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Review Article

A New "Non-Epidemiological" Model of the Covid19 Pandemic - Based on Potential Infection Ceilings [Maximum Number of Infected Persons] and Blocks - Taking in to Account the Results of Simple Calculations of Virus Multiplication as Well as Infection and Infectiveness of Persons

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Abstract

The main objective of part I is to create of a „non-epidemiological" model of the Covid19 pandemic, or more precisely, sets of models/equations with the formulas that allow to calculate changes in pandemic parameters over time, i.e. the number of infected, sick, antibody producing [„recovered"] and dead people, based on the multiplication of viruses and the existence of ceilings and blocks for virus.

The ceilings are the maximum number of viral binding sites [SARS CoV-2] in the human body [thus related numbers of affected people] and the blocks are the viral binding sites [in the blood/extracellular space] such that viruses thus bound do not multiply [subject of separate paper sent to EC Nutrition].

This needed the introducing: a/the concept of „human breath and virus cloud" thus to move on to pandemic calculations from one person to the whole population. b/a simple arithmetic [„2x2x2..."] model/s of virus multiplication in a group of people [and so in the entire cloud]. c/Hill equation [so its constants K_a and X_{max}].

Keywords: *Functional Receptors for SARS-COV-2; Maximal Amount of Viruses Bound Per Person; Binding of Viruses in Blood [Block]; Duplication Time; Exponential Curves; Hill Equation; Infection; Infectivity*

Introduction

Until now, there were actually only „ordinary" epidemiological models in which an attempt was made to fit appropriate curves to the statistical data [the number of infected, sick, convalescent, or those who died over time or their daily increments] [1-4]. The curves were usually exponential, similar to the Gompertz curve, or the so-called logistic curve [5-9]. In such pandemic models, it was common to simply select rates of infectivity, cure, mortality, etc. to fit the statistics [7]. These models did not even use the word virus [or receptor or target cell] or the number of viruses.

My model is supposed to be completely different. I'd like to start with what happens with viruses. How they multiply in one human, in one cell, then in many cells,... etc. until that man falls ill, until his death. I would like to transfer the mathematical model of these phenomena that occur in a single person to the entire population. Let's say it will be the population of Poland, but in fact it could fit into any country where the pandemic has come full circle like Spain, Italy, the United States etc.

The model is based or rather closely related to my two hypotheses: first on necessity of existence of the functional receptors for SARSCoV-2 not just membrane ACE2 to be infected and second on the viruses'block ie binding of viruses to serum ACE2 and some erythrocytes. The paper with these hypotheses was sent to publication [10].

Objectives of the Study

The main objective of the whole paper, i. e. both parts I and II, is to create of a „non-epidemiological" model of the Covid19 pandemic, or more precisely, sets of models/equations with the formulas that allow to calculate changes in pandemic parameters over time, i. e. the number of infected, sick, antibody producing [„recovered"] and dead people, based on the multiplication of viruses and the existence of ceilings and blocks for virus.

The ceilings are the maximum number of viral binding sites [SARS CoV-2] in the human body [thus related numbers of affected people] and the blocks are the viral binding sites [in the blood/extracellular space] such that viruses thus bound do not multiply.

The realization of this goal requires an explanation:

A. Why not all ACE2 molecules in cell membranes are functional SARS CoV-2 receptors and

B. What might be the ceiling and block sizes for four different age groups of the population [dependence on age].

C. What exactly happens „during the block", -in all the affected Mankind; but the data are to be compared mostly with pandemic in Poland. Above appearing point A and justification of point B are the subject of the separate paper explaining the hypotheses I have mentioned.

This needed the introducing:

a) The concept of „human breath and virus cloud" thus to move on to pandemic calculations from one person to the whole population.

b) A simple arithmetic [„2x2x2..."] model/s of virus multiplication in

    1. A group of people [and so in the entire cloud].

    2. one person [say „person zero"] from an infection to death; it is to show what is going on both in target cells and in an extracellular space including an exocytosis and blocking of viruses.

c) Hill equation [so its constants K_a and X_{max}].

So I wanted to:

1. Look what is [are]:

    a. The ratio of the number of infected and infectious persons.

    b. Changes over time in the number of infected (I), sick (S) and antibody producing [„recovered"people].

2. Present the changes over time of the calculated parameters of the pandemic for four age groups and the entire population [of Poland] and try to compare them with the „reported" statistical data for Poland [and in outline for the whole world].

3. Try [eventually as the separate addendum]:

    a. To clear up some common definition ambiguities and data discrepancies, and

    b. To outline the possible expected picture of further changes in the Covid19 pandemic in Poland and in the world.

The implementation of the outlined goals in the following two parts of this article overlaps because it is difficult to separate them. An outline of the main concepts and models of computation is given in Part I as well as more detailed comparison of simple arithmetic models with the Hill equation and their application to the calculation of pandemic parameters for various age groups.

In Part II there is, first of all, the analysis of what happens during the „virus block". Then there is the analysis of data for entire population in Poland, along with comments on the main epidemiological concepts and the situation in the world in 2019 - 2021.

From single infected person to the whole population

Single person

If there were no functional virus receptors in the body at all, there would be no multiplication of viruses and very quickly the viruses would be destroyed under the influence of our immune system, even nonspecific [innate] one.. Practically the same would happen with the minimum, close to zero, density of such receptors. Viruses - come from an „infecting dose", but mainly from multiplication in the cells with functional SARS CoV-2 receptors, i. e. a total amount/number of viruses V:

$V=V_l + [V_{bl} + V_{bd}] + V_{ot} + [V_s + V_{ea}]$..... [1}

Where V_l are viruses from the lungs, but also from the respiratory tract in general, V_{bl} are viruses from the blood of capillaries in the lungs, V_{bd} are those from blood from vessels connected to the gastrointestinal epithelium [beginning downwards from from the esophagus], V_{ot} are those from other tissues, V_s is those from secretions, e. g. urine, tears, V_{ea} are those from an exhaled air. By „blood" I mean the entirety of the extracellular space, including the lymphatic ducts.

For simplicity, $[V_l]_0 = a$ = infecting dose=d_i

And now, β is the fraction of viruses which might be present in an "usual contagious space" [from where the swabs are taken from] during one day [in as only one single portion or as a sum of smaller portions]; d_i is the minimum infecting dose the number of people who can be infected by a given infectious person during the day I_p will be:

$I_p = \beta \times V / d_i$ ..... {2}

I assumed that β = 0. 05 and d_i = 200, so in order to infect 1 person a day, a given person must contain 4, 000 viruses in the whole body, so other formulas for I_p appear:

$Ip = V \times 2.5 \times 10^{-4} = V/4000$ ..... {3}

These formulas [{2}, {3}] can be used to calculate the infectivity of a single person, but also for the amount of infected persons in any area or even the entire population [„in a cloud of human breaths and viruses" - see further text] e. g. with 1 million viruses I = 1, 000, 000/4, 000 = 250 people infected.

If we assume a continuous but passive [diffusive] movement of viruses in the body, there may be a transport of viruses from the lungs [pneumocytes type II] -but also from the cells of the tracheal epithelium, bronchi, mouth either to the blood as well as to other tissues- in

both directions we have to assume that apart from the droplet route there may be infection by blood, urine, faeces, sweat, saliva, sperm, faeces or vomit [11].

Finally:

$V = a \times 2^n$ ..... {4}

[e. g. $V = 200 \times 2^{n]}$..... {5}

The concept of a cloud of human breaths and viruses

In order for the adopting the final formula to the entire population, we must first introduce the concept of a cloud: „a cloud of human breaths and viruses".

Let us note that [in my opinion, everything confirms this], almost everyone, at least in the countries most affected by the pandemic, and even more so in certain centers, such as large agglomerations, but also small towns, we live „in one big cloud" [note that the concept of a cloud has found wide application, for example, in computer science [12-14] and the spread of a pandemic is like... the spread of information]. We can call it the human breaths and the virus/es' cloud. This means that basically in this cloud, we all live a short average distance from each other.

It can even be assumed that 90% of the Polish population, but this may apply to many other countries, live in a kind of cloud in which the average distance of two people from each other is no more than two meters. And such a situation takes place for at least 12 hours a day.

But as we all live in a certain cloud of breaths and viruses, basically an infection is only a matter of time. As it was rightly pointed out by Bromage [15] the most important *de facto* issue is the contact time. Bromage was inspired by paper of Kay [16] which in turn was inspired with ancient studies of Flügge and those from hundred years ago by Borouiba [16]:

1. So anyone can get infected - it is primarily a matter of time!

2. It is enough to take very small portion of viruses [1000 or even less] to be infected; infections with a „sole" big portion [say 1 million] of viruses are absolutely exceptional [17].

3. „The exposure to viruses x time" is the receipt for being infected.

   So indeed, everybody is in danger. Only infection with "big balls"seems to be limited with the protective masks; small droplets could easily pass the masks; first of all is impossible to wear the mask all the time.

4. Almost every infection begins/happens indoors not outdoors. We know most people get infected in their own home. A household member contracts the virus in the community and brings it into the house where sustained contact between household members leads to further infection.

But where and how are people contracting the infection in the community?

A. Especially dangerous is the strong viruses' outburst impetus during coughing, even more sudden sneezing [particles - with viruses – travel then up to 330km per hour!], long loud talking and singing especially in choirs and groups, not just breathing and speaking fairly softly.

B. So there are so called "superspreading events" [SSE]: religious events, weddings, long dinners, mass concerts, sport events, funerals. Mind you, the most dangerous might be singing of national anthem during the football match.

If there are no functional receptors [or their amount is negligible] there is no viral multiplication. So the key thing... is not whether there are viruses, but whether viruses multiply, and they only multiply if there are functional receptors.

Concept of functional receptors for SARS CoV-2

Virus ceilings and blocks.

Certain part of the population lives in conditions where the average distance is clearly greater than two meters, on average > 5m [throughout the day - maybe with the exception of 30 - 60 minutes a day]. And I assumed that such a subgroup [10% of the population and thus one hundred thousand people for every million] do not get infected because the distances between them are long. So these are the vicinity of large forests [like taiga or jungle- [18-20] not only-, rivers and lakes, [even sea coast provided that there are no tourists] and low population density, where - except for some extremely rare and short contacts - imagine that without contact with an infected person/s - this distance is never less than two meters, and usually even 5 or 10m and more].

So every milion all the population might be divided into: A] 900,000 [for every million] living in "a cloud of human breaths and viruses" and B] 100,000 living" far one from the other".

I am assuming that there is a certain group of people who will not become infected even in contact with an infected person, i.e. with their breath/secretions. Why? Because these people do not have functional receptors for the SARS CoV-2 virus. Anotherwords, they are not susceptible. I believe that if everyone had such receptors, the pandemic would spread so much that, in fact, probably more than half of people would be seriously ill, and finally over 15% of the population would die.

The number of cells containing ACE2 is approximately 1. 5 - 2 x 10^9 in a single human body [21,22]. However, if we multiply that potentially by 300, 000. or a million recipients, this will give us numbers of the order of 10^{14}, maybe 10^{15}. Sender., *et al*. [23] tried to calculate total maximal amount of viruses [ie RNA copies] in whole body of infected person and obtained 10^9 - 10^{11}. So their data seem to be consistent with mine assuming that there might be even 10 - 50 viruses in one cel. But I think that with even about 10 - 100 viruses less the infected person would die.

According to my calculations, this threshold [in terms of number of infected people] in the most vulnerable group, over 65, is 330, 000 per million, or one third. But considering that 10% of each group is in a low-density subpopulation and 10% of 330, 000 is 33, 000, the ceiling for the oldest group is 297, 000 [330,000-33,000]. So for every million people over 65, 100, 000 will not get sick [at least in the current phase], because there is no contact [l > 5 - 10m]. Of the remaining [900, 000], 603, 000 will not get sick because there are no functional receptors, and the maximum of 297, 000 can become infected (Figure 1, 2 and table 1).

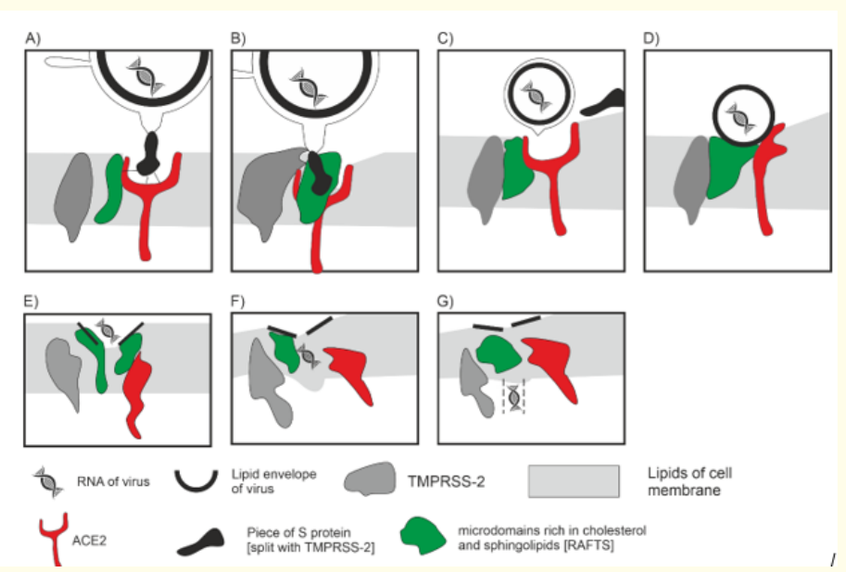


Figure 1A: *Subsequent phases of processes taking place in the contact between SARSCoV-2 virus and its functional receptor [containing suitable membranę ACE-2 molecule]. Explanations see text. !! Above figure is the only one in this paper. It must be exactly in the place I suggested in the text of paper!! [as below is about one page of interpretation of this figure 1.*

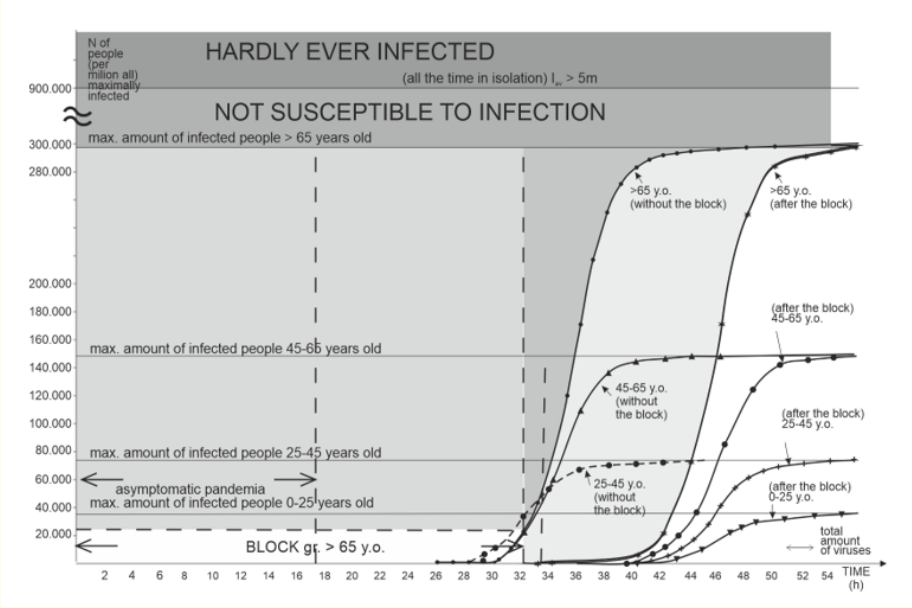
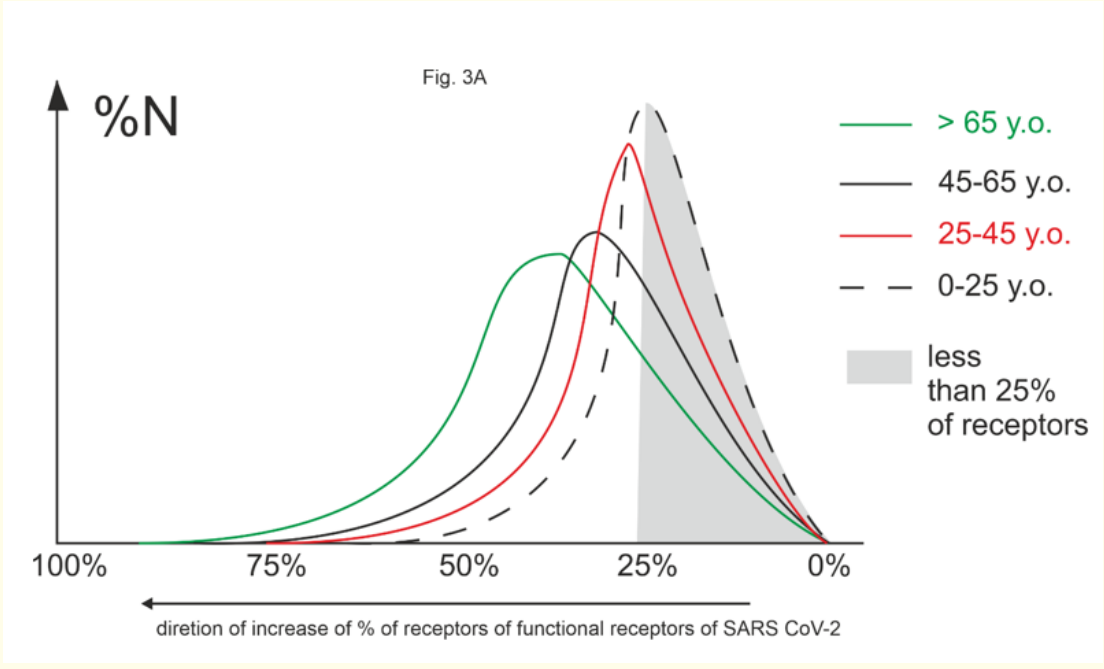


Figure 1B: *Pandemic [assuming different susceptibility and four age groups] and block versus no block comparison [my oldest-initial hypothesis].*
More explanations in text of this [ie I] part-but also in II part.



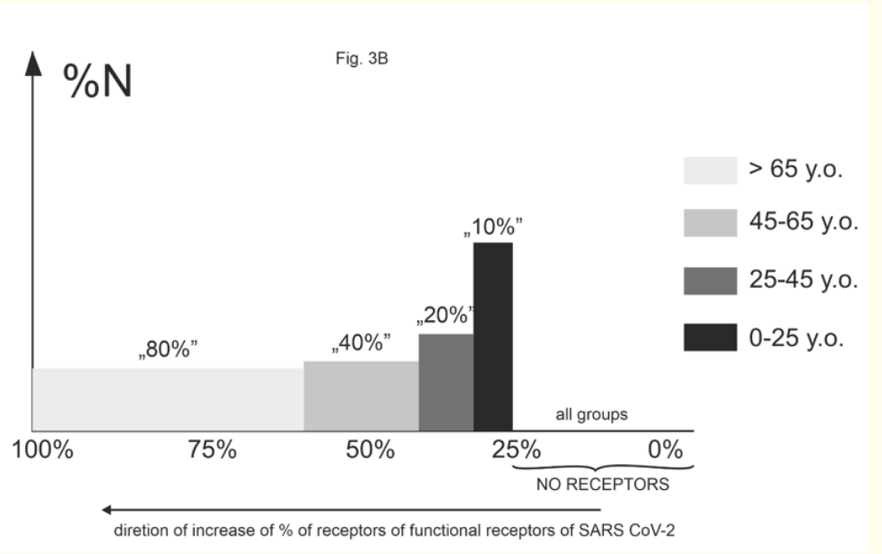


Figure 2A and 2B: *Both for figure 2A and 2B the description on the bottom [] i.e. under the left-directed arrow] should be: Direction of an increase of % of level of functional receptors of SARSCoV-2.*

Figure 2A and 2B: *Distribution in the population [ergo in four age groups] of the "density of functional receptors" of SARSCoV-2 - expressed in% assuming 100% of the amount of all ACE2 molecules in cell membranes - my assumptions.*

Figure 2A: Assumes that density of functional receptors is different for different persons according to Gaussian probability ".

Figure 2B: Assumes that the density of functional receptors is the same in all persons of the same age group.

An area of rectangle for every age group in the figure 2B is about the same as an area under the curves for the same age groups respectively in the figure 2A. Simply, in figure 2B the level of receptors for every person from an age group [0 - 25 years old] is the same: 10% of those present if we assume that every person[regardless the age] has the same ie maximal amount of receptors for SARSCoV-2 [thus remaining age groups have respectively 20,40 and 80%].

So the area represents total amount of functional receptors. The only difference between figure 2A and 2B is that in figure 2A density of functional receptors is different for different persons according Gaussian probability".

One possible justification, but far from sufficient in my opinion, is such that, according to formula {3}, one person, if the viruses had attached to all the binding sites of their body [in the amount given in table 1 - I am talking about the oldest group I] and would survive it for at least a dozen hours [which seems to be impossible], then he/she could infect 333, 000 people ie 297, 000 [with an amendment for 10% of people living „away"] [*sic* !] - such as three mass events at the Maracana stadium.

The second explanation is: a/assuming that 1 million [ie. 900, 000 living „in the cloud"] people 65+ contains 1. 46 x 10^{15} viruses b/ when the binding sites are completely saturated and c/when the density distribution of such functional SARSCoV-2 receptors in their bodies follows the Gaussian curve d/a large% of people have levels of such receptors below a certain R limit, so that it can be considered [?] that they are not functional receptors at all. Such a coincidence would mean presence of functional receptors in about 1/3 of all, and on average each of them has the viral receptor level being 80% that which would be if all ACE2 molecules in epithelial cell membranes were viral receptors.

It is not the shedding ie the liberation of ACE2-or rather its catalytic ectodomain [with the special enzyme sheddase ADAM17 [24]- from the membranes [that quite probably diminishes with age [25-27] the reason enough that with age we have more and more functional receptors for SARS CoV-2. Shedding affects [in my opinion] only fractions of a promille of membrane ACE2 (Table 1), while differences in infectivity depending on age are clearly enormous. I assumed (Table 1) that the % of functional receptors decreases with age exponentially. If, for the oldest group, the mean content of target cells containing fully functional SARS CoV-2 receptors is 80% of all cells having ACE2, this is 40% for group II, 20% for group III, and for the youngest [group IV] on average 10% [from 1. 65 x 10^{9} as 100% for one person]; probably for the 0 - 5 years old group it may be even 10 times less. This is confirmed by the literature data, although there are contradictory opinions about it [28-34].

Table 1 shows also the assumed % of shedding which gives one component of block for viruses ie serum ACE2. We can add the second component of block ie some fraction of erythrocytes [possibly some of those being attacked with free radicals ie reactive oxygen species

[ROS], whose membranes bind [with its sialic acid molecules] viruses with their evident hemagglutinin esterase activity [mind you agglutinating activity is even exerted by spike proteins of virus [35]. Then we obtain the total blocking potential [also shown in table 1]. I assumed the participation of erythrocytes in binding viruses to be roughly the same for all age groups. In such a case there might be justified differences in pandemic course due to the different blood groups [36].

Group	Age	The Ceilings				The Blocks			
		% of target cells	* Number of target cells per person	* Maximal amount of people infected per 1million	* only per people „living in a cloud of viruses" *	‰ of shedding of cells containing ACE2 *	Number of shedded cells(number of ACE2 molecules moved to serum) per person*	Maximal amount of of viruses bound within the blood) per person *	Maximal amount of people „saved -with the „block") [% of maximally infected] *&
I	> 65 years old	80	$1,32x10^9$	330000	297000	$3x10^{-3}$	$4,95x10^3$ ($1,49x10^5$)	$9,9x10^5$	24930 [8,4]
II	45-65 years old	40	$6,6x10^8$	165000	148500	0,03	$4,95x10^4$ ($1,49x10^6$)	$2,33x10^6$	43880 [29,6]
III	25-45 years old	20	$3,3x10^8$	82500	74250	0,06	$9,9x10^4$ ($2,97x10^6$)	$3,81x10^6$	57490 [77,4]
IV	<25 years old	10	$1,65x10^8$	41250	37125	0,1	$1,7x10^5$ ($5,1x10^6$)	$5,94x10^6$	33930 [91,4]

Table 1: *The „ceilings and blocks" of COVID19 pandemic in four different groups of people according to the age. *: My assumptions; &: these values are result of my first conception of block for viruses and finally I changed the idea[so these values are left in the table to help to understand an evolution of ideas concerning block. For further explanations see text.*

At first glance (Table 1) one could think that there is about 1,5 million of people involved within the block [36,1% of them should come from the group III: 25 - 45 years old]. But it is not [compare later] -simply all susceptible people possess blocking sites. Hence the number of people "exposed to block" in four different age groups [shown in table 1] is an artifact "created with the misleading:suggestion due to the calculations [I will explain this later].

Doubling time for the number of viruses [t (2)]. Application of the Hill equation to calculate different symptoms of pandemic

Virus doubling time [t (2)]

I assume the only possible viral multiplication model, i.e. the exponential model, then the given function y is a^x, so it can be 2^x, or 10^x as well as $\cdot e^x$.

Why do I find that the doubling time is 10-11 days? In target cells, viral RNA is transcribed, translated and replicated, and basically apart from one viral enzyme, RNA-dependent RNA polymerase, and yet it is formed on our ribosomes as a result of the so-called early translation], we are dealing with the implementation of the „synthetic potential" of the ordinary epithelial cell [the one that produces ACE2, ie the one that expresses the ACE2 gene]. There are no data in the literature - indicating that the virus could accelerate the biosynthesis of protein and/or RNA in the target cells.

The rate of DNA synthesis was estimated 50 nucleotides per second or less [37]. If we assume that RNA biosynthesis is faster [38] than DNA biosynthesis [although even the truth of this assumption may be called into question [37] taking in mind multiple entry points for replication], the RNA synthesis of a single virus may take 6 - 8.5h [60 - 75 nucleotides per minute, so 30, 000 nucleotides, which is the RNA length of the SARS CoV-2 virus, is 7,5 hour. But with 378 nucleotides per minute [38]-for the slowest stage in transcription;also [39]; it would be just 80 min [1,33 hour] and with 4000 nucleotides per min [the fastest transcription] it would be only 7,5 minutes. But more exact explanation will be bit later.

Well, there are quite a lot of papers dealing with viral RNA biosynthesis and spread of viruses in the body or rather cells [40-45] of the person infected with a virus.

However:

1. They do not concern SARSCoV-2
2. If they dealt with the multiplication of viruses in the body [?] – but rather in an undefined population of cells - they mainly took into account whether the viruses transmitted „cell to cell" [through the so-called viral synapses] or in a „cell-free" manner.

It is true that spreading viruses using the „cell to cell" method is easier than when the virus comes into contact with a cell from the lumen of the extracellular space [e. g. of a blood vessel] - but:

1. Such transmission greatly reduces infectivity.
2. Does not explain - if only this was the way of spreading viruses /- when it comes to attacking even the heart, not to mention distant organs - unless there would be no „attack" on the cells of these organs, but only indirect changes [as a result of e. g. a cytokine storm [46] or changes in the RAAS system [47].
3. The speed of the entire process, and thus the multiplication of viruses in cells and the whole body, is determined by the slowest, not the fastest, stage.

Someone will say that the number of viruses that will enter one cell may be 20, 50 or 100. Well, not at all. According to the research by Kuba., *et al*. [48], it turns out that the attachment of the virus to the receptor in the membrane causes the down regulation for ACE2. This makes the viral receptor essentially a „single-use device". The virus has entered the cell, but this cell will not attach new viruses [well now I overestimate].

The slowest stage determines the speed of a process composed of several stages. There is no data in the literature which stage in the process of creating new viruses is the slowest. I assumed that it is the activity of RNA-dependent RNA polymerase [or actually a multi-protein RNAreplicase-transcriptase complex], because the synthesis of a whole one long RNA molecule must take place: because it is about 5 times bigger than the largest ribosomal RNA molecules and similar to largest mRNA ever; look such RNA detaches from one single RNA template molecule and not earlier the synthesis of another RNA molecule begins.

Some authors claim that synthesis of viral RNA is much quicker [40-45] than I have assumed above. But at the same time they mention that both synthesis and degradation of viral RNA formed take place. In such a case the net dynamics should be decisive; so the multiplication of the viral RNA could be described as the difference of the two exponential curves [that is of RNA replication and hydrolysis-with some cellular ribonucleases and all the defense systems [45] like those involving small intervening RNA [49], formation of double stranded RNA and so called Dicer [50] and the final measurable virus doubling time would be much longer than 1 - 3 days assumed by some authors [40,41,45]; look generally for so called bottlenecks in processes of viral spread and multiplication [45].

During the first ten days [in my opinion], this basically all happens in about 10 - 100 cells, assuming an infectious dose of 200 viruses have been taken. That's a fair amount anyway, given the passive diffusion movement of viruses like „ordinary" small and large particles. Look the papers on viruses' spread over the group of cells or even in one body hardly begin from one virus or even 20 - 1000 viruses, but rather from milion [in an experiment] [40,41,45].

If the speed of viruses'multiplication, thus RNA replication, is 75 nucleotides min^{-1} then one virus is made in 400 min [thus 6, 66 hours per virus]. Thus velocity of viruses' multiplication should be 0, 15 V x $h^{-1}cell^{-1}$. Obviously an effective velocity of viruses' multiplication is paralell to an initial number of viruses'copies in the target cel [See table 2 assuming there are great differences in number of viruses come into one cell-it is the simplification of the real situation when these numbers are subject to Gaussian distribution].

No	No of cells *and	Viruses [V]		Ratio	Time [h] of biosynthesis	Viruses made per 1 cell per 1h
		Come into 1 cell *1/	Made in 1 cell *2/	Made/come		
1	1	20	160	8	53,33	3
2	1	15	150	10	66,67	2,25
3	1	12	180	15	100	1,8
4	1	10	160	16	106,7	1,5
5	1	8	160	20	133,3	1,2
6	1	5	160	32	213,3	0,75
7	1	4	160	40	266,7	0,6
8	1	3	150	50	333,3	0,45
9	1	2	160	80	533,3	0,3
10	1	1	160	160	1067	0,15
Total	10	80	1600	20	.....	12 V h^{-1}/ 10cells
Mean		8	20	20	.....	1,2 V x $h^{-1}cell^{-1}$

Table 2: *Model of viruses' multiplication-assuming different behaviour of different target cells. For explanations see text.*

Thus, if we calculate the final velocity of viruses' multiplication it would be not 0, 15 viruses x $h^{-1}cell^{-1}$ but 8 x more ie. 1, 2 $h^{-1}cell^{-1}$ because there is on average 8 viruses coming into one target cell [See table 2]. So in the first doubling period [n = 1] 80 viruses enter the target cells, so it might be about 1/40 ie 2, 5% of total viruses in the body.

If t(2)= 10-11 days [240-264 h] there should be on average 252 h x 1, 2 $h^{-1}cell^{-1}$ =302, 4 viruses made per 1 cell per t(2), so if there was in the body [at t=0] 3024 viruses [assuming there is 10 cells sucking viruses in first doubling period and 80/3024 ie 2, 64 % of viruses is sucked] the same amount ie 3024 would be synthetized within the target cells during time equal t(2) ie 252h. Thus an effective speed of RNA biosynthesis is 8 x 75- = 600 nucleotides per min. But it could be even bigger but at the same tinme there might happen evident slowing down of this process due to RNA catabolism and inefficient multiplication Meanwhile everything is on average exactly like in table 2 and 5; so there is 20 viruses [on average] made from just one coming into the target cell. An apparent velocity of RNA biosynthesis is of the same range as shown by other authors and still t(2) is about 10, 5 days].

Downloading a larger batch of infection, even 2000 viruses, does not change the whole picture. Anyway, later everything happens „supposedly faster": but in fact the speed is the same, but it takes place in more cells, etc.] that is, only after about 30 days the number of viruses in the intercellular space *ergo* viruses in the nasal/oral cavity is so large that a given person can infect other people [Table 3; especially table 6 in part II of this paper]. And it takes even longer for the number of affected cells to be so large that the body perceives it as a deletion ie a clear loss of the necessary cells for the disease to begin [51].

1/ Time	2/V	3/N x V_p ["n"]	4/A: Infected (new)	5/B: Infectious (new)	6/ A/B	7 / % of viruses :1. "0" 2.B 3.non B-	Number of persons		Number of infected persons assuming:		
							8/Sick …… 9/ Making IgG.	10/ !! Infected (He) group I] *	11/With infection dose		12/ Infection "jumping"
								1] after block ("loos-tight.")	1] 200 viruses	2] 1000 viruses	
1	400	1x400["0"]	1(0)	1(0)	1	1:100 2:0 3:0	0 …….. 0	0 (1) ↑	0	0	1(0)
2	800	1x800["0"]	1(0)	1(0)	1		0 …… 0	1(2) ↑			
3	1600	1x1600["0"]	1(0)	1(0)	1		0 ….. 0	1(3) ↑			
4	3200	1x3200["0"]	1(0)	1(0)	1		0 ….. 0	2 (6) ↑	1		

5	6400	1.x6200["0"] 1x200["5"]	2(1)	1(0)	2	1:96,9 2:0 3:3,1	0 0	5 (12) ↑	2	0	2(1)
6	12800	1.x11800["0"] 1x400["5"] 3x200 ["6"]	5(3)	1(0)	5	1:92,2 2:0 3:7,8	1 ..... 1 ["0"]	10 (25) ↑	3	1	2(0)
7	25600	1.x22600["0"] 1x800["5"] 3x400 ["6"] 5x200 ["7"]	10(5)	1(0)	10	1:88,3 2:0 3:11,7	1 ..... 1 [as abo-ve*]	19 (50) ↑	6	1	2(0)
8	51200	1.x43000["0"] 1x1600["5"] 3x800 ["6"] 5x400 ["7"] 11x200 ["8"]	21(11)	1(0)	21	1:84 2:0 3:16	1 ..... 1 *	38 (50)** ↑	13	3	2(0)
9	102400	1.x81800["0"] 1x3200["5"] 3x1600 ["6"] 5x800 ["7"] 11x400 ["8"] 21x200 ["9"]	42(21)	1(0)	42	1:80,3 2:0 3:19,7	1 ..... 1 *	76 (76)	26	5	22 (20)
10	204800	1.x155600["0"] 1x6200["5"] 3x3200 ["6"] 5x1600 ["7"] 11x800 ["8"] 21x400 ["9"] 42x200 ["10"]	84(42)	2(1)	42	1:76 2:3 3:21	1 ..... 1 *	152 (152)	51	10	22(0)
11	409600	1.x295400["0"] 1x11800["5"] 3x6200 ["6"] 5x3200 ["7"] 11x1600 ["8"] 21x800 ["9"] 42x400 ["10"] 83x200 ["11"]	167 (83)	5(3)	33,4	1:72,1 2:7,4 3:20,5	1 ..... 2["0" + "5"]	304 (304)	102	20	22(0)

12	819200	1x561400["0"] 1x22600["5"] 3x11800["6"] 5x6200 ["7"] ..... 166x200["12"]	333 (166)	10(5)	33,3	1:68,5 2:10,9 3:20,6	1 ..... 5[as +3 persons "6"]	608 (608)	205	41	22(0)
13	1,638x 10^6	Analogical mo de as above 1x43000["5"] 5x11800["7"] 332x200["13"]	665 (332)	21 (11)	31,7	1:65,1 2:14,5 3:20,4	2("0" + "5") ..... 10 [as +5 persons "7"]	1217 (3141) ↑	410	82	347 (325)
14	3,277x 10^6	Analogical mode as above 665x200["14"]	1331 (665)	42 (21)	31,7	1:61,3 2:18,4 3:20,3	5 (3 new) ..... 21(11 new)	2433 (6217) ↑	819	164	347 (0)
15	6,554x 10^6	Analogically as above 1332x200["15"]	2663 (1332)	84 (42)	31,7	1:57,7 2:22,1 3:20,2	10 (5 new) ..... 63 (42 new)	4786 (13403) ↑	1638	328	347 (0)
16	1,311x 10^7	Analogical mode as above 2782x200["16"]	5445 (2782)	167 (83)	32,6	1:54,4 2:25,6 3:20	21 (11 new) ...146 (83 new)	9424 (23398) ↑	3276	655	347 (0)
17	2,621x 10^7	Analogical mode as above 5311x200["17"]	10746 (5311)	333 (166)	32,3	1:51,3 2:28,8 3:19,9	42 (21 new) .....312 (166 new)	18268 (43371) ↑	6552	1310	5595 (5248)

18	5,243x 10^7	Analogical mode as above 10700x200["18"]	Ass. 21464 (10700)	Ass. 667	Ass. 32	1:48,6 2:31,6 3:19,8	84 (42 new) .....645 (333 new)	34401 (75689) ↑	13104	2621	5595 (0)
19	1,049x 10^8	Analogical mode as above 21500x200["19"]	Ass. 42929 (21500)	Ass. 1334	Ass. 32	1:47,5 2:33,2 3:19,3	167 (83 new) .....1310 (665 new)	61659 (75689) ** ↑	26208	5243	5595 (0)

Table 3: *The simple model of the pandemic spread from the very beginning [i.e. From the first infection-that is of person "0"*]. Explanations and comments: */in fact, just before the beginning of first duplication period [n=1]. Say 2 days before,the person "00"[or possibly the animal -in case of Wuhan] infected the person "0". The distinguishing "0" and "00" is necessary as only person "0"belongs to the studied group/population. 1/As the following number of duplication time n [one duplication time corresponds 5 - 6,5 days]. 2/Total amount of viruses (V)after given n. 3/Amount of persons (N)/ x amount of viruses within 1 person V_p [number of infection time: "n"]. 4/ A: Number of infected persons(new cases ie in given duplication period n). 5/B: Number of infectious persons (new cases ie in given duplication time n). 6/ A/B: The ratio of number of persons infected [who took from outside the dose at least 200 viruses and multiply them owing to the presence of functional receptors for SARS CoV-2]to the number of infectious persons [as above but only if number of viruses in their body $V_p \geq_< 4000$]. 7/ % of \viruses present in:1 body of person "0"; 2. bodies of infectious persons[$V_p \geq_< 4000$]except person "0"; 3.bodies of non-infectious persons [$V_p <_< 4000$]. 8/Sick [≥ $4x10^4$ viruses in the body of one such person]. 9/Producing specific[anti SARS CoV-2] IgG[≥ 10^4 viruses in the body of one such person]. 10/ !!Number of infected persons according to Hill equation (He)[in the oldest group I > 65 years old assuming I_{max} ie maximal number of persons per one million of people [ie just 900000 living in a total cloud of breaths and viruses"] as 297000 and K_a=1 x 10^{13} viruses in the "total cloud of breaths and viruses[compare the text of paper]. In fact these numbers refer to the situations: 1 with the block taking place [compare the text of paper] from about time ie duplication period No32[ie No16 according the last interpretation –compare table 8] from the very beginning of pandemic. !! In brackets:the same but with alternative changes: with consecutive successive: a. six periods of doubling [30-39 days] in which there was a „free" approach to the pandemic ("loos") b. the next 6, where there was a tightening of regulations ("tight.") [masks, keeping the distance of at least 2m c. the next 6 „insulation loosening"d. the next 6 tightening of regulations [only first three doubling periods ie 15 - 19, 5 days shown]. ↑: mean the increase of number of infected persons during an evident loosening of restrictions -related to the pandemic. 11/Number of infected persons with "the total cloud"[ie. without differentiating who was the infectious person eg. person "0" or else]-without person "0[such an approach is meaningful for very small amount of infected persons]; with infection dose 1] 200 and 2] 1000 viruses .The amount of infected persons was calculated according to the formula: $I=I_{max} xV/(K_a +V)$ assuming K_a=1x10^{13} viruses and I_{max} = 297000. 12/Infection "jumping": ie taking place only after every fourth doubling period n [1, 5, 9, 13...] without a correction on number of deaths.In brackets only:newly infected persons.*

To calculate the number of viruses, I use the exponential model and since I took 200 as the minimum number of viruses that will infect, the general formula for the total number of viruses [„in the cloud"] depending on the time will be: $V = 200 \times 2^n$, [formula {5}] where n is the number of periods of doubling, i. e. if n = 1, the number of viruses will double during this period, etc. for n = 10 it will be an increase of exactly 1024 times, and for n = 20 it will be an increase of $(1024)^2$ times, of course, that is over a million. The number of viruses [in the „cloud"] increases by 6,82% every day; where t (2) is the doubling time [t(2)= 10, 5 days].

Application of the Hill equation to calculate the various parameters of a pandemic

I decided to use the Hill model, i.e. to use the Hill equation [52] to calculate the number of infected, sick, healed and dead people according to the equation Hill-Langmuir. It is widely used - in various versions - for various effects, e. g. hemoglobin oxygenation and deoxygenation curves [52], but also for enzyme activity, both non-allosteric and allosteric [53,54], for receptor binding of hormones [55], as well as generally for the effects of drugs and poisons [56,57].

Conversely, the Hill equation properly reflects the cellular or tissue response to the ligand: the physiological output of the system, such as muscle contraction. The equation in this or bit transformed form might be applied to evaluate the tissue response [56-58] - not necessarily directly proportional to the binding of agonists with receptors, which usually was studied with Hill equation. So it should be valid in the evaluation of final effects of chain of events beginning with the formation of the complex virus-target cell [or more specific receptor binding domains of viral spike protein with the membrane ACE2 receptor] and resulting in the infection of more and more persons.

The general formula for the amount of infected is:

$I = I_{max} \times V/Ka + V$ ..... {6}

Where V is the total amount of viruses [in the „cloud"] and K_a is the de facto amount of viruses „in the cloud" for which the effect is 50% [respectively infected, but possibly also: sick, producing antibodies, dead [from Covid 19, not from „comorbidities"].

In case of the cooperative [allosteric] model, the number of viruses and K_a should be taken to the n_H power, where n_H is the Hill coefficient.

I tried to use calculations assuming the cooperative nature of this process, but I did not find reasons for assuming that it is a cooperative model [54], in which the subsequent transition of certain important receptor/regulatory units "from the non-stimulated [inactive] to the stimulated [active] form" took place.

Besides, I tried to plot the statistical data for Covid19 pandemic in Poland and other countries-first Belgium-against suspected [assumed] amounts of viruses in the cloud [per 1 million of people]. But there were hardly the evidences pointing to a cooperative process model [n > 1]. Therefore, I adopted a model without cooperation with $n_H = 1$. Then this formula becomes [as to the form] identical to the formula for the rate of reaction catalyzed by a non-allosteric enzyme. But it might be that especially in some phases of pandemic one could elaborate cooperative model.

The curves showing the number of infected persons in a situation there is no block and that after block [an overt pandemic] for the oldest persons [> 65 years old -group I] and for the younger groups [II-IV] are presented in the figure 1.

There is one more important problem. Someone might complain that the equation of Hill [Michaelis-Menten-MM] is not a good representation of the process of infection, let alone the entire development of the pandemic [from very mild to life-risky, antibody production and finally deaths], because:

- It does not give an exponential curve - a practical objection and

- Theoretical objection - this equation is - or at least it was supposed to be according to the authors of this equation and its various versions - to illustrate the change in a given time, e. g. v [reaction velocity], so here possibly dI/dt [daily change in the number of infected persons ?], rather than cumulative numbers of infected/affected people - this should be done with the possibly integrated forms of this equation.

Full answers to these allegations/doubts are beyond the scope of this article. But the short answer must be given. In fact, why are we looking for variants of the exponential curve. Because this is „the logic of the epidemic/pandemic course". They obviously end one day, which means there is always a ceiling [only the reasons for this pandemic slowing down, i.e. its asymptomatic course -the number of infected- may raise doubts]. Therefore, it cannot be just an exponential curve - there should be some kind of its modification, which would have a slower course at the beginning [of the pandemic] and at the end. These are the features of the logistic curve, especially the variants of the Gompertz curve „with an increase, not a decrease" in the number of cases over time [#].

Now let's move on to the non-cooperative case curve of the Hill equation [for MM: enzymes]. There is clearly a ceiling here [like V_{max}], so the curve „slows down" - flattens out „at the end".

And there is slowing down at the beginning and this is.... very large due to the fact that - in the situation of my model - the analog/s of the reaction substrate [or the agonist for the receptor, eg hormone] are viruses. And with a small amount of them [here, even a million viruses is not enough], the effects calculated from the Hill equation [MM] are zero. It resembles a chain process, e. g. free radical polymerization [#] initiated by some catalysts [here, functional SARSCoV-2 membrane receptors] in a very large reservoir [in our case, the whole cloud, or even the population], in which the concentration of the substrate - e. g. monomer [in our case, viruses] gradually changes by many orders of magnitude [e. g. from a few nanomoles to thousands of megamoles per reservoir].

At first the Gompertz curve seems to better reflect the pandemic, because it has the so-called inflection point - where the second derivative after time is equal to zero - where is the maximum speed of the process. But on the scale of the pandemic as a whole [or rather the sum of the two curves - for two different groups of people - compare a lot further] it doesn't matter in the slightest.

Thus, the curve for the infection process [etc] obtained from the Hill equation basically correctly describes what is happening [on a logarithmic scale a straight line - which is typical for the exponential phase - and after exceeding Ka, the curve „flattens asymptotically towards the maximum" I_{max}].

For the theory:

→**V + FR ⇔ V-FR →V in cell (+cell substrates) →new V [then exocytosis] ** +affected cell /s……. →……. → infected person/s ……. →. sick person/s S */producing antibodies A *\ seriously sick S_{ser}* [then →dead person D] or /recovered REC

Where * means the same thing starts all over again, etc.

Well the integrated forms of MM equation are usually applying S_o ie the initial concentration of substrate. In our case it should be form with viruses both as substrate/s and products/byproducts. I couldn't find such a solution. Let us have a look at Henri integrated form of MM equation [59]:

$y + K_M \times 2,303 \times \lg S_0/s_0 - y = V_{max} \times t$ ……. {7} [where t:time;y-amount (concentration of product); K_M: Michaelis constant; S_0 the initial concentration of substrate; V_{max}: maximal velocity. Would be good for our problem [viruses, infection] the following form?:

$I + K_a \times 2,303 \times \lg S_0/ s_0 - I = I_{max} \times t$……. {8}

I and I_{max} mean number of infected and maximal amount of infected [ceiling]. But what is S_0? The only sensible meaning would be the total mass of cellular renewable resources [aminoacids, nucleotides, lipids, sugars] from whose the cells of all infected persons made new viruses [but it has to be expressed as the number of human bodies-equivalent]. But the only way is to assume it as infinity. But then it would be unsolvable. Maybe one should try successively any big number [as $S_{0]}$ beginning from one milion [I_{max} for one milion habitants 65+ I assumed is 297000]. Then one should draw the plot: I/t [ie ? per day or per one doubling period –for viruses-ie 10, 5 days] on x axis and 2, 303 x lg $10^6/10^6$ –I/ t [on y axis]. I did not the story.

But look. If a certain variable is recorded continuously, e.g. every second, then the rate of change of this variable is measured simultaneously, as well as the total [somewhat cumulative] amount of this variable, e.g. produced in a given time [e.g. from 0 to t_1 or between t_1 and t_2] - e.g. for the percentage of oxygenated hemoglobin [#]. Thus, by analogy, we can take the same reasoning for the number of infected persons [as a remote index of virus-receptor binding processes] recorded daily.

But it can be simply assumed that the adoption of the Hill formula [MM] allows to capture the main features of an ongoing pandemic, and it was selected by me intuitively. And it was indeed the case [intuition plus compliance with reality] in a number of studies, eg tissue response [] - without first integration a kinetic formula [#].

Infected and infectious. Simple [arithmetic] model ["2 x 2... x 2"] of what happens in the bodies of a group of people [so in the whole cloud] during an overt pandemic

Infected and infectious - introduction

The genetic tests [for virus RNA: RT-RT-PCR] are so sensitive that you can almost prove that we are all infected. But you have to assume some minimum infectivity, and I assumed that this is a collection of 200 viruses [Bromage assumed [15] that for infection you need to absorb a dose of 1000 viruses - by droplets]. So how many viruses at least would have an infectious person in the whole body?

It would have to be at least about 4000, because I assume that only 5% of the viruses in the body can be „in the breath", nasopharyngeal secretions ie the "usual contaminagious material". So if an individual has less than 4, 000 viruses in his body, he/she will not infect anyone! *Nota bene*, at least with 20,000-40,000 viruses in the whole body there is a real chance of being infectious. Of course, even quite significant changes in these numbers do not change the whole picture; they just slightly change the entire dynamics [Compare table 3]. Summing up, I assumed that the number of people infected I is related to the total amount of viruses [in the body of a single person] or/and in the entire cloud] V with the formula {4} and {5}.

But now let us assume that in the breath of a person speaking [especially loudly] within a distance of 1m there are 1000 viruses and, for example, 200 of them enter our nasopharynx. But if there are only 4, 000 viruses in the whole body of this- speaking loudly- potentially infectious person, then the situation is more difficult to imagine. No one can be infected by viruses that are inside the cells [compare part II of this paper]. If there are half of them, then where „exactly" are the remaining 2000. They move/are displaced/ in the extracellular space, so there is a small chance that at any given moment there will be 200 of them in our breath [i. e. as much as 10%]. There is a chance that once a day such a portion will appear in the nasopharynx [in one or rather some smaller portions -together consisting a dose to be infectious -and will be - by droplet form - given to a person who is then only half a meter from the person who is infecting. We see that indeed, these 200 viruses is absolutely the minimum infectious dose possible ever; the point is if it might be detected even with very sensitive tests for viral RNA.

Simple [arithmetic] model [2 x 2... x 2"] - assumptions and description of calculations

Imagine that viruses are taken from one person to another. So from a person, let's assume „0", for example, who had just come back from China to, say, Poland [and if it is in China, then the individual „000" got infected from an animal, for example: a bat or....] [60]. And

just before the beginning of the first doubling period, may be yet in China, ie n = 0, 200 viruses had been taken by that "person zero" from "person OO" [Table 3]. And "person zero", but not "00", had been living in Poland till then [until his/her death]. Then, apparently not much happens: after 6 - 7 days, i.e. after the first period of doubling from 200 viruses, we have 400 etc. But time runs and nobody infects anyone, because to infect anyone, as I explained before, you need have in whole body at least 4000 viruses.

All this reasoning and the corresponding numbers are presented in table 3; also compare the earlier fragments of the text. The first infection will not occur until the fifth period of doubling. By the end of this period, this individual will have 6,400 viruses [or rather 6200 = 6400 - 200]. This individual will be able to infect 1 person by passing on to her/him - let's say - 200 out of [at least] 4,000 viruses present throughout her/his body.

If we want to know how many people he infects during a given time [a given doubling period with the number n], then the number of viruses that a single person has in the whole body should be divided by 4000, for example: 40 200/4000 =~ 10 people. So in this case everyone infected will receive 200 viruses, so 2000 viruses will „go away"from the body of infectious person, etc.

Infected and infectious persons

Do all infected infect others? Most people believe that if a person becomes infected, he infects others - as long as they are susceptible - which is the canon of classical epidemiology. No, it does not. Imagine what the situation is at the end of the 10^{th} doubling period. We have a total of 204,800 viruses. But there are 155,000 viruses in "person 0" body, 43,000 are in the bodies of individuals with either around 200, 400.. or even 3200 viruses [per one body], which, as I said before, is not enough to infect.

Summing up, we can see that there is a huge difference between the number of infected and those being infectious. This is clearly visible in table 3: from the 11^{th} doubling period, i.e. more than three months of the pandemic [if there was no block, see part II], we have the ratio of the number of infected and infectious people on the order of 32 [but in case of the block it looks like even much more –compare table 6-part II]. This means that out of 32 [or more] people infected, only 1 infects, because only this small fraction, about 3%, has more than 4, 000 viruses in the entire body. The matter is further complicated [Table 6, part II], as only viruses located in the extracellular space should be considered in terms of infectivity.

Let us continue the analysis of the data from table 3. "Person 0" –"the oldest infected"- has as much as 50% of viruses in the population. Non-infecting people contain about 1/5 of all viruses; but the number of such persons is dominating in all group. On the other hand, people who infect, after some time, e.g. n = 15, contain a total of about 30% of viruses.

This seems unbelievable, but this is the result of very simple calculations and it cannot be otherwise, Even if we introduced minor differences in % viruses that they can appear in nasopharyngeal secretions [or exhaled air] or assumed that not 200 but 500 or even 1000 viruses are „contagious dose".. The differences would be quantitative but would not affect the picture of the whole model.

Basic conclusions from the arithmetic model

We can see that this model shows that:

- The number of infectious people is much smaller than the number of those infected.
- About 50% of the total number of viruses of the entire population is found in the body of an „0" individual, generally of a person who is still alive but who became infected first.
- About 20% of viruses in the entire population are found in the bodies of most numerous people who are unable to infect anyone. This conclusion is valid at least during typically exponential phase of pandemic [so up to the time where amount of viruses attains K_a value [according to Hill equation].

Moreover, this simple model enables to estimate possible number of deaths, diseases and people producing antibodies, but this will be explained a bit later.

How does the simple "arythmetic" model ["2 x 2.... x 2"] relate to the ceilings and the increment in the number of persons sick, antibody producing and dead ie to the calculations using Hill equation?

The ceilings and the increment in the number of sick, antibody producing and deaths

Let's start with dying. The first thought is that if death is caused by COVID-19 and not by „comorbidities", then a significant fraction of the cells that contain ACE2 should be damaged. It is not unreasonable to suppose that there should be no less than 10% of such attacked cells for death [#], and at first it can even be assumed that only if an individual had 30 - 50% of attacked or damaged cells of a given type, then death would surely occur [let's think what % of blood loss leads to certain death-it is about 30% if itis sudden].

This criterion can be „mitigated" by assuming that a certain group of cells is particularly sensitive or particularly needed by humans [„key indispensable cells" [61] as a whole. We then assume that for 10% of affected cells is definitely death, but already for 1% is a very probable death. This 1% is about 1 - 2 × 10^7 cells in a body of one person. So it means that in order for someone to die, over 10 million cells would have to be attacked by the virus. But if only attacking 40% of the cells caused death, one would die not earlier if there was half a billion such cells. Taking these numbers into account and looking at the numerical model of simple multiplication presented in table 3, we would conclude that….. no one would die. Only somewhere after 20 periods of doubling, i.e. after more than half a year, would we have the first single cases of COVID-19 deaths. This simple reasoning shows that fewer cells must be attacked in order to cause the death. With this method, I assumed that the limit to die is that a given individual should have at least 20, 000, 000 [2x10^7] viruses, i. e. the total number of viruses „in the cloud/ group should be twice as large [compare the previous text about 50% of viruses in the body of "an individual 0"].

If you need 50 million viruses in your body to die, then how many do you need to get sick? Again, looking at both table 3 and 6, it is evident that most infected people must be asymptomatic. A significant fraction contains less than 4, 000 viruses in the whole body, so it does not infect, and it is such a small percentage of affected cells that there is no chance of any disease. Ultimately, as the absolute minimum for the appearance of the disease, I applied initially 40, 000 viruses per person. Why so much. Again my simple model [2x2x2....] - see table 3. For if we assume that it takes about a million viruses to cause disease, then after n = 13 [after 4 and a half months] it would be [say per million people;but per even almost 10 million or even whole population-see later] one sick person and this would be... "person zero". The next person [person"5" - according to my terminology, which I explained earlier - cf. also explanations to table 3] would be sick only after more than a month [so about n =18]. It is impossible and contrary to what we see. Therefore, I reduced the "requirements for the disease" to 40,000 viruses per body- I will write more about later.

On the other hand, it can be assumed, it is rather consistent with epidemiology, that even if I am not sick, but of course infected so I have already encountered an antigen in an „suprathreshold" amount, I am starting to produce specific antibodies. The threshold for the production of antibodies assumed by me is the presence of 10, 000 viruses per person [Table 7-part II- left side]; but for more meaningful production of antibodies one should assume more than 80000 viruses in the body.

Let us think such an analogy: enzyme (E) = functional receptor for viruses (R_f); substrate (S) = virus/es (V); enzyme-substrate complex (E-S) = complex of virus with its functional receptor (R_f-V); inhibitor (I) = antibody A).

If we assume the so-called fully acompetitive inhibition [59], which -for enzymes- means that the inhibitor bound not to the enzyme itself but only to the enzyme-substrate complex it would mean that the antibodies bind only to the virus-receptor [virus-target cell] complex not the viruses themselves. This would represent an autoimmune model of the body's fight against SARS CoV-2 with all its harmful

effects. However, this does not exclude that specific antibodies [IgG] only bind viruses already connected to the target cell via the fusion peptide [62], thus doing almost no harm to the cells themselves.

Well, why not to adopt the analogy with competitive type of enzyme inhibition? The answer is simple: in such a case the viruses had to bind only with membrane receptor of SARS CoV-2 but not the viruses themselves [in noncompetitive model there is also a fraction of inhibitor binding to the "free enzyme"]. Then we would have-in our case in an analogy to enzymes-full or at least partial intensive auto-immunological mechanism of defense !

From the theoretical point of view, it is generally better to adopt the kinetic model resembling that "one substrate [now virus/es] and two "competing' enzymes" [63] [one is the receptor (s) or the target cell (s), and the other is the anti-SARS CoV- specific immunoglobulin G molecules]. Then the effect of formation antibodies could be expressed by a curve of how many people were „saved" - by producing antibodies -from falling ill [so called "functional antagonism" [64].

Number of sick persons S [shown in table 5 and graphs in figure 3-6 in this part (I) and those in -part II of this paper] shows us in fact how many would be sick if not for the production of antibodies, not the real actual number of people „currently" sick.

A better approximation to the „current" number of sick people [the so-called „active cases"?? [#] is the number U = S-A [where S is the number of those who would fall ill if there was no production of specific antibodies, and A is the number of people who produce specific antibodies]. If U > 0, it means that there are still sick people who have not recovered. [another designation for U would be SS [„still sick"--see later]. These matters will be discussed in part II of this paper.

„Arithmetic" model and Hill equation - selection of the value of K_a

For infection, disease and antibody production, the same model can be used, i.e. the Hill curve, or in principle Michaelis Menten one (?), where simply K_a, i.e. the "half maximal effect" constant, should be greater for number of persons producing antibodies A than for those getting sickness S, but the ceiling [X_{max}] should be higher for people producing antibodies. Suppose a maximum of 60,000 people are sick, 290,000 people are infected, but as many as 150,000 people can produce antibodies: more than those who get sick, but certainly less than number of infected persons. One cannot produce specific antibodies if one is not infected.

If K_a for S > K_a for A the number of apparently recovered people calculated in such a manner would be all the time greater than that of sick people. Analogically, if K_a for I > K_a for S [or A]. Of course it is impossible.

It should be: K_a for I < K_a for S < K_a for A.

Otherwise the calculated number of sick people would be too high to the number of infected, and the number of people producing antibodies would be too soon higher than the number of even mildly ill people. However we cannot exclude the possibility that K_a values do not obey above dependencies but suitable selection of X_{max} might explain the pandemic course's curves.

The data in table 3 make it obvious that the number of persons to be sick is only 1/8 - up to 1/6 of the infected [I am talking about a disease that is „mild", ie such that the total number of viruses in the body is [cf. previous text] > 40, 000 [which would mean - tab. 6 - about 1000 attacked cells].

I have already written about the „ceiling" D_{max} [deaths] and S_{max} as well A_{max}. But the data from table 3 [or actually from a simple "2x2x2... 2"model.....] allow also to calculate/propose, and actually prove, the K_a values for „half maximal effect"; for the Hill formula to calculate the number of infected, sick, antibody producing, dead etc. Why? Simply, if we took too low values, too early [for too small time of pandemic n: a small number of doubling periods] we would get values close to the „ceiling", e.g. for $K_a=10^8$ [for I] the amount of infected I

"already" for n = 19, half of the 297, 000, i. e. 148, 000 infected and there can be no more than about 42, 000 [Table 3]. The same conclusion might come from just looking on world statistics.

But I must say that in some people, rather seldom, there might happen that the concentration of blocking sites in their blood is so low [practically near zero] that there an infection with such a very low K_a evidently take place. This interesting and very important [from the practical and epidemiological side] phenomenon is the essence of what some would call the first wave of the pandemic [March-July 2020] and will be discussed and properly interpreted in the second part of this paper.

The values of all constants necessary to calculate all pandemic symptoms in all four age groups, with Hill equation, are presented/ summarized in the table 4.

No	Age	I		S		A		D	
		I_{max}	K_a	S_{max}	K_a	A_{max}	K_a	D_{max}	K_a
I	> 65 y.o.	297000	$1,0 \times 10^{13}$	59400	$3,0 \times 10^{14}$	148500-50%I_{max}	$3,5 \times 10^{14}$	5600	$7,2 \times 10^{15}$
II	45-65 y.o.	148500	$5,0 \times 10^{12}$	59400	$1,5 \times 10^{14}$	103950-70%I_{max}	$1,6 \times 10^{14}$	1900	$7,2 \times 10^{15}$
III	25-45 y.o.	74250	$1,0 \times 10^{12}$	59400	$4,0 \times 10^{14}$	66825-90%I_{max}	$6,0 \times 10^{14}$	400	$7,2 \times 10^{15}$
IV	0-25 y.o.	37125	$8,0 \times 10^{11}$	34500	$3,0 \times 10^{14}$	37125-100%I_{max}	$4,5 \times 10^{14}$	114	$7,2 \times 10^{15}$

Table 4: *Constants in the hill equation to calculate number of people: Infected (I);Sick (S); Producing Specific Antibodies (A); Dead (D).*

Now about the colossal "influence of the dying". Well, if "the person zero" dies in the 17-19 doubling period and he/she contains 50% of all viruses of the entire population [!], the number of viruses automatically drops by half. If this is the case, and all the calculations [according to Hill's formula] require the current amount of viruses to be substituted into the formula, then automatically if we substitute the number of viruses minus those that „remained in the body of the deceased person", we get different numbers -when calculating-for both people potentially infected (I), sick (S), producing antibodies (A or/and G) or still dying (D) If "next" individuals die [apart from „O"already died], it is because the total number of viruses goes to be greater, what causes, the relative loss of viruses with death of a given person becomes proportionally smaller.

So there is the serious impact of such a correction on the magnitude of calculated parameters of pandemic. For instance calculated I value decreases in n = 48 [100 - 110 days of overt pandemic; explanation later] to 39% [38 for S, 37 for A], but for D [n = 55] to 27,7% [not shown]. But anyway, it does not change the maximum X_{max}. So at the end of the curve, the differences between the curves with and without taking into account % of deaths start to be smaller again because the ceiling X_{max} is the same.

There are reports [65] that after a significantly longer time from infection, there are practically no live viruses [the very term „alive" is absurd], and in any case there are... much less [well but virus RNA was checked in swab area and feces]; severe disease symptoms are interpreted as a result of indirect changes due to "cytokine storm" and disturbances in the functioning of the RAAS system. I find this type of view unfounded. Obviously, the „cytokine storm" and changes in RAAS parameters are taking place. But I don't see any grounds for assuming that the number of viruses in the body of one human being, let alone the whole cloud *ergo* in the population, is decreasing. Viruses are either in cells [including syncytia [66] or in a network of blood capillaries [and probably lymphatic ones] and in the transcellular space. It is therefore - methodologically very difficult to establish the total amount of viruses in the body of an infected person. Of course, this does not exclude that in the body of an infected person, already seriously ill, viruses hardly multiply or multiply, but there is no net increase, because this is balanced by the processes of enzymatic and immunological destruction of them.

Different aspects of infection ["jumping" infection, the effects of tightening and loosening the regulations-the effect of distance]

Results presented in column 14 [Table 3] show us what could have happened if there was "jumping" model of pandemic ie the infections happened only in some days [or better weeks]. Exactly I showed infection "jumping": ie taking place only after every fourth doubling period n [1,5,9,13...] without a correction on number of deaths. In brackets only:newly infected persons. There are shocking lacks of cases of new infections [not day after day but say during a month!]. But sudden increases [during one week "permission to viral infectiousness"] are even more impressive. Anyway, it is obvious that after some longer time of such a kind of pandemic the results will be horrifying but..... not different from pandemic not jumping.

Look at the data in the same column 10 [Table2-from Hill equation- but in brackets]. They relate to a situation [like in real life] when, after periods of carelessness in relation to a pandemic and loosening of regulations, etc. there is a tightening of regulations and a greater

social distance with alternative changes.

With consecutive successive: a. six doubling periods [30-39 days] in which there was a „free" approach to the pandemic ("loos"). b. the next 6, where there was a tightening of regulations ("tight") [masks, keeping the distance of at least 2 m etc]. c. the next 6 „insulation loosening". d. the next 6 tightening of regulations [at this time: only first three doubling periods ie 17 - 21 days shown].

↑ mean that the number of infected persons has increased evidently due to loosening of regulation [and/or social thinking, so behaviour, on pandemic]. And the effects are very clear both in total number of infected persons and the number of new infections in given "doubling [of total amount of viruses] period". The latter are not *explicite* shown, but still are easily visible.

The comparison of number of successive doubling periods [time] for similar amount of infected/affected people- to be attained-between those calculated from the Hill equation [Table 3, column 11] with those calculated using a simple „arithmetic" model [column 4] is very difficult. Why? Probably the best explanation is pretty obvious although unbelievable at first glance. Just "arithmetic "model -by its nature itself-does not predict limits or thresholds or ceilings; on the contrary Hill equation predicts X_{max}.. So in fact values calculated acording an "arithmetic" model should be referred not to just 1 million but to all the population [or at least its quarter -9,6 million in Poland- ie only one age group eg 65+].

So the calculated with Hill equation data [shown in one column of table 3 but also in figure 4-7] from n between 1 and 15 [of course for longer time either] should be multiplied by 9, 6 [as I remind the total number of 65+ people in Poland is 9, 6 million; about the same is for younger poeople from groups II-IV]. Then of course they would be enormously bigger for mentioned n values and one would not have to select data with n = 15 [17] to be comparable with those for n = 1 [3] in the arithmetic model. Anyhow it looks-at first glance- like the arithmetic model seems to be more convincing for the earlier phase of pandemic [say 4 months].

Overview of more detailed changes during the pandemic in four age groups in Poland

The most important in such calculations as those presented in fig. 3-10 is the proper choice of values X_{max} and K_a [at least justified and probable]. So the list of all those values for all age groups [I-IV] is shown in the table 4. Let me to present now [Figure 3] the results for the first group [> 65] "main" group.

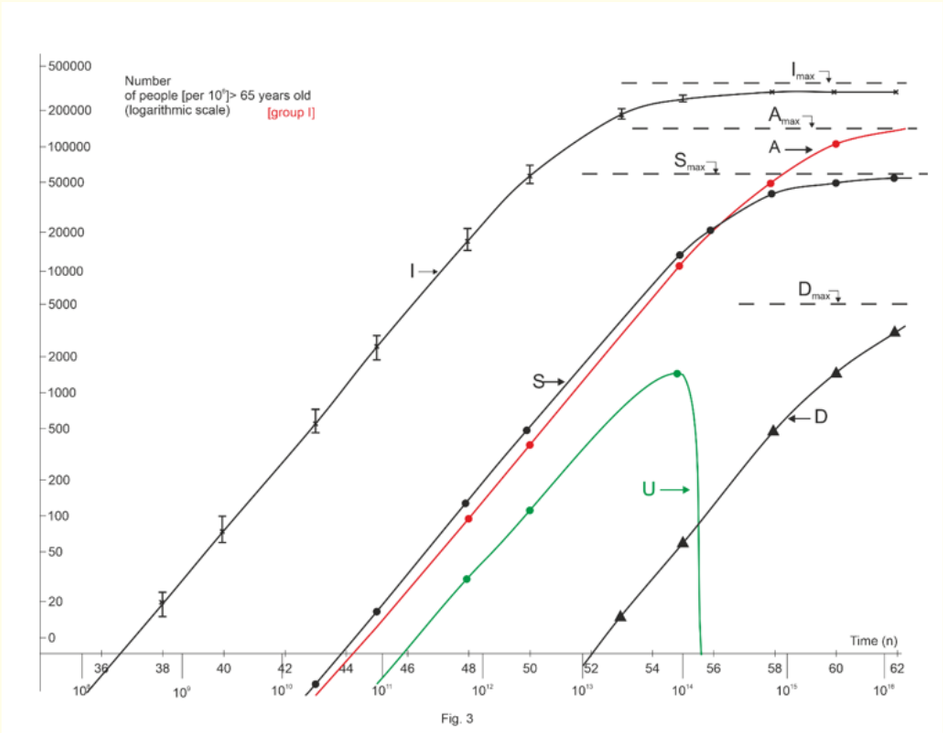


Figure 3: *Pandemic course for people from group I [the oldest: 65+] in Poland-according my assumptions and calculations- per milion people.*

Axis y: The number of infected and affected [eg sick] people -per 1 million people- in logarithmic scale.

Axis x: The time of pandemic as the number of doubling periods [of number of viruses] n, where one doubling period is 10,5 days. The values on axis x begin with n = 32 ie the beginning of "blatant pandemic" [after the end of the block-according my initial conception, which as I explain in text was wrong]; nevertheless the figure shows correctly the course of pandemic [for people with blocking devices [for viruses] in their blood] -see text.The only thing is one should take in mind that real time [on x axis] is by 32 smaller than shown in the picture [e.g. 16 instead 48 and so on].

Figure 3 depicts the pandemic course after about 16th doubling period [i.e. 32th period of duplication from the very beginning of pandemic for I group ie +65- assuming my earlier concepts-see later text]. The curves are in fact the straight lines as it has to be with exponential growth in logarithmic scale, but they flatten after about exceeding [by the number of viruses in the whole cloud] the value for the half-maximal effect K_a thus coming up asymptotically to the ceiling that is the maximal amounts of infected persons [per 1 million of people but in fact per 900000 people evidently living in the cloud- not far each other].

There is only one curve with evidently different shape: straight line but later like parabola with the sharp maximum and after this maximum sharply going down [to values less than zero]. It shows the number of persons still sick as the difference: U=S-A. Let me explain. S mean sick, A mean those producing specific antibodies, [most probably IgG anti SARSCoV-2] [In time n=39,5 [ie. after 22,5 doubling periods from the beginning of evidently overt pandemic [about eight months] -ie after long lasting asymptomatic phase the value- for U attains zero because the number of persons producing specific antibodies is equal to the number of sick persons [calculated]. Taking in mind Gaussian type of distribution of people by the number of viruses in, so the severity of the disease, we should think that real equalization of number of indeed sick people and those producing enough specific antibodies to eliminate viruses would be attained much later [even two months].

The two other curves with maximum would be for "still infected" SI=I-A and for asymptomatic infected persons AS = I–S. If we substract dead people from SI, thus we obtain: I-A-D =AC ie so called active cases [compare the summarizing table 8 in II part].

And once again I remind that I can't know for certain if they are really recovered. Simply, the number of people producing a lot of antibodies exceeded that for sick people and at longer time the number of those producing antibodies is still growing"sharply" and number of really sick diminishes quite quickly up to the negligible values. But number of sick S calculated according to Hill equation still grow but respective curve is flattened and in any case the increase the number of sick [calculated in such a way] are by far smaller that increases of calculated number those producing antibodies. Here it is regrettable that the curves [especially S and A at that time] are on a logarithmic scale, because on a linear scale these differences would be much more visible.

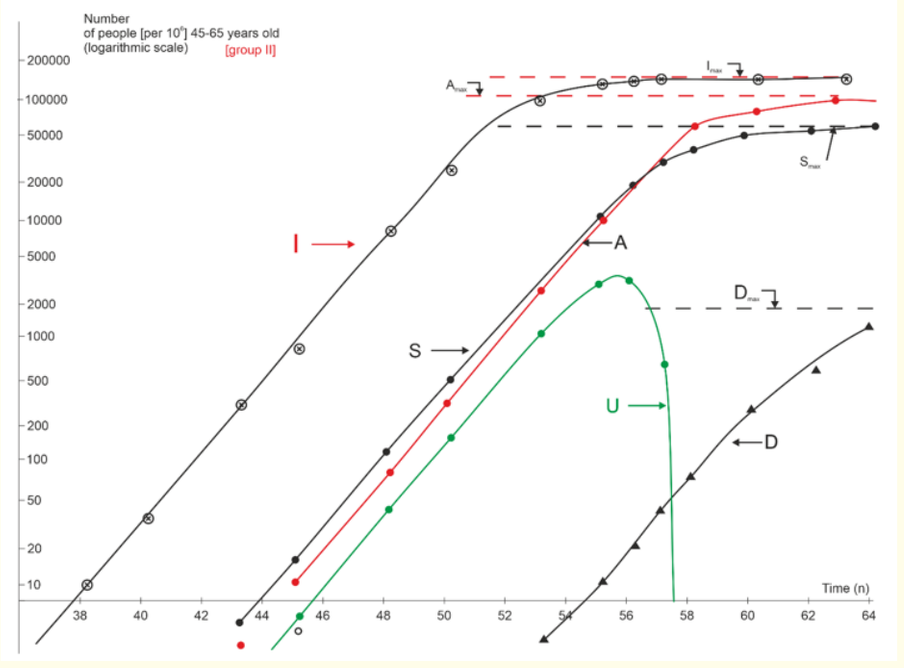


Figure 4: *Pandemic course for people from group II [45 - 65 years old] in Poland-according my assumptions and calculations -per milion people.*
The explanations the same as below the figure 3 [but beginning at about n = 33, compare explanations ti figure 3].

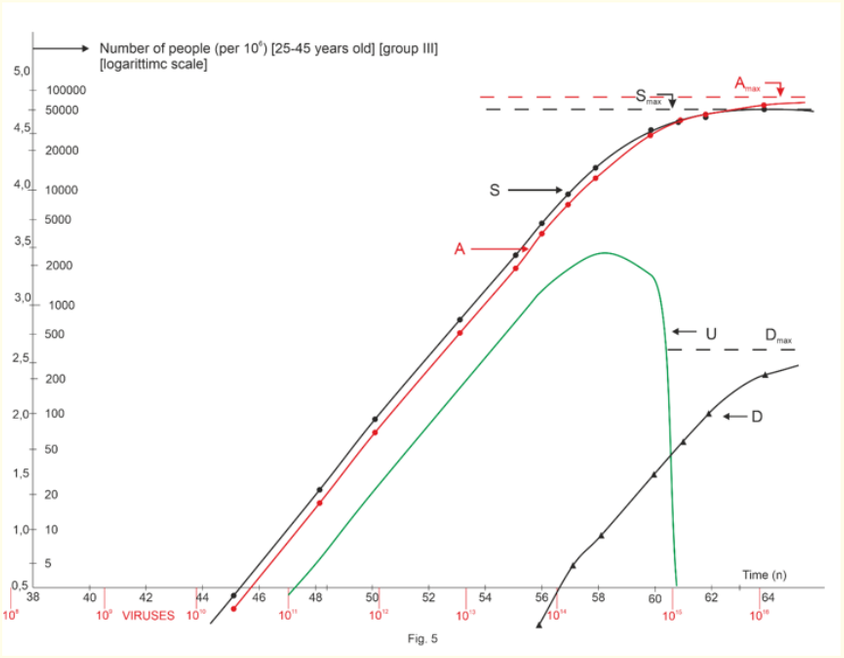


Figure 5: *Pandemic course for people from group III [25 - 45 years old] in Poland-according my assumptions and calculations -per milion people.*
The explanations the same as below the figure 3 and 4.

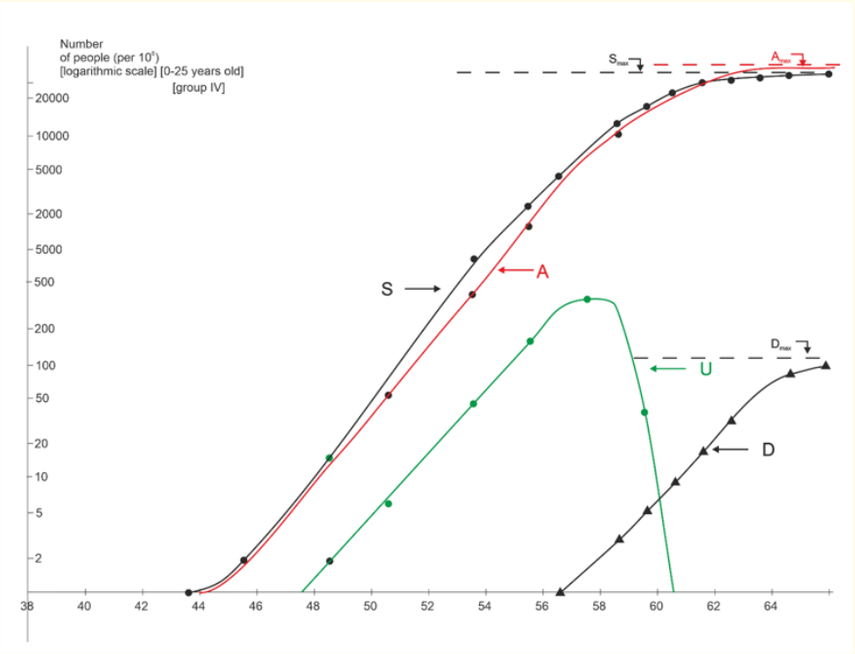


Figure 6: *Pandemic course for people from group IV [0-25 years old] in Poland-according my assumptions and calculations -per milion people.*
The explanations the same as below the figure 3 and 4.

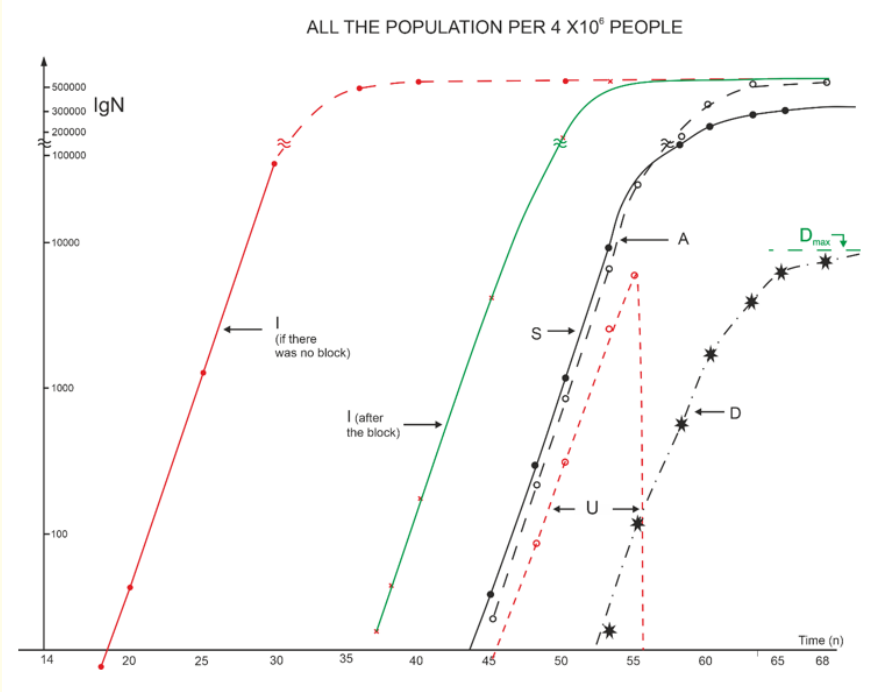


Figure 7: *Pandemic course for whole population in Poland-according my assumptions and calculations -being the sum of values shown in figure 3- [on each per milion people] -so to gether figure 7 shows us the values per four milion of people [of total population ie from all age groups. The values shown with the curves on this figure represent the sum of values shown in figure 3- [on each per milion people] -so to gether figure 7 shows us the values per four milion of people [of total population ie from all age groups]. Notice, somehow the numbers of all age groups mentioned turned out to be approximately the same [each of 9.6 million people].*

I have to remind that curves shown at figure 3 present data calculated applying the kinetic constants shown in table 4-for people 65+ [I group] -per 1 million- assuming that there is after the block. The same was done for remaining three age groups [II, III and the youngest IV] and results are shown respectively on the figure 4-6. Figure 7 just shows us results of summing ie concerns 4 million of people of different age.

Of course as I explained earlier the block concerns every person. But it happened that all the calculations for group I [65+] presented in figure 3 fitted to the newer calculations [Table 6, part II] assuming the block is going on for every person until all blocking sites were saturated. Thus of course both figures 3-7 and summarizing table 7 concern those people who contain in their blood an efficient system of blocking viruses. Simply even then, I did not think that there could be people without such a block or with a relatively very low level of it. But the further analysis convinced me that, however, such people do exist [types A and C-see below and in part III] -which results in fact... further „pandemic waves" - in this case we are talking about people of types A and C.

Of course the number of death cases for younger and especially the youngest groups are much more seldom. But still there is delay so the abundance of death cases would grow long after the growth of amount of sick let alone infected practically arrested even for the youngest group [0-25 years old].

Conclusion

- Only about 3% of infected people are infectious
- About 50 % of viruses present in all the population exists in.... a body of one person ie "person zero".
- About 20% of viruses are located in the bodies of non-infectious people, which consist of 80 - 90% of infected people.
- Hill equation describes the pandemic in a deep analogy with kinetics of non allosteric enzymes [with viruses as substrate/s and functional receptor/s as enzyme and infected people as ...product/s]
- There looks like time of duplication of viruses' number is about 10,5 days.
- The size of the basic kinetic coefficients of the Hill equation [X max and Ka] is discussed and proposed - not only for infection but for disease, antibody production and death taking place.
- It seems that changes in the infection model, sudden or gradual, regardless of their causes, e.g. caused by periodic tightening of the provisions on the „sanitary regime", only delay the course of the pandemic.

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Volume 16 Issue 7 July 2021