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Mini Review Article

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Spread of Respiratory Viruses: Temperature and Physical Environment. Temperature Control May Exploit Virus Hypo-Thermolabity; A Possibile, Immediate Solution for COVID-19

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Bronchial-Tracheal Trast

surface cells work at a specific temperature range. At this range (37-38 C°) their response to viruses and bacteria tend to be optimal and mucus tends to have the specific grade of fluidity to contrast infections [1, 2]. With a decrease of 3-4 C° or more, these cells may be less protected, less active and not ready to fight infections. Most viruses may work (and replicate) only at lower temperatures (i.e. 34-35°C).

There is an evolutionary reason for this: it is possible that the ideal replication-diffusion temperature for a virus is lower than the ideal temperature at which the upper respiratory tract layers most usefully produce the best anti-viral response. Exposure to cold/dry air, lowers the temperature of the upper respiratory tract and the tracheal-bronchial epithelium within minutes, thereby providing a better field for diffusion-replication of viruses and bacteria, as the superficial respiratory cells are stoned by cold and become unable to respond to their maximum antiviral efficiency.

Within minutes, exposure to lower temperatures may also cause important vasoconstriction of the superficial respiratory layers and cells, blocking blood flow, mucin production and generally, any type of anti-viral response. Increasing the temperature of the air, therefore keeping the bronchial temperature higher, may stop the replication and diffusion of the respiratory virus. Thermoregulatory response is altered in older people while children very quickly develop a high body temperature that may halt viral replication. From an evolutionary point of view, individuals able to quickly increase their temperature may have a better chance of fighting infections.

Preventive Implications: Warmer/humid air inhalation (i.e. by aerosol or warm ventilation) may prevent viral contamination and more quickly kill respiratory viruses.

Therapeutic Implications: A warmer aerosol (vapor, 40° C) in the early phases may stop viral replication within hours. In later cases, the use of warmer-humid air (40-41° C) in artificial respiratory systems may kill viruses or halt their replication in the respiratory tree and help the recovery process [1, 2].

The correlation between lower air/environmental temperatures and respiratory infections (particularly acute viral infections) is one of the pillars of 'commonsense' hygiene and medicine.

- 80% of respiratory viral infections happen in the colder months and are related to the low, average levels of temperature. They tend to decrease when the average minimum daily temperatures increase to >10°C. This point needs verification.
- For the same reasons, most viruses may die when exposed to warmer /humid air; therefore a hairdryer may be effective in sterilizing or reducing bacterial-viral charges on surfaces without the need for chemicals that may cause other problems (including an alteration in the immune responses).

According to the World Health Organization there are currently no antiviral drugs licensed by the U.S. Food and Drug Administration (FDA) to treat patients with COVID-19. In the United States, the National Institutes of Health (NIH) is working to develop vaccines and therapeutics for COVID-19. In-vitro or in-vivo studies suggest some therapeutic activity of compounds against related coronaviruses, but there are no results from controlled trials in humans at the moment.

Remdesivir seems to have an activity against SARS-CoV-2. Patients with COVID-19 have been treated with intravenous remdesivir. An NIH trial for hospitalized COVID-19 patients in the United States was approved by the FDA as the first investigational therapeutic. Other trials with Remdesivir for COVID-19 patients in the U.S. are available (subjects with severe and moderate coronavirus disease). Some COVID-19 patients have received uncontrolled treatment with other investigational antivirals.

New Indications: It is possible that local ventilation or instillation of study products, i.e., Remdesivir or other antiviral, directly into the bronchial tree (via warm-vaporization) may be much more effective than systemic doses and may reduce exposure to side effects. Local instillation or vaporization of antivirals with warmer-humid air (>40 C°) may significantly decrease viral replication in 2-3 days in the initial phases of the respiratory disease. The quantity of product needed could be minimal and very cost-effective.

Vaporization with Warmer air may also have a Preventive Role (low dose, in high rish subjects).

It is also Important to Observe that:

- Smoking is the most important cause of bronchospasm and bronchial epithelial vasoconstriction.
- Vasoconstriction – as for cold – may significantly impair the reaction to a virus.
- All smokers should be advised to avoid smoking in this situation.

The evolution of COVID (Figure 1) shows long periods – before the respiratory insufficiency phase (RIP) - usable for management.

However, so far, all efforts or most management methods have been focused on assisted respiration in ICUs. It is not possible to manage a disease, possibly involving 60-80 million of subjects with ICUs. We need to focus on medical preventive methods (not only lockdown) particularly in higher-risk subjects and we need management methods of early symptoms, out of hospitals.

Figure 2 shows our management targets: *hot and humid air* with vaporizators-ventilators may reduce viral spread and replication within the bronchial spaces.

Antivirals, even with limited activity, may affect viral replication. Anti-inflammatory agents may control the inflammatory response due to viral spread. Reconstitution of the mucin layers may block viral passage directly into cells.

Minor quantities of drugs can be used for bronchial vaporization, avoiding side effects and reducing costs. The initial infection is a local viral spread and not a systemic disease. Even with limited antiviral, anti-inflammatory activity and mucin-reconstituting action, a warm-umid athmoshere may produce lower spread and limited symptoms.

The graph in figure 3 shows that daily hot-humid vaporization (WHV) can stop most of the winter respiratory viral infections (associated to fever) in a 3 months follow-up (the graph was obtained during the previous winter).

Finally Figure 4 shows symptomatic subjects (mild-moderate symptoms) managed at home with WHV (warm-humid ventilation), 3-4 times daily for 10 minutes. No drugs were added to the ventilation.

The two comparable groups (7 subjects vs 8 subjects; age range 60-73; mean 63.2;2.2; all males) appear to show a different evolution with most symptoms (cough, throat and eye irritation, fever >38 °C and malaise) being reduced and decreased at 7 days.

This preliminary study could be an indication of the potential of WHV that may be associated to local, low-dose vaporization of antivirals, anti-inflammatory and mucin-protective or reconstituting product agents. The control of viral replication within the upper respiratory tract with WHV may also decrease the possible speading of the virus in the enviroment and achieve a significant community value to this method.

Considering other methods of prevention for non-affected individuals, colostrum has also shown a significant potential in preventing winter-related viral respiratory infections. Its role needs a more specific and larger investigation particularly in high-risk subjects [3, 4].

The key role of planes as fast-super-speaders/incubators should be also evaluated and prevented. Most cheap flights put together hundred of passengers in very close conditions for hours. The speading of any viral problem seems inevitable in this condition and should be carefully controlled. No subject with a minimal suspicion of a viral disease should go into a plane for any reason. In the middle of the COVID-19 epidemic in China – when the problem was clear - thousand of cheap mass-flights to Europe were still operating; the operators new exacltly about the problem but kept their schedules trying to make as much money as possible before the block [5-7]. Filters in planes may filter onl about 40% of the viral particles

Considering the evolution of initial signs/symptoms, predictive analytics (E Siegel) suggests that a sample of 100 symptomatic patients (for 3 weeks) may be valid to evaluate the evolution in most (otherwise healthy) subjects with a relatively simple, low-cost model, without considering hospital patients.

Conclusions

The **thermolability** of this virus may be a significant weak point to attack with relatively simple means, essential when the number of patients is of the present and future magnitude. Solutions must consider costs and simple methods that may be used when the healthcare systems have limited budgets and there are millions of patients. WHV is also an important vector to use, to send targeted low-dose therapies into the upper respiratory tract and in to the bronchial tree. In most patients the initial disease is largely a local condition of the bronchial tree without systemic complications.

This is the place and moment to selectively attack, with all the tools we have, the virus.

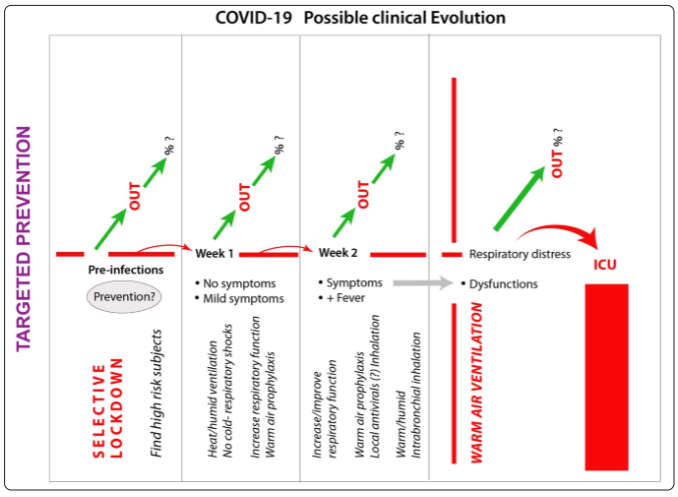

Figure 1: COVID evolution. The syndrome shows long periods – before the respiratory insufficiency phase (RIP) - usable for management. So far most management methods have been focused on assisted respiration in ICUs. It is not possible to manage a disease, possibly involving 60-80 million of subjects, with ICUs. We may focus on medical preventive methods (not only lockdown) particularly in higher-risk subjects and we need management methods of early symptoms, out of hospitals.

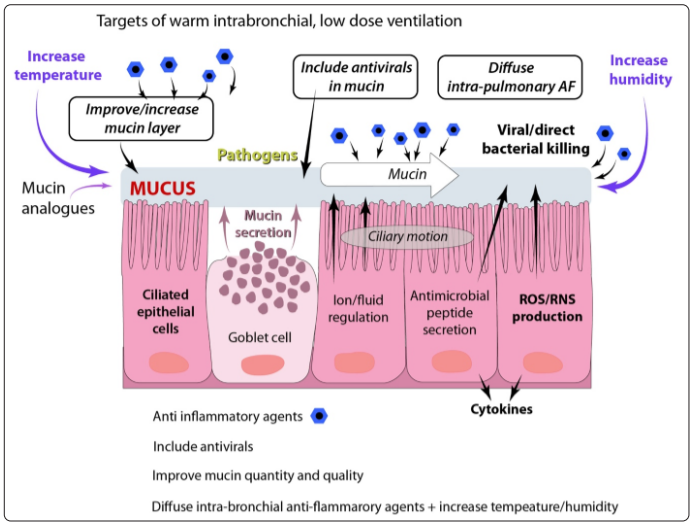

Figure 2: Targets of local, bronchial management: hot-humid athmosphere mass
-improve the mucin layers
-use antivirals
-use anti-inflammatory agents.

This disease should be considered, at least in the early phases, a local disease that requires a local, low-dose, low-cost management, with minimal occurence of side effects.

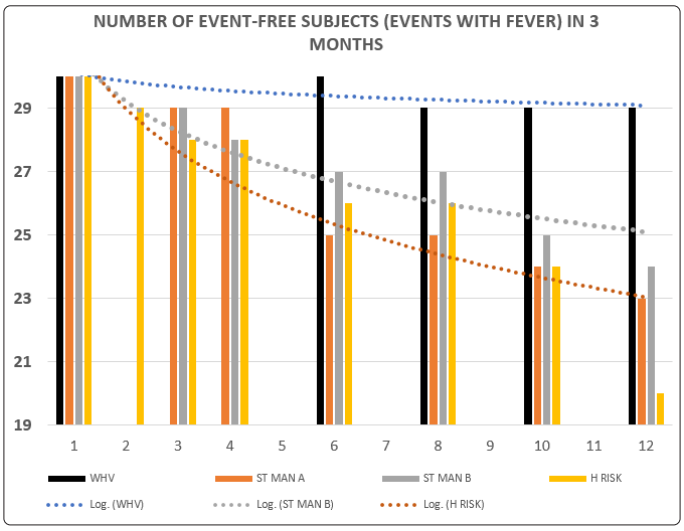

Figure 3: daily hot-humid vaporization (WHV) can stop most of the winter respiratory viral infections (associated to fever) in a 3 months follow-up.

In this graph, groups include 30 comparable subjects (age 50-75). WHC is compared to standard management (SM) A (vaccination, colustrum), only vaccination (SM B) and SM in high risk subjects (only vaccination). The trends for WHV, SM A and high-risk subjects are shown). The 97.7% of event-free subjects with WHV compares with the 66.67% ($p<0.05$) of high-risk subjects not having events.

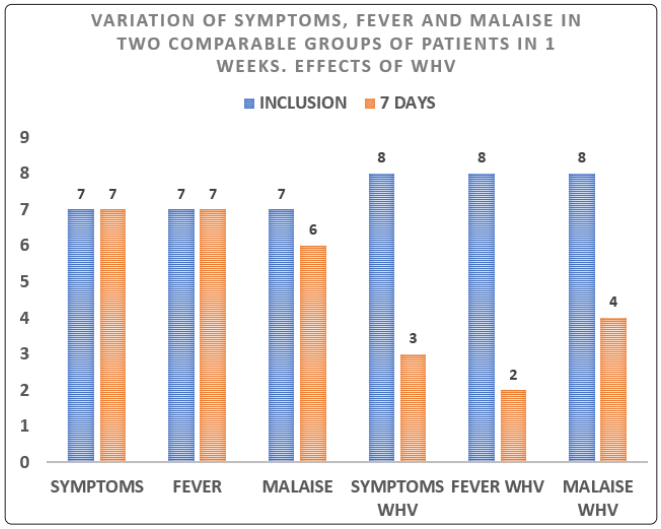

Figure 4: symptomatic subjects managed at home – in a pilot, concept study - with WHV (warm-humid ventilation), 3-4 times daily for 10 minutes
Figure 4 shows patients managed with WHV.
No drugs were added to the ventilation.
The two comparable groups (7 subjects vs 8 subjects; age range 60-73; mean 63.2;2.2; all males) appear to show a different evolution with most symptoms (cough, throat and eye irritation, fever >38 °C and malaise) being reduced and decreased at 7 days.

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