EDITORIAL

THE IMPACT OF COVID-19 ON THE TOURISM SECTOR AND MEASURES TENDING ITS MORIGERATION

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https://doi.org/10.55634/1.5.1

INTRODUCTION

Tourism is one of the essential engines of employment and growth.

But COVID-19 has drastically changed this reality.

We are facing an unprecedented health, social and economic emergency .

Tourism has been among the most affected sectors, with planes grounded, hotels closed, and travel restrictions in virtually every country in the world, dealing a never-before-seen blow to the sector; the COVID-19 pandemic has reduced international tourist arrivals in the first quarter of 2020 to a negligible fraction of what they were in 2019.

Available data points to a 22% decline in the first quarter of 2020 , with a drop in arrivals in March of 57% .

This translates to a loss of 67 million international tourist arrivals and around USD 80 billion in revenue . In addition, between 100 and 120 million jobs were lost, or were in jeopardy .

Forecasts for subsequent years have worsened several times since the outbreak, given the high degree of uncertainty.

The current scenarios make the future remain very uncertain (the scenarios are not forecasts and should not be interpreted as such) .

The impressions expressed by the UNWTO Group of Experts indicate that the recovery of international demand -very slow- started in 2021 and slowly improved in 2022, as we will see later.

According to the experts from around the world that make up the Group, domestic demand would recover faster than international demand.

Considerable challenges remain to be overcome, starting with the lack of knowledge about the duration of the pandemic and travel restrictions, against a backdrop of a global economic downturn.

Countries around the world are implementing numerous measures to mitigate the negative impact of the COVID-19 outbreak and stimulate the recovery of the tourism sector.

2020

Travel restrictions

100% of the world's destinations introduced travel restrictions in response to the pandemic.

According to the UNWTO report on COVID and associated travel restrictions , as of April 20 of that year, 100% of the world's destinations had introduced restrictions.

Ninety-seven destinations (45%) totally or partially closed their borders to tourists.

Sixty-five destinations (30%) had totally or partially suspended international flights.

Thirty-nine destinations (18%) attempted to implement border closures in a differentiated manner, barring entry to passengers from specific countries.

International tourist arrivals January - March 2020

Available data shows a 22% drop in international tourist arrivals in the first quarter of 2020 , with March arrivals falling 57% following the start of lockdowns in many countries, widespread travel restrictions and the closure of airports and national borders.

This represented a loss of 67 million international arrivals in the first quarter of 2020 compared to the same period of the previous year.

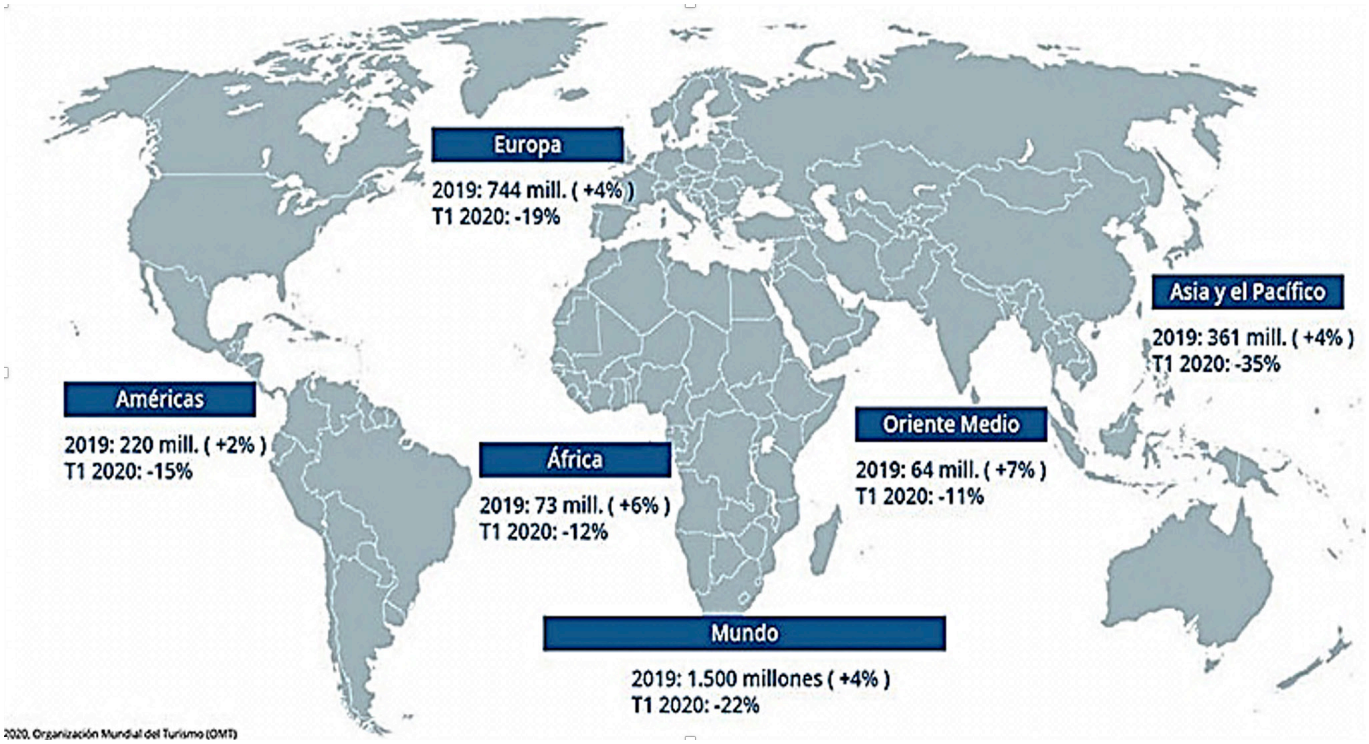
By region , Asia and the Pacific - the first region affected by COVID-19 - recorded a 35% decrease in arrivals during the first quarter of 2020. The second most affected region was Europe, with a 19% decrease, followed by from the Americas (-15%), Africa (-12%) and the Middle East (-11%).

In summary:

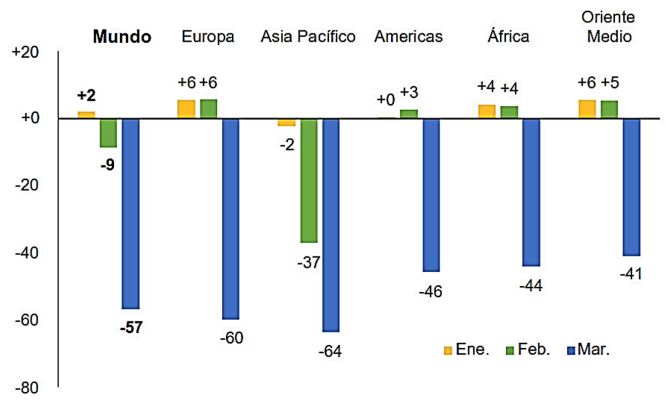
67 million fewer international arrivals.

US$80 billion lost in exports.

100% of destinations with travel restrictions.



International tourist arrivals, january, february, march 2020 (% variation)



Impact of Covid-19 on tourism in the first quarter

2021

UNWTO reported a 4% increase in international tourist arrivals in 2021, compared to 2020.

However, 2021 was another challenging year: arrivals were still 72% below pre-pandemic levels.

International tourism recovered moderately during the second half of 2021, with international arrivals down 62% in both the third and fourth quarters, compared to pre-pandemic levels. Based on limited data, international arrivals in December were 65% below 2019 levels. And by then, the full impact of the Omicron variant and the surge in COVID-19 cases had yet to be seen.

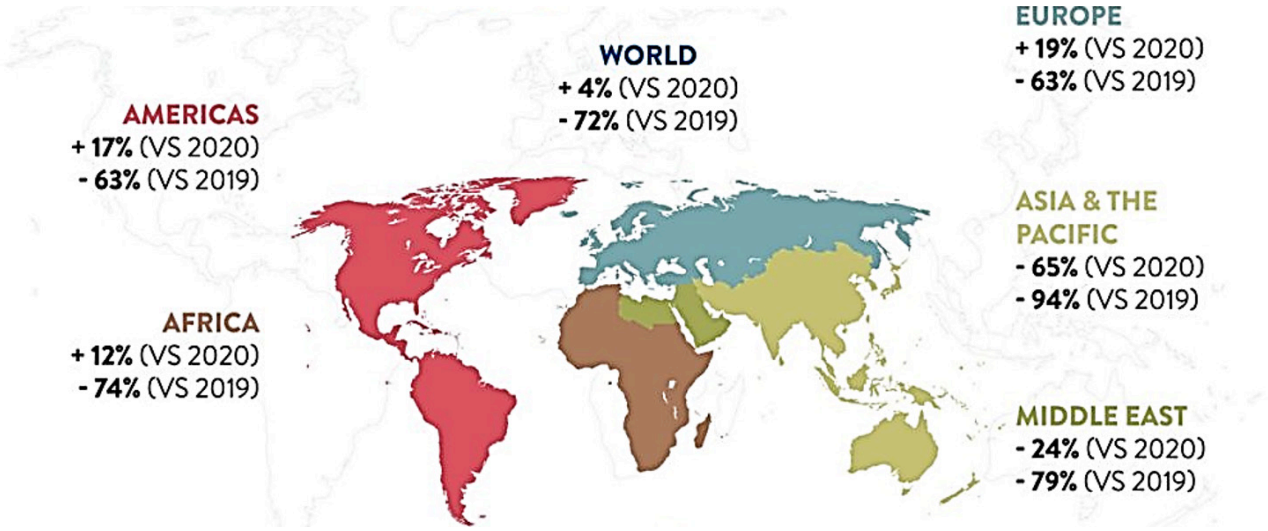
The pace of recovery was slow and uneven across regions of the world, due to varying degrees of mobility restrictions, mandatory travel vaccination rates, and traveler confidence. Europe and the Americas posted the strongest results in 2021 compared to 2020 (+19% and +17% respectively), but still both 63% below pre-pandemic levels. By subregion, the Caribbean performed best (+63% above 2020, though 37% below 2019). Southern Mediterranean Europe (+57%) and Central America (+54%) also rebounded, but were still 54% and 56% below 2019 levels, respectively. North America (+17%) and Central and Eastern Europe (+18%) also exceeded 2020 levels. Meanwhile, Africa saw a 12% increase in arrivals in 2021 compared to 2020 (still 74% lower to 2019). In the Middle East, arrivals were down 24% compared to 2020 and 79% compared to 2019. In Asia and the Pacific, arrivals were still 65% below 2020 levels and -94% compared to pre-pandemic values, as many destinations remained closed to non-essential travel.

The economic contribution of tourism in 2021 (measured in tourism direct gross domestic product) was estimated at US$1.9 trillion, up from US$1.6 trillion in 2020, but still well below the pre-pandemic value (US$3.5 billion). Export earnings from international tourism could exceed US$700 billion in 2021, a small improvement over 2020 due to higher spending per trip, but less than half the US$1.7 trillion recorded in 2019.

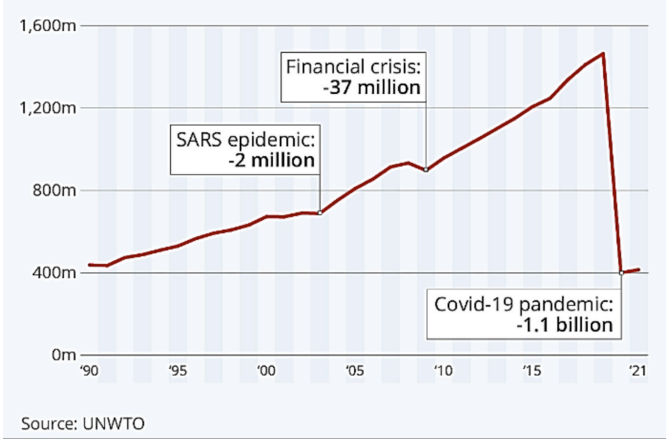
Average revenue per arrival was estimated to reach $1,500 in 2021, up from $1,300 in 2020.

This is due to the large savings accrued and longer stays, as well as higher prices for transportation and lodging.

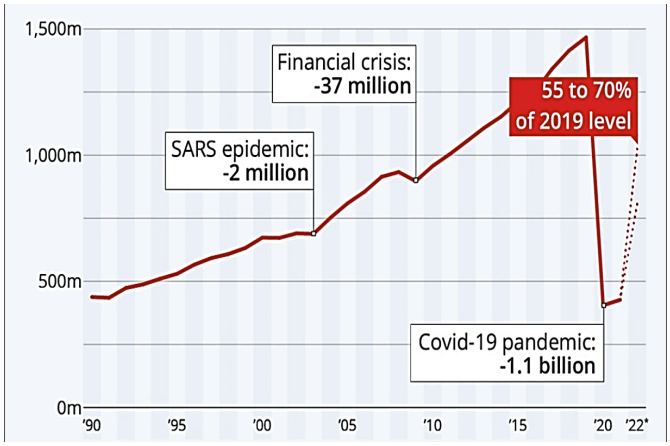
France and Belgium reported comparatively smaller declines in tourism spending at -37% and -28%, respectively. Saudi Arabia (-27%) and Qatar (-2%) also posted somewhat better results in 2021.



International tourist arrivals in 2021



Deterioration of the sector in 2021 (comparative)



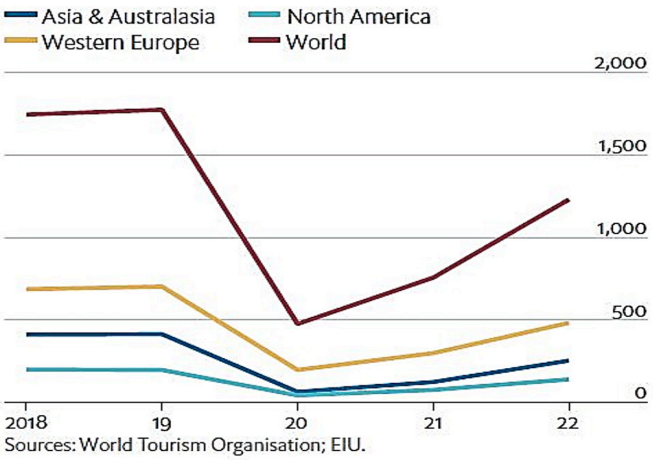
Partial recovery as of may 2022 (compared to 2020 and 2021)

2022

Two years after the COVID-19 pandemic essentially shut down international travel worldwide, the tourism industry rebounded somewhat more markedly as summer arrived in the northern hemisphere.

International tourism saw a year-on-year increase of close to 200% in the first quarter of 2022 and while several related statistics are still well below 2019 levels, the gradual recovery is expected to continue throughout the year, according to an analysis of June from the United States, United Nations and World Tourism Organization. Nearly 50% of experts surveyed by the organization said they expect international tourism to slowly approach pre-pandemic levels in 2023, while 44% said this could happen as soon as 2024 or later.

But the Countries most economically supported by tourism are not necessarily the ones that receive the most visitors. According to the latest UNWTO World Tourism Barometer, international tourism increased by 182% in the three months of 2022, compared to the same period of the previous year, but was still 60% below 2019 levels.

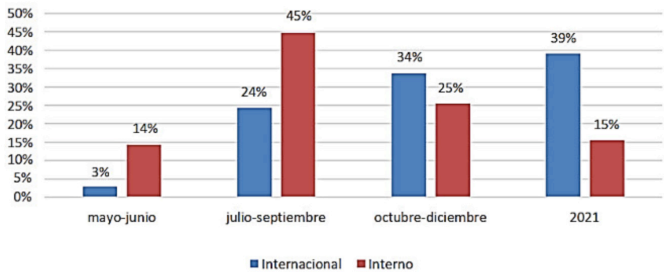


Prospective estimate for all of 2022

LOOKING AT THE FUTURE

DOMESTIC DEMAND IS EXPECTED TO RECOVER FASTER THAN INTERNATIONAL DEMAND

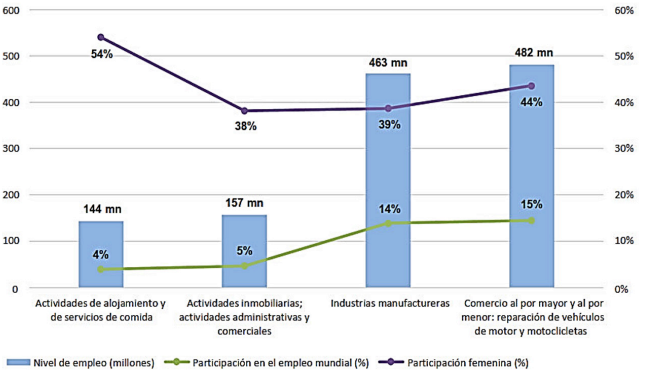
International demand recovered in the fourth quarter of 2021, and mainly in 2022, according to the responses of the UNWTO Group of Experts to the following survey:



Internal and international demand (2021 data)

SUMMARY OF POTENTIAL IMPACTS IN 2020-2022

Between 850 and 1,100 million fewer international tourists.
Between US$910,000 and US$1.2 trillion lost in revenue from tourism exports
Between 100 and 120 million jobs directly related to tourism, threatened
Employment in accommodation and catering services is at serious risk, and more than half of the workers are women.



Workers in the tourism sector with greater risk

DOUBTS AND CHALLENGES

Pandemic

Uncertainty about how long the pandemic will last.

Lifting of travel restrictions and lockdown measures

When and how countries will begin to lift restrictions.
How social distancing rules will affect supply

Consumer and Business Confidence

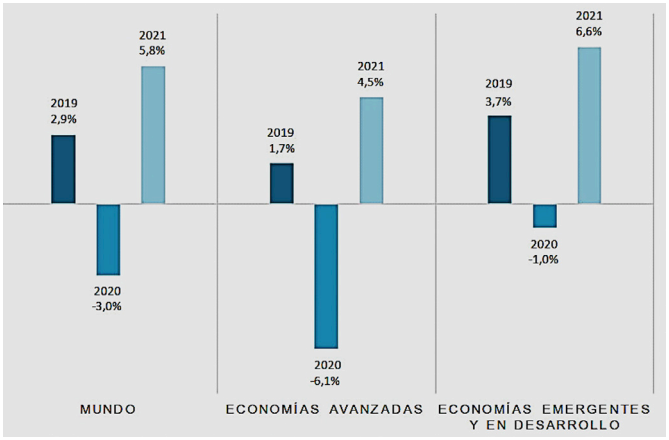
How long it will take for consumers to travel again.
How will travel behavior change?

Economic Impact

How deep will it be , and how long will the global recession last? What discretionary spending decisions consumers will make.

Government measures

How will the government measures support tourism.



The world economy contracted concentrated in 2020, and only 3.0% recovered in 2021

PUBLIC SERVICES

In addition to health workers, all public officials have a role in containing the spread of, and recovering from, the pandemic.
This is true regardless of their occupation: whether they work in state administration (for example, as tax collectors, police officers), or carry out economic or social policies (as labor inspectors); as well as those who provide services to the community (waste collectors), or who support the mandatory social security systems (such as social workers).
Public officials, as guardians of public assets, are essential vehicles for recovery.

MEDIA AND CULTURE

It is worth noting the impact of COVID-19 on the media and culture sector, highly affected by unemployment and closed productions.
Often, the diversity of the sector in terms of types of contracts and occupations creates difficulties in accessing social protection, health and safety programs and financial assistance.

HEALTH SERVICES

The COVID-19 crisis draws attention to overstretched public health systems in many countries and the challenges they face in recruiting, deploying, retaining, and protecting enough well-trained, supported, and motivated health workers.
It highlights the great need for sustainable investments in health systems, including health workers, and for adequate working conditions, training and equipment, especially in relation to personal protection elements and safety at work.
Despite the fact that the infections in the Latin American region appeared in March 2020, since January of that year the interest of tourists in traveling began to decline,

harming the industry since the beginning of the year.
Ostelea, an international university center specialized in training leaders and managers in the Hospitality and Tourism industry, presented a reflection on these effects in these industries.
"The consequences will be, in the short term, notable. In addition, they are very hard for companies as we are seeing, but even more so for workers in the sector. We cannot forget that tourism is a highly seasonal sector and, on many occasions, precarious. This emergency with such complex characteristics will undoubtedly bring a notable level of layoffs, relocations and readjustments on different fronts".
In addition, given all this panorama, a new learning scenario opens for the tourism industry in the face of the different volatile, uncertain, complex and ambiguous contexts.
Likewise, the challenge is to design strategies that are being applied in the affected countries such as Spain, which range from making cancellation policies more flexible, temporary closure of hotels, implementing regulations for the management of temporary jobs, providing facilities to the health service and even requesting to public institutions that activate specific aid for the sector.
Tourism comes from several years of transformation that has affected some participants.
They are not only in trouble because of Covid-19; for example, the acceleration of digitization had an impact, but with the global pandemic, their situation worsened.
In the Latin American space, although the initial impact is less than in Europe, the path is expected to be similar.
Borders were closed for too long, and movement -into countries heavily dependent on foreign visitors- came to a near halt.
The hotel and tourism sector must contribute in some way to tourists, to be in line with corporate responsibility and gain followers, as several organizations worldwide have already done.
Human talent (especially management) must be up to the task of making strategic decisions; where he will highlight the challenge of building teams with proactive people who will provide solutions to the hundreds of thousands of requests that will surely appear during the crisis and after it.
Tourists will want to resume their vacations, request refunds or schedule a break after all the disaster, so the agility of the processes will be vital to reactivate the sector.
With this situation, we must be more resilient than ever and see the opportunities that are opening up, which can be taken advantage of with an in-depth analysis of everything that has happened to tourism as a result of Covid-19.
For example, offering insurance to tourists for cancellations without cause, coverage in the event of border closures and even under parameters of atypical situations.

TRAVEL MEDICINE

What is Travel Medicine used for?

Perhaps the main motivation of travel medicine is prevention.
Diseases acquired during travel are -at the same time- a considerable source of economic losses and the origin of various medical problems, which are sometimes serious.
There are several vaccinations and methods to prevent common and rare diseases during travel that must be evaluated according to the itinerary.
Therefore, it is advisable to receive a medical evaluation in advance (between 4 and 6 weeks is an ideal time for this).
If you require a vaccine, at the time of applying it, you will be given an international vaccination certificate that you must carry with you throughout the trip and return.
In addition, travel medicine is also responsible for making assessments and issuing medical certificates to people who will carry out special activities during the trip, such as diving and mountaineering, among others.
Likewise, in the clinics oriented to this specialization, attention is provided to people who return from a trip with rare diseases in their country of origin.
During the consultation, serologies are requested to assess previous immunity (if necessary).
The vaccines in the calendar are updated and the special and/or required ones are detailed. Prevention measures are indicated for diseases transmitted by mosquitoes such as malaria, dengue, yellow fever and chikungunya , among others. Information on how to prevent traveler's diarrhea and medication for its treatment.
He advises on preventive measures for accidents, sunburns, jet lag and animal bites.
Also about how to deal with special travelers, whether they are small children, pregnant women and immune-compromised persons.
The Medical area that deals with travelers has the objective of not only protecting their health during the trip, but also that of the communities to be visited, and that of the community to which they return at the end of the trip.
Each trip and each traveler is unique: for the reasons for the trip (tourism, business, study, research, visiting family or friends, missionary activities, humanitarian reasons, pilgrimages, ecotourism or adventure tourism, medical reasons, etc.), for the different itineraries of the same, its duration, the time of year chosen, and the particular or personal characteristics of each traveler (age, underlying pre-existing diseases, pregnancy, etc.).
Therefore, the consultation must be individualized and updated in all cases.
There are well-known "old" infectious risks to the traveler, such as traveler's diarrhea and malaria. The so-called traveler's diarrhea is very frequent; it can be acquired during most

of the year and in many areas of our planet it is preventable. Malaria is still present in vast regions highly visited by travelers from all over the world; furthermore, it is preventable.
The risk of acquiring infectious diseases is not static but varies dynamically: in some regions certain risks have decreased, in others previously controlled infectious agents have reappeared, while in some new diseases have emerged that were previously unknown.
For example, in recent years serious infections such as SARS, SARS COV2, MERS, various bird flu, or the one caused by the Ebola virus, or infections such as Zika and Chikungunya , have generated epidemic outbreaks in various regions of our planet. , potentially putting unsuspecting travelers at risk.
Even with so many old and new challenges on the horizon of a trip, timely consultation before embarking on it practically eliminates risks regardless of the chosen itineraries, provided that the recommendations that arise from the consultation with Travel Medicine are carefully observed.
It should also be remembered that the traveler may worsen underlying cardiovascular, respiratory, neurological, endocrinological diseases, HIV, diseases or immunocompromised situations (cancer patients, organ transplants), etc., during their trip.
This possibility must be discussed and planned in advance to avoid and/or treat these possible complications.
The consultation prior to the trip constitutes an unbeatable opportunity to advise, determining the potential risks to which the traveler will be exposed, educating and providing methods for their prevention, recommending vaccines for vaccine-preventable diseases, prescribing medications for use as prevention (for prophylaxis malaria) or self-treatment (for example traveler's diarrhea), or both.
Regarding vaccines, it must be verified if the traveler needs any of the usual vaccines in the National Vaccination Calendar (double adults, measles, etc.), or if they must receive any vaccine that is mandatory to enter a certain country (example: yellow fever), or certain vaccines recommended according to the travel itinerary and final destination (examples: meningococcal vaccines, typhoid fever, Japanese encephalitis, rabies, etc.
In the pre-trip consultation, not only recommendations are generated to prevent infections, but also strategies to avoid and manage other risks should be considered.
The following are also considered and discussed: traffic and swimming accidents, assaults, extreme temperatures, altitude sickness, jet lag, proper handling of food and liquids, sun exposure, risks with sexual activity, risks from contact with animals, risks of infections transmitted by mosquitoes and other insects.
Upon return, some travelers present fever and/or other signs or symptoms of infection. tion: timely consultation makes it possible to adequately investigate and treat unusual and/or little-known infections in the Country of origin and, therefore, difficult to diagnose for Professionals without experience in this branch of Medicine.

PROPOSALS TO MINIMIZE RISKS

They must be:
Reasonable
Easily applicable
Based on demonstrable evidence
Low cost (no impact on the total value of the trip)
Sustainable over time

Temporarily structured, they can be subclassified into:
1) Measures BEFORE the trip
2) Possible measures DURING the trip
3) Measures AFTER the trip

1)MEASURES BEFORE THE TRIP

Risk assessment according to the traditional guidelines of Travel Medicine, referring to the passenger's condition, his background and his specific destination.

PREVENTIVE THERAPEUTIC OPTIONS
carrageenan
ivermectin
HCQ

2)MEASURES DURING THE TRIP

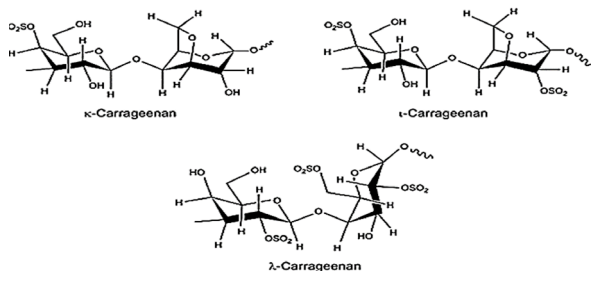
EVENTUAL THERAPEUTIC OPTIONS
Azithromycin, in the case of upper respiratory symptoms.
Bromhexine , in the same case.

3)POST TRIP MEASURES

Medical evaluation regarding prevalent pathologies in the destination visited, and COVID in particular.

CARRAGEENAN

Carrageenans are extracts from Rhodophyceas algae.
There are 3 basic types of carrageenan: Kappa, Iota, and Lambda.
Carrageenans are used in the food industry either as a stabilizer, thickener and/or gelling agent.
The foods most commonly treated with carrageenan are: dairy products; meat products; pastry and confectionery.



Molecular structure of carrageanins

Virucidal capacity of carrageenan, resulting from interference with the first steps of viral replication, has been reported due to its inhibitory action on viral attachment to the host cell.

Iota- carrageenan demonstrates potent antiviral activity in vitro, reducing rhinovirus reproduction and its cytopathic effects.

The same results were obtained against the herpes simplex virus and the Japanese encephalitis virus.

The binding and entry of coronaviruses, including SARS-CoV-2, is mediated by the spike glycoprotein (SGP).

Recently, a SARS-CoV-2 Spike lentivirus was developed Pseudotyping (SSPL) allowing to study spike-mediated cell entry via luciferase reporter activity in a BSL2 environment.

Iota- carrageenan can inhibit cellular entry of SSPL in a dose-dependent manner.

SSPL particles were effectively neutralized with an IC50 value of 2.6 µg/ml iota-carrageenan.

In vitro data on iota-carrageenan against various rhinos and coronaviruses showed similar IC50 values and readily translated into clinical efficacy when an iota-carrageenan-containing nasal spray demonstrated a reduction in the severity and duration of symptoms of the common cold, caused by various respiratory viruses.

Consequently, our in vivo data on SSPL suggest that iota-carrageenan administration may be an effective and safe prophylaxis or treatment for SARS-CoV-2 infections.

The antiviral action of carrageenan is due to the fact that this polymeric compound would function as an electrical barrier that, thanks to its negative charge, would bind to viral particles, whose envelope contains positively charged proteins, thus preventing the virus from attaching to the surface. cells, and blocking their entry into them.

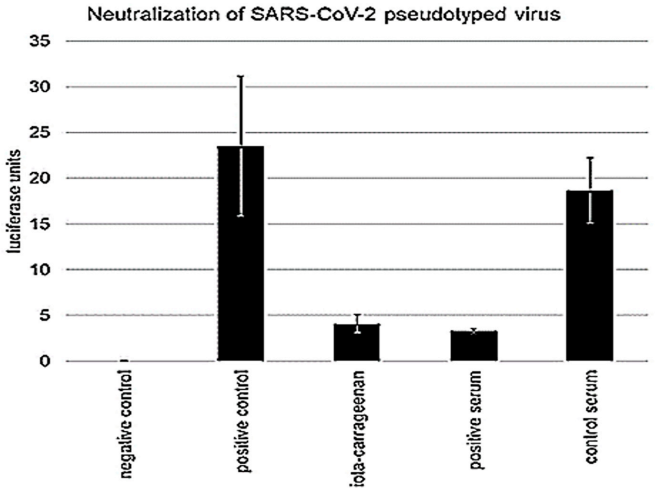
Carrageenan can also capture viral particles released by cells that have already been infected.

Topical carrageenan has two different effects in relation to SARS-CoV-2.

On one hand, it stops nasal infection in healthy individuals by shielding the cells that form the epithelium of the nasopharyngeal mucosa.

On the other hand, in the case of newly diagnosed infected patients, it prevents the viral particles released by dying cells from colonizing new cells, for example of the olfactory epithelium, and this allows the pathogen to spread in new ways, to finally reach to the central nervous system; or infect more respiratory epithelial cells, en route to the lower respiratory tract.

By preventing the virus from reaching the bronchi and lungs, the respiratory system would not be compromised, reducing the number of patients with COVID-19 in severe or even moderate condition.



Viricidal efficacy of carrageanin in COVID 19

HOW TO USE CARRAGEN IN SPRAY

Topical carrageenan is easy to apply; It has no side effects and provides special resistance to the entry, proliferation and subsequent dissemination of viruses.

It has been in the Argentine pharmacopoeia for almost 10 years, and in other countries (United Kingdom, Austria, Australia, etc.) for almost two decades.

The FDA along with the Food and Agriculture Organization (FAO) and the World Health Organization (WHO) recognize carrageenan as a safe ingredient to consume, and several recent studies further support this concept.

James McKim conducted a two-year study looking at the potential health outcomes of carrageenan.

McKim's research confirms that carrageenan has no impact on the human body in the long term, when consumed in food, and even less, when used as a medicine, in the short and/or medium term.

In addition to the antiviral active ingredients, the composition includes at least one pharmaceutically acceptable carrier and, optionally, other additives or active ingredients.

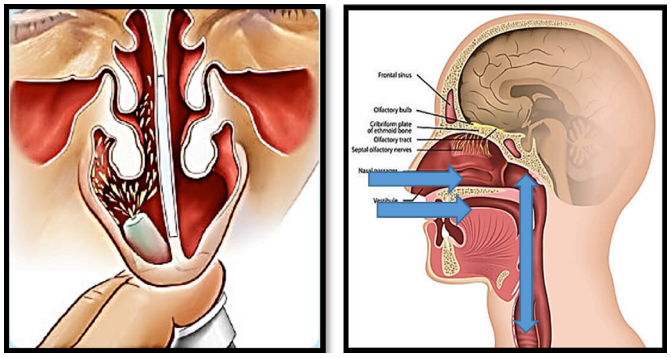
A suitable vehicle may be a diluent, eg, water or saline, an excipient or other vehicle useful for the administration of its active ingredients.

The carrageenan can be used in the form of any pharmaceutically acceptable salt, for example, in the form of "sodium salts of carrageenan ", are available in the Argentine Pharmacopoeia, and can be used for both nasal and buccal application.

Carrageenan is nontoxic by oronasal administration , even when applied at extremely high doses, which is why it has been classified as "generally recognized as safe" (GRAS) by the United States Food and Drug Administration (FDA).

The pharmaceutical antiviral preparation is prescribed

for the treatment or prophylaxis of individuals especially susceptible to or at increased risk of rhinovirus infection, such as a high-risk patient selected from the group consisting of asthma, allergy, or inflammatory disease.



Mode of application and area of distribution oro-naso-pharyngeal of carrageenan

Typically, the composition will be provided as a sterile, non-pyrogenic preparation.

However, the pharmaceutical composition could also be used to coat solid surfaces of hygiene or sanitary articles, for example, hygiene or facial care articles typically used in the oral and/or nasal regions , handkerchiefs or wipes, nasal tissue and tissues. pocket (potential fomites).

More specifically, the pharmaceutical composition can be applied (eg, sprayed) in a manner similar to disinfectants, onto gloves, handkerchiefs, or handkerchiefs, including nasal tissues, to exert a virucidal effect , thus helping to reduce repeated self-infection from contamination from fingertips and viral spread between different people who are in close contact with each other (for example, hand-to-hand).

Depending on the nature of the sanitary or hygiene article, said article may be covered, moistened or otherwise impregnated with the pharmaceutical composition.

Items treated with carrageenan may also include, but are not limited to, cotton swabs, dust masks, or face masks.

Even lipsticks can be formulated to contain an effective antiviral amount of iota- carrageenan .

These hygiene or healthcare items can be used prophylactically or in conjunction with therapeutic treatment against a viral infection, and can help prevent or reduce the risk of infection.

IVERMECTIN

Ivermectin is an antiparasitic, with nematicidal and ectoparasiticidal properties .

It's a lactone macrocyclic derived from the avermectins, a group of highly active endodecicides (antiparasitic agents isolated by fermentation from the soil microorganism Streptomyces avermitilis).

It was discovered in 1960 in Japan by Satoshi Omura.

In 1981, William C. Campbell began the studies that allowed its veterinary use.

Both received the Nobel Prize in Physiology and Medicine in 2015.

In 1985, the French demonstrated its usefulness in onchocerciasis in Africa.

It was approved in 1997 by the FDA for strongyliasis and crusted scabies in AIDS patients.

In Human Medicine it has been used in children from 5 years of age, for the management of ecto and enteroparasitosis .

Orally, and in humans it does not cross the blood-brain barrier.

It is contraindicated in pregnancy.

Ivermectin is an inhibitor of the virus that causes the current pandemic (SARS-CoV-2).

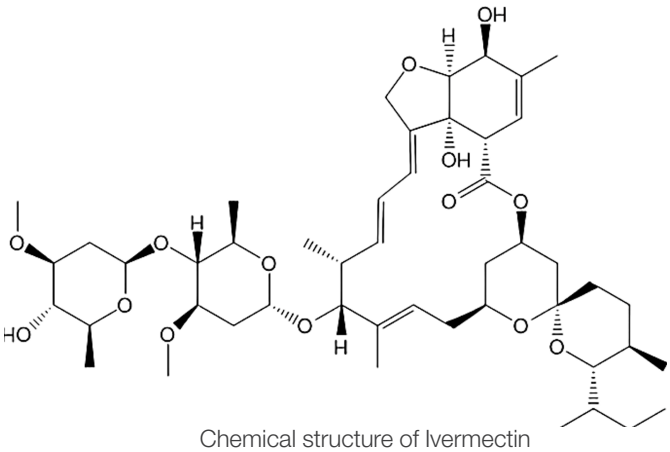
This activity is due to the dependence of many RNA viruses on IMPα/β1 during infection.

Also recently, another mechanism of action has been proposed, assuming its role as an ionophore agent .

Ionophores have many oxygen atoms internally and are essential for binding cations and transporting them across phospholipid bilayers (cell membranes; capsid virus phospholipids).

As a consequence, they would determine an ionic imbalance between the external and internal environment, with the consequent osmotic lysis.

Taken together, these results demonstrate that ivermectin has an antiviral action against SARS-CoV-2 in vitro, with a single dose capable of controlling viral replication in 24-48 hours, and the possibility of repeating it periodically.



Chemical structure of Ivermectin

CONCLUSIONS: THE BENEFIT OF IVERMECTIN + CARRAGEENAN

If we consider the following facts:

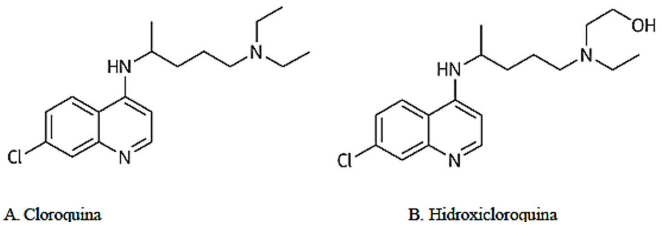
1) Droplets and aerosols are an important source of contagion between humans.

2) The sources mentioned above depend on different sizes of saliva droplets.

3) The contagion comes from symptomatic and asymptomatic patients.
4) The proportion of asymptomatic patients exceeds 30% of all cases.
5) The concentration of ivermectin and carrageenan is adequate in the nasal mucosa and salivary glands.
6) The combined oral solution can offer double protection: on the one hand, it reduces the spread and, on the other hand, it reduces the viral load.
7) Both (ivermectin and carrageenan) are present in the Argentine pharmacopoeia, and their use is accepted by the ANMAT (National Administration of Medicines, Food and Technology, Argentina).
9) Their respective "off label" applications do not imply any risk.
We conclude that by using ivermectin oral solution and carrageenan nasal spray, we may be providing an inexpensive, safe, and effective means to protect people from contagion and severe forms of the disease.

HYDROXYCHLOROQUINE

Chloroquine was first synthesized in 1934, and has been widely prescribed for the prevention and treatment of malaria, as well as for the treatment of autoimmune diseases (rheumatoid arthritis and systemic lupus erythematosus).
The mechanism of action of these drugs against Plasmodium parasites is believed to be partly related to their interaction with DNA and through inhibition of heme polymerization .
The immunomodulatory activity of hydroxychloroquine is related to a wide spectrum of immunoregulatory networks .
In addition to activity against rheumatic diseases, the two antimalarial agents have also shown therapeutic activity or immunomodulatory effects in a wide range of other diseases, including antiphospholipid syndrome , amoebiasis, HIV/AIDS, and some cancers.
These drugs are manufactured as tablets for oral administration as chloroquine phosphate 500 mg, and hydroxychloroquine sulfate 200 mg, respectively.



Chemical structure of Chloroquine and Hydroxychloroquine

The dose varies according to the indication of the treatment.
Doses of up to 2000 mg of hydroxychloroquine and chloroquine have been used for the acute treatment of malaria.
Both hydroxychloroquine and chloroquine are notable for their long half-lives (elimination of 20 to 60 days, respectively).
Hydroxychloroquine and chloroquine have attracted attention as therapeutic agents against COVID-19 .

AZITHROMYCIN

Recent publications by French researchers have raised interest in azithromycin as a treatment for SARS-CoV-2 infection.
In them, the efficacy of the combined therapy of hydroxychloroquine and azithromycin in patients with COVID-19 is evaluated.
In addition, hopes of successfully finding an effective causative therapy against COVID-19 were raised following the comment of Professor Didier Raoult (of the Méditerranée University Hospital Institute of Infections), who announced a "drastic reduction in the number of positive cases".

Clinical picture of SARS-CoV-2 infection	**Hydroxychloroquine with Azithromycin (n=6)**	**hydroxychloroquine (n=14)**	**Control group (n = 16)**
Asymptomatic (%)	0	14.3	25
Nasopharyngitis (%)	33.3	71.4	62.5
pneumonia (%)	66.7	14.3	12.5
Time from symptom remission to trial enrollment (mean, days)	4.3	3.3	2.4

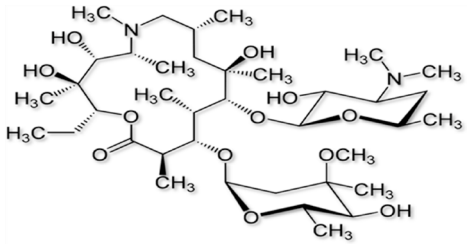
[a] gautret Ph ., Lagier J-Ch., Parola Ph . et al., Hydroxychloroquine and azithromycin as treatment of COVID-19: results of open-label, non-randomized clinical trial, *Internat . J. Antimic . Agents* , 2020: DOI: 10.1016/j.ijantimicag.2020.105949

DISTRIBUTION OF PATIENTS WITH DIFFERENT SYMPTOMS OF COVID 19 IN THE 3 GROUPS ANALYZED

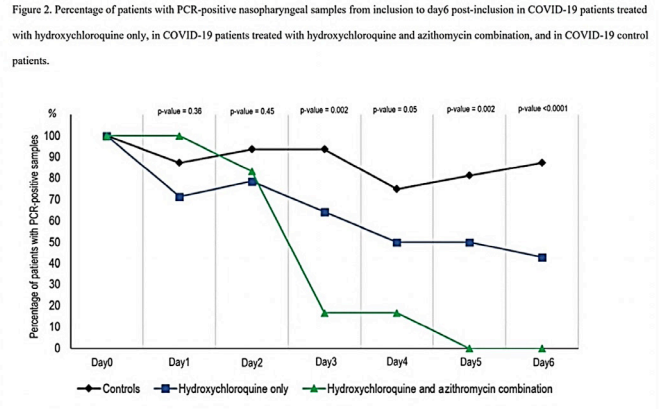
It remains an attractive hypothesis, so we must be very careful when extrapolating these observations to clinical practice without first reliably testing them in sufficiently large and adequate randomized trials.

During the SARS-CoV-2 pandemic, rapid verification is possible, as recently demonstrated by Chinese authors evaluating the efficacy of lopinavir and ritonavir combination therapy .

It is also useful in situations caused by concomitant bacterial infections, and following general antibiotic therapy protocols .



Structure of Azithromycin



Effect of the administration of Azithromycin in patients with COVID 19

BROMHEXINE

CONCEPTS ABOUT TMPRSS2 RECEPTORS AND THEIR BLOCKERS

Overexpression of these receptors has been associated with a higher incidence of prostate cancer.

TMPRSS2 overexpresses ERG in response to androgens.

Structurally, this rearrangement is due to interstitial deletion and, to a lesser extent, reciprocal translocation, and plays a key role in cellular metabolism.

Almost all fusion gene transcripts produce a truncated ERG protein, and the presence of a particular isoform of this gene indicates tumor clonality, such that the metastasis shares the TMPRSS2-ERG isoform with its primary site.

Thus, long before the start of the current pandemic, different receptor blockers have been tested in an attempt to reduce the risk and/or progression of this neoplasm.

Different trials have found various blockers:

TOCILIZUMAB Specific recombinant human monoclonal antibody (IgG1).

CAMOSTAT MESYLATE Approved in Japan for the treatment of pancreatitis, etc.

But their cost, as well as the large number of contraindications and undesirable side effects that they cause, would make their preventive use unfeasible for travelers, and would make the long-term treatment of patients affected by COVID 19 unsustainable, both in the public as well as private sphere.

CONCEPTS ABOUT BROMHEXINE IN PARTICULAR

Bromhexine is a synthetic drug that exerts a mucolytic and expectorant effect.

It reduces the viscosity of bronchial secretions and increases the volume of sputum by inducing the hydrolytic depolymerization of fibrillar secretions (mucoproteins).

It also stimulates the ciliary activity of the epithelium.

Some studies suggest that the combination of bromhexine with antibiotics, in the same formulation, is more effective than the administration of the antibiotic alone for the treatment of respiratory infections.

Bromhexine is well absorbed through the gastrointestinal mucosa, reaching peak plasma concentrations in 60 minutes.

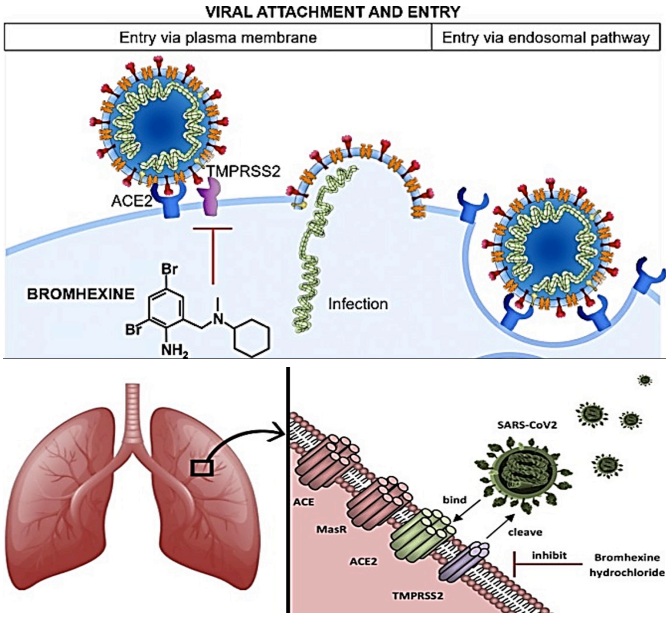
The elimination half-life is 6 hours.

Its main indication is to facilitate expectoration in cases of tracheobronchitis , acute bronchitis, chronic bronchitis, pneumonia.

Due to its mucolytic effect, it has been used to reduce the viscosity of ocular secretions in Sjögren 's syndrome .

It is contraindicated in cases of hypersensitivity to bromhexine , during pregnancy and lactation.

Recently, it has been shown that this drug, widely used in the human pharmacopoeia, is also a TMPRSS2 receptor blocker.



Blockade of receptors by Bromhexine, in COVID-19

Bromhexine provides one more tool to the therapeutic arsenal to deal with COVID 19; its use is not opposed to the rest of the drugs used; its cost (like that of other therapeutic agents) is very low and its dosage is simple.

This medicine has been included in the pharmacopoeia for decades.

Its incorporation does not modify the aforementioned protocol, since the addition of a mucolytic is a precise indication in any patient with a productive cough.

This would translate into two benefits: the improvement of symptoms and the blocking of TMPRSS2 receptors, "closing the path" to COVID 19.

REFERENCES :

1) UNWTO: studies and reviews 2019-2022

2 BALANCE OF THE TOURIST SEASON IN 2022 IN THE NECSTOUR REGIONS 08/29/2022

3) Eduardo L. Ceccotti : COVID-19. Saliva and Tongue Mucosa. Population and Professionals at Risk. ADMIN, MAY 5, 2020. Argentine National Academy of Dentistry

4) Brian Garrod : Crisis around the concepts of hospitality. Route. Hosp. 2022, 3(2), 416-434; https://doi.org/10.3390/tourhosp3020027

5) Emma A. Harden, et al.: Virucidal activity of polysaccharide extracts from four species of algae against herpes simplex virus. Antiviral res. 2009 September; 83(3): 282–289. Published online July 1, 2009. doi : 10.1016/j.antiviral.2009.06.007

6) Katelyn A Pastick , Elizabeth C Okafor , Fan Wang, et al.: Review: Hydroxychloroquine and Chloroquine for Treatment of SARS-CoV-2 (COVID-19). Open Forum Infectious Diseases, Volume 7, Issue 4, April 2020, ofaa130, https://doi.org/10.1093/ofid/ofaa130

7) Yang SN, Atkinson SC, Wang C, Lee A, Bogoyevitch MA, Borg NA, Jans DA. The broad spectrum antiviral ivermectin targets the host nuclear transport importin α/α1 heterodimer. Antiviral research. 2020 May 1; 177:104760 .

8) Hirsch RR, Carvallo HE. Ivermectin as Prophylaxis Against COVID-19 Retrospective Cases Evaluation. Microbiol Infect Dis. 2020;4 (4):1-8.

9) Carvallo HE, Hirsch RR. Ivermectin and Herd Immunity in SARS COV2 Pandemic; from LocalExperience to Broader Possibility. Clin Immunol Res. 2020;4 (1):1-2.

10) Hirsch RR and Carvallo HE.: Covid 19 and Ivermectin Prevention and Treatment Update. J Inf Dis Trav Med. 2020; 4.