3 | 3 | | | | | 1 | 2 | | 1 | | 2 | 3 |
| 10 | LACH | 12 | 26 | 1 | 3 | 2 | 3 | 2 | 1 | | 2 | | | 2 | | | | 3 | 3 | | 3 | 1 |
| 11 | SULPH | 12 | 25 | 2 | 2 | | 3 | 2 | 1 | 3 | 3 | | | 2 | | 2 | | | 2 | | 2 | 1 |
| 12 | LYC | 12 | 24 | 2 | 3 | | 3 | 1 | 1 | | 3 | 2 | | | | 2 | 1 | | 3 | | 2 | 1 |
| 13 | HEP | 12 | 23 | 3 | 1 | 2 | 3 | | 1 | 2 | 3 | | | 2 | | | | 1 | 1 | | 1 | 3 |
| 14 | VERAT | 12 | 23 | 1 | 3 | 1 | 3 | 2 | 1 | | 2 | | | | | | 2 | 2 | 2 | | 2 | 2 |
| 15 | NUX-V | 12 | 21 | | 1 | 1 | 2 | 1 | 3 | | 1 | | | | 2 | 3 | | 1 | 1 | 2 | | 3 |

Then (Kent, Lição III, 1998), proceeding from the general to the particular, as “there is no other way to proceed in homeopathy”, we can adapt the characteristics of each patient to the particularities of each selected drug (therapeutic individualization), because even in individuals of the same family, “a small difference in each case” will be observed.

Therefore, we must also select particular signs and symptoms at each stage of the disease and, subsequently, repertorize and select individualized drugs to administer to the respective patients.

> “Most people infected with the COVID-19 virus have a mild illness and are recovering. Approximately 80% of laboratory confirmed patients had mild to moderate disease, which includes cases with and without pneumonia; 13.8% have severe disease (dyspnea, respiratory rate ≥ 30/minute, blood oxygen saturation ≤ 93%, PaO2/FiO2 ratio < 300, and/or pulmonary infiltrate > 50% of the pulmonary field in 24-48 hours); and 6.1% are critical (respiratory failure, septic shock and/or multiple organ dysfunction/failure).” (WHO, 2020, p. 12)

### II.3.1. Homeopathic medicines of the epidemic genius for the prevention or treatment of mild to moderate disease (COVID-19)

For these stages of the disease, we will use the signs and symptoms of mild to moderate involvement (WHO, 2020), including pneumonia without major complications. (Tables 5 to 7)

**Table 5. Symptomatic totality for prevention or mild to moderate disease**

| **Signs and symptoms in common language** | **Signs and symptoms in repertory language** (repertoire homeopathic rubrics) |
|---|---|
| Fever + dry cough (onset of the picture in general) | COUGH - DRY - Fever, during |
| Dyspnea | RESPIRATION - DIFFICULT |
| Myalgia + Arthralgia | GENERALITIES – PAIN - Muscles, of<br>GENERALITIES – PAIN - Joints, of |
| Pneumonia in the elderly | CHEST – INFLAMMATION, Lungs<br>CHEST – INFLAMMATION, Lungs, old people |
| Anosmia | NOSE AND SMELL – SMELL, wanting, lost |
| Cold and dry weather worsens | GENERALITIES – WEATHER, cold dry weather, agg. |
| Homeopathic medicines used in influenza epidemics in the past | GENERALITIES - INFLUENZA |

**Table 6. Symptomatic totality for prevention or mild to moderate disease**

| Sint. | Selec | Diret | S1 | S2 | S3 | |
|---|---|---|---|---|---|---|
| 1 | X | | | | | NOSE AND SMELL -> SMELL -> wanting, lost |
| 2 | X | | | | | RESPIRATION -> DIFFICULT |
| 3 | X | | | | | COUGH -> DRY -> fever -> during |
| 4 | X | | | | | CHEST -> INFLAMMATION -> Lungs |
| 5 | X | | | | | CHEST -> INFLAMMATION -> Lungs -> old people |
| 6 | X | | | | | GENERALITIES -> PAIN -> Joints, of |
| 7 | X | | | | | GENERALITIES -> PAIN -> Muscles, of |
| 8 | X | | | | | GENERALITIES -> INFLUENZA |
| 9 | X | | | | | GENERALITIES -> WEATHER -> cold dry weather -> agg. |

**Table 7. Repertorization of symptomatic totality for prevention or mild to moderate disease**

| Sin. | Med./Rem. | Cobert. | Pts. | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | BRY | 9 | 21 | 2 | 3 | 3 | 3 | 2 | 3 | 2 | 1 | 2 |
| 2 | RHUS-T | 8 | 16 | 2 | 2 | 1 | 3 | | 3 | 2 | 2 | 1 |
| 3 | NUX-V | 7 | 16 | | 2 | 3 | 1 | 2 | 3 | | 2 | 3 |
| 4 | PULS | 7 | 16 | 3 | 3 | 1 | 3 | | 3 | 1 | | 2 |
| 5 | ARS | 7 | 15 | 2 | 3 | 2 | 3 | | 2 | 1 | | 2 |
| 6 | CAUST | 7 | 14 | 2 | 3 | 1 | | | 2 | 2 | 1 | 3 |
| 7 | LYC | 7 | 13 | 2 | 3 | 1 | 3 | | 2 | 1 | | 1 |
| 8 | BELL | 7 | 12 | 3 | 2 | 1 | 2 | | 2 | 1 | | 1 |
| 9 | PHOS | 6 | 15 | 3 | 3 | 3 | 3 | | 2 | | | 1 |
| 10 | ACON | 6 | 14 | | 2 | 3 | 3 | | 1 | 2 | | 3 |

As in the repertorization of the overall symptomatic totality of COVID-19, there are several possibilities of homeopathic medicines of the epidemic genius to be used in prevention or in the mild to moderate disease, such as: *Bryonia Alba, Rhus toxicodendron, Arsenicum album* and *Phosphorus,* among others.

### II.3.2 Homeopathic medicines of the epidemic genius for the treatment of severe disease (COVID-19)

For this stage of the disease, we will use the signs and symptoms of severe involvement (Chen et al., 2020). (Tables 8 to 10)

**Table 8. Symptomatic totality for severe disease**

| **Signs and symptoms in common language** | **Signs and symptoms in repertory language** (repertoire homeopathic rubrics) |
|---|---|
| Fever + dry cough (onset of the picture in general) | COUGH - DRY - Fever, during |
| Dyspnea | RESPIRATION - DIFFICULT |
| Myalgia | GENERALITIES – PAIN - Muscles, of |
| Respiratory failure (acute) / Acute respiratory distress syndrome (ARDS) | RESPIRATION – IMPEDED, obstructed<br>RESPIRATION – ANXIOUS |
| Pneumonia: in the elderly and bilateral | CHEST – INFLAMMATION, Lungs<br>CHEST – INFLAMMATION, Lungs, old people |
| Cold and dry weather worsens | GENERALITIES – WEATHER, cold dry weather, agg |

**Table 9. Symptomatic totality for severe disease**

| Sint. | Selec | Diret | S1 | S2 | S3 | |
|---|---|---|---|---|---|---|
| 1 | X | | | | | RESPIRATION -> ANXIOUS |
| 2 | X | | | | | RESPIRATION -> DIFFICULT |
| 3 | X | | | | | RESPIRATION -> IMPEDED, obstructed |
| 4 | X | | | | | COUGH -> DRY -> fever -> during |
| 5 | X | | | | | CHEST -> INFLAMMATION -> Lungs |
| 6 | X | | | | | CHEST -> INFLAMMATION -> Lungs -> old people |
| 7 | X | | | | | GENERALITIES -> PAIN -> Muscles, of |
| 8 | X | | | | | GENERALITIES -> WEATHER -> cold dry weather -> agg. |

**Tabela 10. Repertorization of the symptomatic totality to the severe disease**

| Sin. | Med./Rem. | Cobert. | Pts. | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | BRY | 8 | 18 | 1 | 3 | 2 | 3 | 3 | 2 | 2 | 2 |
| 2 | ACON | 7 | 17 | 3 | 2 | 1 | 3 | 3 | | 2 | 3 |
| 3 | ARS | 7 | 16 | 3 | 3 | 2 | 2 | 3 | | 1 | 2 |
| 4 | PULS | 7 | 14 | 3 | 3 | 1 | 1 | 3 | | 1 | 2 |
| 5 | NUX-V | 7 | 13 | 1 | 2 | 1 | 3 | 1 | 2 | | 3 |
| 6 | VERAT | 7 | 13 | 1 | 3 | 2 | 1 | 2 | | 2 | 2 |
| 7 | NIT-AC | 7 | 12 | 1 | 2 | 3 | 1 | 2 | 2 | | 1 |
| 8 | OP | 7 | 12 | 2 | 3 | 2 | 1 | 1 | 2 | 1 | |
| 9 | BELL | 7 | 10 | 2 | 2 | 1 | 1 | 2 | | 1 | 1 |
| 10 | PHOS | 6 | 14 | 3 | 3 | 1 | 3 | 3 | | | 1 |

As in previous repertorizations, we could assume several possibilities for individualized homeopathic medicines of the epidemic genius to be used in the serious situation of COVID-19, such as: *Bryonia alba, Arsenicum album, Nux vomica* and *Phosphorus,* among others.

### II.3.3 Homeopathic medicines of the epidemic genius for the treatment of critical states (COVID-19)

For critically ill patients, we will use the signs and symptoms of the very serious involvement of COVID-19 (Yang et al., 2020; Shi et al., 2020). (Tables 11 to 13)

**Table 11. Symptomatic totality for the critical state**

| **Signs and symptoms in common language** | **Signs and symptoms in repertory language** (repertoire homeopathic rubrics) |
|---|---|
| Respiratory failure (acute) / Acute respiratory distress syndrome (ARDS) | RESPIRATION – IMPEDED, obstructed<br>RESPIRATION – ANXIOUS |
| Pneumonia: in the elderly, bilateral, peripheral (pleuropneumonia), diffuse and in the right lower lobe<br><br>Radiological changes: ground-glass opacity (interstitial thickening or alveolar collapse); septal and pleural thickening (infiltration or fibrosis) | CHEST – INFLAMMATION, Lungs<br>CHEST – INFLAMMATION, Lungs, old people<br>CHEST – INFLAMMATION, Lungs, right<br>CHEST – INFLAMMATION, Lungs, right, lower lobe<br>CHEST – INFLAMMATION, Lungs, pleura-pneumonia<br>CHEST – INFLAMMATION, Pleura |
| Multiple organ failure / sepsis | KIDNEYS – SUPPRESSION of urine (anuria)<br>GENERALITIES – SEPTICEMIA, blood poisoning |

**Table 12. Symptomatic totality for the critical state**

| Sint. | Selec | Diret | S1 | S2 | S3 | |
|---|---|---|---|---|---|---|
| 1 | X | | | | | KIDNEYS -> SUPPRESSION of urine (anuria) |
| 2 | X | | | | | RESPIRATION -> ANXIOUS |
| 3 | X | | | | | RESPIRATION -> IMPEDED, obstructed |
| 4 | X | | | | | CHEST -> INFLAMMATION -> Pleura |
| 5 | X | | | | | CHEST -> INFLAMMATION -> Lungs |
| 6 | X | | | | | CHEST -> INFLAMMATION -> Lungs -> right |
| 7 | X | | | | | CHEST -> INFLAMMATION -> Lungs -> right -> Lower lobe |
| 8 | X | | | | | CHEST -> INFLAMMATION -> Lungs -> pleura-pneumonia |
| 9 | X | | | | | CHEST -> INFLAMMATION -> Lungs -> old people |
| 10 | X | | | | | GENERALITIES -> SEPTICEMIA, blood poisoning |

**Table 13. Repertorization of the symptomatic totality to the critical state**

| Sin. | Med./Rem. | Cobert. | Pts. | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | PHOS | 9 | 20 | 2 | 3 | 1 | 2 | 3 | 2 | 2 | 3 | | 2 |
| 2 | BRY | 8 | 19 | | 1 | 2 | 3 | 3 | 3 | | 3 | 2 | 2 |
| 3 | MERC | 7 | 14 | 1 | | 2 | 2 | 3 | 2 | 2 | | | 2 |
| 4 | NIT-AC | 7 | 13 | 1 | 1 | 3 | 2 | 2 | | | | 2 | 2 |
| 5 | BELL | 7 | 12 | 2 | 2 | 1 | 2 | 2 | 2 | | | | 1 |
| 6 | IOD | 7 | 11 | 1 | | 2 | 2 | 2 | 1 | 1 | 2 | | |
| 7 | CALC | 7 | 10 | 1 | 1 | 1 | 2 | 2 | | | 2 | | 1 |
| 8 | ARS | 6 | 16 | 3 | 3 | 2 | 2 | 3 | | | | | 3 |
| 9 | ACON | 6 | 15 | 3 | 3 | 1 | 3 | 3 | | | | | 2 |
| 10 | LACH | 6 | 14 | 3 | 2 | 2 | | 2 | | | 2 | | 3 |
| 11 | SULPH | 6 | 14 | 2 | | 2 | 3 | 3 | | | 2 | | 2 |
| 12 | ARN | 6 | 12 | 3 | 2 | 1 | 2 | 2 | | | | | 2 |
| 13 | DIG | 6 | 11 | 2 | 2 | 1 | 2 | 2 | | | | 2 | |
| 14 | HEP | 6 | 11 | 1 | 2 | | 2 | 3 | | | 2 | | 1 |
| 15 | KALI-C | 6 | 11 | | 2 | | 2 | 2 | 2 | 2 | | | 1 |

In turn, for the critical states of COVID-19, the repertorization of the respective signs and symptoms suggests other possibilities of individualized homeopathic medicines of the epidemic genius, such as: *Phosphorus, Bryonia alba, Mercurius solubilis* and *Arsenicum album,* among others.

To those who question the possibility of using individualized homeopathy in critically ill patients, some studies have been carried out in the area (Intensive Care Unit or Intensive Therapy Unit), showing the benefits of complementary and adjuvant therapy for homeopathic treatment in these cases. (Oberbaum et al., 2005; Teixeira et al., 2008; Frass et al., 2011; Frass et al., 2015)

As mentioned in the teachings of Hahnemann and Kent, the different individualized homeopathic medicines of the epidemic genius, selected for the different stages of COVID-19, must be individualized according to the particularities of each patient, because “no remedy must be given because it is in the list, for the list has only been made as a means of facilitating the study of that epidemic” (Kent, 1998, Lesson III). Hard work of the homeopathic doctor before his patients, to whom he dedicates his individual care and takes responsibility for his actions.

**However, if you want to indicate a homeopathic medicine of the epidemic genius to treat or prevent an epidemic disease in a given population or community, without individual monitoring and prescription, it is essential**

**to submit it to a properly designed clinical research protocol in order to that its effectiveness and safety can be assessed.**

Only then, in line with the bioethical principles of 'beneficence' and 'non-maleficence', could it be suggested for large-scale use. As Hippocrates said, "primum non nocere".

## II.4. Ethical and bioethical aspects of research in human beings

Any research project involving human beings, such as the administration of a supposed homeopathic medicine of the epidemic genius to a population or community, without previous scientific proof of its efficacy and safety, must comply with Resolution No. 466 of December 12, 2012, Ministry of Health/ National Health Council (Brazil, 2012), which "incorporates, from the perspective of the individual and collectivities, bioethical references, such as autonomy, non-maleficence, beneficence, justice and equity, among others, and aims to guarantee the rights and duties that concern research participants, the scientific community and the State".

Among the ethical aspects of research involving human beings, several fundamentals must be observed, such as: respect for the research participant, balance between risks and benefits, guarantee that predictable damages will be avoided and social relevance of the research.

On the other hand, the research must observe numerous requirements, among which: be adequate to the scientific principles that justify it and with concrete possibilities to respond to uncertainties; be based on scientific facts, previous experimentation and/or assumptions appropriate to the specific area of research; be carried out only when the knowledge to be obtained cannot be obtained by other means; always seek that the expected benefits prevail over the foreseeable risks and/or discomforts; obtaining free and informed consent from the research participant and/or his legal representative; to assure research participants the conditions for follow-up, treatment, comprehensive assistance and guidance, as necessary; among others.

All research involving human subjects must be submitted to the appreciation of Research Ethics Committees (CEP) or the National Research Ethics Committee (CONEP), which, when analyzing and deciding to approve it, becomes co-

responsible for ensuring the protection of participants. The ethical review of research projects involving human beings must be associated with their scientific analysis, which must be correctly based on the text.

The researcher's responsibility is non-delegable and indeclinable and includes ethical and legal aspects, and the researcher is responsible for: submitting the protocol duly instructed to CEP or CONEP, awaiting the decision for ethical approval, before starting the research; prepare the Informed Consent Form (ICF); develop the project as outlined; preparing and presenting the partial and final reports; among other duties and responsibilities.

Among countless other ethical and bioethical aspects of research involving human beings, we have brought some basic premises to exemplify the serious shortcomings committed by those who intend to distribute homeopathic medicines indiscriminately to an entire community without observing the ethical and bioethical principles, fundamental for that the safety of the participants and the effectiveness of the measure are guaranteed.

For the administration of a specific homeopathic medicine of the epidemic genius to a population, or any other therapeutic proposal without scientific proof, it is necessary to carry out previously controlled clinical trials, in accordance with the steps mentioned in that Resolution.

This protocol is intended to exemplify the indispensable aspects for the elaboration of a clinical research project, as well as the dynamics necessary to execute a protocol according to ethical and scientific guidelines, clarifying homeopathic colleagues as to the premises that must be followed in clinical research involving human beings.

On the other hand, we are submitting this protocol to researchers and health managers, requesting an opportunity to propose, discuss and apply this proposal in the research institutions and health services that work and/or administer it, in order to research and select medicines homeopathic drugs of the epidemic genius of COVID-19 appropriate for the various stages of the disease, as well as, in a second moment, to be able to apply it in a preventive and community way.

In addition to previous expectations, the disclosure of this protocol in an online and freely accessible form (indexed in the VHL Regional Portal) also aims to raise awareness and invite other researchers, homeopaths or not, to apply the

method proposed in their work or research units, allowing the increase in the sample of patients (greater accuracy of the results) and the elaboration of a multicenter research project on the use of homeopathy in epidemic diseases.

## III. STUDY JUSTIFICATION

In view of the absence of preventive and/or curative therapies for the current SARS-Cov-2 outbreak that plagues humanity, of the hundreds of thousands of infected individuals worldwide, of millions of infect individuals by COVID-19, among which hundreds of thousands died, and since Brazil is the actual epicenter of this pandemic, with an exponential increase in patients and deaths, it is essential to search for other therapeutic and/or prophylactic approaches that can act in an adjuvant and complementary way to the measures hygienic and isolation standards, with homeopathy being a low cost and safe alternative.

Just as it has acted in the prevention and treatment of several epidemics in the past, the individualized homeopathic medicine for the epidemic genius of COVID-19 could be adopted in all segments of health services and society, as long as it proves to be effective and safe.

After the in-depth study and the survey of some drug hypotheses that can act therapeutically and preventively in the current epidemic, we are proposing to conduct a double-blind, placebo-controlled study to test the efficacy and safety of the homeopathic medicine(s) X, Y and/or Z (one must choose which or which drugs to be tested) in the adjuvant and complementary treatment of the various stages of COVID-19.

If the hypothesis is confirmed in the treatment of the initial stages of the disease (mild to moderate disease), the drug may also be used on a large scale in the prevention of the current epidemic, as Hahnemann observed in the use of *Atropa belladonna* in the treatment and prevention of scarlet fever: “a medicine that is capable of quickly blocking a disease in its beginnings should also be your best preventive” (“Cure and prevention of scarlet fever”, Hahnemann, 2006b).

## IV. STUDY OBJECTIVE

The objective of this study will be to evaluate the effectiveness of the homeopathic medicine(s) X, Y and/or Z (one must choose which or which medicines to be tested) in dynamizations/potencies 30, 200 and 1000cH as treatment adjuvant and complementary in the various stages of COVID-19, through a randomized, double-blind and placebo-controlled clinical trial.

## V. PATIENTS AND METHOD

With this project, we propose to conduct a randomized, double-blind and placebo-controlled short-term clinical trial (2-3 months) administering the homeopathic medicine(s) X, Y and/or Z (one must choose which or which medicines to be tested) (dynamizations/potencies 30, 200 and 1000cH) or 'placebo' to patients with COVID-19 at different stages of the disease, concomitant with conventional support and treatment measures.

This study will be carried out with patients admitted to ward/infirmary or ICUs of ___ (Institution where the study will be carried out).

The ethical, practical and biosafety principles stipulated by the Ministry of Health and the institution's Human Research Ethics Committees will be respected, as well as the technical protocols of the hospital and the doctors involved. The study will be initiated only after approval by the Institution's Research Ethics Committee.

### V.1. Sample calculation

For each stage of COVID-19 (mild to moderate disease, severe disease and critical state), 50 patients (25 in each group: 'active' and 'placebo') with manifest disease and diagnosed by quantitative examination of the load will be studied viral (RT-qPCR), followed up on ___ and/or ___ (ward and/or ICU of the referred Institution). All patients and/or their companions/guardians will be previously informed about the study and will sign the Informed Consent Form (Annex 1) before entering the protocol.

### V.2. Inclusion and exclusion criteria

Inclusion criteria will be considered: ___ (if any, include according to the population chosen to participate in the project)

Exclusion criteria will be considered: ___ (if any, include according to the population chosen to participate in the project)

### V.3. Study dynamics

To participate in the project, the medical records of patients monitored at the ___ and/or ___ (ward and/or ICU of the referred Institution) will be evaluated in order to confirm the general inclusion/exclusion criteria. If so, patients and/or their companions/legal guardians will sign the Informed Consent Form (ICF) (Annex 1).

**V.3.1. Randomized, double-blind and placebo-controlled clinical trial**

Once the inclusion/exclusion criteria are fulfilled and the ICF is signed, patients and/or their companions/legal guardians will be referred to the performing researcher to be informed about the dynamics of the proposed homeopathic treatment and will receive the 'active' homeopathic medicine(s) (X, Y and/or Z at dynamization 30CH) or 'placebo', according to a randomization scale previously stipulated according to the number of the patient entering the protocol (01, 02, 03, etc.) or bed number of ward room/ICU, each with its specific bottle, previously randomized and 'blinded' to the drug in use ('active' or 'placebo'), so that the researcher and patients are unaware of the allocated group.

Every patient will remain in the same allocated group ('active' or 'placebo') until the end of their hospital treatment and the administration of the medicine(s) ('active' or 'placebo') to patients will be performed by the team of nursing in the prescribed dosage.

The drug(s) ('active' or 'placebo') will be administered initially in the dosage of 3 drops, 4 times a day (can be individualized, increased or decreased, according to the stage of the disease and the evolution of the framework). Any change in dosage must be included in the patient's medical record, in order to enable future analysis of the evolution of the groups ('active' and 'placebo').

In the case of randomization by bed number of ward room/ICU, with patient discharge, the new patient will remain in the same group ('active' or 'placebo') as the bed room initially randomized, facilitating the work of distribution and medicine administration by the nursing team.

Patients will be evaluated daily (or several times a day) by the performing researcher(s), during the hospitalization/treatment period. Each day, the effects of the drug ('active' or 'placebo') on the general evolution of the clinical picture will be assessed by reading the medical record, talking to the medical team and/or individual anamnesis, allowing for an adjustment in dosage (doses and

potencies of the homeopathic medicine) depending on the clinical response: in case of constant and progressive response, the 30cH potency will be maintained; in case of absence or insufficient response, the potency will be increased to 200cH and 1000cH, successively.

This 'potencies individualization' becomes necessary to obtain progressive gains in the homeopathic therapeutic response, due to the tolerance to the same potency observed after a period of use (analogous to oral immunotherapy).

As a mandatory premise for assessing the security of the proposal, possible adverse events will be assessed periodically, being reported on the Adverse Events Form (Annex 2).

Patients and their companions legal guardians will have easy access to the researcher (phones and whatsapp), so that possible changes in the clinical condition are communicated and the inherent measures (adjustment in dosage) are quickly instituted.

At the end of the hospital treatment period, patient data will be computed and stored, so that the evolution of the groups can be analyzed statistically.

### V.3.2. Preparation and delivery of medicine

Will the preparation and supply of the 'active' drugs (X, Y and/or Z in the dynamizations 30, 200 and 1000cH) and 'placebo' for the study period be carried out by the ___ Laboratory or Pharmacy (responsible pharmacist and contact).

The medicine will be made available in liquid form, in a 20% hydroalcoholic solution, packaged in 60ml bottles with droppers and dispensed according to the Brazilian Homeopathic Pharmacopoeia (Farmacopéia Homeopática Brasileira, 2011). The vials with a volume of 60 ml will be sufficient for the proposed dosage for each patient for a period of 2 months (3 drops, 4 times a day, which corresponds to 720 drops), being replaced when they are finished.

### V.3.3. Statistical analysis

The different variables of the clinical evolution of COVID-19 will be analyzed statistically (global analysis between 'active' and 'placebo' groups), to verify the possible existence of a significant clinical response to interventions.

Quantitative variables will be described according to groups using summary measures and compared between groups using comparative tests, t-Student tests or Mann-Whitney tests according to the probability distribution of the variables.

### V.3.4. Work plan

This project has a perspective of duration of n (weeks or months) divided as follows: n1 (days or weeks) for the selection of patients, n2 (weeks or months) for the clinical trial and n3 (weeks or months) months for analysis and publication of the results, according to the work plan below. (Table 14)

**Table14. Work plan with project phases and procedures**

| Project phases | Responsible | Procedures |
|---|---|---|
| Selection of patients | Institution professional | Anamnesis and/or reading of the medical record to confirm the inclusion/exclusion criteria and signing the Informed Consent Form. |
| Start of treatment | Performing researcher(s) | Clarification on the dynamics of treatment and start of the dispensing of 'active' and 'placebo' medicines according to the randomization scale. |
| Throughout the treatment period | Performing researcher(s) | Daily assessment of patients in order to adjust the dosage in accordance with the evolution of the clinical picture. |
| End of treatment period | Performing researcher(s) | Patient data will be computed and stored. |
| Analysis and publication of results | Performing researcher(s) | Data tabulation, statistical analysis, writing and publication of results. |

### V.3.5. Budget

The estimated budget for carrying out this project is based on the cost of medicines, being estimated at $$ (value of costs).

### V.3.6. Work team

1. Researcher in charge: Prof. Dr.Marcus Zulian Teixeira
2. Performing researcher:
3.

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# VII. ANNEXES

## VII.1. Annex 1 – Informed Consent Form (ICF)

### Informed Consent Form (ICF)

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**Research data**
Research title: "Clinical research protocol to evaluate the effectiveness and safety of individualized homeopathic medicine in the treatment and prevention of the covid-19 epidemic"
Researcher in charge: Prof. Dr. Marcus Zulian Teixeira
Department/ Institution:

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**Identification data of the participant or legal guardian**
**1**. Name:
Identity document No.: Sex: M□ F□
Date of birth:
Address:

**2**. Legal guardian:
Nature (degree of kinship, guardian, curator, etc.):
Identity document No.: Sex: M□ F□
Date of birth:
Address:

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Introduction: You are being invited as a volunteer to participate in this clinical research because you have coronavirus disease (COVID-19), are experiencing symptoms of the disease and are receiving conventional treatment. This is a study on the efficacy and safety of homeopathic treatment in patients with COVID-19, associated with conventional treatment (complementary homeopathic treatment). The aim of this study will be to evaluate the efficacy of the homeopathic medicine X, Y and/or Z, compared to the use of placebo in the complementary treatment of COVID-19. For this, all participants will receive 'active' homeopathic medicine (X, Y and/or Z) or 'inactive' or 'placebo' medicine (inert substance with no pharmacological effect) during the period of n2 weeks (randomized, double-blind and placebo-controlled clinical trial). All patients will be randomly distributed in these two groups ('active' medicine or 'placebo' medicine) and, like the homeopathic doctor, you won't know which group is allocated (double-blind).

Procedures: Patients under conventional treatment and at all stages of the disease will be included in this study.
If you agree to participate, you will be referred to the homeopathic doctor to start treatment during your stay at this hospital, with daily evaluations of the homeopathic doctor in conjunction with the other teams.
The medicines will be given at a dose of 3 drops, in the mouth, 4 times a day (every 6 hours). These doses may be increased or decreased according to the evaluation of the homeopathic doctor, seeking a progressive improvement of his condition.

Discomforts and risks: All types of clinical research may involve some risk, and not all are predictable. You may experience some discomfort during treatment due to the occurrence of adverse reactions. Although homeopathic treatment does not usually

present serious adverse effects, it is important that any bothersome event that may occur during the study is promptly reported to the homeopathic doctor.

Benefits: No direct benefits are guaranteed to participants. This is an experimental study testing the hypothesis that homeopathic treatment can help in the improvement of patients with COVID-19. Only at the end of the study can we conclude about the presence of some benefit. Its participation may contribute to the development of a therapeutic alternative to the current epidemic caused by coronavirus.

Alternative therapies: There are several conventional medications to treat disorders caused by the disease and you do not need to participate in this study for your problem to be treated with the therapies already approved. If you decide not to participate in the study, you will receive treatment deemed appropriate for your condition.

Guaranteed access: At any stage of the study, you will have access to the professionals responsible for the research to clarify any doubts. The main investigator is the Dr. ___ which can be found in this ward (or CTI) or by phone/ whatsapp ___. If you have any consideration or questions about research ethics, please contact the Research Ethics Committee (CEP) (address and contacts).

Participation and closure: You are free to refuse to participate or withdraw your consent and discontinue treatment at any time. Participation is voluntary and refusal to participate will not incur any penalty or loss of benefits. Refusal or interruption shall in no way prejudice the benefit of receiving any treatment, now or in the future, at this Institution.

Secrecy and confidentiality: Your doctors will treat your identity with professional standards of secrecy. Your chart will remain confidential. The information obtained will be analyzed together with other patients, and the identification of any patient is not disclosed. The researcher undertakes to use the data and the material collected only for this research. A copy of this informed consent will be archived in your medical records and one will be provided to you.

Update on results: During the course of the study, you will be informed about the partial results of the research. If these new findings make it necessary to reassess your individual situation or interrupt your participation in the study, the homeopathic doctor will inform you. There may be circumstances in which you will be removed from the study. These include marked worsening of your condition, not adherence to the medication under study, if the researcher considers that it is in your best interest or if the study is interrupted. You may be removed without the need for your consent. In case of personal damage, directly caused by the procedures or treatments proposed in this study (proven causal link), the participant will be entitled to medical treatment at the Institution.

Expenses and compensation: There are no personal expenses for the participant at any stage of the study. There is also no financial compensation related to your participation.

Patient statement: I believe I have been sufficiently enlightened about the information I have read or that has been read to me, describing the study **"Clinical research protocol to evaluate the effectiveness and safety of individualized homeopathic medicine in the treatment and prevention of the covid-19 epidemic".** I discussed with Dr. ___ about my decision to participate in this study. It was clear to me what are the purposes of the study, the procedures to be performed, their discomforts and risks, the guarantees of confidentiality and permanent clarification. It was also clear that my

participation is free of charge and that I am guaranteed access to conventional treatment. I voluntarily agree to participate in this study and may withdraw my consent at any time, before or during it, without penalty, injury or loss of any benefit I may have acquired, including my care at this Hospital.

_____
Signature of patient or legal representative Date: _____ / _____/ _____

_____
Witness signature Date: _____ / _____/ _____

*(Only for the project manager)*
I declare that I have obtained in an appropriate and voluntary manner the Informed Consent Form of this patient or legal representative for participation in this study.

_____

Signature of the responsible for the study Date: _____ / _____/ _____

## VII.2. Annex 2 - Adverse Events Form

| **Patient:** | | | | **Identification:** | |
|---|---|---|---|---|---|
| **Adverse Events Form**<br>(include all adverse events that the patient has had since the previous visit, whether or not it is related to the drug) | | | | | |
| **Adverse Event** | **Start/ Finish** | **Event Type**<br><br>(C) Constant<br>(I) Intermittent<br>(A) After dosing | **Severity**<br><br>1. Mild<br>2. Moderate<br>3. Severe<br>4. Potentially fatal | **Relationship**<br><br>0. Unrelated<br>1. Possible<br>2. Likely<br>3. Related | **Investigator's Action**<br><br>0. None<br>1. Change in dose<br>2. Medication withdrawal<br>3. Introduction of new medication<br>4. Discontinuation of the study |
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