

Analysis of Some Worsening Factor Involved with Covid-19 and Other Respiratory Virus Diffusion, How Some Preventive Measure and Therapeutic Strategy Can Improve Clinical Outcome

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Abstract

The epidemiology of covid-19 and other related virus show relationship also with climate condition, air pollution and humidity [3].

The same it is clear the role played by air pollution (PM 10, NO₂, O₃ and other) as worsening factors in many respiratory disease.

The respiratory mucociliary clearance in respiratory apparatus is influenced by air pollution and especially if chronic exposition of pollutants.

All this factors that contribute to a more rapid diffusion of respiratory virus as showed in great polluted World regions.

A deep knowledge in this environmental toxicological condition make possible to evaluate preventive measure to reduce this effect like depurative strategy.

Keywords: Covid-19; Respiratory Virus Diffusion; Therapeutic Strategy

Introduction

Observing the different velocity rate of diffusion of covid-19 disease and other relevant respiratory virus is possible to verify a relationship with air pollution in some world regions characterized by great industrial activity and determinate climate condition.

The air pollutant whit various mechanism produce in respiratory tract an environment able to favour.

Also respiratory virus attack.

This especially in some kind of patient like elderly and with polipathology.

It is related whit level of some air pollutant but also to the global time of exposition (in example for 3 - 5 years).

But to prevent this, in past, various measure was introduced like use of musk to avoid intake of pollutants, reducing level of industrial production, control of civil house emission and also in some cases thermal aerosol therapy to depurate pulmonary tract. (BPCO, ASTHMA).

Materials and Methods

Whit an observational approach some relevant literature for the scope of this work are analyzed to produce a global conclusion.

All literature is present or in PUBMED or as OPEN LITERATURE and indexed by scientific research website od university digital library.

Results

From literature according Prof. G. Tarro related covid -19 spread in Italy: “In Italy the regions more hit are the same ones that have the greatest productive activity and therefore more millions of tons of special products” [1].

In book “Pianura Padana geo-morphology, climate condition prevalence and distribution of COVID -19 and some other respiratory virus: Hypothesis of work: “The HYPOTESYS of this research work It is ranged as opinions of the authors to verify if the climate condition of PIANURA -PADANA and air pollution level may contribute or not in the speed and severity of global covid -19 great diffusion in north of Italy as a severe disease. Factors such kind of geo-morphological environment with specific climate condition and natural separation by mountains presence at north and south of Italia. In this study the strange velocity in diffusion in north vs south of Italy need new research: observing lethality rate of Lombardia 17,9% vs 9% of the rest of Italy it seem that could be 2 different AREA in Italy related this virus diffusion. Latitude, climate, air- pollution and what other factor acts? as well as to known people direct attachment (contamination) and those subclinical infected persons? Only The lockdown strategies produced this? And the role played by high way diffusion (trucks and other road transport of goods) in cross APPENINI- MOUTNAINS is a fact to be taken in consideration? The relationship between air pollution and respiratory disease, acute and chronic are a scientific Proof of relationship” [2].

And in article <https://www.ildolomiti.it/ricerca-e-universita/2020/coronavirus-i-luoghi-piu-colpiti-sarebbero-quelli-piu-inquinati-lingegnere-ambientale-venuto-aggressivita-del-virus-proporzionale-allesposizione-alle-polveri-sottili>: according coming “In all cities and provinces with a higher contagion rate, roughly all in Lombardy and Emilia-Romagna, the data on concentrations of fine dust in February marked very high peaks, in a clear temporal coincidence between exposure to pollutants and the beginning of the infection by counting the incubation time of the virus. The case of the province of Sondrio, for example, is useful for understanding in comparison with the rest of the region to which it belongs.

Evidence emerges, in fact, that this prolonged exposure to pollutants could have influenced the aggressiveness of the virus.

The Val-Seriana starts from the plain of Bergamo, where there are industries, highways, one of the most polluted areas in Italy. It is a narrow and long valley. A cycle of winds engages that during the day brings the air from the valley floor upwards, while at night it blows in the opposite direction”.

Città	n° superamenti del limite di Pm10	Tasso di contagio 1(ab provincia/casi accertati) ⁻¹
Bergamo	12	1/216
Brescia	17	1/272
Cremona	14	1/150
Sondrio	2	1/1111
Piacenza	10	1/182
Firenze	0	1/2522
Roma	0	1/7571
Bari	0	1/7588
Napoli	2	1/7416
Reggio Calabria	0	1/7507
Palermo	1	1/21230

Tabella 4.2: Superamenti delle concentrazioni di Pm10 e tasso di contagio in alcune provincie italiane.

Figure: Overcome of PM10 concentration and contagious rate in some Italian province (Figure from reference 15).

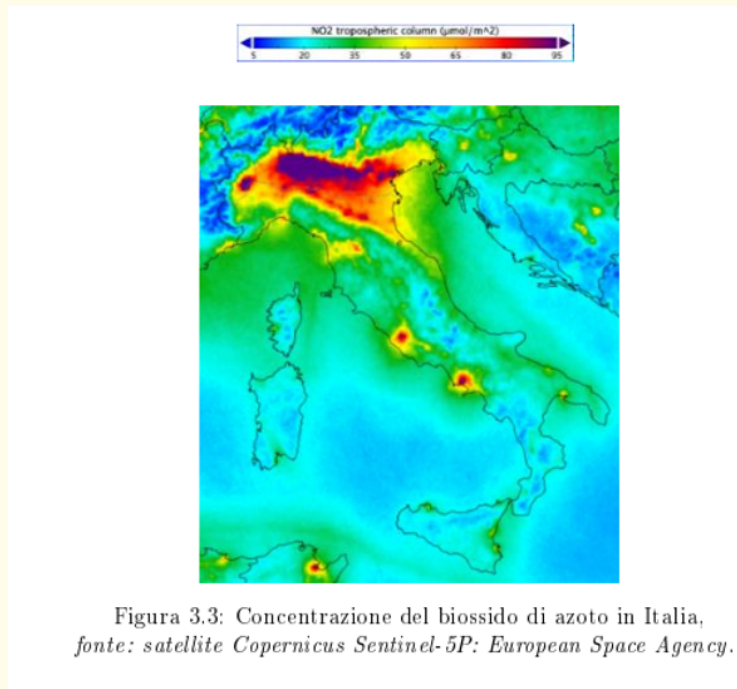


Figure 1: Nitrogen dioxide concentration in Italy, Source: Atellite Copernicus Sentinel-5p: European Space Agency.

“it is clear by science the role played by air pollution related some relevant respiratory disease and related toxicology and death- related. The same is clear that in COVID 19 diffusion in some industrial- area it induced the stop of great part of industrial activity with high reduction of air pollutants release as easily seen in the figure in this work. It is also interesting the diffusion of some virus disease like COVID 19 in other region whit high- level of air pollution (north Italy)” [3].

M Pedersen: “The mucociliary -clearance is an important part of the nonspecific defense mechanism of the human airways. Coordinated beats of cilia in the nose, trachea, and bronchi propel the mucous layer toward the pharynx, and with it inhaled micro-organisms and other particles captured in the mucus. Normal function of this system depends on the efficacy of the ciliary beating and the properties of mucus. Primary ciliary dyskinesia--a congenital respiratory- disease characterized by ultrastructural defects and motility disturbances of cilia--has provided us with valuable information about the role the mucociliary function plays in the protection against harmful agents in the inhaled air. Secondary ciliary dyskinesia is described in inflammatory disorders of the respiratory tract, but also some components in air- pollution results in malfunction of cilia, damage of ciliated epithelium, or alteration in the mucus” [4].

“All The authors agree with the fact that depurative -strategies involving PM and other pollutants from respiratory apparatus can help in reducing pulmonary pro- inflammatory-status in elderly and In subject with poli-pathologies to prevent some respiratory viruses pathology” [5].

“Related the various mortality-rate and diffusion velocity of the covid-19 disease is possible to conclude that not all the strategy- adopted by different countries present the same result.

A clear evidence of the pathogenetic process that can explain the various phases of the disease since from first- phases to pulmonary phases to cytokine explosion and related phenomena can help in choosing the really best therapy in the right time as well as using the best

imaging strategies to stratify the patient risk in objective way. [6] The right therapy in the right phases of the disease (first phases) seem by literature to avoid the most severe -consequences” [6].

M. Pellegrini, *et al.* “In conclusion, treatment with inhaled salt-bromide-iodine thermal water in COPD is associated with a reduced proportion of neutrophils in induced sputum suggesting that thermal water may have a mild anti-inflammatory -effect on the airways. the short-term improvement in some components health-related quality of life was not related with changes in lung function or with the degree of airway inflammation” [7].

Ogen Y: “The extent to which the COVID-19 virus induces respiratory- stress in infected individuals may also be influenced by the extent to which an individual’s respiratory- system is already compromised.

The high levels of PM pollution in China may increase the susceptibility of the population to more serious symptoms and respiratory complications of the disease.

The simultaneous inhalation of chemical pollutants in PM along side COVID-19 virus may also exacerbate the level of COVID-19 infection. Pro-inflammation, injury, and fibrosis from inhaled PM combined with an immune- response or cytokine- storm induced by COVID-19 infection could enhance the infection severity. Larger numbers of patients displaying more serious infection symptoms also created an increased risk of enhanced- transmission potential” [8].

Brian A Kuzik, *et al.* “The use of nebulized 3% HS hypertonic saline is a safe, inexpensive, and effective treatment for infants hospitalized with moderately severe viral bronchiolitis” [9].

Amar Safdar, *et al.* “Early studies in the 1990s indicated that increasing concentrations of aerosolized sodium chloride (saline) solutions result in increasing rates of mucociliary clearance” [10].

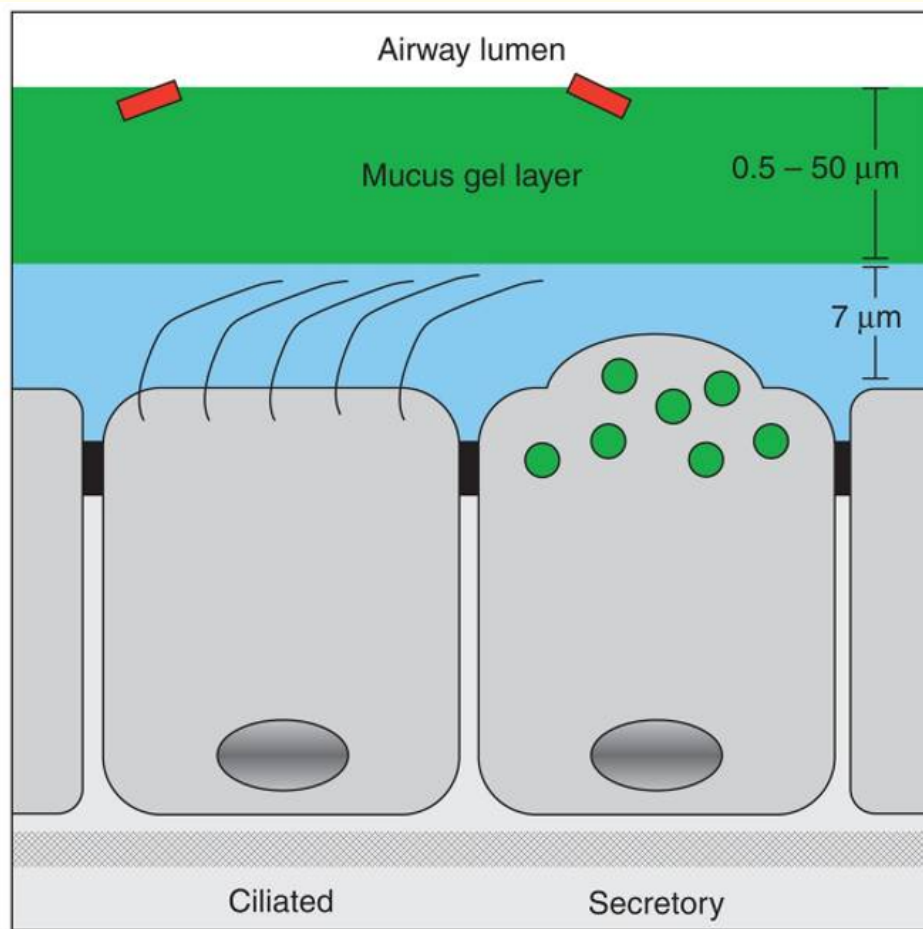


Figure 2: Airway epithelium with overlying surface liquid [10].

The conducting airways are lined by numbers of ciliated and secretory epithelial cells. Secretory cells contain granules that include peptides and mucins (green), although the intracellular mucins may only be detected in small distal airways by sensitive immune-histochemical techniques or during inflammatory metaplasia when their production is increased. The airway- surface liquid consists of a periciliary layer 7 μm in depth (blue), and an overlying mucus gel- layer (green) that varies from < 1 μm in thickness in distal airways to > 50 μm in proximal airways of humans. Cilia- beat directionally to propel the mucus gel layer cephalad towards the larynx. The mucin glycoproteins MUC5AC - MUC5B are the principal components of the mucus gel layer and are exocytically released both from the underlying surface epithelium (shown) and from submucosal glands (not shown). While the mucus gel layer is important in clearance of inhaled pathogens (red), excessive mucin production or airway surface liquid depletion can lead to mucus impaction of the airway- lumen, providing a sanctuary for microbial infection.

According Sean D. McCarthy, *et al*: "Another mucolytic, hypertonic saline has been shown to attenuate the severity of ALI acute lung injury when nebulized, by reducing inflammatory cytokine production" [16].

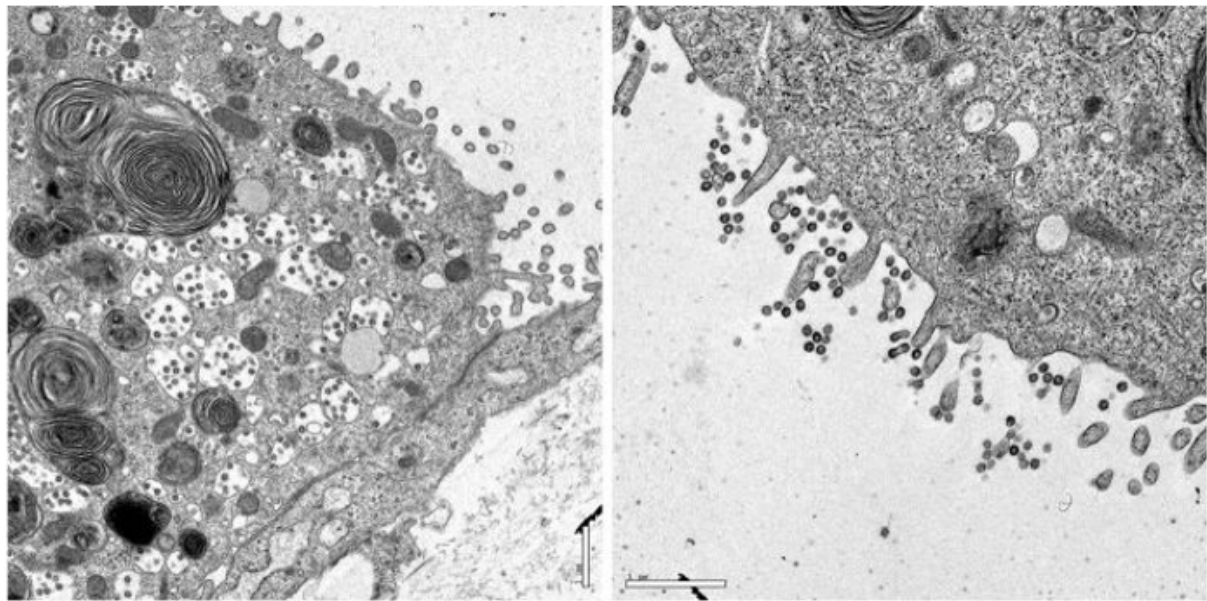


Figure 3: Human alveolar type cells infected with SARS-CoV. Human type cells were isolated, cultured *in vitro*, and then infected with SARS-CoV. Viral particles are seen in double membrane vesicles in the type cells (left panel) and along the apical microvilli (right panel) (from reference [17]).

Amy C Sims., *et al*. "SARS-CoV in 2002 an important cause of severe lower respiratory tract infection in humans, and *in vitro* models of the lung are needed to elucidate cellular targets and the consequences of viral infection.

The SARS-CoV receptor, human -angiotensin 1-converting enzyme 2 (hACE2), was detected in ciliated airway epithelial cells of human airway tissues derived from nasal or trachea-bronchial regions, suggesting that SARS-CoV may infect the proximal airways.

To assess infectivity in an *in vitro*- model of human ciliated airway epithelia (HAE) derived from nasal and trachea-bronchial airway regions, we generated recombinant SARS-CoV by deletion of open reading frame 7a/7b (ORF7a/7b) and insertion of the green fluorescent

-protein (GFP), resulting in SARS-CoV GFP. SARS-CoV GFP replicated to titers similar to those of wild-type viruses in cell lines. SARS-CoV specifically infected HAE via the apical surface and replicated to titers of 10^7 PFU/ml by 48h postinfection. Polyclonal antisera directed against hACE2 blocked virus infection and replication, suggesting that hACE2 is the primary receptor for SARS-CoV infection of HAE. SARS-CoV structural proteins and virions localized to ciliated epithelial- cells. Infection was highly cytolytic, as infected ciliated cells were necrotic and shed over time onto the luminal -surface of the epithelium. SARS-CoV GFP also replicated to a lesser extent in ciliated cell cultures derived from hamster or rhesus monkey airways. Efficient SARS-CoV infection of ciliated cells in HAE provides a useful *in vitro* model of human- lung origin to study characteristics of SARS-CoV replication and pathogenesis” [17].

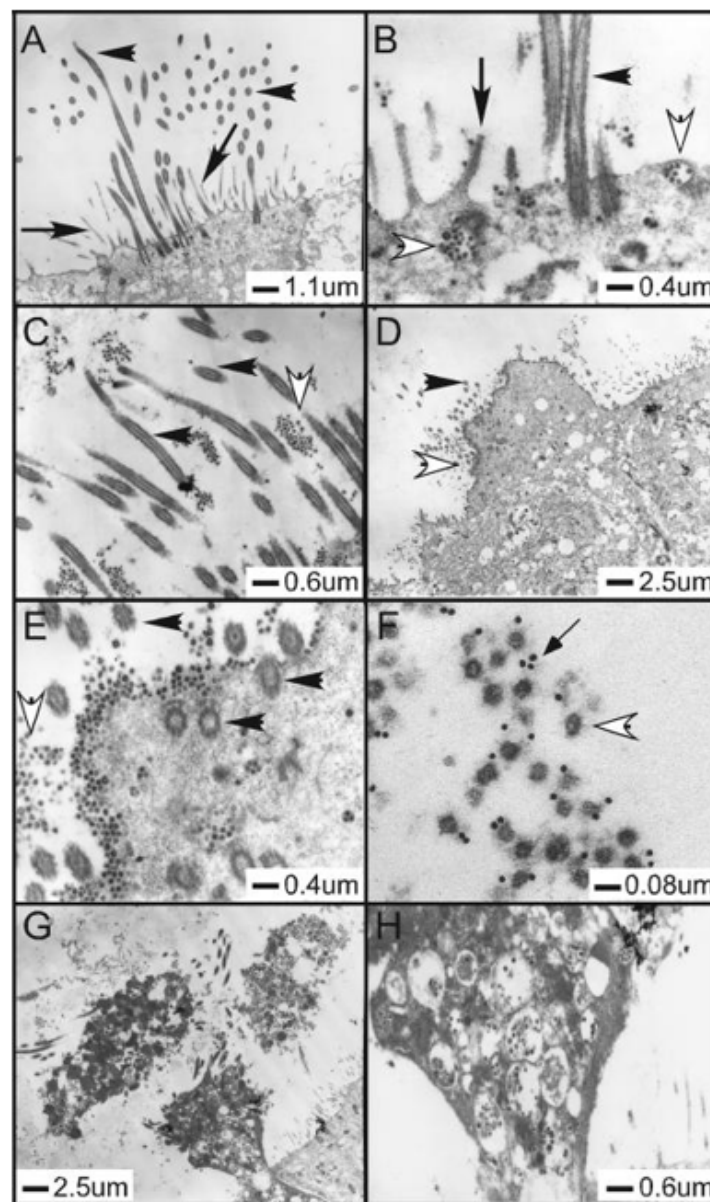


Figure 4: Ultra-structural localization of SARS-CoV in HAE. Representative transmission electron-microscopic photomicrographs of HAE infected with Urbani SARS-CoV. (A) HAE inoculated with vehicle- alone, demonstrating the typical morphological- features of the apical surfaces of ciliated cells with prominent cilia and microvilli. (B to E) HAE inoculated with Urbani SARS-CoV 48 h before fixation and showing the presence of large numbers of virus -particles in vesicles inside ciliated cells (B and E) and on the surface of ciliated cells (B, D, and E) or shed into periciliary regions (C). Large quantities of virions were noted on the surface of ciliated cells, where ciliated- cells were identified by cilia basal bodies (E). (F to H) To confirm that the observed virions were SARS-CoV, immuno-EM was performed using polyclonal mouse antisera against S with secondary antibodies conjugated to 12-nm colloidal gold (F). SARS-CoV infection resulted in extrusion and shedding of infected ciliated cells into the airway -surface microenvironment (G and H). Similar observations were seen with HAE infected with icSARS-CoV and SARS-CoV GFP. Scale bars are shown for each panel. Filled arrowheads, cilia; filled arrows, microvilli; open- arrowheads, virions; thin-tailed arrow in panel F, immuno-EM colloidal- gold [17].

Discussion and Conclusion

Observing the result of the scientific literature presented is possible to verify the effect played by some secondary aggravating factor in some respiratory virus disease and also by covid-19 disease.

It is possible also to divide this factor in two phases: The preventive phases and the therapeutic phases.

Related the first it is interesting to observe the common measure adopted in many industrial high polluted cities like musk use to avoid intake of pollutants or reducing home heating emission in winter or car movement in centre of the city.

Some kind of more old cars are stopped in some winter month.

In the second phases relevant for the outcomes of patient surviving (covid-19) it is relevant to apply the most efficacy therapy in early stage of the disease to prevent cytokine explosion.

Also imaging contribute to the global clinical outcome: "A clear evidence of the pathogenetic process that can explain the various phases of the disease since from first phases to pulmonary phases to cytokine explosion and related phenomena can help in choosing the really best therapy in the right time as well as using the best imaging strategies to stratify the patient risk in objective way" [12].

Related the first phases it is possible to verify that some preventive measure can help in various respiratory disease reducing also the effect played by dangerous air pollutant. (masks use not only to prevent virus transmission by droplets or airborne but also to prevent air pollution intake).

What happen in a pulmonary apparatus of an elderly subject and with polipathology when Exposed to air pollutant from many years?

And what is the full role in pathogenesis of coronavirus disease played by ciliar respiratory apparatus?

Why the most fragile patient are not deeply depurated by air pollutant before the winter season?

It is opinion of the author that some depurative strategy can be evaluated by researcher also in next Hypotesys of new respiratory virus pandemia.

Acknowledgement

This work is produced with a pharmaceutical, pharmacological and toxicological point of view, without any diagnostic or therapeutic intent only to produce hypothesis of research to be submitted to the researcher. A reference is added in Italian languages to preserve the original meaning. All figure in this work are introduced only for scientific and research scope.

Conflict of Interests

No.

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