SARS-CoV-2 COVID 19 SPIKES CHEMICAL REACTION WITH CLIMATE HUMIDITY

Yves PIOVAN Institut National Polytechnique of Toulouse, Legal expert in chemistry

ABSTRACT

The analysis consists of daily monitoring of pandemic fluctuations and climatic fluctuations over a period of two months in France.
A comparative analysis survey in 27 European countries determined the effect of climatic conditions, temperature and humidity on differences in the extent of the disease. From the molecular composition of Spikes, we established their hygroscopic property and showed the essential role of air humidity on the spread of COVID-19 disease.

Keywords: COVID-19, SARS-CoV-2, Vapor, Model, humidity, Propagation

INTRODUCTION

The medical community has carried out today in the world, very numerous and important works for decades through the successive appearances of the different forms of Coronavirus. But although the latest medical studies have been widely increased recently, there have been few studies and scientific research about a link between the modes of transmission of the pandemic and the physical characteristics of the air inhaled through the respiratory tract. Doctors are now finding, without explaining it, that the most active spread is that of asymptomatic patients who do not have visible symptoms of breathing. It is for this reason that we focus our research on pulmonary aerosols of invisible spectrum. The medical studies carried out to date have been devoted to main clinical knowledge such as the definition and biological representation of the genome, the medical description of the viral cycle, that of receptor binding, fusion, transcription and replication of the virus propagation cycle. These studies have clarified the biochemical structure of the virus as well as the modes of action of the proteins in the Virus, such as the role of ACE2 receptors.
Epidemiological studies found in the scientific literature have addressed the epidemic potential of MERS-CoV and the identification of the basic reproductive rate of patients infected with MERS-CoV without addressing the role of climatic variations.

Among these studies, the first was that of the first human coronaviruses studied, 229E (HCoV-229E) and OC43 (HCoV-OC43). These coronaviruses were isolated by researchers in the 1960s. They are classified respectively among the Alpha coronaviruses and the beta coronaviruses.
In 2002, the first highly pathogenic coronavirus appeared in the human population: the beta-coronavirus SARS-Co (2). It was responsible for epidemic of severe acute respiratory syndromes that started in China. The following coronaviruses 229E (HCoV-229E) and OC43 (HCoV-OC43) were isolated in the 1960s. Following these epidemics of SARS-CoV, new coronaviruses, human beta-coronaviruses NL63 (HCoV-NL63) and HKU1 have were discovered in 2004 and 2005 respectively. They are responsible for mild infections. Then there was the appearance of beta-coronavirus in Saudi Arabia. It was named Middle East Respiratory Coronavirus Syndrome (MERS-CoV). It emerges from all studies carried out in the medical environment that coronaviruses are mainly transmitted by aerosols of biological fluids and by contamination of surfaces. They are said to infect the human respiratory route by entering the cells of the respiratory epithelium through the apical pole. Recently, medical studies have been able to prove that new virions are also excreted from the apical pole, facilitating the spread of the virus by coughing and sneezing (15).

Despite all the high-level medical studies carried out, despite modern medical imaging tools, the results of therapeutic prescriptions are stagnating. Attempts to eliminate the proliferation of the new coronavirus have so far been unsuccessful. Recent theoretical knowledge on the COVID-19 chemical attack is today at the highest medical level. But paradoxically, they are late in obtaining effective medical treatment. Because of these noted difficulties, it becomes important to redirect scientific research. We hope to obtain more encouraging results by concentrating our efforts on research on invisible pulmonary aerosols. As a scientific basis for our new study, we use the recently made observation that the virus is transmitted by aerosols from asymptomatic patients who are infected without contact. Inhaled air is said to be a major factor in the transmission of the virus. For this reason, we have devoted ourselves to examining the impact of changes in atmospheric characteristics on propagation speed. With these data, we have better known the biological mechanism of COVID-19, and in particular the role of it's Spike. The first parameter chosen is the daily variation of the atmospheric relative humidity, the reason is it is linked to the water vapor inhaled during respiration. The second parameter chosen is the variation of the daily air temperature because the effectiveness of viruses is known to be sensitive to temperatures. Indeed, we know that coronaviruses desappear for very high temperatures, proliferate at moderate temperatures between 10 and 40 degrees and doze for negative temperatures.

We first identified the daily fluctuations in atmospheric data in France. We compared them with the pandemic spread data. The conclusions obtained were the subject of a verification of the results on a series of 27 European countries. These countries have very different climates. Some have a hot and humid Mediterranean climate, others a cold and dry continental climate and the latter have a cold and humid northern climate. We compared the climatic effects by presenting our results in the form of a graph with comparative evolution curves and in the form of correlations on the XY axes.

Therefore, the novelty of our approach is to direct scientific interest towards examining the characteristics of inhaled air during a pandemic period, in order to determine and understand the role of atmospheric humidity as a carrier vector of COVID-19 in the pandemic.

EXPERIMENTATION

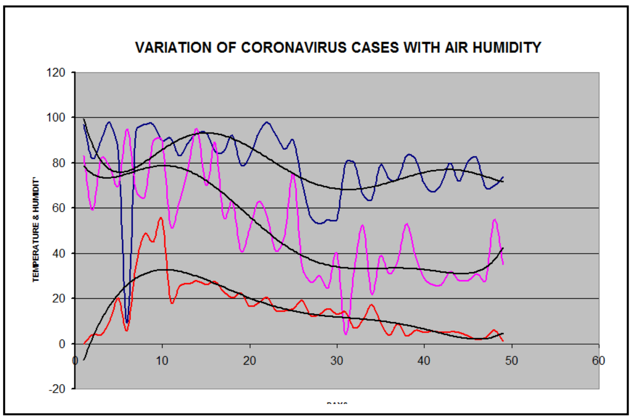
The examination of the mode of transport and spread of the virus is based on a survey of official atmospheric surveys for the periods of February, March and April 2020. The atmospheric data used are extracted from the France Meteorology Institute in the northeast region of the hexagon due to the significant presence of viruses. The coronavirus data come from the French governmental bases of pandemic of COVID 19.

The extracted data of the analysis are130,000 cases of coronavirus declared, 1,620 temperature readings, 32,400 humidity readings in 27 European countries. We have with these data carried out analyzes of correlation between the various collected data. Calculations and graphs are carried out with the Excel software. The measurement point curves were smoothed by degree 6 polynomial regression of type aX6 + bX5 + cX4 + dX3 + eX2 + fX + g.

For the study of daily monitoring, the two parameters are daily humidity in France as well as the increase in cases of COVID19. Daily measurements were taken at 7 a.m. and 4 p.m. This scenario was chosen because the results at 7 a.m. reflect the relaxation of absolute humidity during the cooling of the night, i.e. the increase in relative humidity until saturation in the morning. The results at 4 p.m. correspond to the time at which the daytime temperature is maximum, and correspond to the time of day with the maximum humidity accumulation between 9 a.m. and 4 p.m. The monitoring of daily fluctuations is illustrated in Figure 1. The results of the linear correlation analysis of the 7 a.m. and 4 p.m. readings. are shown in Figures 2 and 3 respectively

RESULTS

Figure 1 presents a comparison graph with superimposed curves of the simultaneous variations of two parameters, humidity at 4 p.m. and cases declared over a period from February 3 to April 30. The days are numbered from 1 to 40. Two characteristic periods emerge: At the start of the pandemic, a first period characterized by a rapid increase in the number of confirmed cases (days 1 to 8). A second period of 36 days is characterized by a short plateau of values followed by a continuous decline until the last day. Period 2 between days 6 and 15 shows a daily fluctuation relationship (Figure 1)
between the number of cases and the humidity.



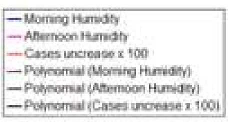


Figure 1

The existing relationship between these two parameters is shown again in XY representation (Figures 2 and 3). The results in the figure show a relationship between the daily humidity values and the cases of coronavirus with a correlation coefficient of 45% for the 7 hour readings

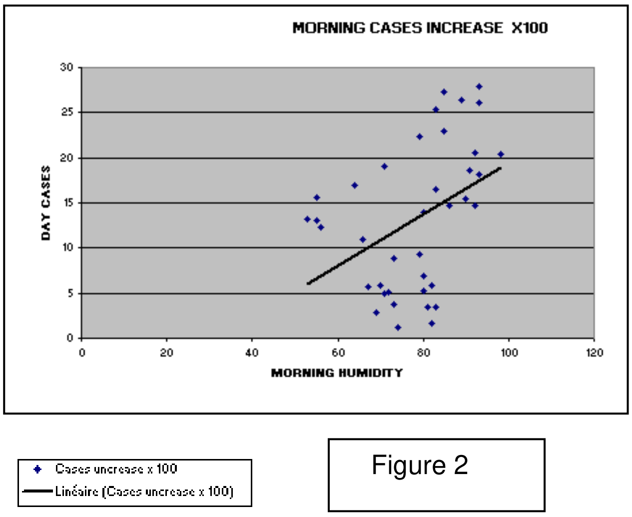


Figure 2

For the 16 hour readings (figure 3). the figure show a relationship between the daily humidity values and the cases of coronavirus with a correlation coefficient of 69%.

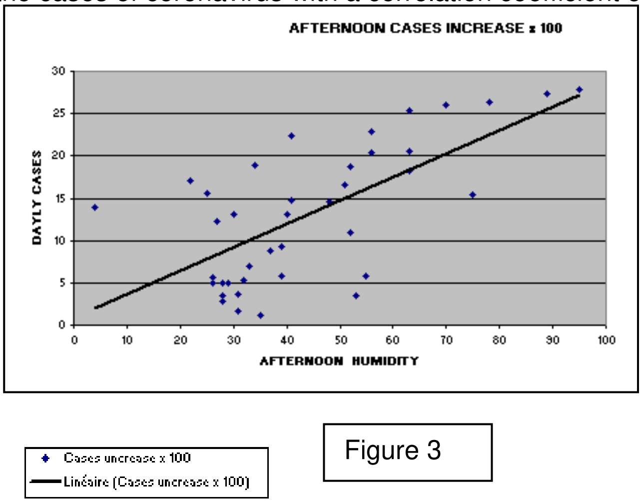


Figure 3

Country	Cases 01 May per million	Average Humidity March April (%)
Germany	1966,1	56
Austria	1753,4	55
Belgium	4285,8	67
Bulgaria	227,8	52
Chipre	715,7	50
Croatia	513,7	49
Denmark	1639,9	56
Spain	4560,2	73
Estonia	1285,9	64
Finland	924,8	63
France	2497,9	65
Greece	242,3	44
Hungary	296,6	51
Ireland	4273,7	62
Italy	3432,5	63
Latvia	451,5	59
Lithuania	499,6	58
Luxembourg	6250,0	70
Malte	964,9	62
Netherlands	2321,4	64
Poland	345,0	54
Portugal	2469,9	67
Czech Republic	724,4	51
Romania	647,3	43
United Kingdom	2688,8	66
Slovakia	256,9	51
Slovenia	675,1	51
Sweden	2113,0	66

Table 1

Conclusion: The humidity readings represent a regional sample of 80% of people in France (northeast region). The COVID 19 case reports in France correspond to the entire national population. As the correlation coefficient obtained is equal to 69%, this is a sufficient confidence result to establish that there is a cause and effect relationship between relative humidity measured at 4 p.m. and cases of coronavirus. The relative humidity at 7 a.m reflecting the relaxation of absolute humidity during the cooling of the night, is over 95% all month long , that is a quasi saturation. It doesn't cannot daily fluctuations, that is, a representative correlation coefficient.

European 27 countries results: Figure 4 is an epidemic representation of 27 European countries in XY axes. This figure compares the relative humidities and the numbers of coronaviruses. (See Table 1 values).

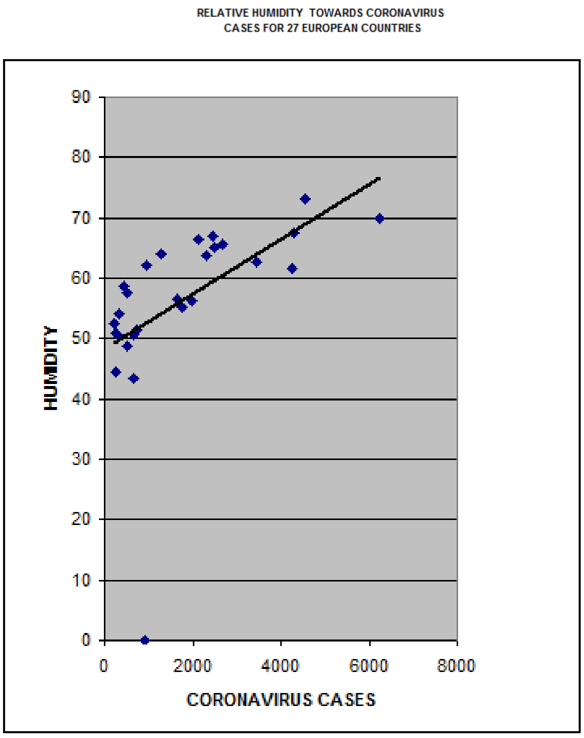


Figure 4

The elongated shape of the points reflects the existence of an increasing relationship between humidity and cases of coronavirus with a correlation coefficient of 77%. On the linear correlation curve, we find singularities related to temperature: several countries with the same X, Y coordinates, that is to say, with the same humidity and quantities of coronavirus, have very different temperatures. As an example, Spain and Ireland, which are known to be two countries with different climates, one Mediterranean, the other Nordic, have the particularity of having similar values of humidity and number of coronaviruses while the temperatures are very different (11 and 18 degrees).
The COVID 19 case reports in France correspond to the entire national population. Since the correlation coefficient obtained for values at 4 p.m. is 69%, this is a confidence result sufficient to establish that there is a cause and effect relationship between the relative humidity measured at 4 p.m. and the cases of coronavirus. However, the relative humidity at 7 a.m. reflecting the relative humidity after the accumulation of the night, is greater than 95% throughout the month, i.e. almost daily saturation. In the absence of daily fluctuations, the humidity correlation coefficient at 7 a.m. is not representative
However, in Figure 5 showing the temperature and the number of coronaviruses in the XY axes, the point cloud is random with a very low correlation coefficient of 45%. The example of these two countries among others, presented in Figure 4, shows that temperature is not a basic cause and effect parameter with the pandemi.

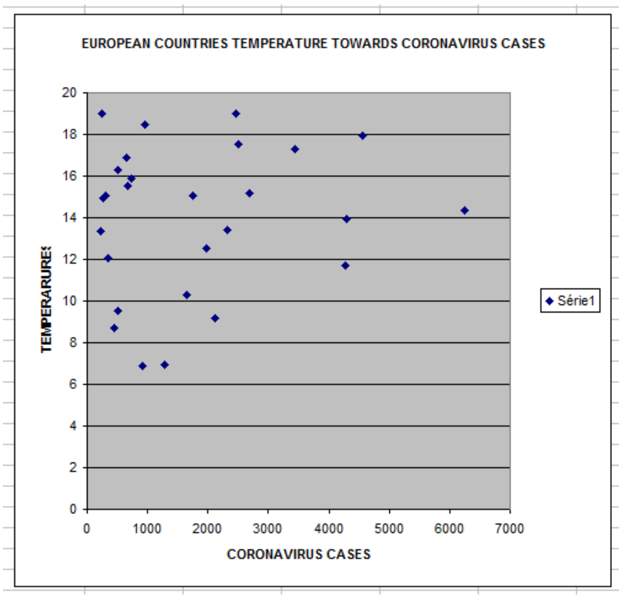


Figure 5

DISCUSSION

Medical institutes at this time know that active spread of the virus is present in asymptomatic patients who do not have visible breathing problems, such as coughing or sputum. Researchers at GUANGZHOU University in China have obtained medical images that the lungs of asymptomatic patients have pulmonary MRI coronavirus profiles. It follows from their work that invisible spectrum aerosols are contagious. The characteristic of aerosols is that their existence is dependent on a process of enlargement of droplets according to the dimension scale below. In this scale, the spectrum of water vapor is located between 1 Angstrom to 1 mm Figure6).

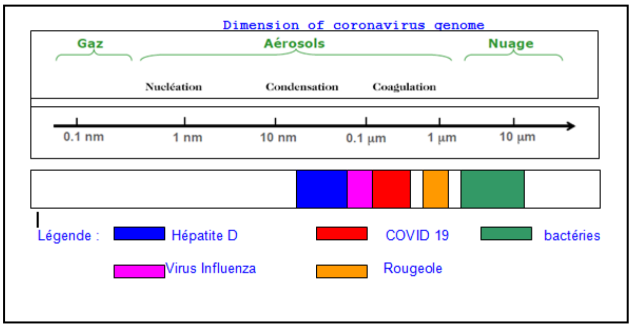


Figure 6

Principe of development of an aerosol

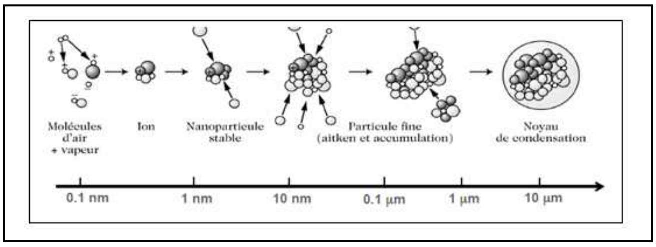
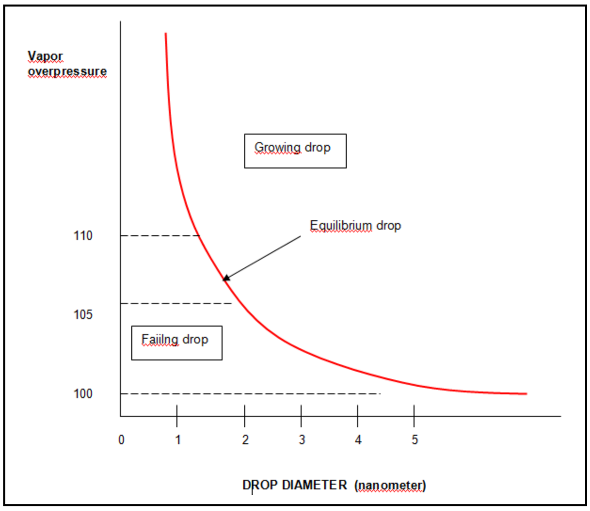


Figure 7 Ref 16*

The existence of a stable aerosol is linked to specific thermodynamic conditions. In order for water vapor molecules to agglomerate, accumulate and condense, they must comply with Kelvin's thermodynamic law figure 8.

For the aerosol of a patient, (17 *) the mucous membranes of the upper airways being abundantly vascularized, they ensure the humidification and warming of the inspired air. Under normal conditions, the inspired air is brought to around 32 ° C and has been completely humidified when it leaves the pharynx. It is in the middle trachea that, normally, the air is brought to body temperature (37 ° C) and that it reaches the required degree of hygrometry, namely: 44 mg / l.



Relation Steam overpressure and droplet diameter

Figure 8

Therefore, in the opposite direction of the flow, when the air is discharged from the middle trachea to the pharynx, due to the passage from 37 ° to 32 ° the air is in supersaturation of vapor. Clapeyron's thermodynamic law of vapor pressure gives for a saturation 100% at 37 degrees, a supersaturation pressure or relative humidity of 130% at 32 degrees rejection (Figure 9)

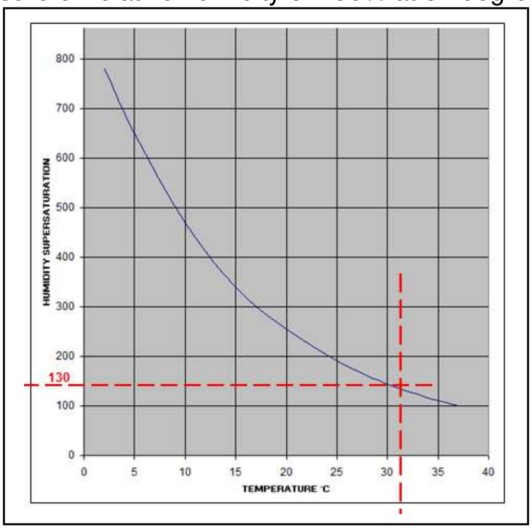


Figure 9

According to an expiration scenario using this data, the aerosol of supersaturated vapor cools from 37 to 32 degrees when it leaves the pharynx, condenses under the conditions of Kelvin's thermodynamic law The calculations of this law, for a saturation vapor overpressure (in other words Relative Humidity) coefficient located between 100 and 130% , give a diameter of drops in thermodynamic equilibrium, between 4 and 20 nanometers (red curves intervall). See figure 10 below.

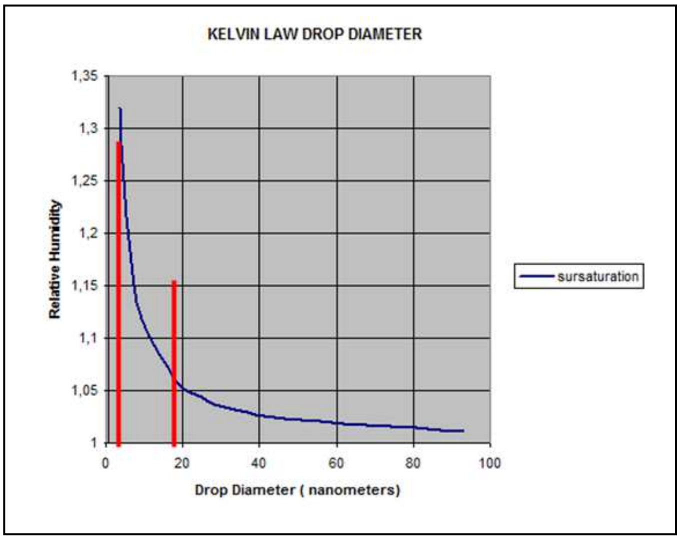
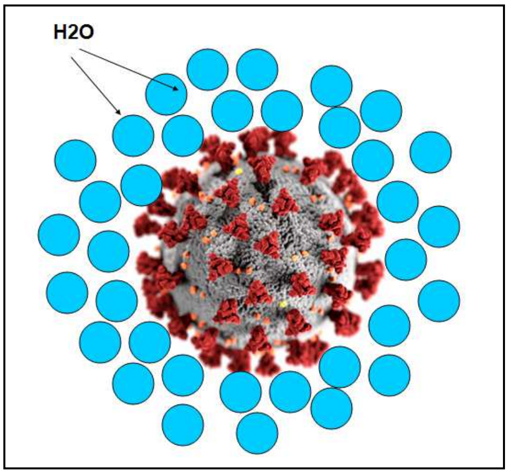


Figure 10

So drops of dimension greater than the equilibrium curve fulfill the conditions of agglomeration and accumulation with each other. The law therefore demonstrates the existence of an aerosol invisible to the eye (less than 20 nanometers) when the expelled aerosol is close to an inhaled atmosphere of 100% humidity (130% expelled humidity).

The measurements obtained during april and may were an average relative humidity measured of 80% in March and 65% in early April, 55% in late April. Taking into account the amount of added humidity when brathing out, these humidities correspond to 110% and 95% and 85% of relative humidity rejected. According to Kelvin's law, the aerosols give coagulation condition of droplets over 11 nanometers in March, 100 nanometers in early April and >100 nanometers in late April. Taking int account that expelled aerosol is between 4 and 20 nanometers, in consequence in late April coagulation diameter is too large to maintain an aerosol. The result corresponds to the observation at the end of April of the tendency to decrease in the number of coronaviruses declared.

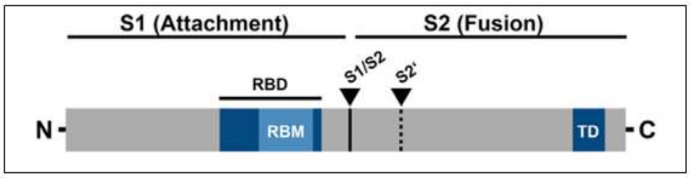
Knowing that the spikes of coronavirus ends are hydrophilic, when the coagulation conditions of the vapor molecules allow it, the aerosol coagulates on the crown of spikes (Figure 11)



coagulation of molecules on hydrophilic spikes

Figure 11

Indeed, the coronavirus polypeptides have two endings (figure 12), one S1 with amino terminus NH2, the other S2 with carbonyl end COO- and the NH2 end is hydrophilic (ref 2 *).



Spike **configuration with N termination of hydrophilic S1 branch (ref 8)**

Figure 12

<u>COVID-19 spikes are hydrophilic:</u>

First of all, water is attracted to the hydrophilic functional groups of other proteins, due to its particular molecular conformation. The oxygen atom of the water molecule has four sp3 orbitals. Of the six electrons in the electron layer, two electrons are taken up by the two covalent bonds with hydrogen, so the other two orbitals carry a non-binding electron doublet. Free electrons create an imbalance of charges, the oxygen atom is changed negatively $(\delta-)$.

This atom attracts hydrogen atoms from other positively charged hydrophilic functional groups $(\delta+)$ and creates a hydrogen bond.

The laws of chemistry demonstrate that the Spikes S1 and S2 meet the conditions of molecular configuration to create hydrogen bonds with water.

<u>hydrophilicity of the N-terminal NH2 group of Spike S1</u>

In the N-terminal group of Spike S1, the functional group NH2, the nitrogen atom has an hybridization sp3. The free doublet carried by the non-binding orbital is located closer to nitrogen than the H bonding doublets, which repels them.

As N is more electronegative than H, there is an excess of negative charge $(\delta-)$ on this one. The molecule therefore has a dipole moment. The nitrogen atom has a negative charge $(\delta-)$, the H atom has a positive charge $(\delta+)$. In consequence, a dipole-dipole interaction of the polar group NH is created with the electronegative oxygen atom in water. The H atom at the amino terminus of the Coronavirus Spike will create a hydrogen bond with negatively charged water oxygen. So, water is attracted to the polar NH group due to the hydrophilic nature of the NH group.

<u>hydrophilicity of the Carboxylterminal COO- group of the spike S2</u>

In the Carboxylterminal group of Spike S2, the carbon atom is of type AX3, or sp2. The oxygen atom carrying the negative charge is of the AX3 type. The oxygen atom with the negative charge is carrying three non-bonding doublets. It is of AX3 type, ie a hybridaton sp3. The second oxygen atom is a AX2 type, an sp2 hybridization. Due to the mesomeric form, the carboxylate has three sp2 orbitals. The binding orbital mobilizes two electrons for bonding with carbon. The other two non-binding orbitals have four free electrons. The doublets carried by the non-binding orbitals are located closer to oxygen than to carbon. For this reason, the oxygen atom is negatively charged, $(\delta-)$, the carbon atom positively charged $(\delta+)$.Due to the charges, the oxygen atom at the C-terminus of the Coronavirus Spike will create a hydrogen bond with the hydrogen in negatively charged water. Consequently, water is attracted to the polar group COO- which has a hydrophilic character.

<u>Consequence of the effect of humidity and the attraction of Spikes for water</u>

Coronavirus infection causes an additional release of water, the virions being carried away by the water vapor. These high humidity conditions exist in the lungs of an infected patient: Mucous fluids in the lungs have been found to be overabundant during COVID 19 symptoms. Recent findings by hospital services obtained from patients with COVID 19 show images of MRI examination with a tapestry significant viral mucus in the alveoli. Biological analyzes show that the alveolar mucus is made up of 99% H2O (13*). However, the mechanism of attack of cells by the coronavirus consists in creating protein ruptures by hydrolysis, that is to say with the production precisely of H2O.

In detail of the attack mechanism, the COVID 19 viruses are characterized by their crown of proteins known as “Spike” or S. The SARS-Cov2 virus (COVID 19) begins by undergoing a “priming” stage for spikes, a kind of 'activation. COVID 19 Spikes are activated by their own enzyme. As a result, at the start of the viral attack, COVID 19, with its own enzymes, produces H2O.

Once the Spike protein is "awarded" or activated, the coronavirus will once again release water by hydrolysis. It will attach to one of the receptors on the surface of our cells, called ACE2. (Figure 13). Since the SARS-Cov2 has an envelope (Figure 13), it must indeed combine it with the membrane of our cells or of our cellular compartments to penetrate it.

This step, called endocytosis, requires that the Spike protein be cut again by a protease and therefore produce water a second time. Again, this is furin and TMPRSS2. Furin is a serine protease which catalyzes the cleavage of a polypeptide typically at the level of a basic sequence of the form –Arg – Xaa–(Arg / Lys) –Arg- | - where Xaa represents an acid residue any proteinogenic α-amino. TMPRSS2 codes for a protein in the serine protease family. Serine proteases are a family of different proteases called peptidases, which share the same mechanism of action. Like all proteases, their function is to cleave proteins or peptides by hydrolyzing their peptide bonds.

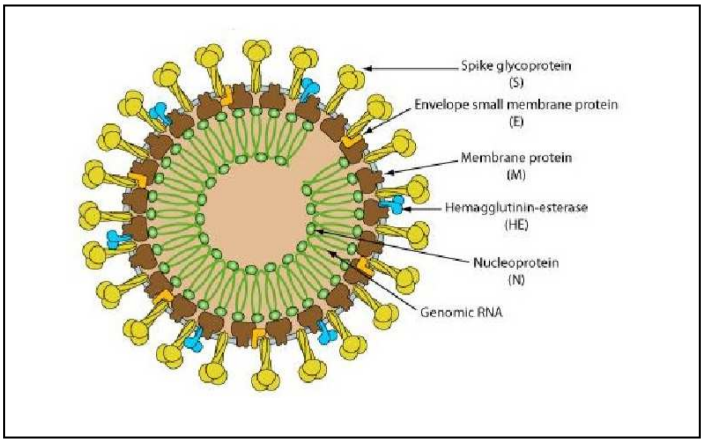


Figure 13

The coronavirus also releases water a third time, by repairing errors in its RNAs. It does this because it has its own enzymes in the genome whose role is, on the one hand, to repair the errors of its RNAs and, on the other hand, to ensure the replication of virions. Its own proteases therefore create additional hydrolysis, thus an addition of H2O. Therefore, the mechanism of the coronavirus produces a cascade of water molecules.

The finding of overabundant liquid in medical imaging is evidence of the excess of hydrolysis reactions, the so-called hydrolysis. When this excess alveolar mucus, in the terminal stage of the disease, invades all the pulmonary alveoli, it constitutes a thick barrier which reduces the exchange of oxygen. In addition, the excess alveolar mucus, because it consists essentially of 99% (13) of H2O actively participates in an overabundant evaporation of water vapor at the time of expiration. COVID 19 is not destroyed by H2O but on the contrary, it adapts perfectly to the abundance of liquid mucus: For this, Figure 13 shows that it is made up of three main layers, the RNA genome in the center, an envelope of proteins and esterase and an outer crown of Spike glycoproteins. The COVID 19 Spike glycoprotein is located in the outer ring and at the same time is hydrophilic. Looking on its affinity for water and the abundant presence of particles of water vapor exhaled by the lungs, the virion, being surrounded by coagulated H2O on its crown, is entrained in the exhaled humid air. Then, water vapor from the pulmonary alveoli brings the COVID 19 virion

Other climatic worsening

The increase in water vapor can also be increased by the high humidity of the air in winter. The more the amount of water vapor expired, the more the amount of virion entrained. Not only the amount of vapor exhaled by a healthy patient is increased by the hydrolysis effect of the coronavirus, but even, it can be increased by the inspired atmospheric humidity. During a period saturated with humidity (95%) such as the period of days 1 to 15 of our survey, the excess of inspired atmospheric water vapor is more important

than usual. In this case, the production of H_2O by hydrolysis of the coronavirus is superabundant on breathing out. Otherwise, for less humid periods, such as days 15 to 45 of our survey shown in the graph of Figure 1, the atmospheric supply of breathe in vapor is less, and therefore the quantity of exhaled water vapor is more limited. We found these trends in the results of Figure 1. We observe on our curves such variations, that is to say increases during humid atmosphere of declared COVID 19 cases, and conversely, decreases in cases in a drier atmosphere. These correlation findings clearly show that there is a cause and effect relationship between the humidity of the inspired atmospheric air and the daily number of reported cases.
Looking on our results, water vapor plays a major role in the proliferation of the COVID 19. Other Studies support our conclusions: It is indeed known through the multiple studies of all the viruses that have developed for twenty years, that excess hydrolysis has come from the action of proteases. We have proof of the role of protease hydrolysis because the blocking of proteases has been successful in stopping the pandemic of the ZIKA virus which belongs to the same family of viruses. Like the COVID 19, the ZIKA virus is an envelope virus encapsulating an RNA genome, as does the COVID 19 Coronavirus. More precisely, regarding hydrolysis, the ZIKA virus has been proven to be hydrolyzed into three structural proteins. (E, prM / M and C) and seven non-structural proteins (NS1, NS2A, NS2B, NS3, NS4A, NS4B and NS5) by the host and viral proteases.
ZIKA has been successfully treated with drugs that block proteases. So, the hydrolysis of viral proteases from COVID 19, because the virus belongs to the same family of enveloped viruses, can also be blocked by blocking drugs as has been done for the ZIKA virus in which the activity of proteases and in particular NS2B -NS3 has been blocked.

Our results can help to carry out a prospective study on the date of the end of proliferation of COVID 19. We have shown that the relative humidities allow only the propagation of the virus by transport with water vapor when they are higher than 80%. Sufficient humidity in March, became insufficient at the end of April, and the values coincide with the slowdown of the pandemic. As a result, our encouraging correlation calculations make it possible to estimate of the likely date on which the pandemic's proliferation will stop. Extrapolating the measurements represented by the correlation in Figure 3 shows that the minimum humidity obtained between 15 and 20% corresponds on our graphs to the number of cases declared from 500 to 600 per day. If we base on the reference of the climatic conditions of the year 2019 (figure 14), the waited humidity rates of 15-20% are at the beginning of May, which corresponds on the curve to the end of the pandemic. Note that the correlation curve (Figure 3) does not pass through the origin. This property of the curve could indicate that an activity has not become zero, and that the coronavirus is slippy. In such a case, the return of humidity to the winter seasons could allow it to reappear.

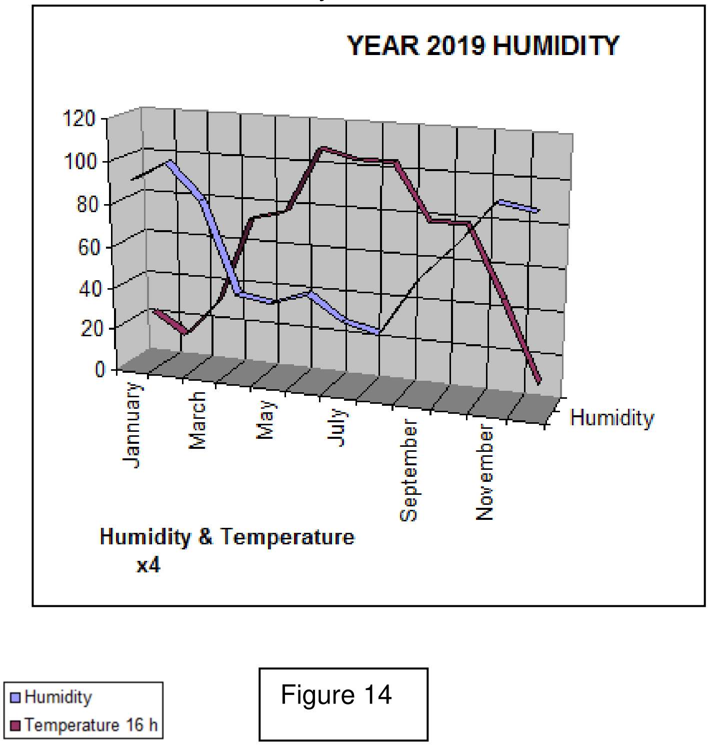


Figure 14

CONCLUSION

Our results on the study of reported cases of COVID 19 and humidity were obtained with 130,000 cases of coronavirus declared, 1,620 temperature readings, 32,400 humidity readings in 27 European countries over a period of two months. They revealed relationships between humidity and a pandemic proliferation during the two months of March and April. The effect of the meteorological environment observed in France and in 27 European countries reveals a cause and effect relationship between the humidity level and the daily occurrence of new cases of coronavirus reported. For the period studied, there is a perceptible correlation in the period studied for the pandemic. The laws of molecular chemistry made it possible to know the role of the N-teminal groups of SpikeS1 and Carboxylterminal of Spike S2, and to determine the affinity of Spike with relative humidity.
We have shown that the viral mechanism is favored by the expired aerosol with droplets of 4 to 20 nanometers, that is, invisible to the eye. We have concluded from our work that proliferation is transmitted by exhaling vapor through the respiratory tract. The mechanism that we describe is that the water vapor contained in the alveolar mucus is the transport vector for the aerosols of COVID 19. We have explained that the spikes of COVID 19, because they are hydrophilic, create special bonds with hydrogen bonds with H2O. COVID 19 is surrounded by the coagulation of water molecules and entrained by exhaled water vapor. We read on the data curves that the low humidities at the end of the pandemic (20%) on the graphs coincide with minimum cases of coronavirus, of the order of 500 per day, without the values of new cases of coronavirus reach zero. This discovery has a major novelty effect, that the spread is caused by the expulsion of aerosol of invisible droplets smaller than 100 nanometers, that is to say on patients without declared symptoms.

End Matter

Author Contributions and Notes

The author did not benefit from any contributory intervention for the writing of the manuscript and declares the authors no conflict of interest.
This article contains publicly available online support information and images.
He declares to be in compliance with the availability of all the data mentioned in the manuscript, as well as links to all the data hosted in an external repository.

He states that all relevant ethical guidelines have been followed, all necessary IRB and / or ethics committee approvals are not required, no patients have been diagnosed or consulted. No clinical trials have been performed and needed to be registered.

Acknowledgments Thanks

Funding for the work comes from the author who heads the SEIT research firm
This research was carried out in part using France Météorologie data available to the public and COVID 19 government propagation data available online.
The author declares that he has not received payments or services from a third party which could be perceived as influencing or giving the potential appearance.

REFERENCES

1-Cristallographic and Biochemical Investigations on Coronavirus Replication Proteins – Non-Structural Proteins 8 and 9…. Aus dem Institut für Biochemieder Universität zu LübeckDirektor: Prof. Dr. rer. nat. Dr. h.c. Rolf Hilgenfeld

2-CARACTÉRISATION DE LA PROTÉINE S DU CORONAVIRUS HUMAIN 229E Centre d'Infection & d'Immunité de Lille (CIIL), Inserm U1019, CNRS UMR 8204, Ariane BONNIN
Institut Pasteur de Lille, Équipe Virologie Moléculaire & Cellulaire

3-Crystal structure of the SARS-CoV-2 non-structural protein 9, Nsp9
Littler D. R. a,b,1, Gully B. S. a,b, Colson R.N. a & Rossjohn J a,b,c,1

4-La structure des protéines Hervé Darbon herve.darbon@afmb.univ-mrs.fr http://www.afmb.univ-mrs.fr/

5-[Covid-19] Comment le coronavirus pénètre dans nos cellules et s'y réplique... Et comment le contrer LA RÉDACTION D'INDUSTRIE ET TECHNOLOGIES Publié le 24/03/2020à 10h30 Mis à jour le 26/03/2020 à 17h28

6-Approche moléculaire et physico-chimique de la détection du coronavirus entérique bovin dans l'environnement Jocelyne Collomb UNIVERSITE DE NANCY 11991

7-Coronaviruses and the human airway: a universal system for virus-host interaction studies Hulda R. Jonsdottir & Ronald Dijkman Virology Jornal Article number: 24 (2016)

8-SARS-CoV-2 Cell Entry Depends on ACE2and TMPRSS2 and Is Blocked by a ClinicallyProven Protease Inhibitor Hoffmann et al., 2020, Cell181, 1–10April 16, 2020ª2020 Elsevier Inc.https://doi.org/10.1016/j.cell.2020.02.05

7-La Rédaction d'Industrie et Technologies Publié le 24/03/2020à 10h30 Comment le coronavirus pénètre dans nos cellules et s'y réplique... Et comment le contrer

8-MS-Médecine sciences MEDECINE/SCIENCES *2003 ; 19 : 885-91*

9- Des photos du nouveau coronavirus prises au microscope Spuutniknews 16-04 19-03-2020

10- La couronne du virus assure sa liaison avec ses cellules cibles Sciences et Avenir Par Héloïse Chapuis le 02.04.2020 à 09h22

11- How Furin and ACE2 Interact with the Spike on SARS-CoV-2 27th Mar 2020 Paige Dougherty MSc. Assaygenie https://www.assaygenie.com/how-furin-and-ace2-interact-with-the-spike-on-sarscov2

12- Thema Radiologie Covid 19 scanner 3D d'une patiente 6 mars 2020 imges Radiological Society of North of America http://www.thema-radiologie.fr/actualites/2612/covid-19-le-scanner-3d-d-une-patiente-infectee.html

13- EMC Salivation2010 *Elsevier Masson SAS.* L. Devoize, R. Dallel https://www.researchgate.net/publication/230752238_Salivation

14- Crystallographic and Biochemical Investigations on Coronavirus Replication Proteins – Non-Structural Proteins 8 and 9 Aus dem Institut für Biochemie der Universität zu Lübeck Direktor: Prof. Dr. rer. nat. Dr. h.c. Rolf Hilgenfeld Lübeck, 2009

15- Proteolytic activation of the SARS-coronavirus spike protein: Cutting enzymes at the cutting edge of antiviral research Graham Simmons, Pawel Zmora, Stefanie Gierer, Adeline Heurich, and Stefan Pöhlmann Blood Systems Research Institute, 270 Masonic Ave, San Francisco, CA 94118, United States 2013 Dec; 100(3): 605–614.

16- IT Industrie &Technologies 24/03/2020à 10h30 **Alicia Aloisi** Industrie & Technologies Antony Parc 2 10, place du Général de Gaulle 92160 Antony