

Hi all,

So sorry but in French for rapidity and thanks to B to translate... (i'm so sorry and a BIG thank you!)

First of all, we did not test an HRH1 - HRH2 blockers association, but, the following therapeutic combination

refers indirectly in my opinion to what K and M are setting out in relation to patients taking long-term antihistamines.

Indeed, our experience on the subject shows that these patients, treated for allergies with ENT manifestation and / or pulmonary and / or cutaneous manifestations, by antihistamines, are not immune to developing a Covid!

From memory I only remember 3 cases.

We were able to understand the origin of this using a reasoning diagram, admittedly trivial but which allowed us to offer a support which, in the end was proven effective each time, for now.

We have called this between us the "theory of the bucket" (Who said "medicine" was not fun... even during a Covid pandemic?).

Again, it is very theoretical and simplistic, but it allows us to grasp the idea.

In fact, "chronic" allergies treated with antihistamines have a balance between spontaneous allergic process (and more or less permanent) and effectiveness of antihistamines treatment.

Therefore, they don't develop any symptom, thanks to this balance.

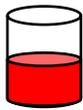
After contagion, SARS-Cov2 would generate according to our primordial hypothesis, a release of histamine, the starting point of the immuno-inflammatory cascade (here, we called it the "corridor theory"... but that's another story!).

In this way, although on antihistamines, some chronic allergic treated patients would see their quantity of histamine exceed that of HRH1 blockers and the immuno-inflammatory cascade would begin (with more or less potency depending on the flexibility/leeway of antihistamine available).

Thus, to take care of these patients it is necessary either to increase the dose of antiH1 or to change antiH1.

With the 'bucket effect' it gives the following:

No SARS-Cov2:



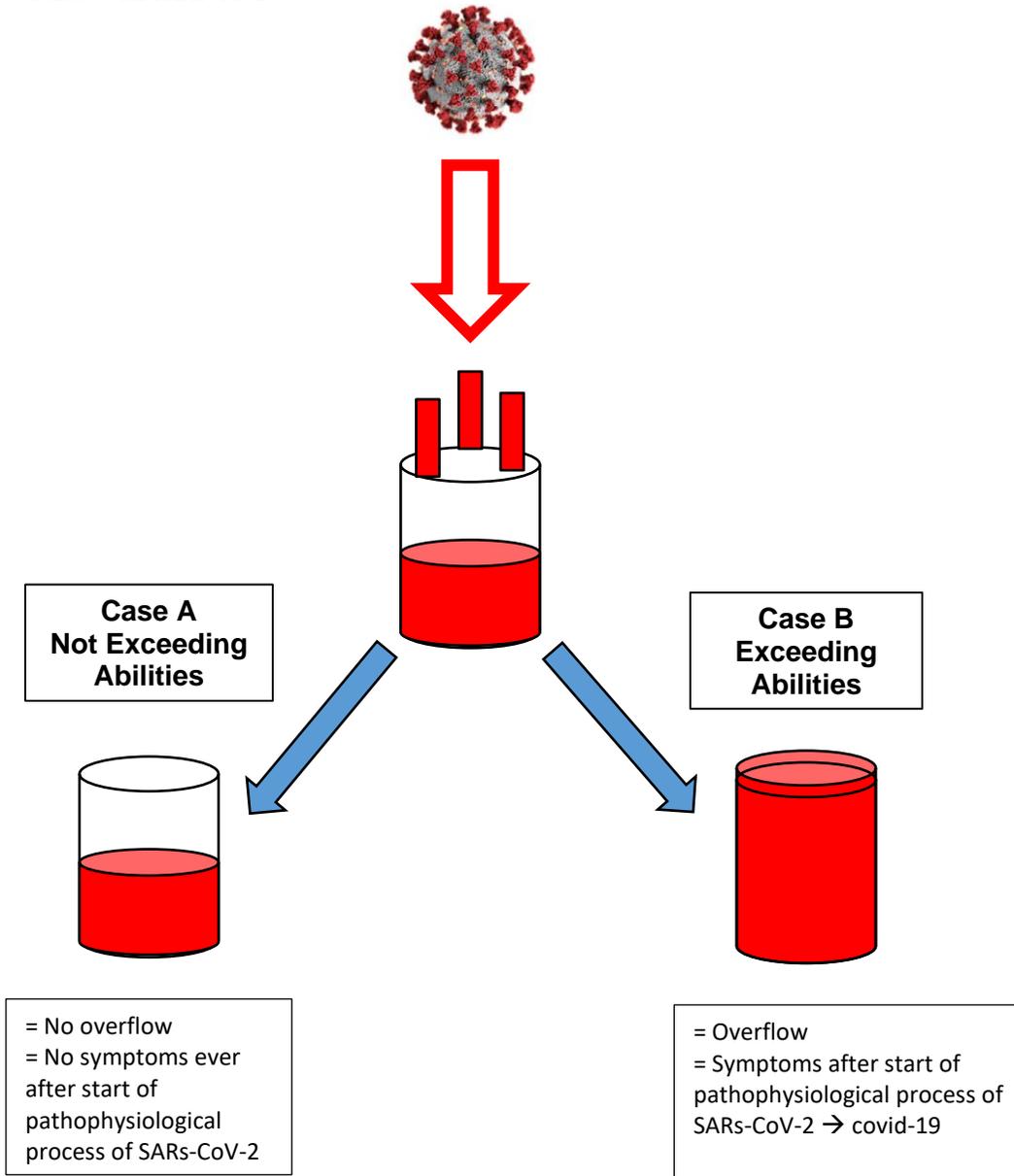
(nothing overflows = no symptoms)

With:

 = effect of histamine in chronic allergic patients linked to the abnormally total "histamine quantity" produced (= H, for Histamine)

 = response capacity in relation to antiH1 (the "bucket"!)(= M for Drug)  
Here we have:  $H < M$  = no symptom

Contact with SARS-Cov2:



Legend:

 = effect of histamine in chronic allergic patients linked to the abnormally total “histamine quantity” produced (= H, for Histamine)

 = response capacity in relation to antiH1 (the “bucket”!) (= M for Drug) Here we have:  $H < M$  = no symptom

 = Sars-Cov-2

Here we have:

Case A:  $H < M$  = no symptom

Case B:  $H > M$  = symptoms

Therefore, by increasing the capacity of the container, overflow is avoided and therefore symptoms are avoided (the Covid)....

Based on this reasoning, we proposed to increase the dosage of antiH1 in patients chronically treated with antiH1 and who develop symptoms after contagion with SARS-Cov2

It is also possible to take a larger container, therefore a more powerful antiH1 (but what is the power of an antiH1?)

By the way, this 'bucket' theory also has an advantage which is to allow us to propose an explanation for an effect observed in many patients: the "arousing" effect in Covid of antihistamines.

It is indeed common to see it develop, more or less rapidly during the evolution of the Covid, a somnolence which, unusually, is less difficult to distinguish from fatigue in the Covid. Patients sleep a lot (= more than usual).

In our experience of Covid, the initiation of antiH1 treatment is accompanied by a clear and rapid decrease in this drowsiness.

The reflection then focused on the origin of this effect in the Covid, knowing that, the antiH1 of second generation do not (to my knowledge) pass the blood-brain barrier (thanks to the pharmacologists to confirm it to me or not). Thus, only the decrease in intracerebral injection of histamine and the retro-control mechanisms associated with sleep on HRH3 are believed to be at work. The Bucket Theory gives us here perhaps, a trivial understanding but satisfying one to the clinician that I am.

In short, all this to say that:

- the HR1 - HR2 blockers association could come as an additional treatment plan for treating allergic patients developing a Covid (we can add the HRH2 blocker 'bucket').
- K and M: I am very interested and eager to know the results of your

research

In my opinion, they should show that allergic patients treated with antihistamines develop Covid, but in my opinion, the incidence should be expected to be lower than in the general population (= not chronically affected) and still in my opinion, the severity of the Covid they develop should perhaps be lower (margin of absorption of the histamine increase) ???

Thus, it would be interesting if you had in the future collection of data, a matched control population as well as elements to assess the severity in these two populations (death, ventilatory assistance, length of hospitalization, etc.) ... in short, some extra work but it would be fascinating to see if the 'bucket' theory does exist.

Thank you to you for these discussions and perspectives!

Kinds regards

S

Traduction B, diagrams Philip Fremont-Smith