A GUIDE THROUGH THE COVID-19 JUNGLE

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ПУТЕВОДИТЕЛЬ ПО ДЖУНГЛЯМ КОВИД-19

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EDITORIAL

This is a position paper, created for and with members of the International Academy of Science-Health & Ecology and partners*. The current situation, which is also unique due to the worldwide social action, challenges us to elaborate such a paper to form an opinion and to make it available to others. We are — to put it simply — alienated by two seemingly irreconcilable groups, each of which, in its own way, sees the situation in a highly simplified way: Those who deny COVID-19 or belittle it despite the horrible images, and those who do not want to take note of the antiseptic and even against better information. But every life-experienced mother, every sweaty construction worker and every smart athlete knows that you can protect yourself and your child from the threat of infection by quickly putting on appropriate clothing: without affecting the contact with others or the viral load in the nose and without replacing a vaccination! Both conflicting positions lead to the same result in one point: the «Semmelweis phenomenon» is repeated: that obvious knowledge is not applied for extra-scientific reasons: In the 19th century, because people did not want to accept its effectiveness against puerperal fibers, with the consequence that two decades longer mothers had to die unnecessarily. In the 21st century because the historically known possibilities and limits of non-specific defenses are being suppressed. This time, millions are affected.

It should also be borne in mind that governments can only set their measures on the basis of the legal powers vested in them. This almost inevitably leads to an imbalance (bias) in the selection and differentiation of measures toward the options that can be prescribed by means of laws and regulations. This has consequences at different levels:

a. For example, the impression is given that the epidemic was only the late consequence of inadequate legal bases, for example, in space use and food production, so that new pathogens such as SARS-CoV-2 were able to jump to humans. Therefore, the Intergovernmental Platform on Biodiversity and Ecosystem Services (IPBES, a global advisory body to the UN), rightly calls for appropriate measures aimed at «escaping the era of pandemics» [1]: important, but too little.

b. The bias addressed also leads to a focus on the expectation of science on how far it can support policy arguments as a supplier of knowledge and techniques: Important, but too little! Rightly, the presidents of the National Academies of the G20 countries have recognized that for this to happen, corresponding preconditions must be fulfilled by politics, e.g. with regard to the equipment of research and development, lack of economic foresight, etc., but without going into fundamental aspects of SARS-CoV-2 and COVID-19 [2]. Important, but inappropriate limitation of actual tasks!

c. Understandably, the actions of the UN and WHO are also guided by the capabilities of their members, i.e., states. Therefore, the criticism of the previous procedure is only directed at these possibilities: The «independent, comprehensive and impartial review of international health measures against the pandemic» initiated by the World Health Assembly is now available as the report «Making COVID-19 the last Pandemic» [3]. It contains several calls, particularly regarding the elimination of inequity, (e.g., vaccine inequity), the improvement of the international warning system, and the legally binding International Health

* Prepared by the President and the Secretary General. An essential insight in the creation was that each individual should be able to contribute his or her position without running the risk of having to give it up. The merit of an argument should be seen independently of the individual and their particular circumstances.

Regulations (IHR). This should allow for better coordinated determination of actions at the global and national levels. Also fundamentally important, but essential possibilities remain unconsidered! The report is criticized (only) that the local, national and cultural conditions are to be considered strengthened [4].

d. But also the value-free scientific journals like Nature, Lancet, or Science, which are committed to scientific progress, seem to see the decisive key in the management of this pandemic in the optimization of the adopted prescribable social measures [5–7]. Also important, but too focused on «normal», traditional science.

e. The negligence of considering systems thinking in attending complex social and health problem such as COVID-19. COVID-19 effected all the human and non-human systems worldwide (illustrated by its consequences on health system, legal system, biodiversity and eco-system, transport system, education system, employment system, industry system, defense system, economic system, etc.) has vividly brought systems interconnectedness to the forefront of human thinking. The human, social and economic costs of COVID-19 pandemic are enormous [8]. Systems thinking is an indispensable tool for understanding the root cause of complex problems.

For legally binding can be established only commandments and prohibitions for the behavior of citizens. This approach would be sufficient if COVID-19 is caused by behavior. But one cannot prescribe from which degree of susceptibility a healthy person has to do this and to leave that. Nevertheless, susceptibility can be influenced. Therefore, this approach falls short. COVID-19 is an infectious disease and therefore a biological process between pathogens and cells. But the behavior of viruses and cells cannot be regulated by regulations. Where everywhere and how one can effectively intervene in these processes and which inevitabilities are unavoidable in the process only becomes comprehensible by obtaining clarity about all partial steps of the cascade, regardless of whether they can be regulated by a legal basis or not: The cascade begins with the fact that the virus could jump to humans and put concrete persons in danger of infection. It ends with the fact that one person does not even fall ill, but the other suffers a torture-like death. That all the important arguments listed in the documents quoted above have their importance is indisputable. But the implications arising from the nature of the processes and their dynamics deserve at least to be considered.

For in none of the papers referred to above, for example, is the possibility even raised, the assumption would have to be questioned, that the «human factor» in the infectious process is regarded as constant and influenced only by vaccination or recovery thanks to specific immunity. As said, any person experienced in life knows that this is false and an assumption contrary to nature. And Kermack & McKendrick, the fathers of models for predicting the effect of delaying contact between infectious and infected people, have made it clear that «a small increase in infectiousness can cause a very pronounced epidemic in a population that would otherwise be free of epidemics». They acknowledge that changes in susceptibility are to be expected in reality and therefore «no conclusions should be drawn about the actual values of the various constants» [9].

The skewing of the weighting of measures in the direction of socially influenceable, even prescriptive behavior of the citizens under renunciation of possibilities with consideration of the nature of an infection in our society lets expect that influencing variables are overlooked, which would become obvious with a purposeful argument with the appropriate processes [10].

The aim of this position paper is to make a contribution to opening up such options.

In the specific case of COVID-19, it is also important to note that the majority of individuals who come into contact with SARS-CoV-2 do not become ill. This should not lead to the conclusion that COVID-19 is insignificant. After all, polio is not harmless just because less than 1% of those who first come into contact with these viruses become ill. The potentially horrific consequences of COVID-19 alone justify its importance. Therefore, Public Health (PH) measures must take into account that the presence of SARS-CoV-2 is the necessary, but not the sufficient explanation for the individual event and in sum so socially significant: several components must obviously coincide for this misfortune to occur: as Leo Tolstoy already says: «All happy families resemble each other, every unhappy family is unhappy in its own way!» It is generalizable that every single person, who died of COVID-19 suffered this fate due to their individual unfortunate constellations. Any future-oriented PH strategy for COVID-19 must also take this fact into account [11]. The principles of a person's individuality as a bio-psycho-socio-cultural being and his interactions with and expectations from his environments must be considered. For the anticipatory social strategies, this means that different precautionary measures have to be planned for, as, for example, modern concepts of risk management demand (e.g., Reason).

Also complicating COVID is the fact that the pathogen is unknown. One can, therefore, only draw on prior experience to a very limited extent. We are therefore in a phase in which only «eminence-based medicine» is possible for essential questions, which must be gradually and ethically responsibly converted into «evidence-based medicine» and ultimately into a causally based procedure, even if not everyone sees it that way [12]. Semmelweis can also be seen as a pioneer in this respect: He founded «evidence-based medicine» in 1848 with the empirical testing of his «eminence-based» idea of the efficacy of chlorine as an antiseptic against an unknown causative agent in ani-

mal experiments. Koch and Pasteur provided causal evidence that pathogens were these unknown causative agents about 20 years later. Our current knowledge of SARS-CoV-2 and COVID has not reached the level of empirical proof of a Semmelweis or the causality of Koch and Pasteur in important areas. Therefore, there should be a high degree of willingness to repeatedly put the overall strategy to the test and, if necessary, even to make profound extensions and modifications. But there is little evidence of this.

From this diversity arise considerable formal requirements to a position paper: Even the highly qualified representatives of the individual disciplines are laymen in most of the other disciplines, but they are indispensable for the understanding. Nevertheless, many assume that the interlocutor, as an educated person, has mastered at least the basic knowledge and terminology from their fields. What a momentous mistake! Nobody is able to do this, even if he does not want to admit it. But nobody should feel caught as a layman, if in this position paper — «only» because of the needs of the life partners — terminologies and connections from all fields of expertise are presented in a simplified way. Rarely is it so essential to strive for a constructive error culture. Now it is still possible to learn before the mistakes are implemented or wrong decisions are repeated. Especially when dealing with momentous risks, this has proven its worth [13].

This position paper can and will only provide arguments so that everyone can put their own limited conclusions to the test. This is less about factual knowledge. One also does not need to know the techniques of the different disciplines that are practically relevant especially for dealing with COVID-19 and SARS-CoV-2. In this regard, one can rely on the experts. It is more a matter of understanding the process flows and interconnections. In doing so, you have to venture into the world of thinking of the most diverse and mostly foreign disciplines. Whether you like it

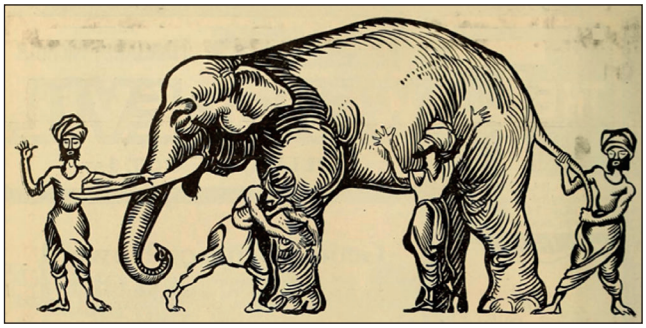

Fig. 1. Four blind men examine an elephant. Lewis J. Selznick, Wikipedia common

or not, you have to get an idea of whether the position of a decision-maker or a statement by an expert — no matter how recognized he may be in his field — is meaningful overall for the complex issue at hand. Can one be sure that this person has appropriately brought his or her specialized knowledge to bear on the complex issue at hand, or that he or she is only selectively representing a position from one point of view? In order to be able to assess this, one must be prepared to form a complex opinion oneself. To do this, you need — of course, open to discussion — positions on the various partial aspects. One should not expect more and only demand that others are also prepared to state why they take this or that position. Such controversial arguments have been considered in the position paper: Contributed by members and friends from the most diverse scientific disciplines, from art and culture. In particular, however, also from their life partners who want to live together with them in everyday life, although they concentrate most of the time on their own — foreign — world of thoughts.

That is why this position paper has to be so multilayered and sometimes — but only seemingly — give the impression of being away from the core problem.

РЕДАКЦИОННОЕ ВВЕДЕНИЕ

Настоящий документ излагает консолидированную позицию членов Международной академии наук (Здоровье и Экология) и их партнеров. Текущая ситуация, которая является уникальной из-за всемирного социального действия, побудила нас разработать такой документ, чтобы сформировать общее научное мнение и сделать его доступным для других: Нам, проще говоря, противостоят две, казалось бы, непримиримые группы, каждая из которых по-своему видит ситуацию в сильно упрощенном виде: те, кто отрицает COVID-19 или принижает его значимость, несмотря на ужасные последствия пандемии, и те, кто не хочет принимать к сведению возможности антисептики несмотря на факты. Но каждая опытная мать, каждый строитель и каждый спортсмен знает, что можно защитить себя и своего ребенка от угрозы инфекции, быстро надев соответствующую одежду (безусловно, не отрицая значимость социального дистанцирования и вакцинации)! Обе противоречивые позиции приводят к одному результату: повторяется «феномен Земмельвейса»: очевидные знания не применяются по вненаучным причинам: в 19 веке потому, что люди не хотели признавать эффективность вакцины против послеродовых фибром, в результате чего матери умирали преждевременно на 20 лет дольшеж в 21 веке — потому что подавляются/игнорируются исторически известные возможности неспецифической защиты. На этот раз страдаютмиллионы.

Следует также иметь в виду, что правительства могут устанавливать свои меры только на основе предоставленных им юридических полномочий. Это почти неизбежно приводит к дисбалансу в выборе и дифференциации мер в пользу тех, которые могут быть предписаны с помощью законов и постановлений. Это имеет последствия на разных уровнях:

a. Например, создается впечатление, что эпидемия была лишь поздним следствием неадекватной правовой базы, например, в области использования космоса и производства продуктов питания, так что новые патогены, такие как SARS-CoV-2, смогли «мигрировать» к людям. Поэтому Межправительственная платформа по биоразнообразию и экосистемным услугам (IPBES, глобальный консультативный орган при ООН) справедливо призывает к принятию соответствующих мер, направленных на «выход из эры пандемий» [1], что, безусловно, важно, но недостаточно.

b. Рассматриваемая предвзятость также приводит к тому, что в центре внимания оказываются ожидания от научных разработок в качестве аргументов для политических решений: также важно, но слишком мало! Справедливо президенты национальных академий стран G20 признали, что необходимы скоординированные политические предпосылки, например, в отношении оснащения исследований и разработок, отсутствия экономического предвидения и т.д., даже без углубления в фундаментальные аспекты SARS-CoV-2 и COVID-19 [2]. Важное, но неуместное ограничение актуальных задач!

c. Понятно, что действия ООН и ВОЗ также определяются возможностями их членов, т. е. государств. Поэтому критика предыдущей процедуры направлена только на эти возможности: независимый, всеобъемлющий и беспристрастный обзор международных мер здравоохранения против пандемии», инициированный Всемирной ассамблеей здравоохранения, теперь доступен в виде доклада «Сделать COVID-19 последней пандемией» [3]. В нем содержится несколько призывов, особенно в отношении устранения неравенства (например, неравенства в отношении вакцин), улучшения международной системы оповещения и юридически обязательных Международных медико-санитарных правил (ММСП). Это должно обеспечить лучшую координацию действий на глобальном и национальном уровнях [4]. Однако в докладе критикуется только то, что местные, национальные и культурные условия недостаточно координированы.

d. Но и, казалось бы, свободные от политических аспектов научные журналы, такие как Nature, Lancet или Science, которые привержены научному прогрессу, похоже, видят ключ в управлении пандемией в оптимизации принятых предписанных социальных мер [5–7]. Это тоже важно, но слишком ограничено традиционными научными подходами.

e. Пренебрежение системным мышлением при решении сложной социальной и медицинской проблемы COVID-19. Влияние COVID-19 на все человеческие и «нечеловеческие» системы во всем мире (на примере последствий для системы здравоохранения, правовой системы, биоразнообразия и экосистем, транспорта, образования, трудовой занятости, промышленности, обороны, экономики в целом и т.д.) наглядно продемонстрировало взаимосвязь систем на переднем крае человеческого мышления. Личностные, социальные и экономические издержки пандемии COVID-19 огромны [8]. Системное мышление является незаменимым инструментом для понимания первопричины этих сложных взаимовлияний.

Юридически облигатные запреты и регуляторы могли бы быть эффективными в борьбе с COVID-19, но не поведение человека является причиной пандемии. Невозможно предписать регламенты поведения человека в зависимости от его индивидуальной восприимчивости к вирусу. Тем не менее, на восприимчивость можно влиять. COVID-19 — инфекционное заболевание, а значит, биологический процесс между патогенами и клетками /организмом. Но поведение вирусов и клеток нельзя регулировать нормативными актами. Как эффективно вмешиваться в эти процессы — становится понятным только при получении полной картины всего патогенетического каскада. Он начинается с того, что вирус может подвергнуть опасности заражения конкретных людей, а завершается тем, что один человек даже не заболевает, а другой умирает мучительной смертью.

То, что все важные аргументы, перечисленные в приведенных выше документах, имеют важное значе-

ние, бесспорно. Но следствия, вытекающие из природы пандемических процессов и их динамики, заслуживают, по крайней мере, более внимательного рассмотрения.

Ведь ни в одном из упомянутых выше документов, например, даже не дискутируется то, что «человеческий фактор» в инфекционном процессе считается постоянным и на него влияет только вакцинация или выздоровление благодаря специфическому иммунитету. Однако это не совсем так. А В. Кермак и А. МакКендрик, отцы модели прогнозирования эффекта отсрочки контакта между заразными и зараженными людьми, ясно дали понять, что «небольшое увеличение инфекционности может вызвать очень выраженную эпидемию в популяции, которая в противном случае была бы свободна от эпидемий» [9]. Они признают, что в реальности следует ожидать изменений восприимчивости, и поэтому «не следует делать выводы о фактических значениях различных констант».

Крен в сторону социальных и поведенческих регламентаций при отказе от возможностей с учетом природы инфекции демонстрирует, что упускаются из виду важные влияющие переменные, которые стали бы очевидными при более целенаправленной аргументации [10].

Цель настоящего документа — внести свой вклад в открытие таких возможностей.

В конкретном случае с COVID-19 важно отметить, что большинство людей, контактирующих с SARS-CoV-2, не заболевают. Это не должно приводить к выводу о несущественности проблемы COVID-19. В конце концов, полиомиелит не является безобидным только потому, что менее 1% тех, кто впервые вступает в контакт с этими вирусами, заболевают. Потенциально ужасающие последствия COVID-19 сами по себе оправдывают все принимаемые меры. Таким образом, меры здравоохранения должны учитывать, что наличие SARS-CoV-2 является необходимым, но не достаточным объяснением отдельного события и в сумме столь социально значимого: для того, чтобы произошло это несчастье, очевидно, должны совпасть несколько компонентов; как сказал уже Лев Толстой: «Все счастливые семьи похожи друг на друга, каждая несчастливая семья несчастлива по-своему!»

Можно констатировать, что каждый человек, умерший от COVID-19, пострадал от этой участи в силу сочетания своих индивидуальных «неудачных» особенностей. Любая ориентированная на будущее стратегия здравоохранения для COVID-19 должна учитывать этот факт [11]. Необходимо учитывать принципы индивидуальности человека как био-психо-социо-культурного существа и его взаимодействия с окружающей средой. Для опережающих социальных стратегий это означает, что необходимо планировать различные превентивные меры, например, на сонове современных концепций управления рисками.

Также осложняет ситуацию с COVID-19 тот факт, что возбудитель недостаточно изучен и опираться на предыдущий опыт можно лишь в ограниченной степени. Таким образом, мы находимся на этапе, когда для решения основных вопросов возможна только «авторитарная медицина», которая должна постепенно и этически ответственно преобразовываться в «доказательную медицину» и в конечном итоге в процедуру, основанную на причинно-следственных связях. В этом отношении И.Земмельвейс может считаться пионером: он основал «доказательную медицину» в 1848 году, эмпирически проверив в опытах на животных свою «основанную на авторитете» идею об эффективности хлора как антисептика против неизвестного возбудителя. Кох и Пастер представили причинные доказательства того, что патогены являются этими неизвестными возбудителями, лишь 20 лет спустя. Наши современные знания о SARS-CoV-2 и COVID-19 не достигли уровня эмпирического доказательства Земмельвейса или причинности Коха и Пастера в важных областях. Поэтому должна быть высокая степень готовности неоднократно подвергать общую стратегию борьбы с пандемией проверкам и, если необходимо, даже вносить существенные модификации.

Из этого разнообразия вытекают значительные формальные требования к представленному нами документу: даже высококвалифицированные представители отдельных дисциплин являются дилетантами в других областях знаний, но они важна для выработки общих подходов. Тем не менее, многие полагают, что собеседник, как образованный человек, овладел хотя бы базовыми знаниями и терминологией из их научных областей. Как правило, это не так. Однако никто не должен почувствовать себя неспециалистом, если в настоящем документе — «только» из-за потребностей партнеров по жизни — терминология и связи различных областей знаний представлены в упрощенном виде.

Представленный Вашему вниманию текст с изложением позиции авторов содержит только аргументы, с помошью которых каждый может проверить на практике свои собственные заключения. Речь идет не столько о знании фактов. Нет необходимости знать методы различных дисциплин, которые имеют практическое значение, особенно для борьбы с COVID-19 и SARS-CoV-2. В этом отношении можно положиться на мнения экспертов. Это скорее вопрос понимания «технологических» решений и взаимосвязей. При этом Вам придется окунуться в мир мышления с использованием мультидисциплинарногых подходов. Хотите Вы этого или нет, но вы должны понять, является ли позиция лица, принимающего решение, или заявление эксперта — каким бы признанным в своей области он ни был — значимым в целом для рассматриваемого сложного вопроса. Можно ли быть уверенным, что этот человек должным образом привнес свои специальные знания в рассматриваемую проблему, или он лишь выборочно представляет позицию с одной, специальной, точки зрения? Чтобы иметь возможность оценить это, нужно быть готовым самому сформировать собственное мнение.

Вот почему этот программный документ имеет такую «многослойную» структуру и иногда, но только на первый взгляд, создает впечатление, что он текст уходит от основной обсуждаемой проблемы.

INTRODUCTION

Almost everyone's daily life has changed since March 2020 as a result of SARS-CoV-2 and COVID-19. People have had to restructure their priorities. More and more people feel threatened not only because of a possible infection. They fear or have already gone through, for example, a collapse of the basis for their individual economic existence, their psychosocial integrity and integration. They are affected in a different way than the politicians who have to lead the community through the pandemic and its also unexpected consequences. Both groups, however, have choices to make: The owner of a restaurant or the minister of health or the single mother in the home office and home schooling with three children in a 60 square meter apartment. All need sufficient information: Information that allows for coherent reasoning to decide what to do or not to do, and how to deal with the unavoidable. Each individual needs such information to accept constraints, especially under the pressure of limited resources and options. Otherwise, one feels unlawfully restricted in self-determination (reactance) [14]. Meanwhile, negative health effects of deficiencies as well as the positive effects that can be achieved with successful coping even under extreme conditions have also been scientifically proven [15, 16]. Who decides needs the cooperation of the affected persons. However, both must be able to integrate the complex interactions including their uncertainty aspects into a comprehensive view. However, uncertainty is now often part of daily life with and without the disease itself. This also easily leads to unmeasured fears and panic because risks are often classified irrationally [17].

Whether the individual or the official decision maker, both need support to understand the options for addressing individual challenges. Official decision makers can convene experts into task forces; the ordinary person cannot. But it is the individual who becomes ill. His risk may be reduced if options, not just limitations, are also offered. Both can be more adequately managed by those who can better assess the possible influences and interactions. This would suggest more hope.

The purpose of this paper is to provide an aid to self-help. It draws in particular on possibilities in applied hygiene, social medicine and public health, and physiology. These subjects often collaborate with other disciplines. This, too, is incorporated into the texts. This interdisciplinary approach, which is also open to non-experts, is atypical for scientific articles. Usually, these offer new results for a scientific discussion within a subject discipline. The present text offers selected information for interactions. At the same time, much is uncertain, so it can only be estimated by applying the laws of reasoning and the experiences of daily life. But this situation is typical for daily life: In everyday life, too, one has to make decisions, and one has to do so with a limited level of knowledge. Here, the precautionary principle is given special importance. As an optimist, it is better to assume that, given our state of knowledge, it is wiser to count on the less favorable. Then one will probably go into the future prepared. One will gladly take note of improvements in the state of knowledge! The situation also requires the readiness to imagine new kinds of processes that have not yet been discussed. Possibly, however, they will become necessary to make phenomena understandable, which are in need of explanation because they point to otherwise overlooked threats. Therefore, it is necessary to deviate from the usual approach in science on a case-by-case basis: Conjectures lead to experiments in normal situations. But there is no time for that in a new kind of epidemic. One has to act, because non-action is also relevant to health and therefore has to be justified in the same way as action. Thus, there is often nothing left to do but to evaluate the available experience and the limited available knowledge, to make assumptions and to implement them. But the reader must be clear: Such speculations are indispensable only in order to be able to do justice to the precautionary principle. It is often to be hoped that they will later turn out to be unnecessary.

The current situation therefore requires two approaches: The first is the pragmatically short one: Where do we stand? Where can we go from here? Does it fit at all? An offer is made for this in Part 1. But then, when you realize that you have come to a conclusion that differs from the one that is being advocated all around, you need further foundations. These are offered in Part 2. Part 2 is also about working out the question of individual concern and showing what relevance the individual influencing factors can have for oneself and what measures one can take personally. This question is relevant for everyone: For the individual who can only make decisions for himself and his family, as an expert or as a political decision-maker.

However, one thing should already be anticipated at this point because time is pressing: In the current situation, it is recommended that two measures be tested for their usefulness. These should be used IN ADDITION to the currently planned measures:

1) The use of a well-tolerated antiviral active antiseptic for regular inhalation of those admitted to normal hospital wards with COVID-19.
2) The use of a well-tolerated antiviral active antiseptic as a nasal spray for those individuals who are scheduled to have a negative antigen test as a requirement for selected activities.

This is expected to reduce personal risk to fall ill, the risk of infecting others, and the possibility of mutants forming. Individuals with a negative test and an acutely used antiseptic nasal spray should not pose a higher risk than vaccinated and recovered individuals. But there is absolutely no such thing as zero risk.

THE FRAMEWORK: MULTI-CAUSALITY-MULTI-INTENTIONALITY-TURNAROUND?

I. MULTICAUSALITY: understanding necessary sufficient causes, implementing locally and internationally in a legally compliant manner.

In 2020, a novel virus hit the world. Its presence and successful contact with a person who has reproduced this

virus and passed it on to others is the so-called «condition sine qua non» i.e. the indispensable condition for the infectious disease. This is the so-called «sufficient reason» for every single case of infection, illness and death from COVID-19. However, the successful contamination of cells of a person is not sufficient for the infection to occur, the infection is not sufficient for hospitalization and certainly not for death. So there are other — necessary — reasons in this multi-causal chain of causes. However, this does not change the fact that neither old age, overweight, poverty, nor heavy physical or mental stress, lack of trace substances, nor lack of vaccines or lack of oxygen supply caused death from COVID-19. ALWAYS the causative agent is the sufficient cause. However, it is indisputable that death would not have occurred if the necessary reasons had not been present: if the body had been supplied with sufficient oxygen in time, the person would not have been 85 but 12 years old and would have been able to ward off the penetration of the virus into the organism thanks to non-specific defenses. The significance of the necessary influencing variables can be recorded with meaningful epidemiological studies as differences in the RISK that a person has. But risk is not causality. Conditio sine qua non — the REASONABLE reason is in each individual case the INFECT, i.e. the biological process, how well it can be strengthened and weakened by a multiplicity of influencing variables. How significant these possibilities of influence are, especially in the case of COVID-19, is shown by the extreme difference in the risk of death, which persons have only as a result of their age compared to identical exposure to the virus: Ioannidis reports a difference of 1: 10,000 between the young and the very old threatened by COVID-19 [18]. He also reports that epidemiologists typically work with risk differences of 1: 1.3 or so.

If one wants to understand COVID-19 better, one must first deal with the processes that start from the — in itself preventable — transfer of novel viruses from animals to humans, via the spread in the environment to contact with persons, the contact between persons, so that viruses enter the respiratory tract of the infected, penetrate there at best the outer boundary of the body, then lead at best to illness with or without symptoms, so that hospitalization becomes necessary, which can lead to death in the absence of sufficient supply, especially with oxygen and specific therapy. Since COVID-19 has appeared for the first time, in many areas one starts from «assumption» and not from «understanding».

Nevertheless, targeted action and inaction must be taken currently from presumption and understanding.

The individual can take these actions herself or himself. Often she or he is dependent on community and social structures (pharmacies that can also deliver the remedies) being in place or being created. Since the individual falls ill and not the society, the measure must ALWAYS arrive at the individual. This also applies to the many measures and regulations that can only be initiated by the «authorities».

This presupposes in constitutional states also legal possibilities, in order to be able to react in the case of epidemics on short way to the fact that the standard way for permission of e.g. medicine products or medicines presupposes a depth of knowledge, which cannot be present at present: No one can know all the characteristics of a pathogen that has appeared for the first time. The legislator has therefore established the right and the duty of the decision-maker to be able to prescribe the best current course of action in such cases beyond the state of knowledge by applying the laws of reasoning and the experiences of daily life, also by means of emergency ordinances. Proportionality must be taken into account in weighing all direct and indirect health consequences, as well as fundamental rights and economic consequences.

Pandemics that occur worldwide will not be overcome until they are overcome worldwide. They therefore require the appropriate international cooperation. The Independent Panel called for by the World Health Council concludes that the pandemic could have been prevented with changes in the international legal framework. The IPBES rightly points out that fundamental changes in the relationship between ecology (biodiversity), food habits and the close relationship between animals and humans, which obviously must be made legally, would be a prerequisite for stopping the era of pandemics. For this, however, a balanced integration of influencing factors would be necessary, which so far from a sectoral point of view by very many, methodically often seemingly incompatible scientific disciplines prerequisite. However, the S20, the body of presidents of the National Academies of Sciences of the G20 countries, does not address this issue: they were also asked only for advice on economics.

II. MULTI-INTENTIONALITY: as already evolutionarily limited and self-referential with novel possibilities.

This brings up another underestimated aspect: MULTIINTENTIONALITY, which must be considered in all actions and inactions. Decisions are not made with a two-value logic. Weighing up desires and fears, which by their nature do not seem to be connectable, such as ethics, hunger for power, the pursuit of profit, and the laws of nature, determine the everyday life of the individual — whether any common person, corporate boss, or health minister. Th. Kuhn has already proven this for research. It is a fact that the gap between rich and poor has widened even in Western countries during the pandemic and that the wealth of the wealthy has increased in a way that has not been the case since the boom after World War II. According to the NZZ, there was a gold-rush atmosphere at Zurich airport on 16.7.2021: 380 francs for an express PCR test! Actions and blockades of action in the context of COVID-19 must therefore also be viewed from this perspective. Politics seems to be closely intertwined: for example, President Trump would probably have won re-election without COVID-19. Currently, every election is in tension with the measures against COVID and the current epidemic events. Is COVID-19 the occasion for a turning point?

III. The methodological interlinkage: approaching the problem from multiple dimensions applying systems-thinking (MULTI-DIMENSIONALITY).

The third aspect that is not thought about generally is MULTI-DIMENSIONALITY. Multidimensionality and systems thinking are closely connected. Multidimensionality refers to various components of a system and the dynamic behavior of these components at different scales. It highlights complexity of the problem and demands analytic skills to recognize the interconnections between parts of the system (applying basic systems-thinking). This also means interdisciplinary, multidisciplinary, and transdisciplinary research is required to improve health and related cross-disciplinary research problems [19, 20]. «Every existent is either a system or part of a system» [21]. This essential means that every disciplinary individual must be a systems-thinker, having the skills of identify influences on other parts of the system when one part of the system is affected. Multidimensionality includes multilevel perspective (macro-, meso-, and micro- levels) of social-technical system and multiple implications of driving forces (system-agents), decision-making (governing rules that force system-agents to take actions), and evaluation (resulting performance of interconnected factors) [22] in the multifaceted consequences across the community [23] to capture, analyze and adopt the cultural narrative of the people's perspective of the given problem (for example, pandemic) [24].

The pandemic has highlighted many dimensions that are fragmented and disconnected, such as fragility of contemporary economics [25], dependency on industrialized urban infrastructures [26], failing governance institutions [27], vulnerability to climate disasters [28], dislocation from the natural world [29], societal inequalities, and the loss of cultural memory [30]. This raises questions on how to integrate these dimensions and look at a coherent and holistic picture that help us understanding the dynamic situations, allowing us to cope with them.

Finally, trans-disciplinarity goes in hand in hand with multidimensional, again bringing the essence of systems-thinking. It transcends disciplinary (dimensional) borders and brings systems-knowledge together with target-knowledge to integrate and offer transformative-knowledge [31–34]. It facilitates cross-disciplinary understanding between diverse groups of people. The complexity theory underpinning complex adaptive system [35] offers framework to address challenges of multidimensionality by accommodating multiple perspectives of the multiple agents and interactions between them in a dynamic context. As a result of which 'emergent properties' evolve. These properties are different than the past properties [36, 37]. These emergent properties result into new set of strategic governing rules, strategic systems-outcome, and strategic challenges, which must be translated to all levels [38].

Presumably, few will have fundamental objections to such a comprehensive approach. However, the problem remains how to integrate the individual scientific approaches, which provide valuable information for their traditional field of application, into a self-contained, causally based system of thought. If this does not succeed, the individual statements have to be placed next to each other in an unconnected way. This problem was faced by Bertalanffy with his General System Theory [39] and Engel, who proposed the biopsychosocial model for medicine in 1977, based on the General System Theory [40]. This has proven itself in practice, although for epistemological reasons it has not yet been possible to establish a causal link between the different evolutionary levels that have to be taken into account. Therefore, psychosomatic medicine would have to be located unconnected between natural sciences and humanities [41]. If this linkage succeeded, the possibilities of systemic thinking in practice would be expanded [42]. This will be discussed in Part 2.

IV. ANTICIPATED: AS IF THEY WERE «TAKE HOME MESSAGES»

It has proven useful to preface this section with a few key statements that seem obvious without a specific derivation, but which one might not think of in everyday life. They are intended to facilitate the reading of Part one.

- The pathogen is the primary enemy not the person: it is not the meeting with the friend that is the starting point of the health problem. It is the penetration of the virus through the nasal mucosa. This can be counteracted.
- But where are the measures against SARS-CoV-2? The priority goal should be the destruction of the germ, only secondarily the indisputably important contact restriction.
- In a non-ideal world, one should not expect that anything can be ideally implemented. One must reckon with deviations. The risk can be reduced by combining DIFFERENT principles of action. In most cases this is more economical than using only one principle.
- Mis-judgements and other errors will probably be unavoidable if one has to act against an unknown pathogen. Due to the precautionary principle, one must expect the most unfavorable theoretically POSSIBLE characteristics. Therefore, the situation must be permanently reviewed and adjusted.
- During an epidemic, the scientific expert is in a fundamentally different situation than in everyday research: he/she is obliged to advise the most probable, applying the laws of reasoning and experiences of everyday life, even if there is no confirmed knowledge about it. This is obviously especially true when an epidemic is caused by an unknown pathogen.
- Action and inaction must be equally well justified.
- During an epidemic, the government has special competences: it is therefore obliged to use the legal framework specifically assigned for this case in order to act commensurable (at least after logical examination).
- As long as it is not proven that the disadvantage of antiseptics, especially the substitute for the currently too little available physiologically formed

N-chlorotaurine (NCT), is greater than the effects to be expected without the use of these options, it seems imperative that these substances be used. This is already necessary to comply with the intentions of the International Health Regulations for cross-border traffic. Comparable considerations apply when assessing the necessity of, for example, lockdowns, home schooling, etc.

- In any case, the possibility of substituting the currently missing physiological non-specific defense substance must be examined. After all, ALL variables influencing the process of the epidemic must be taken into account, not only those for which mathematical models are available:
- «Thus a small increase in the infectivity rate may cause a very marked epidemic in a population which would otherwise be free from epidemic» [9].
- The influence of behavior and emotional, cognitive and intellectual evaluations in the individual bio-climatological, ecological and socio-cultural environments affect the success or failure in the fight against SARS-CoV-2 so strongly that it is rightly spoken not only of a COVID-19 pandemic, but also of a COVID-19 syndemic.
- How long can a financially well-situated state and ultimately the individual citizens cope with the fact that every half year a vaccination of the entire population as well as the necessary accompanying measures have to be financed? How are developing countries and their inhabitants supposed to manage this? Does the key to the medium and immediate comprehensive consequences lie acutely in the extent of solidarity with the developing countries and in the medium term in the success against the fight against the new emergence of pathogens?
- A pandemic results not only in direct health effects, but also in indirect ones. Both deserve the same consideration, as do non-health systemic effects.
- This pandemic is not over until it is over worldwide.
- The era of pandemics is not under control until the transmission of human pathogenic viruses from animals to humans is under control.

PART 1
A GENERAL APPROACH

1) THE ROAD MAP.....

The structure of the booklet is based on the premise that while urgent action is needed now because of COVID-19, it is also now determining the medium- and long-term trajectory for the future. COVID-19 is therefore more than a health challenge. The pandemic therefore compels fundamental reflection, if only because it and the way it is being dealt with present fundamental challenges. For the application-oriented scientist, it is particularly painful that it has not yet been possible to combine the different approaches, each of which admittedly concerns an important partial aspect, into a balanced problem-oriented and holistic approach. Essential aspects and especially the «intellectual band» are missing. The situation is characterized by the fact that in the minimum five principles determine whether COVID-19 and its consequences occur, but in practice only two are consistently taken into account within the political strategies. From a pragmatic point of view, it is possible to draw conclusions from this and work out what additional things should and should not be done in order to be more successful at present. This is the approach taken in Part 1. But it does not address the root cause of why this incomprehensible situation has come about. Obvious essential influences have been left unconsidered up to now. How does one get this «spiritual bond», which is the prerequisite for being able to link the different aspects in a networked way of thinking? Only with it does the hope germinate that in the medium and long term solutions for COVID-19 and its networking with all the other upcoming reorientations will be chosen, which are more future-oriented already from the approach. This is the subject of Part 2, which requires more intensive discussion and is therefore deliberately separated from Part 1: However, in order to ensure that the proposals for the current pragmatic approach remain compatible with the necessary overall orientation, some of the contents of Part 2 must already be anticipated in Part 1.

The pragmatic approach presupposes corresponding preliminary work: starting points are analyses of the current status and the successes achieved by the measures taken so far, but also of the strategic considerations that can be imputed to the current measures. The Australian virologist Mackay seems to have modeled this very well and expressed it in a visually impressive way in his version of Reason's Swiss cheese model. Therefore, Mackay's Swiss cheese model is well suited both as a starting point for analysis and for presenting the necessary supplements. It turns out to be helpful that Reason's approach offers many more possibilities for reducing the risk of disasters, despite the error-proneness of human actions, than can be seen from Mackay's graphic, which is widely used today.

Reason assumes that humans are error-prone. Therefore, they must expect errors and develop a constructive error culture. Risks can only be reduced, but not fundamentally avoided. Therefore, one should develop as different instruments as possible to cushion the effect of any errors that may occur: Then it can be expected that the consequence of an error that occurred despite protective measure A will be compensated by measure B. Cheese slice C would compensate for faults that happen to A and B, so that no catastrophe occurs. However, Mackay's model describes the reality of the actual politics very well: it contains a large number of protective measures against SARS-CoV-2. They have only one crucial drawback: they are based on the same protective goal: to avoid that a person comes into contact with the virus. If, for example, someone was infected because their neighbor was not wearing a mask, then having to pass a special check when entering the country after-

wards will not help them. But that should not occur. Mackay and the political concepts do not assume that people make mistakes. They have to implement the requirements correctly. Mackay also built into his model the measure that is envisioned worldwide against COVID-19: vaccination. Both conceptions are necessary. Even if all people avoid contact as planned, their susceptibility to SARS-CoV-2 does not change. You cannot do lockdowns, home schooling, etc., in perpetuity. Therefore, you have to vaccinate, assuming that everyone will then be permanently immune, never get sick again, and never infect anyone else. So much for the theory. The practice looks different.

The analysis of the causal chain that ultimately leads to death from COVID-19, however, reveals that six steps, different in nature, are necessary for this. Thus, five principles are also possible in the effort against death from COVBID-19: SARS-CoV-2 had to form first. If SARS-CoV-2 can be made to disappear or inactivated locally, it cannot enter the environment. Then it also cannot reach people who can carry it further. If the virus does not reach the nose or lungs, contamination cannot occur. However, this only occurs if the non-specific defense cannot prevent penetration into the organism. Then the phase of non-specific defense inside the body begins. It can, but does not have to end with manifestation. In case of immunity, the manifestation does not lead to a severe disease. With appropriate therapy, one need not die from COVID-19.

It is possible to intervene at all these levels. As exemplified in Part 1.

Political decision-makers can seek advice from experts. This is an unfamiliar role for many scientists, who are accustomed to making statements only within their narrow field of expertise and relying on the state of the art. Both are incompatible with the requirements arising from the interconnected problems with a new pathogen. The legislator has taken this situation into account and clarified that the most appropriate conclusion is to be derived «by applying the laws of reasoning and the experiences of daily life». The responsibility for action and inaction remains with the responsible e.g. minister or government. These have been endowed with far-reaching rights and duties for the duration of the epidemic. The review of the appropriateness of their decisions is the responsibility of the competent supreme court, which must examine whether the measures taken were proportionate. This presupposes that at least an attempt was made to take less disadvantageous measures before fundamental rights were suspended. From a medical point of view, it is expected that the same standards for assessing the justifiability of measures will be used for the immediate (such as death as a result of the breakdown of intensive care due to the high number of COVID-19 patients) as for the indirect health hazards. Thus, for example, because of the increased risk of suicide among children as a result of their special situation during the epidemic.

Decisions in the private sphere depend strongly on one's own possibilities. What to use or not to use often does not depend on oneself. Especially in the case of limited possi-

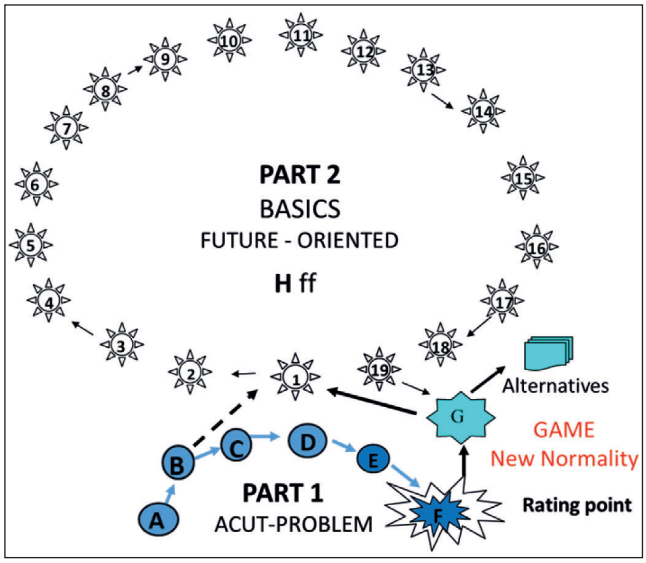

Fig. 2. THE ROAD-MAP (details see in the text).

bilities, it is essential to know which one to choose. This requires information and the willingness to think through alternatives on a trial basis. To facilitate this, the «Game of the New Normality» is developed. In order to be successful here, however, one needs better basics. These are offered in the second part. Its structure corresponds to the classical sequence of steps in application-oriented science. But this structure is also helpful for the one who wants to acquire key information for «The Game of New Reality». For this purpose, it is helpful to make clear what one should think about in order to be able to understand one's own situation and the field of tension in which decisions have to be made. The list of questions below can help. Each question also identifies where in the text considerations for answering them are presented for discussion. Page references for Part 2 are shown in Part 2.

a. Road map to answer important questions

This guidance document justifies the designation «Signpost». [The text passages in Part 1 and Part 2 that are helpful in forming opinions on each question will be identified after Part 2 is completed]

- Why is a scientist's job as an expert on an epidemic occurring for the first time fundamentally different from his job as a researcher?
- Why, with the same viral load, do equally old, severe, etc. healthy persons NOT contract COVID-19, although others do, some severely?
- Why is the mother and the sweaty athlete right in demanding the wearing of protective clothing, even though the number and type of contacts with others, and therefore the viral load of the breath, is not affected?
- Why do some people get a cold sore just because they are so disgusted?
- Is polio a harmless disease, even though fewer than one in a hundred people become infected with the virus on first contact?

- Why has tuberculosis been radically reduced even in countries without vaccination and antibiotics as a cause of death per year between 1900 (e.g., 500 per 100,000) and 1950 (to about 50 in 1950), even though certain e.g., immigrant populations are still at the same risk today as in 1900?
- Is pain (and other subjective experience) always THE guardian of health, although one does not feel the radiation exposure, the increased blood pressure, already inoperable tumor?
- How quickly could nonspecific defenses change with the use of a tolerated antiviral nasal spray such as NCT if changes in effect are as rapid as if an asthma spay immediately prevents impending death, the cold spray allows the fouled spar to continue, and the eye can grossly adapt to darkness in a fraction of a minute?
- Should death under torture conditions not be a social challenge merely because a virus causes it?
- Is the preventable suicide of a student less relevant just because it is the indirect consequence of action against a preventable death in a viral epidemic?
- How responsible is it to forego a proven diversity of methods and, despite unexpected failures, continue to rely only on diverse techniques that are all built on the same principle (interrupting contact of infectious persons with germ carriers)
- Is a government free to consider whether or not special powers delegated by Parliament (e.g., in medical device and drug law) can be used in an emergency?
- In case of imminent danger due to a new pathogen, may one base one's measures only on established knowledge and is otherwise obligated to inaction.
- Every Complex Problem has a simple answer, but the answer varies depending on the area of expertise of the expert consulted. Therefore, each must be wrong, although each may contain a «kernel of truth»: How does one deal with this problem? What should be given priority, e.g., because of the terms used?
- Why doesn't everyone who is infected with a SARS-CoV-2 that can lead to death die even though they don't receive medical services?
- Why hasn't humanity died out beautifully long ago, even though there are so many deadly infectious diseases?
- Why do pathogenic viruses disappear and what influence do our measures have on this?
- Why doesn't everyone who is infected with a virus that can lead to death die even though they don't receive medical services?
- Why hasn't humanity died out beautifully long ago, even though there are so many deadly infectious diseases?
- Why do pathogenic viruses disappear and what influence do our measures have on this?
- Is it even correct to expect that all chains of infection can be traced, should there be a dark net and its dynamics?
- What is cross-immunity? Does it exist in COVID-19 — comparable to cross-immunity between cowpox virus and «real smallpox»?
- Does a person have to have symptoms of COVID-19 to infect others?
- How long does a person remain protected from further infection after having been exposed to COVID-19 or successfully vaccinated, and how long can others remain uninfected? What is the protection against mutants?
- Who infected the person who carried the germ home, how long ago can this be and why is this person so often untraceable?
- How can you influence the clearance of viruses in your own body?
- Why don't you change the strategy if it obviously doesn't do what you told everyone it would?
- Is it allowed to set measures as a society without empirical experience that are also known to be detrimental to health? How does the legislator regulate this?
- Why were other countries (China, New Zealand ...) so successful, but not Europe?
- Could a different strategy have eradicated SARS-CoV-2 or at least limited the pandemic?
- Is the price paid by China, New Zealand, etc. on a permanent basis justified?
- What do I need to know, how exactly, what do I need to understand, so that I can form my own opinion or check my current opinion?
- How meaningful are the results of the tests? Can it really all be calculated? How meaningful are these numbers?
- Why are methods based on Kermack & McKendrick [9] used in ways that they have testified are inappropriate for these questions?
- Why have the predictions for effectiveness of interventions been so unsatisfactory while the predictions for ICU occupancy have been so accurate?
- What can and cannot be predicted by the models used?
- Will vaccination bring a return to normal as in 2019?
- At what point does one become immune to SARS-CoV-2? How long will one remain so? How does one become this again and how does this affect whether I might infect others4?
- What ways does the body have to protect itself against infections caused by viruses? What possibilities does the person have to protect himself and his own against the virus, and what possibilities does the community and society have?
- What possibilities does the virus have to prevail against inactivation and the cell barrier?

- How does the body defend itself against infection by viruses? How the virus defends itself against inactivation
- How can you influence the risk yourself, especially when you are exposed to this stress?
- Is it possible to use other tools besides vaccination in this process?
- If the pandemic threat is over, should COVID-19 have been successfully lowered to the relevance of «normal flu waves»? What are the arguments in favor, what are the arguments against?
- Is it possible to influence the occurrence of mutants?
- What makes COVID-19 so special? What is «long COVID?»
- How can asymptomatic courses with full antibody formation occur? Why, for example, can asymptomatic antibody-bearing children become life-threateningly ill with PIMS (Pediatric Inflammatory Multisystem Syndrome) weeks later?
- How long is someone infectious and how sure can this be known?
- What is the booster effect? What influence does it have in determining the duration of immunity protection?
- How is the fight against COVID-19 related to other challenges?
- What has been learned in the fight against epidemics over the centuries and therefore what can be expected now in terms of development?
- Can lessons be lost, and if so, might that affect strategy? Why is the experience of TB not being used.
- Not only the intellectual understanding of epidemics and the resulting possibilities to understand and fight them have continuously expanded. Does this evolutionary process also apply to the understanding of all processes, i.e. also the physical, chemical, biological ones in the body and its use for performance claims of the person on it?
- How do such dynamic processes at the different levels enter into the disease process? For example, how do the communities of life and function on our external surfaces (esp. intestines, lungs, nose, throat) influence the occurrence of infections?
- What is the current and long-term role of nonspecific mechanisms in the effort to prevent an era of rampant pandemics?
- What is the intended goal in the fight against COVID-19?
- How capable is science in general and during periods without sufficient knowledge?
- « Is it permissible as a society to set measures that are known to be detrimental to health without empirical experience? How does the legislator regulate this?
- To err is human — Can risks be reduced to zero? How can one deal with it? No
- What influence do therapy and vaccination have on the spread of the pandemic?
- What is the benefit to whom if I get tested?
- What is needed today, what is needed in the medium and long term? Who is responsible for what in the process?
- Is there evidence why COVID-19 can cause systemic disease, not just lung disease, and pre-disabled and seniors are at particular risk?

b. As in a circumstantial trial:

Some questions will take us to the limits of available knowledge. That is precisely why it is important that they be asked. Take the example of PIMS (Pediatric Inflammatory Multisystem Syndrome). This very rare disease has only been around for a few months. Children and adolescents, although they had no symptoms for weeks but had antibodies against SARS-CoV-2, suddenly become ill unexpectedly with severe multiple symptoms in different organs. What does this tell us about the virus, about the interaction between the cells of the organism and the virus? What is the role of the diseased person? Only a model that can give an insightful answer to all these questions will ultimately help. For the mother, of course, it is enough to know that a very successful therapy is available, especially with cortisone. The process and the importance of SARS-CoV-2 will only be understood when it becomes clear how these and all other reproducible phenomena in connection with the infection, manifestation of COVID-19 as a respiratory disease and its transition to the various systemic processes can be integrated into a framework of thought. The scientific way to this resembles a circumstantial trial, in which the accused — i.e. the virus — and the potential voluntary or forced accomplices — i.e. the diverse cells and structures of the organism — steadfastly refuse to testify, and the injured party — i.e. the diseased child — is only a very poor witness of the events. But all are affected: the viruses up to the person! One can understand the process therefore only if one can make the interaction between them comprehensible in a single access. Isolated knowledge about the virus, the individual cells and the person is of limited help. It is just like in a trial of circumstantial evidence: Without complete proof why all circumstantial evidence can be assigned to whom, the perpetrators will go free and will be allowed to continue their mischief: In case of doubt for the accused! Surely it is comforting that the currently affected child can be cured. But wouldn't it make sense to prevent the next illnesses through prevention? For this, science would have to be able to do something that works without problems in everyday life all the time: The causal interaction of the most diverse types of physical, chemical, biological, intellectual, etc., effects. effects to an overall effect. But science has not been able to do this so far, because the individual disciplines have only developed an approach oriented to their specific problems [43]. But this can be done differently, as will be shown in Part 2.

If one applies a comprehensive approach coherently built up in this sense, which is in harmony with the diverse sectoral theories, it corresponds to the so proven

requirements for Einstein's principle theories. Nevertheless, it must not be claimed that the so helpful thought building offers the only useful solution. Also this approach is only «a free invention of the human mind» in the best possible agreement with the facts, as Einstein has formulated this [44]. At best, it can become a recognized «conjectural knowledge» in the sense of Popper's «logic of research» [45]. But the way developed by Einstein for this purpose has the advantage, especially in phases of time pressure, to be able to present novel conclusions, which can claim to be a logical application of different positions, which is recognized as state of knowledge thanks to empirical proof. This substantiation of a new position is much faster than Popper's epistemic technique, which is widespread in the natural sciences: after all, it is based on the fact that sufficiently frequent unsuccessful falsification is necessary. This shows that it can be useful to deal also with the techniques how knowledge can be extended [46]. Therefore, Part 2 will also deal with this and its concrete application for COVID-19.

Currently, however, the focus is on the need to stop the epidemic, and to do so with the limited knowledge that is currently available, and with insightful conclusions that may be assumed «using the laws of reasoning and the experiences of everyday life». Thus it remains of only to apply «Eminence based Medicine», to test this empirically parallel to the effort for solutions and to reach thereby the step to «Evidence Based Medicine»: Which is far from achieving the goal to which science has dedicated itself: to explain processes causally.

2) OVERVIEW

What information can the reader expect in Part 1. On the one hand, it is about the necessary analyses. On the other hand, the connectivity to a comprehensive approach must be established. Therefore, it is unavoidable to present core information from different fields of knowledge for discussion. They touch very different fields of knowledge, which would have to be linked to each other in an unusual way. Therefore it makes sense to work out the core statements in an overview. This should make it easier to grasp the importance of the individual aspects in the holistic view.

a. The situation

In spring 2020, the world was overwhelmed by the first wave of the epidemic with SARS-CoV-2. The causative agent was unknown. Therefore, only measures that have proven effective in other epidemics could be put in place. The focus was on reductions in personal contacts until lockdown. Forecasts suggested a return to normality once new infections had dropped to extreme levels. This occurred surprisingly quickly, as if SARS-CoV-2 and COVID-19 were actually adequately detectable by the forecasting models. Contact restrictions were relaxed again to varying degrees during the summer, in line with continued low contact rates, without striking increases in new cases and deaths in large areas of Europe over a period of months. With the end of the travel and holiday season in September, however, there was a second wave in numerous countries, e.g. in Europe, which had not been foreseen on this scale. Nevertheless, many European countries still gave the impression in late fall that they were doing very well in combating the pandemic. However, despite all the restrictive measures taken in accordance with the repeatedly adjusted forecast models, the increase was not only not brought under control: There was an increase in the number of new cases that led to fears of a collapse of the health system, as had occurred in the first wave in Lombardy. Since then, the fight against this collapse has been at the center of societal efforts, rather than the fight against SARS-CoV-2. Contact restrictions and all measures to implement them in a more targeted manner (testing, border controls, contact tracing, masks, hand disinfection...) have been reinforced, and new lockdowns have been imposed. In the meantime, the unintended consequences of these measures dominate the present in practically all areas: Public life largely came to a standstill. Economic burdens are rising to unimagined heights, health consequences are appearing in areas that were virtually ignored during the planning in the spring and in the further aftermath. The situation can be summed up by the statement, attributed to German Chancellor Merkel: «The thing has slipped away from us».

If a comparable situation occurs in medicine, e.g. that a therapy that has proven itself does not and cannot prove itself contrary to the prognoses, it is state of the art to fundamentally reconsider the course of action — even at the risk of replacing or supplementing the obviously insufficient therapy. This did not happen in the case of COVID-19

The bright spot that everyone is hopeful about is the surprisingly rapid progress in vaccine development and production. This provides tools to expect that the overall number of diseases will decline, especially the severe courses and deaths. This is what can be expected from vaccination. Whether the vaccinated may also be neglected as carriers of the viruses is another matter. This is of particular importance because new, more aggressive mutants have appeared in the meantime, which also give rise to fears that vaccinations against them will be less effective. Obviously, it is only a matter of time before mutants «escape» vaccines. Moreover, it must be clear: animals in close proximity to human habitat are hosts to approximately 625,000 and 800,000 virus species that can easily mutate into human pathogenic forms. Thus, an era of pandemics is looming [2]. The currently available vaccines are unlikely to protect against this, irreplaceable as they are today.

The conclusion of the Independent Panel, which was initiated by the WHO to evaluate the effectiveness of the measures taken worldwide, is thought-provoking. According to the panel, the pandemic could have been prevented if certain international measures had been taken. This also raises the question of the adequacy of local measures. Furthermore, this question becomes relevant because — not foreseen — it has turned out that

COPVID-19 is not only a respiratory disease but systemically affects many organs and that with Long COVIDF a pandemic has occurred within the pandemic. The message disseminated at the time that life would be restored to 2019 levels with a single vaccination coverage has also turned out to be an unjustified hope. Due to the mutants that have appeared in the meantime, it seems necessary to carry out booster vaccinations repeatedly and in surprisingly short time circumstances.

b. Central: Pathogen virulence vs. susceptible infection manifestation

To date, however, there is no fundamental change in the strategy currently being pursued. The associated measures have been depicted in a graphic that is going around the world as the «Swiss Cheese Model» in many languages [47]. Many see their implementation as the solution to all the problems ahead. That is why this chart is so well suited to show what possibilities are overlooked if only this approach is taken into account: Namely, it envisages only two types of intervention: 1) various ways of restricting contact of not-yet-infected persons with infectious agents, and in particular with infected persons, and 2) vaccination. Of course, there can be practically no infection if no one who is infected has contact with someone who is not yet infected. However, contact with others is only the (most important) condition for becoming infected. To become infected it needs the contact of the virus with the cells of the outer boundary of the body. This is not the same as contact of one person with another! However, the presence of SARS-CoV-2 in the nose does not mean that one has to be infected either. The person, more precisely the cells of the «outer boundary» of his body, can defend himself against the invasion and thus against the infection. And if this fight was unsuccessful and the pathogen was able to penetrate the outer barrier, so that the infection of the body came about, then even this does not mean that one gets sick. The body also fights against this. If this fight is not successful, the so-called manifestation occurs. This can lead to observable effects of illness (with subjective symptoms) or to asymptomatic disease. In the asymptomatic course, the effects of the body are not subjectively experienced. We all know that asymptomatic diseases do not have to be harmless, e.g. from cancer. There, too, one often notices the consequences only when it is too late. The physician notices that an asymptomatic disease has occurred by the fact that specific antibodies can be measured. The course of the disease also depends on the characteristics of the pathogen and the reactions of the organism, influenced by the behavior of the sick person. Here, too, one can intervene non-specifically (bed rest, oxygen administration..) and specifically therapeutically and preventively (especially by vaccination). From a medical point of view, the process from contact with a germ carrier to the severe course of the disease in the intensive care unit is a sequence of extremely complex interactions, which offer a variety of consciously and unconsciously effective possibilities of influence.

i. The contents of terms are summarized or differentiated in a problem-related way

A widow will not choose this sober description of the sequence of individual steps to tell her sister how her beloved husband died so terribly: «He came back from the choir still so happy. That's when he caught it. Three days later, he got such severe symptoms that we had to take him to the hospital the next day. 10 days later he died in the intensive care unit despite artificial respiration. I wasn't even allowed to visit him». With that, she expressed what was essential to her.

Kermack & McKendrick, two progenitors of infectious disease epidemiology, might have emphasized quite different aspects [9]. They would have reported, for example, that they were not surprised that the members of the choir who could not attend the performance did not become ill. However, it was noticeable that only one of those who stood at the very back next to the window fell ill, and even those who only brought in the new sheet music and left right away remained healthy. Then only the intensity of contact was decisive for whether a choir member was infected and fell ill. Thus, one could imagine how the two researchers came up with the idea of demonstrating the importance of contact intensity as an additional, independent factor influencing the epidemic. For this purpose — as will be explained later — it was legitimate to assume the plasticity («adaptability») and other characteristics of the pathogenicity of the pathogen as well as all influencing factors of the infected person together with the time span between contact and the appearance of the symptoms as constant and to summarize them with a term, e.g. «infectivity», «force of the epidemic» or similar. Then one can use the frequency and intensity of contacts between the infected choir director and the non-infected choir members as the only variable remaining as different and also make it mathematically tangible. Then one can calculate, for example, when how many of the choir members' contacts thus generalized will be newly infected or newly ill. But Kermack & McKendrick were aware, of course, that in the practice of an epidemic, the partial aspects that were summarized by method will vary independently. But to demonstrate the usefulness of the sub-aspect of the epidemic event they were interested in, they did not need quantities for variable cellular and organismal non-specific defenses, nor for the possibly changing strength of infectivity/pathogenicity of the pathogen (mutant...). After all, they only wanted to prove the basic principle of the effectiveness of delaying contact on the course of an epidemic!

ii. The content of the terms used determines the conclusions

However, applying these formulas to real-world processes has far-reaching consequences for misconceptions: If the observed frequencies of new cases deviate from the calculated value, there can only be one answer for this: The contacts occurred differently than assumed. After all, the model does not provide for any

other possible explanations. But possibly the reason lay somewhere else: e.g. because the non-specific defense was weakened. But this method cannot make any statement about that. And the researcher, who uses terms with such summarizing contents, will possibly not be able to get the idea that the process described by him in a general way would have to be differentiated, so that one can correctly seize the relevant single processes. Not only that: if word-similar terms with different contents are used, there is a danger that the interlocutors will talk past each other: One then believes that the other has understood that infectivity means a characteristic of the pathogen and not susceptibility, i.e. the characteristic of the host to be infected. The other person, e.g. a representative of the Robert Koch Institute, thinks that he was talking about a characteristic of the host [48]. But which host did he mean?

This shows how important it is that all possibly changeable influences on the substeps of a process sequence can be recorded exactly separately. The first prerequisite for this is that a clear term is used for each relevant substep. All those involved in a process should also always be clearly recorded. If, for example, it is the chain of interaction that is to be interrupted, it must be made clear what interaction is to be interrupted, by whom and with whom: Only when this is stated, the reader's or the listener's attention is also drawn to the different possibility of interruption. The one «partner» will therefore ALWAYS be the infectious virus. Whether the «partner» to be interrupted otherwise gets contact to the air, a sink, the hand or the cell in the nose is immaterial. But already from this it is clear that the partner can NEVER be the person, but always only a physical part of him. So when speaking of «host», one should not mean the infected person. «Host» of a virus can always be — precisely -only a cell. A person can «infect» another with an idea, an aversion, etc., but not with a virus.

However, one can be infected when visiting a person, but with a virus exhaled by him with the air. Of course, the behavior of the person influences whether contact of the pathogen with the hands, mucous membrane cells in the nose, etc. can occur.

This is not a quibble but crucial to realize where one can intervene everywhere to break the contact [49]. This is also important because the virus itself is changeable and shows reactions e.g. with surfaces, under solar radiation. Therefore, detecting the presence of parts of the virus does not have to prove that the affected object is infectious or that one is infected. This is also essential when dealing with contact in the nasal cavity between virus and mucosal cell. Contact does not automatically mean «infection». The effective contact with the nasal cells necessary for infection depends, after all, also on the current characteristics of these cells, but also on the viral load and the characteristics of the virus. Each of these aspects is significant.

iii. Important terms used

Therefore, the terms used in this paper are clarified as follows: SARS-CoV-2 is a (human) pathogenic virus. «Pathogenic» — because SARS-CoV-2 is, in principle, capable of infecting any non-immune human. The PATHOGENITY of a pathogenic virus indicates the degree of INFECTIOSITY. This can be measured, for example, by the number of viruses that must be present in the nose for the viruses to penetrate the cells of the «outer boundary» of the organism (e.g., the nasal mucosa) of a «standard person». If this succeeds, the person is considered infected. The infectivity of a virus — as well as e.g. its dangerousness (virulence) and the resistance to vaccines — can be changed by its plasticity (= its adaptability), however one wants to imagine this process. Obviously, the consequence of plasticity is the changed characteristics of the mutants in comparison with those of the initial virus.

In the organism, a second characteristic of the virus becomes essential: its VIRULENCE. It influences the severity of the course of the disease. Virulence and pathogenicity/infectivity do not depend on each other: thus, the infectivity of the virus for polio is very low, its virulence is terribly high.

Whether SARS-VoV-2 viruses in the nose lead to an infection = penetration of the «outer boundary» depends not only on characteristics of the virus, but also on the RECEPTIVENESS or SUSCEPTIBILITY of the person, more precisely of the affected cells of his outer boundary. Everyone can defend himself against the infection more or less successfully with the help of his cellular and exudative — by releasing substances like NCT e.g. into the nose — non-specific defense (or also called «non-specific innate immunity»). Since their performance is individually variable, the susceptibility or susceptibility can even change rapidly under certain circumstances. If one wants to compare pathogens in their infectivity among themselves with regard to the standard population, one assumes an equal distribution of the capacity for non-specific defense in a collective. This is expressed by the CONTAGION INDEX. This indicates the proportion of non-immune individuals in a collective who are infected with a virus on first contact — ideally by a standardized viral load.

Unfortunately, people also talk about an infected person being infectious. Strictly speaking, this is not true: the germs that the person gives off are infectious. Often one speaks also of the fact that e.g. SARS-CoV-2 is particularly infectious for this or that group of people (e.g. fringe groups). With this choice of words one summarizes the «human» sphere of influence of the unspecific defense of this group of people and the virus-related sphere of influence, as if they were an inseparable whole. The important questions of why viruses penetrate more frequently in these groups of people and whether this can be influenced are thus practically excluded: this is also because they are more susceptible.

The onset of infection and the penetration of a correspondingly high number of viruses is only the begin-

ning of an interactive process that can, but need not, lead to the classic disease. Again, the non-specific defense — this time that of the organism — influences whether and when it comes to manifestation and thus to the classical disease. It is not known for SARS-CoV-2 how high the proportion of those is who do not develop a manifestation, but the MANIFESTATION INDEX is known: However, this usually only covers those patients who also show classical symptoms. (As the example of PIMS shows, other types of disease can also manifest themselves later without passing through the stage of «classical lung disease») For this subgroup, the INCORPORATION TIME can be determined, i.e. the time interval between contact with the person who spread the germs and the manifestation. In simplified terms, it can be said that the more effective the nonspecific defense, the longer the incubation period. From an epidemic hygiene point of view, it is not only their mean value that is of interest. The extreme values are also significant: since the nonspecific defense can be changed individually and via societal measures, it must be assumed that the average incubation time (or the so-called «serial interval» or «generation time» derived from it in the formulas of experimental epidemiologists) can also change approximately within this range, even in the case of longer-lasting epidemic events. Thus, one must reckon with this possibility in the current long duration of the epidemic of more than one year.

1. confusion possibilities due to different questions

It is important to be aware that the incubation period itself has nothing to do with detection of viruses e.g. in the nose by a laboratory test (like PCR test). The person with positive laboratory test may or may not have clinical symptoms. She is infected. So, she is in the stage when viruses could infect cells of the outer boundary of the body, for example, the mucous membrane of the nose, so that they could reproduce the viruses and release them into the nasal cavity. Therefore, the number of viruses in the nose could increase so much that they could be detected by the test. Therefore, these viruses can be released into the environment through sneezing, etc. This can lead to a viral load of persons, which becomes the starting point of an infection. According to experience, the viral load in the nose of the spreader must be so high that the viruses can also be detected in his nose with a correspondingly sensitive test method. For this reason, for example, the PCR test is essential from a medical point of view: to be able to detect whether people who do not yet and possibly never show symptoms themselves are the cause of infection of others. Since each test is a snapshot, it says little about how significant the person was as an excretor on the day and the days before: after all, the test can be done in the waning phase. It does, however, suggest that the person who tested positive and is symptom-free is already a carrier and will be even more so, especially tomorrow, possibly with symptoms of his or her own. The person, tested positive is considered a «proven case».

We only know from the persons on whom the test has been performed whether they are «cases» or not. Their daily number does not tell us anything about the collective to which they belong: After all, we know nothing about those not tested: they may or may not be positive. There is no generalizable reason why those who have been tested have been tested.

It is possible to determine the time that elapsed between the contact of the first infected person and the appearance of the criterion to be used for evaluation in «his» secondary infected person. This information is used in the calculation of the «serial interval». If the criterion used is laboratory detection, e.g. with PCT, the «serial interval» is shorter than the incubation period. After all, the test becomes positive before the subjectively ascertainable symptoms appear. However, if evidence of the onset of the disease — i.e. the presence of such symptoms — is used, this «serial interval» corresponds to the incubation period. However, investigations of the time intervals between the first sufferers of the disease and the subsequent sufferers who can be assigned to them provide the best information on both the serial interval and the incubation period.

But the data, which are related to laboratory-detected cases, strictly speaking have nothing to do with the incubation period in the classical sense. Their definition dates from a time when PCR tests, etc., did not exist. The condition of the person was ascertained on the basis of the presence of symptoms agreed upon by the scientific community. Since these symptoms are expected to be the reason for going to the doctor and they are judged by the same criteria, it is much more justified to use this figure if one wants to compare collectives. Even more meaningful for comparisons between collectives would be the daily new hospital admissions with COVID-19 and their individual length of stay. The hardest data are the deaths from and/or with COVID-19 related to a collective. But it is essential how the collective is defined to which the number of deaths is related. In medicine, a «classical» distinction is made between lethality and mortality. The lethality refers already historically to the number of persons who died with the classical symptoms. Mortality to the number of deaths per 100,000 persons in a state. Thus, lethality is obviously different from other figures, such as the number of deaths related to proven cases (case fatality rate). But these figures belong to the domain of model calculators. These have different questions than the disease hygienists and clinical physicians, even if in public these differences tend to blur. Therefore, not all data are mutually helpful.

2. on the interface medicine — model calculations

Various models of infectious disease epidemiology assume that there are only ill persons with symptoms. Therefore, only these are taken into account. If this were the case, it should be possible to trace back all chains of infection without gaps, provided that enough personnel are available and no interviewee is lying or forgetful.

However, if asymptomatically ill persons (persons in whom positive antibodies can be detected) or COVID patients with inconspicuous symptoms could also become the starting point for the infection of others, this assumption would no longer be conclusive. In that case, the course of the epidemic could be quite different. However, the sources of infection of the children carrying/ill for weeks inconspicuous germs, who then suddenly fall ill with PIMS, remain just as hidden as possible third parties, who could have already infected these children [50]. This fact alone shows the relevance of the «dark figure» of germ carriers and challenges us to think about the consequences: not only with regard to the claim of a 100% success rate in tracing.

The German National Academy Leopoldina, for example, points out the consequences as follows: «A substantial part of the infected population is hardly or not at all ill even for the entire duration of the infection. Therefore, the so far strongly symptom-guided surveys lead to a distorted perception of the infection occurrence, which hardly allows robust (data- or even model-based) estimates regarding the efficiency of measures [51]».

All these interrelationships, which are essential for understanding the processes and for considering which measures can be targeted to get the epidemic under control, must remain hidden if the computational models used, against whose correspondence of the forecasts and the results that actually occurred the success or the additional need for measures is determined, do not incorporate the individual variables that are actually possible. However, typical models summarize these and assume constancy of the few variables over the total duration of the epidemic, such as the serial interval.

This position paper is based on medical principles, but strives for connectivity with all other disciplines concerned with researching and influencing health-related aspects.

c. Why does not every infected person die?

COVID-19 can lead to death. Why doesn't everyone die if the pathogen has the potential to do so? And why hasn't mankind died out long ago, even though there are so many pathogens that can lead to death? Why do so few get infected and fall ill with identical exposure to SARS-CoV-2 viruses in the nose, while others who are comparably healthy sometimes even fall seriously ill, even die? The answers to the biological processes are provided by physiology, i.e. the science of how the organism organizes health biologically. Pathophysiology provides information about how these processes take place when the organism is no longer able to establish health equilibrium (homeostasis). The human being is therefore not infected because the organism of the human being has possibilities to inactivate the pathogen in time. The individual person will not be infected if the structures whose functionality is the prerequisite for penetration through the external barrier of the organism are denatured, for example, by oxidative processes. Then the problem of how to deal with the penetrated viruses does not arise. Once the virions have entered the organism, denaturation processes can only be expected again inside the phagocytes. For this purpose the formation of the antigen-antibody complex is essential. However, in case of the disease, not all virions are captured in time with the help of antibodies. They can enter other cells and are reproduced there. During this phase, the plasticity of the virus may also change, resulting in the formation of mutants. Thus, the diseased person may become the starting point for the spread of a new mutant. The longer it takes for the viruses to be denatured in the organism and thus eliminated, the greater the risk for the diseased person that further cell systems will be affected with the typical impairment of functions. On the other hand, the risk of evolutionary further development of the viruses into mutants with higher pathogenicity, virulence and the ability to evade the effectiveness of vaccines also increases. This must therefore also be expected in phases in which there is not yet complete immunity or in which immunity has declined again. Latent phases, in which viruses remain functional in a kind of equilibrium with the cells over a longer period of time, therefore also deserve special attention with regard to the evolutionary development of new mutants.

Thus, the infected person will survive the infection, which would basically lead to death, whose organism — possibly supported by a vaccination — can destroy the viruses in time. Lethality expresses the «average» failure in these efforts. This figure indicates the average number of patients in a collective whose denaturation processes are no longer sufficient to prevent death. It depends not only on the infectivity of the pathogen and its virulence, both of which characteristics may be altered in mutants. Numerous host-related processes also exert a promoting and inhibiting influence on the denaturation processes. Therefore, the lethality of the disease can be expected to change over the course of an epidemic and between affected groups. One influencing factor is vaccination, even when there is only partial immunity or only partial immunity.

Mortality, i.e. mortality per 100,000 inhabitants, includes not only lethality, but also how many inhabitants are infected. This depends, for example, on the frequency and the way in which people come into contact with each other. The strategies currently used to control the epidemic are based on this. But the decisive factor is whether contacts with infected persons also lead to infection. This is influenced by the non-specific defense of the cells of the outer border of the respiratory tract. The more successful the denaturation processes there are, the fewer people will be infected and the viral load that can penetrate the outer boundary will be correspondingly lower. This increases the chance of overcoming the disease with the help of the natural organismic defenses. If this succeeds, mortality will decrease radically, even without vaccination and specific therapy. How this was achieved with tuberculosis in Austria between 1900 and 1950 is described in Chapter B 1.

Mortality and lethality can be altered by the evolutionary development of viruses into new mutants. How relevant this is, especially in COVID-19, is shown e.g. by the «English», the «South African» mutants and «P 1» from Manaus. The evolutionary dynamics of viruses depends on the length of time viruses remain in the organism and their transmission: Partially immune individuals pose some risk in this regard. This could have importance in the context of the prolongation of the two vaccination steps, which are carried out for lack of available vaccines. However, since partial vaccination already leads to a reduction in lethality, Harvard researchers nevertheless see a preponderance of the benefits of using the limited available vaccines on more individuals at the expense of the interval to the second vaccination.

d. The holistic response to COVID-19

COVID-19 is an infectious disease. Therefore, the pathogen is the number one enemy and not the person. However, the infection takes place in the body of a person. This suggests interactions, on the one hand, with the influences on the complex biology, and on the other hand, behavioral and evaluative influences of the individual person on the organism. In this context, the person is integrated into psychological, community and social structures. These influence the situation of the individual in many ways. Therefore, the fight against the pandemic is a societal, indeed a global challenge that cannot be won without adequate consideration of the person and his or her biology in its diverse environments.

i. Biology influences the person

Infection is first and foremost a process between a virus and a cell. It only indirectly affects the person, as long as no functions are impaired by the cell, that are relevant for the person. This is just as true for all processes that take place on a purely biological level. Therefore, we do not feel the growth of cancer cells, even if the cancer has grown so large and is scattered throughout the body with metastases that it has become inoperable. However, the doctor makes the diagnosis based on biological changes. After attending a soccer game, however, you may be hoarse for hours because you shouted so loudly to cheer on the team. The doctor will not call this a disease. You see: Pain is thus not a good guardian of health. It communicates much more whether functions can be retrieved by the body or not. The person feels sick, although so according to medical point of view.

Therefore, it is understandable that during the incubation period the person does not notice that the viruses are multiplied more and more by the cells. However, more and more cells in the organism are affected. Therefore, functions in the organism have to be reorganized in order to maintain the so-called homeostatic balance despite the needs caused by the infection (or cancer). The messenger substances necessary for this can be measured under certain circumstances. The structures that the organism forms to defend itself against the infection (or cancer) can also be measured. Thus, the detection of specific antibodies proves that the person has or has had COVID-19. Regardless of whether the person feels symptoms or not. Therefore, in children, for example, infection with SARS-CoV-2 can go unnoticed for weeks, but in the meantime result in impaired functions in multiple organs without being noticed.

The reorganization will sooner or later affect functions that are significant to the person. This leads to subjective experiences: One feels weakened, lacking drive, etc., gets fever, headache, e.g. after vaccination. Or the weeks of conflict in the body of the children then suddenly lead to massive symptoms in them. They have to be hospitalized immediately with multi-organ defects. There they are diagnosed with PIMS.

1. implications for COVID-19

In order for the organism to be able to perform the services required in dealing with the disease, it needs resources. These are limited and must therefore be withdrawn from other demands. This is why cancer patients often lose weight. The multitude of theoretically possible biological processes are in competition with each other, so to speak. In order for one function to be enhanced, others must be curtailed. If this leads to restrictions in the currently necessary demands of the person on his body, there is a reduction in performance and at best subjective sensations. That is why the sick tooth hurts as soon as it comes into contact with ice or you bite on it. But the organism prepares itself for expected performance: Therefore, antibodies remain in the blood even against pathogens that are not currently present.

ii. The person influences the biology

The person also has current demands on the organism or is in anticipation of coming demands. Therefore, athletes warm up before competition and one prepares for a discussion by mentally considering the possible issues. The mind and body are therefore aligned accordingly. Ultimately, all functions that a person performs must be implemented by cells of the body. Therefore, the person also intervenes in these interconnected processes in the organism between cells, tissues and organs with his considerations. Thus the requirements of the person are in competition with the biological requirements of the organism. The person has no other possibilities to become effective than to organize the biological modes of operation accordingly, which are just as available to the organism. Since neither the organism knows what the person wants, nor the person what the body needs, surprising consequences can occur from the person's demands on the body. Many people are familiar with the placebo phenomenon. Here, unconscious control processes of the brain trigger biological functions that can also be triggered by, for example, toxins or drugs. But this is only one example of how the person influences biological processes with evaluation processes. However, these central control processes can also be detrimental to the person. As said: The brain cannot know, which demands are actually delivered, if a help call of the body

takes place. Then it would be of better, the message would not reach the brain at all. Who does not know this from soccer games: Despite a heavy foul, after which one could not go for hours, the soccer players run after few minutes as before, because with a cold spray the transmission of the stimulus to the brain was interrupted and therefore the disservice was omitted, which would have occurred otherwise by the controls of the brain. The effectiveness of anesthesia and artificial deep sleep prove to everyone how fundamentally different the consequences would be if central control were not prevented by the interruption of the flow of information. Many biological processes would occur differently, and often more efficiently, if they were not centrally interfered with.

1. conclusions for COVID-19

In principle, this must also be expected for infections, e.g., SARS-CoV-2, if only because effective influences on physiological processes are needed to make it understandable that so many healthy, non-immune persons do not become ill despite comparable viral loads.

iii. The interdependence of organism and person

Such influences can also be expected on the effectiveness of non-specific defenses, and within a short time. This is proved e.g. by the following experiment: The influence was investigated which the intellectual assignment of meaning has on the one hand on a subjective perception and on the other hand on a biological effect which can neither be influenced consciously nor chemically [52]. For this purpose, students were invited to participate in an experiment. The aim was to determine how strongly the odor threshold varies between young people and whether odor has an influence on the concentration of the antibody IgA in saliva. Healthy volunteer students were alternately offered one breath (2.2 seconds) of odorless air and one breath of test gas at continuously increasing concentrations via a breathing mask. The administered dose is harmless even at high concentrations because of the short exposure time. Students entered the odor threshold and pain threshold and again provided a saliva sample. Offered in both tests was the much more harmless sulfur dioxide. However, in the second test, it was stated to be the much more toxic sulfur trioxide. Both odor threshold and pain threshold decreased significantly when the students believed they were being exposed to the more toxic SO_3. The concentration of antibodies in saliva also changed significantly: the third with the highest sIgA values before the experiment dropped abruptly and massively, the concentration of the third with the lowest sIgA values increased slightly [53].

These effects occurred within a short time. This means that one should expect meaning attributions to influence whether an objectively given biological burden is subjectively perceived or not. These scientifically supported conclusions are in good agreement with countless empirical socio-medical studies that have provided evidence between intellectual, emotional, and cognitive evaluations with biologically beneficial and detrimental

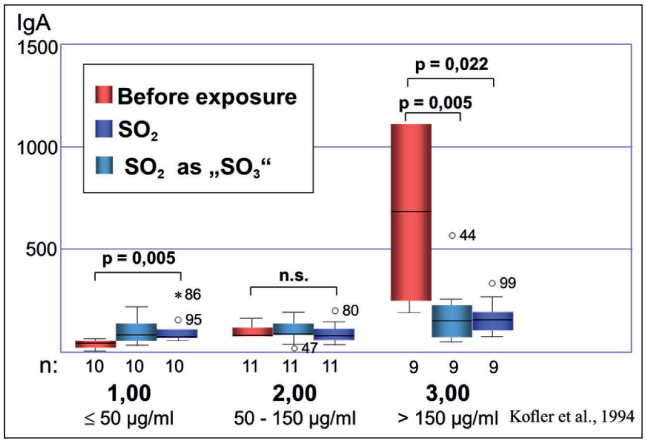

Fig. 3. SIgA (µg/ml) in healthy students sorted according to their SIgA concentrations before exposure

effects. This is discussed in more detail in Part 2. Evidence between such assessment processes and the genome (telomere and telomerase) has been pointed out several times by Nobel Laureate Blackburn [54], e.g., improvements in neglected children after successful training of parents [55]. These approaches open the understanding of bio-psycho-social processes leading to the evidence of the link between social situation, poverty, helplessness etc. and increased COVID-19 risk [56].

1. Consequences for COVID-19

Assuming such interactions also in the context of assessment processes and COVID-19, it makes sense why asymptomatic individuals can be germ carriers and infectious. The subjective experience is not triggered, but the biological processes run. However, these connections also make it understandable why it becomes conceivable why even short-term changes in immune defenses become conceivable, which can cause viral loads that would be successfully repelled by nonspecific defenses in the absence of the change in meaning to lead to penetration of the organism's outer boundary and thus to infection..

Such processes make it understandable why persons can be germ carriers without an increased viral load being detected in the nose and why they do not need to be additionally infected to suddenly show symptoms themselves. Under stressful conditions, however, this initial load may be sufficient for the onset of manifest symptoms: Then a lower viral load is sufficient for penetration. Such stresses are conceivable under homo office, home schooling, etc. in close living conditions. Such considerations would also make it understandable why, without additional infections acquired outside the home, members of a family at home can suddenly infect their roommates.

The reason for the poorer organization of previously appropriately adaptable processes can be seen in the fact that the potential for coping with challenges is limited. When a new, even more significant requirement arises, this potential must therefore be subtracted from a function and assigned to this more significant one [57].

This leads to causally unspecific effects as demonstrated by Kofler et al. These considerations are consistent with the conservation principle — the most fundamental theorem of physics. Epidemiological proof is accessible in Kofler 2019, among others [58].

iv. Limitation, subjectivity, and rhythmicity.

This experiment to demonstrate the effect of intellectual evaluations on biological processes is stimulating in several respects: the capacities needed to tune biological processes are obviously available only to a limited extent. Therefore, an additional demand must lead to a change in the allocation of the available adaptive potential. Whether the consequences are experienced or not obviously depends not only on the concentration of the chemical (physical, biological) stimulus, but also on the subjective assignment of meaning to the experienced situation. This explained why lower concentrations of SO_2 were already perceived and then triggered pain if it was assigned more importance because of the subjectively assumed higher relevance, whereas the same biological interactions were not perceived if they were subjectively assigned a lower importance.

However, this assignment of importance is also related to the amount of adaptive capacity that is «freely available» and also used according to the conservation principle. Thus, it becomes clear why a process unrelated to the evaluation of airborne agents, such as the precautionary stockpiling of antibodies without the simultaneous presence of corresponding pathogens, could be influenced by intellectual evaluation processes, and the level of secretory IgA is adjusted after an increased need for adaptive capacity has occurred.

1. I. Sechenov and I. Pavlov: Inhibition — Reinforcement and the Evolutionary Process

Both processes confirm a long-established principle in physiology: attention to one aspect leads to aversion or devaluation of other aspects. Since the key works of I. Sechenov and I. Pavlov «reinforcement and inhibition» belong to the state of knowledge. Surely everyone has already personally experienced their practical relevance: You cannot do everything you can in principle at the same time. Therefore, one must concentrate on one and disregard the other. This personal experience helps further to understand two kinds of principles: First, the principles of directing with the possibilities of automated control and consciously made control. For this, the experience of learning to drive a car helps: In the beginning, you have to concentrate highly, you hold on to the steering wheel convulsively, you don't listen to the advice of the co-driver, and still the car bounces to the intersection like a billy goat. Two weeks later, everything runs in a resource-saving manner via the control circuits that have been acquired in the meantime, so that you can comfortably talk to the co-driver.

The second, related principle concerns the resource-saving, efficiency-increasing good organization of the daily routine with the variety of activities that are successfully performed in rhythmic sequence in succession of sleep and wakefulness.

Sechenov's research also provides valuable additional information in this regard. «Inhibition vs. reinforcement» and «automation» of recurring requirements not only contribute to solving everyday problems more efficiently. They are also essential to better understand the interconnectedness of a person's functional carriers and modes of functioning, which vary in age with respect to their initial occurrence. He has studied reflexes, automated biological processes, such as the speed with which a frog withdraws its paw from an acid bath. Removing parts of the frog's brain gradually according to their initial evolutionary appearance, the reflex occurred faster the more recent brain parts had been removed. In ticklish subjects asked to suppress tickling while having a hand in the acid bath, he was able to demonstrate that the reflexive withdrawal of the hand was delayed in time compared to the situation without tickling when the subject made a voluntary effort to [59]. Thus, Sechenov proved that the principle of inhibition is valid across biological, psychophysiological, and intellectual levels. It leads to time-related effects of meaning assignment in relation to the affected evolutionary levels in the organism.

2. Rhythmic change of effectiveness

These considerations suggest that the incorporation of ever new evolutionary structures and associated novel possibilities into highly complex organisms was possible because the needs of the different evolutionary levels were made compatible by an appropriate temporal sequencing that gave priority to the different levels over other demands. Connected with the principles of guidance, i.e. the transition from resource-consuming control processes to economical and automated appearing cybernetic systems, largely self-acting rhythms are to be expected, to which corresponding characteristic frequencies should be assigned. According to the principle of inhibition and amplification, it is to be expected that these automatisms can be modified within limits in order to be able to face the actual requirements in a dynamic way.

These considerations are connected to the research of chronobiology and the corresponding biological, psychological and social rhythms. Particular attention is paid to circadian rhythms, a term which, like «chronobiology», was introduced by F.Halberg, the father of chronobiology, in the 1950s. At the latest since the 2017 Nobel Prize was awarded to Jeffrey C. Hall, Michael Rosbash and Michael W. Young for their discoveries of the molecular mechanisms underlying the circadian rhythmicity of cells, this approach has become part of the accepted state of knowledge. The different biological rhythms in the organism are integrated into the circadian 24 h rhythm. This means that within this time span, biological functions are given priority over others at one time, but are devalued at other times. This also changes the biological effectiveness of a stimulus relevant for this function. This can be seen, for example, in the fact that the identical dose of a drug can have a completely different efficacy if it is given at noon or at midnight. The correct dose at time A of an anesthetic (e.g., of

lidocaine [60]) may result in death at time B. It is essential to keep in mind that the intensity of the rhythms can also be amplified or attenuated in the short term. This is also true for the influence of intellectual, emotional and cognitive unconscious evaluations, as in placebo and nocebo phenomena. For example, the already classic studies by Hildebrand and Pöllmann not only show the characteristic circadian differences in the pain sensitivity of teeth to cold stimuli. They also prove that this sensitivity can be raised or lowered with the help of placebo — i.e. by pretending the administration of a drug by administering a substance that is pharmacologically ineffective per se [61]

3. The metaphor of the cabbage

Consideration of rhythms in the context of thinking about how to optimize action against epidemics requires a change in approach to the processes that are important in the process:

We are accustomed, when considering the appropriate strategy against an epidemic, to start from the strengths and weaknesses of the possibilities and that the individual or society has in doing so. If one wants to represent these graphically, one arrives at representations such as the Swiss cheese model described in detail later: The individual cheese slices then stand for the basic possibilities to be able to act against the epidemic, the holes for why one will not achieve the ideal imaginable goal with it and also for where there is a need for compensation.

However, one can also assume that every living being is repeatedly exposed to threats, such as a viral infection, and has only survived because it has so far successfully overcome these threats. One can also choose a metaphor for this and represent it graphically. Cornelissen and Halberg have developed the cabbage head model for this purpose [62]. The structure of a cabbage differs from that of a bulb in that the individual leaves cover only parts of the plant, can overlap, and have a certain independence of their own. Therefore, the cabbage head is suitable as a metaphor for the complexity of, for example, a person. During the ontogenesis of the human being, multicellularity, tissues, organs and the organism of a person with its specific needs are formed from the fertilized seed. Comparably from the seed the single leaves form individually and nevertheless basically predictably. Also each leaf has its own needs, but also contributes to the protection of the whole plant by the fact that the leaf — comparable to the cheese in the Swiss cheese model — impairs the penetration e.g. of the virus, however depending on the correct positioning also of the other leaves. For the usefulness of the cabbage head as a metaphor, however, Cornelissen and Halberg have to assume that the different leaves of this cabbage head shift in their position according to their rhythms, the thickness of the superimposed leaves and thus the overall protective effectiveness is changed. This process is currently influenced by the guiding processes. This can lead to constellations in which, for example, one and the same viral load can penetrate the interior without any significant resistance, whereas a much stronger resistance would be expected if shifted in time.

4. Conclusions for COVID-19

For essential steps of the infection process or its defense, F. Halberg, G.Cornelissen and co-workers present numerous already classical studies on circadian rhythmicity. For example, they demonstrate the dependence of phagocytosis [63] and of T, B, and natural killer cells [64] on circadian rhythms. H. Borrmann et all. recently presented a review on the influence of circadian rhythms on viral infections [65]. These rhythms exert a decisive influence on the severity of infections. Therefore, understanding the role of circadian systems in regulating viral infection and the host response to the virus is of great importance for prevention and therapy. So it makes a big difference when you are exposed to a virus, and it also makes a big difference when you are vaccinated to protect yourself from that virus. But it's not just circadian rhythms that have an impact. The same is true of numerous other rhythms. This will be discussed in more detail in Part 2.

v. The accumulation of unexplained cases of disease

That such processes will more often lead to manifestations when the resources necessary for the biological processes are limited (poverty, physical overload...) is conclusive. This demonstrates the biological bridge to the higher risk of marginalized groups. These groups of people are also more likely to be exposed to assessment-related stresses, e.g., due to their housing conditions. Such processes provide insight into why there may be an increased incidence of new disease within families, even if the available evidence does not provide any indication of the origin of the germs that have been introduced into the family.

The dynamics between the pathogenicity of the pathogen and the variable susceptibility of the person or, more precisely, his organism explains the variability of the incubation period, but also the option that pathogen latency occurs.

These processes deserve attention not only because they could lead to the formation of a viral dark net: That is, a network of symptom-free infected individuals who can spread viruses to individuals who also need not become manifestly ill. When and in whom this network leads to manifestation can be predicted just as little as it is possible to trace who passed on the infection.

Such considerations would make the graph below understandable: Carinthia, with a population of about 560,000 and an area of about 9,400 km?, is an intensively touristic used area, especially in the, summer of 2020, because of its lakes, mountains, and diverse cultural offerings. Despite the probably strong increase of the contacts during the tourism months (June — September) the new disease rate sank so strongly that over weeks the reproduction number could not be computed any longer. Dead Nr 13 died on May 5, dead Nr 14 from October 23. The second wave struck with an intensity that had not been predicted.

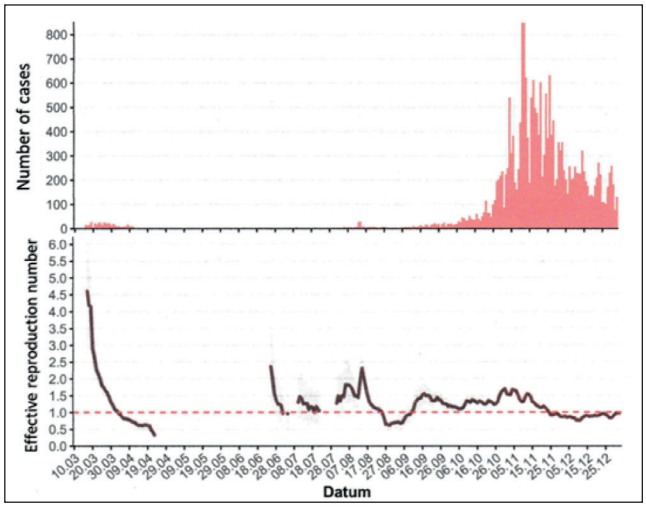

Fig. 4. Epidemiological curve of daily incidence by laboratory diagnosis and the time course of the estimated effective reproduction rate in Carinthia, Austria. In each case, 13 epidemic days were used. Data after January 2, 2021 were excluded from the model calculation. (AGES 2021)

All processes that influence the duration of the presence of viruses in the body — from the formation of an increasing viral load e.g. in the nose before manifestation to death from COVID-19 — are also significant because they contribute to an increased risk that mutants can form.

Both this and the personal risk of becoming infected and manifesting disease, such as the likelihood of passing the viruses to others, should be able to be reduced by the prophylactic administration of antiviral antiseptics, e.g., as a nasal spray.

e. Illness and disease and COVID-19

Meanwhile, the question of whether and how to recognize excretors of SARS-CoV-2 is gaining more and more attention, regardless of whether they also individually experience symptoms or not. This question is also becoming more urgent because it has so far been open to what extent individuals who have already experienced the disease and have therefore acquired specific immunity or vaccinated individuals are possible carriers. Therefore, the preliminary results of the SIREN study are briefly mentioned [66]. In this study, more than 25,600 employees (average age about 47 years) in English hospitals were regularly examined for one year (from March 2020) for their antibodies, PCR values and objective and subjective clinical findings. Of these 25,600, 32.3%, or about 8200 individuals, had contracted COVID-19 by about mid-July. These 8,200 were screened for recurrence of COVID-19 by January 2021. The antibody-negative (approx. 17,300) employees up to mid-July were examined in parallel for the occurrence of first infections using the same methods. In the period up to January 2021, «only» about 10% contracted COVID-19 for the first time, despite the largely similar composition of the study groups. Of these individuals, about 66% exhibited the classic subjective COVID symptoms. These persons therefore also felt ill. About 17% stated that they had never noticed any symptoms at all. However, according to objective criteria, they had COVID-19. In the case of COVID, therefore, a distinction must be made between being ill and being sick.

At 17%, the proportion of atypically ill persons in this collective was thus remarkably high. Even more strikingly, a further 14% of individuals with now positive AK detection reported subjective symptoms. However, these symptoms were atypical for COVID-19, which is why it would probably not have been assumed that they had COVID without the study. Thus, about 31% had COVID-19 but would not have been recognized as such.

In order for antibodies to be formed, the phase must have been passed in which the viral load, e.g. in the nose, has become so large that others can be infected, but there is still no manifestation. This phase may last individual days [67]. Therefore, it can be assumed that both symptomatic and asymptomatic patients were potential carriers.

The authors of the SIREN study also present a graph and data from 155 suspected reinfections among the approximately 8,300 people who had contracted COVID between March and July and had therefore acquired immunity. That immunity declines after illness is not unusual. Therefore, it is not surprising that reinfection occurs and at an increasing rate with an increase in the distance from the initial illness. For our considerations, another statement is of importance: the suspected reinfections are namely distributed significantly differently among those with typical COVID symptoms, those with inconspicuous symptoms and those with atypical disease: Now, instead of 66% percent suffering from COVID-19 as in the initial infections, only about 33% do so. The proportion of persons with inconspicuous symptoms (approx. 18%) and asymptomatic sufferers (approx. 49%) rises to 67%. Thus, the ratio has reversed. If one assumes («thumb times pi») that this collective had approximately the same risk of being infected as that of the 10% who were infected for the first time, then it is reasonable to assume that those who had already been infected in the past (approx. 7.5%) (difference of approx. 10% and the calculated approx. 2.5% of those who were reinfected) were also more successful in avoiding infection. This is also not a really surprising result for the epidemic hygienist. It has been observed time and again that once an infectious disease has been successfully overcome, protection against a new infection is improved. Thereby, a shift of the proportions on the continuum from «not infectable» — over «infected» — to «manifestly slightly» — to «manifestly severely ill» can occur in the direction of an increase of the «not infectable». With increase of the time distance of the new infection from that of the healing at the first illness the continuum shifts again more in the direction of the illness. Something similar has been found with vacci-

nation against cholera in comparison with non-vaccinated individuals.

However, this means that the possibility of virus transmission must be expected in all persons in whom corresponding antibody increases — due to the new disease — are found, which entitle to the diagnosis «COVID-19». The increase must have been caused by a specific stimulation of the immune system by virions, which succeeded in penetrating through the cellular outer boundary of the organism. This penetration is also preceded by a phase in which the viral load, e.g. in the nose, is sufficient to infect others. This can lead to infection followed by asymptomatic disease, which can then lead to symptomatic disease «sometime and somewhere» when the virus infects a person with weakened defenses. This situation is not unknown either: We know it, for example, in infectious hospitalism. There, symptom-free persons with a good immune system transmit the so-called «facultative pathogenic germs» not only between other persons with a good immune system without any consequences, but unfortunately also to immunocompromised persons, who then fall ill. This is particularly problematic when it comes to germs that have become resistant to conventional antibiotics over the years. Fundamental problems could also arise in connection with the emergence of particularly pathogenic mutants of viruses.

f. Not static monocausal — interactive multicausal and multi-intentional.

Thus, understanding the infectious disease for each of the sub-steps from transport of the virus in the environment to death from COVID-19 requires a comprehensive process approach that takes into account physical, chemical, biological, psychosocial, legal, economic, etc., aspects in a balanced manner. Multiple causes will need to be considered simultaneously in order to incorporate diverse goals, as well as existing concerns, into a process. This results in interactions, which themselves have an influence on the events and intentions. This requires a scientifically correct approach that allows statements about the cause — i.e. causality. This encounters the methodological problem that the scientific disciplines used are based on different world views or paradigms. Therefore, they cannot be causally linked. The problem can be solved by using a comprehensive paradigm in which the sectoral views are integrated like subsets in a common basic set. This has been achieved in the model used here because it has been implemented that all sectoral disciplines used agree on two assumptions:

1) Everything that is today is only a consequence of yesterday's circumstances and processes, yesterday's the consequence of the day before yesterday, and so on. All thus accept a comprehensive evolutionary understanding.

2) At least partial aspects of our world can be explored and predicted. Therefore all statements of all disciplines can also be related to these basic assumptions and therefore be connected with each other.

Thus three directions of looking at one and the same problem are open to us:

a. the classical approach of the respective discipline

b. the comprehensive approach resulting from the assumption of a continuous evolutionary process from the «Big Bang» to the «Big Mac» and

c. the approach using the laws of thought and the experiences of everyday life.

The third approach will possibly be even more surprising than the second. But it has a key significance in an epidemic with a completely unknown pathogen. Crucially, action and inaction must also meet the requirements of our legal system: And this system provides, in cases where only limited knowledge is available but a decision must be made, that the decision must be «based on the experience of everyday life and the application of the laws of reasoning. These issues, which are particularly significant from a scientific point of view, will be discussed in more detail in the «long road» (Part 2).

The current situation cannot be answered by anyone who has to decide with the help of already secured knowledge alone. «Compared to the pond of our knowledge, our ignorance is Atlantic», already said the R. Duncan and M. Weston-Smith, the editors of the Encyclopedia of Ignorance, supported by numerous Nobel Prize winners [68]. Thus also this route finder can point out in many areas only, with what one should count for precautionary reasons. Nobody knows the future, nevertheless one must act today in such a way or differently or decide not to act. Not acting also needs the same good justification.

g. Necessary and sufficient justification

Despite this often severely limited knowledge, rapid and correct decisions are needed in epidemics. Measures that may or must be taken or avoided to protect health and prevent deaths need sufficient justification. What is sufficient is determined, on the one hand, by the principles of science. Ultimately, however, the determining factor is whether the action is in accordance with the law. Parliaments have delegated special authority to responsible decision makers in the event of an epidemic, pandemic, or other disaster. Scientists who are appointed, for example, as experts to advisory bodies to these decision-makers are thus in an unfamiliar situation. Arguably, they are required to state what would be considered reasonable, unreasonable, hazardous to health, etc., using the laws of reasoning and their experience of daily life. In doing so, the health expert will have to point out both that SARS-CoV-2 can lead directly or indirectly to death from or with COVID-19, for example [69]. He will also have to point out to the decision-maker the consequences of the measures planned to prevent such deaths, e.g. that lockdowns may increase the risk of suicide among children. Whether and to what extent this is followed is not the responsibility of the experts, but of the decision-makers. The proportionality of the measures taken is a matter for the competent supreme court.

In practice, numerous problems arise in this process. The strong specialization of the disciplines involved proves to be particularly significant. They differ so fundamentally in the world views they use and the theories and methods they derive from them that they are not compatible with each other at the causal level. Particularly relevant is the fact that science focuses on proving what is generalizable, but each disease affects an individual person. These significant problems will be addressed in more detail in Part 2 and a solution will be presented for discussion.

h. Conclusions

This leads to the fact that among the correct techniques to expand knowledge, the scientist should also use the possibilities that allow to use the empirical and logical experiences of different disciplines that until now seemed incompatible. For this purpose Einstein obviously successfully developed a technique which can be used also in medicine [70]. This has the additional advantage that its expressiveness extends, but does not replace, the possibilities offered so far by the state of knowledge. The «third leg» for the sufficient scientific justification is provided by the legislator with the requirement to close any remaining gaps even without further empirical proof «by applying the laws of reasoning and the experiences of everyday life».

A strategic concept is required for the measures in order to be able to achieve the short, medium and long-term goals efficiently. This requires a regular review to determine whether the expected goals have been achieved. Deviations are to be expected, since people are not ideal and also technical aids can fail and organizational structures can be deficient.

As the timeframe changes, so does the emphasis placed on local, regional and global aspects of pandemic response. Currently, the focus will be on the avoidance of medium and immediate fatalities and the functioning of the health care system. However, the impact on education, jobs, cultural and sporting diversity, etc., is also significant from a health perspective. Without ecological, spatial planning measures with consideration of the international interdependencies, there will be no adequate long-term handling of COVID-19 and the next pandemics and their integration into the other structural changes that are currently pending (keywords climate change, mobility, local and global inequalities).

Basic adjustments are necessary when the epidemic cannot be stopped at the stage of new emergence, but there has been a spatially and temporally uncontrollable spread of germ carriers. In principle — as described below-, although five different principles are theoretically available to stop the epidemic and prevent death from or with COVID-19. However, since none of these principles can be implemented in an ideal way, it is necessary to combine all methods so that the consequences of insufficient protection in one area are offset by the effectiveness of another. In this way, risk can be reduced. But there is no such thing as zero risk in a non-ideal world. Rather, the fear is that paying attention to one approach to a solution may lead to unexpected consequences in an entirely different area. This appears to have occurred in the course of the fight against COVID-19. Unexpectedly, mutants of SARS-CoV-2 have appeared and continue to appear, including those that are more infectious and dangerous. Most ominously, they could also escape vaccine efficacy (escape mutants). Such a mutant could condition a situation similar to that in March 2020. This represents a threat that was not anticipated in March 2020.

From a health perspective, such considerations lead to numerous suggestions and deductions. At the top is the avoidance of the occurrence of escape — mutants. The likelihood of their occurrence is related to the duration of persistence of SARS-CoV-2 in cells of the host organism. The most efficient way to reduce this is to denature the virus before it penetrates the outer boundary of the organism in the nose, throat, or larynx. The use of, for example, appropriately effective and tolerant nasal sprays also temporarily reduces susceptibility. It would reduce them already in the nose located virus loads. This reduces the relevance of infected persons as carriers and the probability of manifestation of the disease in the infected person. Inhalation with such substances should also reduce the recent infection of patients hospitalized in normal wards by viruses formed by themselves and released into the lung and nasal cavity.

3) A BRIEF HISTORY OF CONCEPTS TO COMBAT THE HOSTAGE OF EPIDEMICS

Living beings have had to deal with viruses and other pathogens for billions of years. They survived and were able to evolve until now — thanks to the successful fight and — in part — successful cooperation with them (mitochondria as viruses «integrated» into the cell, etc.). Therefore, the tools for interaction have also changed over time.

a. Different methodological approaches

Additional tools had to be developed for situations where the non-specific and specific biological tools were not sufficient: Since the Stone Age, the secretion of infectious agents has been used as a tool against epidemics. Since then, the available tools and focus areas have expanded as knowledge has increased. As a result, a variety of tools can now be integrated and sequenced into a comprehensive approach to epidemics.

In parallel with the possibilities that have been possible individually, and which may have been implemented collectively and socially, more and more far-reaching legally binding precautions have also been enshrined. So far, however, these obligations are practically oriented only to measures to prevent the transmission of pathogens from one state to another. The Independent Panel sees this weakness as the reason why the COVID-19 pandemic occurred.

1) Isolation and quarantine: since the Stone Age... social norms and laws.

2) Influencing virulence: Jenner, Pasteur, Koch, (1796, 1895, 1896).

I. Indirect improvement of nonspecific physiological defenses and comprehensive coping capacities: Virchow (1848 hygiene, social medicine, PH), Bismarck (1883, social insurance laws).

II. Behring (1890, passive immunization thanks to antitoxins)

III. Metschnikow (1863): phagocytosis thanks to white blood cells

3) Antiseptic and asepetic of medical activities: Semmelweis and Lister: (1847, 1865)

4) Contact avoidance and natural herd immunity: Kermack & McKendrick: (1927)

IV. specific therapy: Ehrlich (1909 Salvarsan), Waksman (1943 Streptomycin),

V. «Immunology as usually understood»: Alick Isaacs & Lindemann 1957 (interferon); Porter R 1959 antibody globulin structure.

5) International legal regulations (International Health Regulations e.g. 2005)

VI. The Independent Panel for Pandemic preparedness & response 2021

6) «Test, test, test» WHO 2020.

VII. individual comprehensive and controlled daily live behavior

7) Mucosal antisepsis in a comprehensive understanding of health (Kofler et al. 2020/2021).

8) One World concept «Escape the Era of Pandemic» thanks to comprehensive sustainability: International Science-Policy Platform on Biodiversity and Ecosystem Services 2020

9) One Health concept with «COVID-19: Make it the last Pandemic» The Independent Panel and IPBES (2020)

The «naïve evidence-based» responses against an epidemic consisted of keeping a distance from the sick and agreeing on norms that such people must or want to live segregated even in special valleys (leprosy). This is evidenced not only by data on humans, but also for animals [71]. Epidemic areas were consistently demarcated: No one was allowed in-no one was allowed out.

The principle of contact avoidance also works less radically. Kermack & McKendrick proved its usefulness mathematically [9]. Their approach became the basis of various models (e.g. SEIR). The extension by WHO with the requirement for «testing, testing, testing» takes into account the fact, specific to COVID-19, that the infectious individual can pass on viruses asymptomatically or presymptomatically. Therefore, these individuals must be recorded, isolated, and their contacts identified, and the potential carriers of germs thus recorded must also be isolated.

Jenner used evidence-based experience that infection with a less pathogenic virus caused protection from the «black death» — without knowledge of immunology and infectious agents such as microbes or viruses. Pasteur and Koch developed the «germ theory» of infectious diseases. They recognized the possibility of artificially altering the virulence of pathogens. Behring discovered that an antitoxic substance could be the cause of a curative effect. This could be obtained from the blood of cured people and artificially infected animals. He used it, for example, against diphtheria and tetanus. Kermack & McKendrick referred to the influence on virulence as the second tool against an epidemic, which has been used in addition to radical secretion, when they developed the third approach.

Virchow made references to the relationship between poverty and risk of infection (1848). The fight against poverty, social insecurity, work overload, inadequate nutrition and housing conditions was a non-specific tool against almost all infectious diseases. This manifested itself in a decline in the contagion/contagion and manifestation index. For example, mortality from tuberculosis — the most important cause of death at the time — was reduced in Austria from about 500 deaths per 100,000 persons per year (1900) to about 50 in 1950 without the influence of vaccination and antibiotics. The physiological explanation for the decrease in infections and manifestations is the increase in the efficiency of the non-specific defense. However, the non-specific defense does not cause specific immunity. Therefore, even if individuals have come into contact with and successfully repelled e.g. SARS-CoV-2, they remain fundamentally susceptible to e.g. SARS-CoV-2. Thus, they may later contract COVID-19 upon renewed contact with SARS-CoV-2 if their nonspecific defense status is worse. The nonspecific immune status can change rapidly, as will be shown below. The risk of infection can therefore increase — if the exposure to SARS-CoV-2 viruses remains constant — even in the short term, e.g. in the wake of a severe physical strain. However, the risk can also be permanently improved or worsened by the living conditions that are so essential for contracting the disease, e.g., with tuberculosis. Therefore, contagion and manifestation index may vary within the same collective and depending on the currently given situations in the individual. The success of the non-specific defense against contamination with respiratory pathogens is based on the antiseptic efficacy of substances produced, for example, by mucosa cells of the nasal mucosa.

Semmelweis discovered the basic principle of antiseptic in 1847 in his special form of disinfection. Disinfectants can destroy viruses but are too aggressive for the mucosa. Semmelweis applied chlorine-containing solutions to disinfect the hands of obstetricians. This made him the «savior of mothers,» although university and ministerial authorities prevented its implementation for about 20 years. Lister rediscovered the principle in 1865 and applied it to surgical operations. Since then, antisepsis has been the most fundamental principle of every medical activity worldwide. And Semmelweis has also gone down in history because the Semmelweis effect is named after him: that obviously effective measures are not implemented for unscientific reasons and social harm is accepted as a result.

Using mathematical techniques, Kermack & McKendrick demonstrated a third principle with the

delay of contacts between infected and infectious persons, by which one can influence the course of an epidemic (1927): One does not have to lock infectious persons away permanently. One can also start with the non-infected. If the number of those who are no longer infectious thanks to immunity increases above a critical value, then the — now time delayed — contact of an infectious person with infectious persons leads to fewer new cases of the disease than at the same time persons who are (permanently) healthy, become permanently immune and no longer infectious. Kermack & McKendrick also assumed that genesis becomes permanently immune and no longer infectious. Under these premises, the so-called reproduction number falls below 1. The reproduction number can also be reduced by measures of contact restriction and quarantine of (potential) germ excretors. Then the epidemic will change to an endemic or sporadic occurrence. Kermack & McKendrick are thus the intellectual fathers of herd immunity and reproductive numbers. However, they understood this way to contain an epidemic only as an additional offer and not as a substitute for the possibilities of permanent segregation or influences on virulence, on pathogenicity and on susceptibility.

Ehrlich, thanks to the invention of Salvarsan against syphilis, opened the way to be able to act with drugs against infectious diseases. Waksman discovered streptomycin in 1943, the first drug produced by microbes (antibiotics).

Immunology «as normally understood [72]» and occurring only from mammals onwards, is based on cellular immunity (e.g. phagocytosis thanks to leukocytes; Metschnikow 1883) and globulin-based specific antibodies (e.g. Porter 1961). Therefore, Kermack & Kendrick in 1927 could only consider the possibilities of quarantine and virulence or susceptibility, but not modern vaccination. Recently, many techniques have become available to construct an artificial vaccine, including RNA techniques. They made it possible to extend the concept of Kermack & McKendrick thanks to vaccination by artificial herd immunity.

Contact with a virus is not identical with infection, and infection is not identical with manifestation: this is because the non-specific (innate) physiological defenses intervene in these processes. The resulting indirect means of combating infectious diseases have been used since Virchow and the legal initiatives of Bismarck. It has since been demonstrated that deficiencies in the physiological defense against infection can be compensated for by administration of a synthetically produced substance of the nonspecific defense, namely N-chlorotaurine (NCT) or by other antiseptics. The use of N-chlorotaurine (NCT) as a mucosal antiseptic may therefore help to bridge the gap between the outbreak of such an epidemic and the prevention of the severe illnesses and deaths with the help of a specific vaccine. NCT was discovered in 1970 by a group of Polish researchers. In the 1990s, Gottardi developed the technology at the Medical Faculty in Innsbruck to synthesize this substance of innate defense on a large scale. Together with Nagl, therapeutic applications were tested, including tolerability and efficacy against SARS-CoV-2 [73, 74]. W.Kofler et al. proposed its preventive use to prevent SARS-CoV-2 infection and COVID-19 manifestation [10].

Efforts to prevent the spread of diseases to other countries were regulated in an internationally binding manner centuries ago, for example in the maritime sector. The UN has addressed this issue through the WHO and agreed on International Health Regulations. But these are — like the Independent Panel called for by the World Health Council — a toothless tiger that inhibits more than it promotes. The Panel therefore calls for a fundamental strengthening, under the leadership of the WHO. Thus, success stands and falls with the strength of the WHO. This is discussed in more detail in an article by Pradetto in the focus issue.

The Director-General of WHO proposed an additional tool in March 2020 to break the chains of contact for COVID-19: «We have a simple message for all countries: test, test, test; test every suspected case. If they test positive, isolate and find out who they were in close contact with for up to 2 days before they developed symptoms, and test those people as well» [75]. This takes into account the fact that people infected with SARS-CoV-2 are infectious before they show symptoms. In March 2020, however, it was impossible to know that these tools would not achieve the predicted goal. It was predicted by virtually all decision makers at the time that the measures recommended by WHO would stop the epidemic.

The IPBES (Intergovernmental Science-Policy Platform for Biodiversity and Ecosystem Services) presented the sustainable measures concept to escape the «era of pandemics» [1]. It is necessary to prevent the threat of about 620,000 to 850,000 potentially pathogenic viruses for which animals are the host and can easily become human pathogens, he said. The next pandemic is therefore only a matter of time — with all the direct and indirect consequences that we are currently experiencing, at least until adequate vaccines, therapies and the necessary preventive measures would be available.

The One Health concept is based on the Millennium Goals of the UN and the WHO. Its goal is to raise the level of health on earth for all people, regardless of their wealth, religion, etc... Therefore, it goes beyond fighting pandemics, but if successful, it would have a decisive impact on pandemics and their consequences, especially in developing countries. This justifies that this concept is cited here. Its implementation poses a particular challenge to the international community to implement this shared commitment.

The independent panel initiated by the WHO World Health Council recently presented its report. It outlines the extent to which the global response to the COVID-19 pandemic to date has contributed to achieving this goal, and what changes would be needed to more suc-

cessfully integrate pandemic response into the One Health approach.

The concept of IPBES can also be seen as a contribution to the implementation of the One Health concept.

b. The underestimated framework conditions

Unfortunately, it is not only factual arguments and the techniques developed in the meantime that determine the fight against the COVID-19 pandemic. The existing infrastructural framework conditions inevitably set limits. Politically divergent interests, especially in the context of upcoming elections, lead to competitive behavior that is mostly not conducive to coping with the pandemic. The extreme cost movements lead to a dynamic in which the focus is not on the desired goal — protecting the health of the population and minimizing the medium and immediate other impacts — but on maximizing personal interests. The significance of this has been demonstrated by the WHO Independent Panel, for example, with the following graph on the change in prices for pandemic aid.

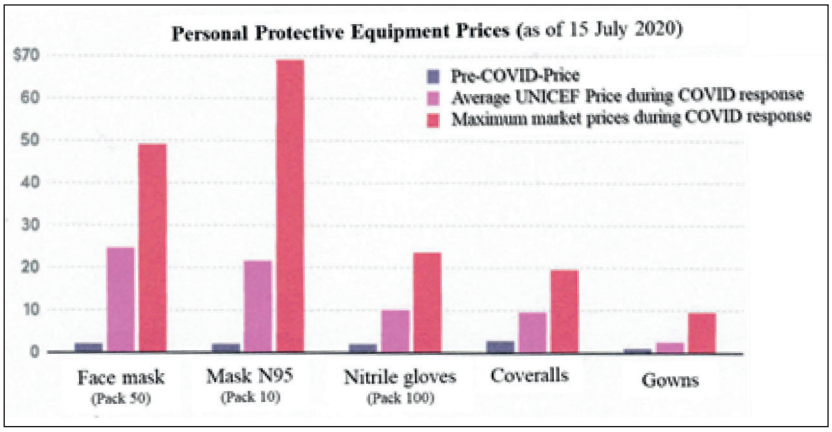

Fig. 5. Personal Protective Equipment Prices (as of 15 July 2020). The Independent Panel for Pandemic Preparedness & Response, 2021. Data: UNICEF Global COVID-19 Special Interim Report, August 2020

Price increases of 1000% were therefore not uncommon. These framework conditions will therefore also be discussed in more detail.

4) A PRAISE OF NON-SPECIFICITY.

In the discussion of necessary measures, the importance of specific procedures is emphasized. This is particularly evident when talking about immunity, as if there are only specific immunological effects. But nonspecific processes are indispensable, e.g.

a. The success of the nonspecific (innate) defense ensures the survival of the infected individual until the specific defense of the individual has developed to the point of being effective against the disease.

b. Nonspecific defenses reduce the number of infected and diseased individuals. This reduces the reproductive number, i.e., the average number of individuals infected by a diseased individual. This is particularly important in the period before vaccines increase the proportion of immune individuals and thus artificial herd immunity.

c. Artificial boosting of infectious defenses is also effective against any kind of mutants. Their widespread use helps to reduce the development of mutants.

d. Nonspecific processes can contribute in several ways to combating the collapse of the critical care system, e.g., also by being effective against other viruses. The demand for beds due to «other» infections, e.g. with Influenca, therefore decreases. If used in a targeted manner, an increased protection of e.g. the staff in intensive care units can be expected.

e. The best remedy against the formation of mutants is to prevent mutant formation from occurring. This can be achieved by preventively preventing the penetration of viruses through the outer boundary of the organism, but also by targeted measures to reduce viruses in the air (cleaning by filters, etc.).

f. Currently, there is a controversial discussion whether RNA of SARES-CoV-2 could enter the host DNA [76]. The fact alone that phenomena give rise to this discussion, which is conducted at the highest scientific level, should urge us to use all possibilities for precautionary reasons, so that this is prevented as far as possible. The inactivation of the virus before it can penetrate serves this purpose.

g. Nonspecific processes also contribute to improving the level of health in general, quality of life and coping with a variety of challenges, independently of the defense against infections. For example, increasing the potential to absorb and transmit oxygen is helpful not only to combat infection and the severity of COVID-19, but also to enable the elderly, for example, to care for themselves for longer.

h. Long-term success against many infections (and behavioral diseases) relies on non-specific elevation of health levels (e.g., against tuberculosis).

i. The tools to escape the «era of pandemics» cannot target specific viruses or microbes. After all, today we do not know which pathogens will cause the next pandemic. So today, prevention can only be achieved with non-specific methods.

A strategy without the integration of non-specific tools would thus forego relevant, indeed irreplaceable, opportunities.

5) THE GOALS OF A HEALTH-ORIENTED STRATEGY

The goals have changed profoundly from a medical perspective since March 2020:

- It began with the intention of eliminating the impact of the newly emerged infectious agent on

health, disease, and well-being by eradicating the virus.

It has since become clear that, at least now, it is no longer possible to eradicate SARS-CoV-2

- The goals of medicine and public health (PH) are now oriented toward combating the manifestation of COVID-19: the goal is to be able to deal with COVID-19 as with «any other infectious disease, even the far from harmless influenza» — thanks to successful prevention, promotion of health, and cure.

This includes the appropriate impact on the global import and export of the virus.

But these goals have not yet been satisfactorily achieved. Vaccine development, on the other hand, has been successful and provides hope for addressing the threat of severe disease progression and many deaths resulting from SARS-CoV-2.

- However, the actual defining goal is currently (early 2021) based on preventing a collapse of the intensive care system with the possible consequence of a collapse of the entire healthcare system. This fight is directed against premature, unnecessarily painful or forced death. It is pointless to fight against death in principle or to believe that one can exclude risks in principle.

With the appearance of Long COVID, a pandemic has occurred in the pandemic. It also affects younger individuals. It is reported that approximately 38% of those with COVID-19, regardless of severity, have long-term symptoms [77]. Drake et al, in a prospective study, found Long COVID in 48.8% of men younger than 60 years and 36.6% of women [78].

In the meantime, it has been possible to prevent a collapse of the health care system in numerous countries. This was and is connected with extreme also health-relevant side effects as a result of lockdowns and other measures, which are set to inhibit the contact of persons among themselves as a precaution. This technique also reduces contacts between asymptomatic germ carriers. However, the approach of interrupting contact between individuals has no relevant impact on future population susceptibility. It should also be borne in mind, in a strategy aimed at avoiding the collapse of intensive care, that patients with COVID-19 are not the main reason to occupy ICU beds. Therefore, other measures, e.g., against other serious infectious diseases, against traffic accidents, etc., must also be considered to prevent the collapse of the ICU system. In addition, the available personnel in particular limits the resilience.

It should also be taken into account that it is not only the overload of intensive care that can lead to triage. A similar situation is reported for psychiatric care of children: Priority must now be given to those at risk of suicide.

It is time for all disease-related intermediate and immediate effects of the pandemic response to be included in the assessment of the appropriateness of interventions.

The strategies of local, regional, and global institutions will vary. («Think global, act local») The importance of health levels is obviously of significance that goes beyond health: both the EU and WHO confirm that the development of health levels is the relevant measure of effectiveness in overall policy [79].

The political strategy should be prepared for the next pandemic. Therefore, the fight against COVID-19 is just a model example of how to be prepared against epidemics and pandemics in the future.

MULTI-CAUSALITY
A) Understand causal chains better:

1) FIVE PRINCIPLES AGAINST SARS-COV-2 AND COVID-19

Following Einstein's theories of principles, the term «principle» here refers to a solution approach for a precisely defined problem that is not derived from other solution approaches. This solution approach can be applied via different methods: For example, the occurrence of COVID-19 deaths can be avoided by the principle of preventing contact between germ carriers and infectious agents. This can be achieved by quarantining infected persons or those who have become conspicuous by testing, by blocking borders, lockdowns, etc. Another principle, which is therefore independent of the principle of contact prevention, would be, for example, the inactivation of viruses.

The primary goal is to prevent death from COVID-19. Death is the final step in a sequence of conditions without which death would not have occurred. Therefore, everyone will agree that the goal can be achieved if the substeps can be prevented. The substeps involve processes based on different principles. Suitable techniques can be used for these. If one succeeds in implementing them in an ideal way, the goal should be achievable.

These principles are:

a. Principle 1: If SARS-CoV-2 did not occur at all or disappeared, then there would be no transmission of SARS-CoV-2;

b. Principle 2: Without transmission of SARS-CoV-2 — no contact with germ carriers of SARS-CoV-2;

c. Principle 3: Without successful contact with SARS-CoV-2 — no infection with SARS-CoV-2.

d. Principle 4: Without infection with SARS-CoV-2, no manifestation with COVID-19 and no need to hospitalize a COVID patient.

e. Principle 5:

a) If all individuals were successfully and permanently immunized, e.g., thanks to an appropriately qualified vaccine, no one would be able to contract COVID-19 and would — hopefully — never be contagious again

b) If we had a successful specific therapy, the risk would decrease that a high number of the

scarce number of beds in intensive care units would be occupied for COVID-19 for such a long time

and would not have the risk of a collapse of the health care system

f. If 1–5 are successful: no more risk of lockdown because of the threat of health care system failure — no need for repeated lockdowns with their inevitable long-lasting side effects (e.g. risk of «Lost — COVID generation», economic consequences only comparable to the post-war period)

No more risk of a breakdown of the HCS — no need on repeated lockdowns with their unavoidable long-lasting side effects (e.g. risk of lost COVID generation...).

2) ARE ALL PRINCIPLES EQUALLY VALID AND ALSO IMPLEMENTABLE?

The argument is conclusive that the pandemic could be blocked by SARS-CoV-2 even if only one of the principles 1–5 is realized in an ideal way. However, this does not mean that each of the principles is equivalent in application. Therefore, they are not interchangeable. Therefore, there must be good reasons for choosing principle 2 and not principle 1, for example. If Principle 1 could be implemented in an ideal way, the measures for Step 2 would not be necessary. Then SARS-CoV-2 viruses could not develop into threatening mutants. Principle 2 has virtually no effect on the inactivation of viruses, so it does nothing to prevent mutants. It is possible that the decision against Principle 1 came about because there was a fear that Principle 1 could not be implemented ideally. This would be a very good argument.

a. Inhibition — Enforcement

Since principle 1 does not promise a resounding success, it is clear that one looked for an alternative. Principle 2 offered itself: It has been implemented in a radical way for centuries. Thanks to Kermack and McKendrick, a more «humane» way of implementation was available, which also allowed mathematically tangible predictions. Therefore turning to principle 2 and turning away from principle 1: Connoisseurs of physiology will connect this with the principles which Sechenov and Pavlov proved for physiological processes. However, it is also true for these that they are not ideally balanced: Inhibition is often overemphasized and attention and resources are inappropriately allocated to the chosen path: This is consistent with the distribution of recommended measures (e.g., WHO)

b. Collective forgetting?

Breaking the chain of infection suggests that the epidemic can be brought to a halt. But it does not make individuals in the population immune. In a pandemic, there is always a fear that the pathogens will be reintroduced. Therefore, the risk of falling ill is only postponed. If one assumes that the dangerousness of the disease remains constant and can be described by the probability of dying in the case of illness, it can be determined how many deaths must be expected if the pathogen has not been eradicated and the population has not become naturally or artificially immune. By interrupting the chain of infection, it is not possible to change this number, but it is possible to extend the time period in which people will die. This can help ensure that hospitals are not overburdened and that patients receive the available therapy for which lethality has been identified. On this basis, the chief ideologist of the Charitee had to come to the prognosis in March 2020 that in the long run ultimately more than 250,000 people would die of COVID-19 in Germany alone and that an exponentially increasing wave could be expected in the fall of 2020. Only immunity of about 85% of the population could stop the epidemic [80]. Principle 2 was obviously not sufficient. Immunity can be achieved artificially through vaccines. This may have been the impetus why the responsible politicians were willing to massively promote vaccine development. But no one assumed at the time that development could be completed before the summer of 2021, let alone the necessary licensing, production and vaccination coverage. It was therefore necessary to bridge at least 20 months without vaccination protection and also without specific medication.

It would have been possible to build on the positive experience gained with the improvement of nonspecific immunity. It is undisputed that the massive decline in the incidence of tuberculosis in the 20th century can be traced back to the improvement of nonspecific immunity. This will be discussed in the example of Austria below (B 3a) and in Part 2. It would also have been open to promote scientific interest in this option in a similar way as has been done for the development of vaccines worldwide. Any systematic literature search should have come across NCT, for example. But this has not happened worldwide. It is possible that this is a process that is well known to historians: they are repeatedly confronted with the phenomenon that millennia-old technical and intellectual achievements can no longer be made today: Just think of the processing of the enormous building blocks of the Minoan fortress walls, between which no sheet of paper fits. Or the technology required to build the pyramids. There seems to be a process that leads to collective forgetting. Otherwise, it is difficult to explain why worldwide hygienic knowledge, banal in itself, has been disregarded by recognized medical experts. Not only this: This consideration of non-specific defenses would, after all, open up the possibility of a temporary reduction in susceptibility. Nevertheless, there is no reference to these possibilities in the Saudi Arabia Communiqu? of the Presidents of the National Academies of Sciences of the G 20 countries. The experts had access to the leading specialists in all fields of science. The Communiqu? deals, among other things, with immunity, but expresses verbs only with specific immunity [2].

It is obvious: It is an ethical/moral obligation to deal with the possibilities which threaten to be lost by the decision for a paradigm which is now recognized as dominant. Thereby the problem already raised by Th. Kuhn is

that the representatives of the new paradigm assume that they would dispose of the final and only correct world view. Therefore, all world views even successfully used so far would be falsified, and all statements would have to be rejected as unscientific. But also the new paradigm is only an invention about the world. Also here one can learn from Einstein: The refuted paradigm of Newton does not lose its usefulness, if one restricts its range of application appropriately [81].

Already Sechenov has pointed out the principle that attention allocation is connected with an inhibition of other, at best essential aspects [82]. The danger of omission (Occam's razor) should not be underestimated. Therefore it needs Comprehensive simplicity (Einstein: As simple as possible but not simpler) Simplifying is helpful, but only so far that everything observable can be described separately and everything explicable remains explicable [83].

c. What was not thought of.

The first wave was caused by the wild form of SARS-CoV-2. This corresponded to the situation as given in the epidemics that have been used as examples of the course and influenceability of epidemics worldwide, e.g. in the cases described by A.Cori et al. [84]. At that time, there was therefore no reason to worry about whether mutants would occur and what influence the chosen strategy could have on them. In the meantime, this has changed fundamentally. In the meantime, there is talk of the evolution of viruses and it is understood that more aggressive, more virulent viruses and so-called escape viruses — viruses that evade the effects of vaccination — must be expected to assert themselves more and more against the «more harmless» wild form in the future. Since the development of these viruses is tied to their presence in host cells, strategies that also lead to inactivation are superior in this respect to strategies that only interrupt the chain of infection.

During the first wave, the obvious prerequisite for manifestation was that the virus, now appearing for the first time, entered the nasal and pulmonary cavities. It was therefore obvious to attribute the frequency of manifestation only to the infectivity of the virus. But this was not enough, as could be seen in the course of the summer with the decline of the epidemic to a sporadic occurrence of the diseases (e.g. graphic Carinthia) distributed over the entire province despite the increase in contacts thanks to the high season in tourism. Thus, one must also reckon with infected and infectious persons who are asymptomatic and never show symptoms and those who are not recognized because their symptoms are atypical. Indisputably, this was already the case in March for a short period before the infected person shows the characteristic symptoms. However, there are now increasing findings that such transmissions cannot be ruled out in general. They give rise to fears of a viral dark net in which inconspicuous germ carriers infect other persons who themselves remain inconspicuous. This can be explained by the fact that the occurrence of classic symptoms not only presupposes that a pathogen is present, but also that the non-specific defense is weakened, at least for a short time. In this «window of weakness» during the incubation period — which may last a long time — a manifestation may occur, preceded by a high viral load in the nose, which is necessary for the infection of others.

Precautionary testing is of little help against this. Measures to inactivate the viruses before and during the incubation period would be necessary. Overall, it seems essential to plan for these three stages in all planning and to adjust measures as the epidemic progresses.

d. The result: two monocausal approaches

No matter how the deliberations have proceeded. The result is the same worldwide: people rely on one principle to tackle SARS-CoV-2: Interrupting transmission. A second is directed against COVID-19: Vaccination. These two approaches are being pursued «with all available means» and increasingly sophisticated techniques (e.g., the collection of infected but still asymptomatic individuals by antigen mass testing). The aim may well be to reach the last unteachable. At the same time, the danger of being able to recognize others without their own infectivity should be eliminated. With it ideal effect should be attainable nevertheless.

Of course, it is true in theory that the causal chain only has to be interrupted at one point. But is this mathematically logical conclusion also applicable to the real world. We do not live in an ideal world! We have to accept: No principle can be realized in an ideal way.

3) OBJECTIVE ACTION AND INACTION ACCORDING TO THE LEGAL SITUATION

A scientist who is called as an expert to advise a decision-maker cannot be presumed to know about the particular legal situation in which he finds himself, since he is to make recommendations for action in a situation where there is «imminent danger». It is therefore assumed in the considerations below that the experts have had their particular situation and responsibilities unambiguously communicated to them by legal experts.

a. The special legal situation of an expert in an epidemic

This includes making it clear that it is not the experts who decide what happens. Exclusively the responsible minister is authorized to decide. But if he relies on the unanimous vote of the government on a regulation, all members probably share that responsibility. After all, they would not have had to agree.

The situation is particularly challenging for the scientific expert in the case of an epidemic with a pathogen appearing for the first time: As a scientist, he is accustomed to making a statement only if he can rely on the state of knowledge. But at this point in time, this can only exist in partial areas. Nevertheless, action must be taken quickly. The procedure has been clarified by law: the expert, applying the laws of reasoning and the experiences of daily life, has to represent the most probable

effect in such a clear way that this becomes understandable for the decision-maker — in proceedings under plant law, in which situations with a limited state of knowledge occur very frequently, the lawyer conducting the proceedings, in the context of the pandemic, for example, the Minister of Health [85].

A similar procedure is provided for in the WHO International Health Regulations, which have been transposed into local law in the individual member states (e.g. in Germany [86]). This legal basis is significant not only because it is designed to prevent pandemics from spreading through interstate traffic. But in doing so, the IHR also mandate that health measures must not have a greater adverse economic impact than «alternatives available at reasonable cost that are expected to provide an adequate level of health protection». The «available alternatives» naturally include all measures, e.g., the use of agents to prophylactically compensate for currently existing deficits in nonspecific defenses.

The expert must therefore also consider anticipated possibilities that can be classified as conceivable from experience with other viruses and recommend measures against them from the precautionary principle. This concerns, for example, the possibility that SARS-CoV-2 could lead to latent infections. Of course, it may later turn out that a precautionary measure was unnecessary. But nonaction must also be justified in the same way as action. But the state of knowledge should be expanded as quickly as possible. Therefore, the scientist may suggest studies for clarification in parallel with the recommendation for precautionary action.

b. The limits of the scientist's responsibility

Neither the individual scientist nor the scientific community is responsible for ensuring that the scientific facts are available that are needed to safeguard health and prevent avoidable illness and death. The responsibility for this has been placed by the legislature on policy makers. Governments have met this responsibility in the context of vaccine development. Virtually in all other areas of Principles 1–5, there is a need to catch up.

c. The equivalence of health effects caused indirectly and directly by the epidemic

For the physician and all other health scientists, there is no difference in the value of protecting premature, inhumane, and forced death. Thus, for example, protection from an increase in the rate of child suicide as a result of the collapse of the health care system deserves the same value as protection from death from COVID-10 or other preventable death as a result of the collapse of intensive care.

d. The fundamental importance of the difference between medical devices and medicines

Injury to the body by injection or ingestion of a drug by absorption is physiologically a fundamental difference from an action that is relevant to health or healing without penetration of the organism. Aids used in this process are therefore not considered medicines but medical devices. This is also reflected in the legal system: medicines are more strictly regulated than medical devices. However, in epidemics, both can be made freely available via emergency ordinances even without the proof of these conditions required under normal circumstances. In this way, the government in Israel made an antiseptic nasal spray available even to children over 12 years of age in March 2021 [87].

Obviously, two standards were and are applied: For the proof of the justifiability of a drug, empirical evidence is required that the benefits clearly outweigh the possible health disadvantages to be concretely ascertained accordingly. Double-blind studies are required for this purpose.

This is quite different for measures that do not penetrate the organism. There are no double-blind studies to prove that lockdowns, closing schools, etc. have more health advantages than disadvantages. The considerations do not even seem to include what health disadvantages might occur in the first place. One is content with the logical proof that the measure is expected to lower the specific impact on COVID-19. Whether this is legally compatible seems worth examining.

e. The obligation to make appropriate use of delegated authorizations

It also seems legally remarkable that the legislator has created the possibilities of being able to force the production and distribution of medicines and medical devices even by decree. For example, President Trump has forced General Motors to produce respirators. Obviously, the legislator has provided for the possibility of being allowed to interfere with fundamental rights in this respect as well, if this seems unavoidable from a health perspective. The presumption is that all coercive measures are only proportionate if a comparable harm-preventing effect cannot be achieved or could not have been achieved by other, less burdensome measures if the possibilities had been exhausted that Parliament has delegated to the decision-maker during an epidemic. If this reasoning is correct, then the responsible minister would probably be obliged to make available by emergency regulations a substance for which there is scientific evidence that it is tolerable and antiviral, not absorbed into the body and not injected, even if there is no CE marking.

The substitution of a current shortage of a natural defense substance (NCT) by the same but artificially produced substance seems to be one of those measures that hardly give rise to fears of adverse effects. As long as this option has not been used, it will probably be legally difficult to justify why profound cuts in fundamental rights are unavoidable and, for example, interfere with the international economy (e.g., through lockdowns).

However, the task of the experts is only to point out that such substances exist. It should be known that in Israel, in March, a nasal spray based on NO was approved by the Minister of Health as an antiseptic even for children 12 years and older by emergency decree.

f. The need for testing of laboratories

The discussion on the origin of SARS-CoVB-2 shows that it is possible to produce pathogenic viruses artificially.

According to a paper published in Science, it is known where mutations would have to be made to produce mutants that escape the effectiveness of currently available vaccines. The extortion of states with computer viruses — which was also successful — shows that every state and the community of states must be prepared that criminals could produce such viruses to cause comparable threats.

4) ADDITIONAL CHALLENGES: FIGHT AGAINST MUTANTS, LONG COVID, ETC.

This means that the tools available in the fight against the epidemic are no longer to be used only against SARSA-CoV-2 and the classical disease pattern of COVID-19. The focus is increasingly shifting to prevention of the impact of mutants, Long COVID as a pandemic within a pandemic, protection against e.g. PIMS and other specific manifestations of COVID-19 as a potential multisystem disease. Until specific therapeutics are available against the disease entities, prevention of contamination and vaccination remain the focus of options.

B) Spotlight on currently applied political strategies

1) Reason's Swizz Cheese Model and Pareto's 80: 20 Rule

Every strategy needs not only a clear goal but also clarity about the available resources and any systemic consequences associated with their use. Both have to be considered strategically. In this context, experience with risk management can be helpful. Reason has made valuable contributions to the health care sector [13].

a. Reason's approach

A discussion of risk and risk management should start from the realization: It is impossible to eliminate risk. «Life is always life-threatening» (E. Kästner). Risk management, therefore, means weighing different risks or undesirable aspects and allocating available resources accordingly. Reason analyzed man-made disasters (e.g., Chernobyl, Seveso). He came to the conclusion: the best trained and organized personnel and the use of sophisticated machines are not enough to reduce accidents as effectively as one could. The starting point of his considerations was the recognition of the fact that people are not ideal. They make mistakes. Moreover, no one can predict exactly when and under what conditions mistakes will occur. Therefore, he suggested that organizations that use sophisticated technical methods (e.g., hospitals, aircraft manufacturing, etc.) should integrate their own structures that develop and implement methods to manage the risk for as yet unknown combinations of errors [88]. In doing so, he said, one should not so much look for the culprits of errors, but rather assume that people make mistakes all the time. Therefore, he said, there needs to be an appropriate system with a culture of error in which there can be open, free discussion: What has been overlooked? What could still lead to mistakes, etc.? Outstanding people and key employees in particular make mistakes, which are then often particularly serious. In addition, mistakes that people make due to inattention, fatigue, etc. are often ultimately mistakes in the system: lack of qualified personnel, overload, poor planning, lack of technically possible safety precautions, etc. Of course, what is needed first and foremost is first-class technical, logistical and personnel equipment. But even this is only ideal in theory. People make mistakes [13]. But the cleverly structured system is built so that the types of errors of one kind are intercepted by the protections of another kind. Reason's focus, therefore, is not oriented toward combating human inadequacy, but toward building systems in such a way that several different goals, or approaches, are used so that they collectively reduce the risk of momentous errors. The diversity of different principles gives hope that an error not inhibited by principle A will be captured thanks to principle B. And if an error cannot be detected and offset by, for example, management principle A or the technical precaution of B, its effects could be detected and neutralized by a third safeguard that does not rely on the approaches of A and B. This strategic approach can be extended by many additional risk management methods. This approach would also have the advantage of capturing very different types of failures with this system. The major man-made disasters, such as Chernobyl, were characterized by the simultaneous occurrence of different types of errors. For this reason alone, different approaches are needed for management. One can compare these errors with holes that people drill into the various only theoretically dense protective walls of the system. Therefore, they appear perforated like a Swiss cheese. The catastrophe occurs because the last layer could not prevent the additionally caused error. After all, the catastrophe is only avoided if there are enough slices that de facto act like hard cheese due to their differently positioned weak points: Nothing goes through any more, although no measure could be ideally implemented. The well-known graphic (in graphic 3, top left) therefore describes the occurrence of the catastrophe — although the yellow structures (symbolizing the risk management) have been built into the structure of the aircraft production according to Reason's recommendation.

b. Mackay's interpretation

Follow-up of cheese slices with holes has recently been used to address the need for tools to combat COVID-19 in a comprehensive manner. J. M. Mackay, an Australian virologist, developed the «Swizz Cheese Respiratory Pandemic Defense Model» based on J.T. Reason [89]. It has since been modified and translated into many languages. It serves as a demonstration of the steps necessary to adequately fight the COVID-19 pandemic. The wide acceptance of this clever graphic is reflected in the high number of translations (more than 20) and the discussions in blocks of famous newspapers, e.g., the Wall Street Journal or the New York Times. Even leading scientific journals refer to the presentation, e.g. in the BBC [90]: no word goes in the direction that this model would not be sufficient.

This model is later used to characterize the current situation in many countries (e.g., Austria) at the end of 2020. However, Mackay's concept already differs significantly from Reason's concept: Now it is not used preventively, but as a guideline for concrete action, and this without taking up Reason's recommendations for the additional services needed to make Reason's special approach to risk management about the benefits of error culture effective. In addition, no one is asking: are the «traditional» resources, sufficient staff, etc., available for the challenges currently being encountered?

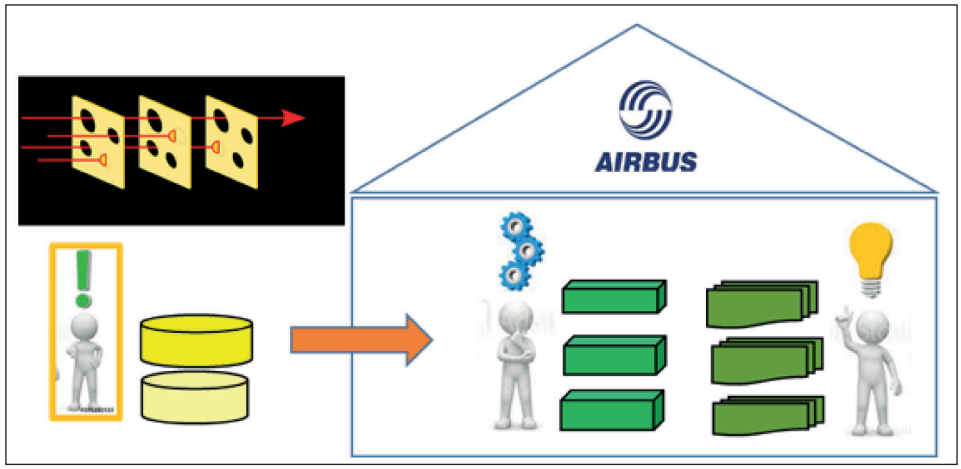

Fig. 6. The integration of a risk management unit into a well-organized enterprise

Other deviations from the concept:

a) Reason proposes his own approach to managing the risk of highly complex machines and techniques that can be inadequately managed by individuals within a complex organizational system. In doing so, he assumes that people make mistakes all the time. We must learn to live with the errors and develop appropriate systems so that the errors are reduced rather than compounded. In his examples, Reason assumes that systems are necessary and that they are constantly improved as a precaution through an appropriate error culture. The problem of errors thus concerns processes of quasi-ideal man-made techniques and organizational structures. However, an infection is not a technical process, but a natural biological process. It runs without machines, supervising persons or complex organizational structures. The natural processes involved are therefore not planned on a drawing board. Much of it is not yet known to us. But we intervene in these processes in many ways, consciously or unconsciously. Our systems must therefore be much more flexible. Error culture is already essential in the «standard case». Here it becomes indispensable. However, the approach does not address this.

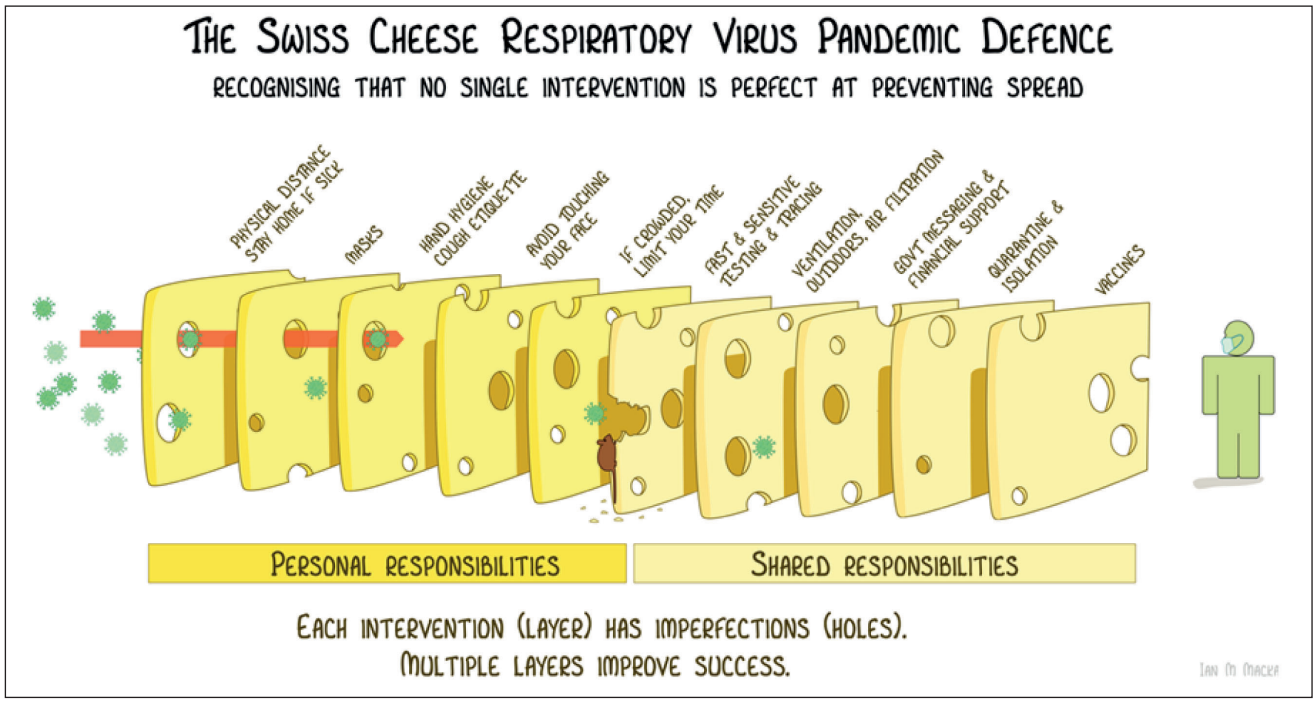

Fig. 7. The version of MacKay of a Swiss Cheese Model according to J.T. Reason for a comprehensive fight against COVID-19 (MacKay I. M. virologydownunder.com)

b) The reasons why people are responsible for errors when operating machines can also have many causes: They range from distraction, drunkenness, forgetfulness, fatigue, lack of practice in dealing with new situations, to sabotage. This can be counteracted in a targeted manner. But often personal errors are also consequences of system errors. This alone shows that a mix of methods is indispensable. Risk management basically needs different approaches for this, not only different methods, in order to reach the SAME final goal — in the chosen approach, the avoidance of contact with infectious agents. But this is not what the modified model provides.

c) The holes in Mackay's diagram exist regardless of what the acting persons do. This means that the individual techniques, systems, etc. are inherently assumed to have severe deficiencies in prevention. But that is not what Reason was implying at all! Theoretically the procedures etc. would be quasi ideal. But the persons make the mistakes! Moreover, Mackay arranges the cheese slices one after the other. This is supposed to give the impression that the third slice normally compensates for the error of the second slice. But this is not the case in Mackay's approach against the spread of the pandemic: If viruses get through any Emmental slice, infection can occur. Then it doesn't help if so many more holey slices are supposed to protect you. Once you have been infected, e.g. as a result of «maskless» contact, the strict controls at the airport no longer help.

d) Mackay's graphic contains two creatures, a mouse enlarging an existing hole and the threatened person. The mouse can stand for «corona deniers». These undermine so-and-so's already holey effectiveness. Just as well, this mouse could stand for those who deny the biological nature of the infectious process, or even those who purposefully prevent the options provided by it from being considered («antiseptic deniers» etc.). But this kind of presentation underlines the systematic weakness: The holes in the cheese just belong to an Emmentaler — even without human intervention. Humans can still increase the risk out of malice. But this idea does not correspond to Reason's position. The system of cheese slices would be tight if it were implemented ideally thanks to the dynamics between the individual system approaches. People are flawed — even without bad intentions. Therefore, only one symbol for people should be used.

e) The core problem, however, lies in the fact that — with one exception — all the measures listed are only modifications of a single principle to achieve the same goal: To prevent contact of the infectious with the infectious. That this is a principle to prevent the cascade of steps from the appearance of pathogenic agents to death from infectious disease is indisputable. (See Principle 2) But one should not expect to be able to implement a concept ideally in a non-ideal world with non-ideal people. The contact of the infectee with the germ carrier is — like the presence of SARS-CoV-2 — a necessary but not a sufficient explanation: neither for a peron to become infected with SARS-CoV-2, nor for the infected person to also manifest COVID-19.

f) There is, however, one exception to the set of listed measures: The Emmental disc for vaccination. It belongs to the principle No. 5 listed under B. It is good that this slice is also shown with holes from the beginning.

The graphic of Mackay is therefore very helpful to show the different tools of the same «principle». A variety of tools for a principle is also consistent with the principles of risk management: there are usually several ways to increase the efficiency of a given principle. These must be skillfully integrated, not only for the goal of reducing risk from contact with vectors. Therefore, this type of graphic will be used later to illustrate the different tools of the different principles.

c. Pareto's 80:20 rule

However. A hospital or a company that manufactures airplanes must also use the money available for risk management. When allocating resources, one can rely on the Pareto principle: One can achieve 80% of the achievable effectiveness by using 20% of the resources. For the remaining 20%, one would have to use 80% to achieve the total possible 100%. This is another reason why it makes sense to combine tools: This applies equally to the different tools used according to the same principle and to the allocation of resources to different principles. Thus, using 100% resources for risk management could theoretically achieve 400% if resources were allocated according to 5 different equally effortful and effective principles to achieve the same end goal.

The increasing use of resources to persuade people to vaccinate after all shows the effectiveness of Pareto's approach here as well. It seems worth examining whether it will be possible to achieve the 85% vaccination rate that is now required, even with maximum effort. Doesn't it make more sense to consider how to achieve the goal of epidemic hygiene by other means?

d. The «post-hoc» application.

Mackay does not use Reason's proposal to be prepared for a risk that is to be expected. He applies it as a guide to action for a disaster that has already occurred. The first question, therefore, is: Are the conditions for a successful fight in place? If not — then make sure that all the necessary equipment, qualified personnel, premises, etc. and a clear strategy are available! If the available means have been deployed, but the expected success has not occurred, there needs to be an appropriate open fault analysis — preferably without attributing blame. Is it the people? Is it the system?

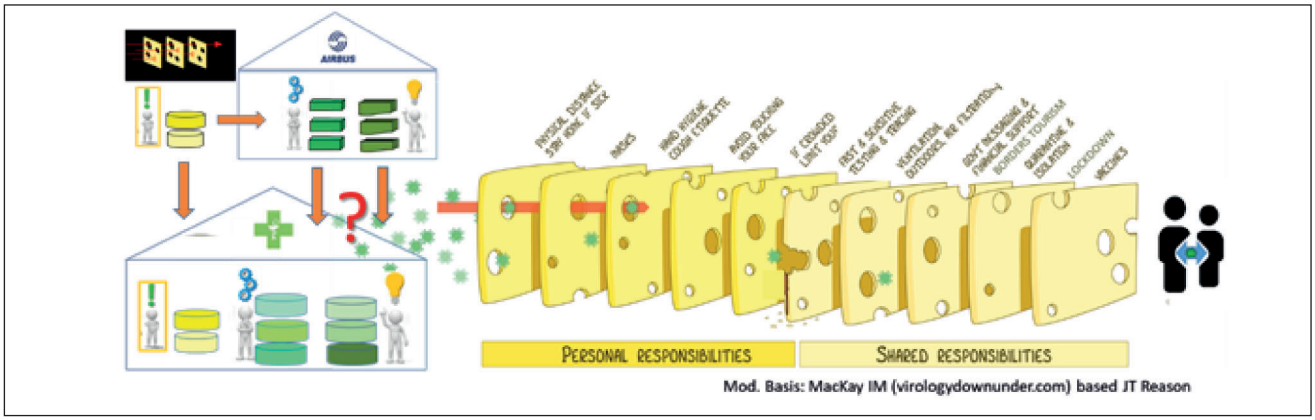

Fig. 8. For «MacKay's Swiss cheese model», the application-oriented framework conditions must first be created so that they correspond to the starting point of Reason's well-equipped ventures: There was/is a need for infrastructure expansion in virtually all areas to address the ongoing epidemic

- Then there are two conclusions:then expand or adjust the range of services through an additional precautionary principle in the hope of thereby being able to lower the threat to an acceptable risk, at least in the future.
- change the emphasis in the access, arrange the distribution of the resources including the manpower in such a clever way that the given problem can be treated appropriately! Personnel, etc., must therefore be shifted from their traditional activities to fighting the disaster, perhaps in terms of the 80: 20 rule. Otherwise, an unjustifiable lack of otherwise necessary efficiency must be expected, e.g., if all police officers have to do is to check the correct application of the quarantine and removal rules, or if hospital beds are not allowed to be occupied according to need in order to keep them free for COVID-19 patients.

2) The changes in the situation.

a) Initial situation — integrated into the «Swizz Cheese Model».

Mackay's graphic contains the planned elements of the strategy used in the West, but leaves out the question of resource availability. However, it was precisely their lack that determined the initial situation in many Western states: Pradeto's analysis showed the differences worldwide [91]. He points to a multiple failure of WHO, the EU and Germany in the Corona crisis by June 2020, a situation without collapse and with low incidence and mortality rates. He pointed out the shortcomings in the availability of adequate technical resources, logistical structures, national and international communication systems, a lack of well-trained personnel, sufficient space, etc. Various countries in Asia and on islands were much more successful: these had drawn the consequences from MERS and SARS.

So far, these deficiencies have been remedied only partially and at extreme financial cost. The consequences can also be seen in the large differences in the declines in, for example, gross national product in different states.

This situation forces the relevance of a comprehensive medium- and long-term strategy. Training well-qualified staff, e.g. for the intensive care unit, takes years. Is there a need for health-oriented land use and urban planning due to the negative consequences of the proximity of infection departments in the center of hospitals? There are experiences that the fear of being infected in the hospital was a reason not to go to the hospital. How do you solve the education problem if epidemics are expected to continue in the future? How do you integrate the currently deferred but overall determining restructuring (climate change, energy demand...) into the overall concept, etc.?

Therefore, Mackay's graphic had to be modified to fit the initial situation: It needs infrastructure, not «mice». It needs the basic structures of the system for the people involved and cared for according to Reason's considerations.

b) The situation at the turn of the year 2020/2021.

Contrary to forecasts, the pandemic could not be controlled in many states. This was not achieved despite several lockdowns, which have now lasted for months, and only more or less significant facilitations of everyday life. Currently, the fight against the imminent collapse of the health care system determines the measures. We have thus reached stage 2 of the epidemic and no longer stage 1! In addition, new mutants determine more and more the events. They force the reorientation e.g. of the adjustment of the vaccines and limit again the possibilities to turn with indirect health consequences and the lining up general structure problems. There are therefore good reasons to assume that we are in the transition to stage 3.

The strategy adopted in spring 2020 has not been fundamentally scrutinized. The range of measures has also not been changed significantly to date. What has

increased is the duration and consistency in prosecuting those who do not comply with the measures to avoid contact with those who may be infected.

Therefore, the Mackay's Swizz Cheese model is well suited to represent the current situation along with the measures taken so far, if some measures are added: These are border control, lockdowns, and the CORONA APP. But the thrust of these measures is the same: to detect (potentially) infectious persons early, to keep away from infectious persons also thanks to simple hygiene principles, to successfully trace back the contact chains.

However, the situation is determined by the inevitable, unintended effects as a result of the fight against the collapse of the health care system. Currently, in many countries, the danger of having to allocate beds in intensive care units according to the patient's chance of survival seems to have been averted. But this is not the case everywhere. The stresses of the restrictions on freedom of movement that have now lasted for so many months, the compulsion to home schooling and the consequent increasing threat of loss of irrecoverable influences on personal development and teaching units (Lost COVID generation?), home office, the increasing tensions in families, the economic consequences, being locked away without culture or sport, etc. are probably having long-lasting effects. On various occasions, there have already been public violent confrontations. Is it really only a matter of time before civil war-like conditions arise? Unemployment has reached levels not seen since the end of World War II. And this despite the fact that short-time work is an irreplaceable means of preventing the collapse of the economy. The confidence of many in those responsible, but also in each other and in their own ability to shape the future for themselves and their own, is dwindling more and more. Worries about basic rights are depressing many. The willingness to show solidarity within one's own sphere of life, but also globally, is being put to the test. Important indicators of stability in communities are deteriorating, such as the Gini index. This indicates how wealth is distributed in society.

Many people probably find it particularly depressing that not even the next few weeks can be planned in advance. Everyone is given the hope that at the latest when enough people — supposedly about 60% or even 80% or more — would be vaccinated, everyday life would return, without masks and restrictions in leisure time, travel, school attendance, etc. However, more and more reports, e.g. of mutants, which may currently be difficult to address by vaccination, make it clear that this «light at the end of the tunnel» could once again be just a mirage. The number of scientific papers showing that COVID-19 cannot be defeated by vaccination alone is increasing almost daily [92]. This is also the view of key figures in the

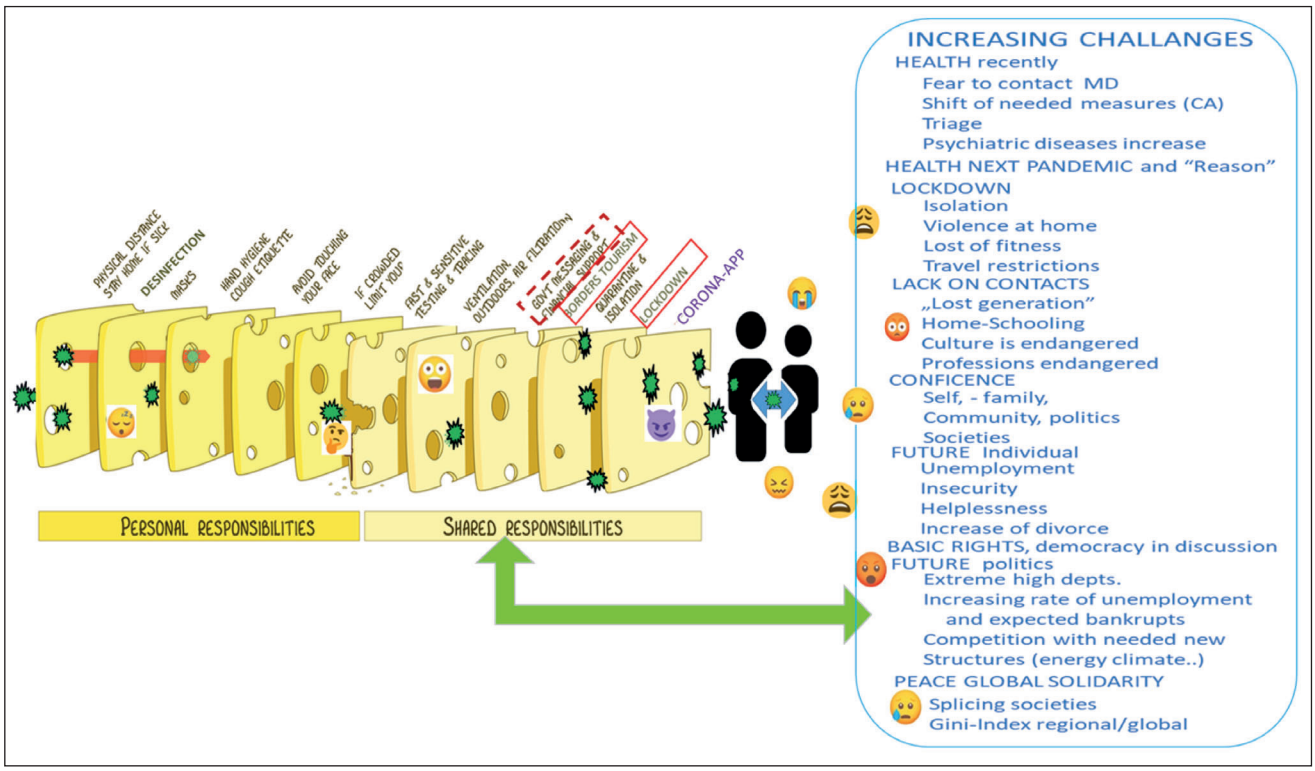

Fig. 9. Balance sheet of one year of adherence to the effort to fight the pandemic practically exclusively by preventing contact of people with germ carriers and hoping that vaccination will ensure the return to the state of 2019 not only in terms of individual hygiene, but also in terms of epidemic hygiene

day-to-day fight, such as the president of the Red Cross [93]. But this has hardly been communicated to the general public. The shift of societal activities from the focus on «stabilizing intensive care» to other even indirect health challenges could therefore take even longer than hoped.

It is now far from any scientific conclusion to assume that the health consequences of unemployment, for example, can only be attributed to the lack of money. The cause of much of this damage touches on the essence of the processes that make Homo sapiens Line? a psycho-socio-cultural person: The way situations are individually evaluated and how these intellectual, cognitive or emotional classifications lead to a holistic response. This also relates to the modification of biological processes. Part 2 will discuss this in more detail. In Part 1 these connections were briefly pointed out: There also the profound effects on the concentration of immunoglobulin A in the saliva are presented, which the change of the meaning to the identical and harmless substance in the air had, if it was classified once as more, the other time as less toxic [94].

The graph 9 illustrates that all these processes and the related evaluation processes and other consequential effects also have influences on the susceptibility of individuals to SARS-CoV-2. However, this cannot be detected by the prediction models, which are only designed to detect the sufficient or insufficient interruption of contacts.

3) Frameworks and experiences

a. Experiences from Europe including Austria

However, almost all European countries have decided to follow the path described above in the fight against SARS-CoV-2 and COVID-19. Accordingly, those responsible still believe that they will ultimately be able to implement these principles in an ideal manner. This approach has one more advantage. It can be implemented by means of a decree: Its effect also appears to be mathematically detectable. If the calculated effect in the reduction of new infections does not occur, one seems to be justified in assuming that the measures were not implemented correctly. «Blame» is then placed on the citizens. Therefore, nothing helps but to tighten control and extend the duration of restrictions. This will be understood by all those who have complied with the measures: We must manage to bridge the time gap so that the specific vaccines can be developed and distributed to all.

Again, it is assumed that after vaccination coverage all problems would be solved. Life would be the same as in 2019. Everyone knows such stories in different variations, which are repeated similarly even now. The only problem, he said, was finally implementing the restrictions that individuals were ordered to inhibit transmission. But if one would take into account that already Kermack and McKendrick pointed out that even small deviations in susceptibility can have decisive consequential effects, one would have to think of other causes as well.

Austria and many other European countries began an immediate lockdown in March 2020. They gradually weakened the restrictions thereafter, in line with expected declines in the rate of new cases. Their extent was based on the predictions of descriptive and experimental epidemiology. The measures were limited to reducing, in particular, contacts between healthy persons with infected persons or possible other carriers of SARS-CoV-2, so that the so-called R-value (reproductive number, i.e., the number of secondary infections caused by each ill person on average) should be below 1. This was realized over many weeks in May 2020, but COVID -19 did not disappear. On the contrary, after a phase in which the epidemic seemed to have ended in wide areas (see the curve in Carinthia), the second rise began with unexpected intensity, not only in Austria.

For Austria, a new start was then made in forecasting and implementing the measures. Suddenly, the need for a third «hard lockdown» with massive restrictions was appropriate. But as with the previous forecasts, the expected improvements did not materialize. The risk of a collapse of the critical care system remained. Such mispredictions do not only characterize the situation in Austria. Press and Levin therefore called for the introduction of additional U.S. federal authority to model pandemics «to be better prepared to save lives in the future». Kofler and Nagl supported this editorial by suggesting that the overall strategy for COVID should also be adjusted-beyond the need for better modeling in the future. [95]. Kofler, Glazachev, Lysol, and Tellnes began the discussion, «Is the fight against COVID-19 enough?»[11].

b. What can be learned from others?

The only global commonality seems to be that all countries have the same emphasis in the methods used: Contact restriction by all socially acceptable means, reliance on vaccination as a solution where financial strength permits. Nevertheless, successes vary.

i. «Nip it in the bud».

Some states have succeeded in becoming «SARS-CoV-2 free». What they have in common is that they have succeeded in keeping the carriers localized. The basis for this in all cases was that germ carriers were rigorously shielded and contacts were massively restricted. This was implemented particularly radically in WUHAN. The «Diary from a Blocked City» provides evidence of this from the point of view of one of those affected [96]. By interrupting the chain of infection, it is possible to stop the epidemic and, at this stage, the spread of the germ outside the quarantined area. It does not change the susceptibility of the individuals. As long as immunization is not achieved, the sword of Damocles of a COVID-19 epidemic continues to loom as long as SARS-CoV-2 viruses are present somewhere on earth. Therefore, profound measures are permanently necessary. In China and other countries, it has been made compulsory to carry a cell phone at all times. With it the position of each citizen is centrally seized. Nevertheless, clusters occurred in China. These were controlled with rigorous and wide-ranging quarantine measures. Systematic controls continue to be

carried out on who is allowed to enter the country, e.g. to South Korea. The goal here is also artificial herd immunity through vaccination. China is the only country whose economic output increased — albeit slightly — in 2020. The decline in economic output in South Korea is remarkably small.

Various island states (Australia, New Zealand, Iceland...) have also managed not to be included in the pandemic with a broad epidemic and without being able to permanently monitor the position of each citizen. They have been able to «nip the epidemic in the bud», also through consistent contact avoidance. The risk of introducing a new epidemic remains. To ensure that this does not occur, Australia and New Zealand have currently imposed massive travel restrictions. And anyone who enters the country nevertheless has to endure long and expensive quarantine stays in special hotels. Thus, travel to these countries will be prevented for foreigners for practically the entire year 2021. Again, hope lies in herd protection through population-wide vaccination. The two far-flung island states of New Zealand and Australia are among the countries with particularly high economic consequences. But this is likely to be primarily due to the global consequences of the temporary collapse of the transport system, and thus of supply chains, rather than to the cost of testing, large-scale construction of new infrastructure to combat the epidemic. Countries such as Australia and New Zealand are therefore particularly affected by the global consequences of the pandemic in other countries. As a result, issues such as stockpiling, «basic self-sufficiency», etc. become important not only from the point of view of epidemic hygiene. Fundamental considerations will probably also be necessary in the context of «tourism», not only in Australia.

The global management of the pandemic in the low-income countries should therefore be an indispensable focus, at least in the medium-term strategy of combating the disease, if only out of self-interest.

It might also be of interest there to consider more complex preventive approaches in order to be prepared in one's own country if the protection provided by vaccination is not as far-reaching and lasting as hoped.

ii. «The thing got away from us».

Despite considerable efforts, the majority of countries did not succeed in using the initial phase of the epidemic to eradicate the viruses. It may be that this would have been possible in the initial phase of the epidemic, or would be possible in a new pandemic using more complex approaches. This is a question that should be addressed today as a precautionary measure. In principle, the same two monocausal approaches (contact interruption — vaccination) were used, but with less success. But currently the German Chancellor Merkel describes the situation correctly: «The thing has slipped away from us». Therefore, in countries where the local distribution of germ carriers can no longer be estimated, the question should be openly asked today whether this nevertheless very one-sided concept can still be promising under the now fundamentally changed epidemic hygiene conditions?

The framework conditions for the feasibility of measures, which are already given by cultural-historical differences between systems in China and Western Europe, indicate that increases in the intensity of measures that are basically oriented toward the same coping strategy will sooner or later reach their limits. Necessary adjustments and expansions of the range of measures can be implemented more easily if one is still allowed room for maneuver.

iii. The beacon from Manaus

The whole world looks with pity on Manaus with its more than 2 million inhabitants. Nowhere was the incidence of disease and death as high as in Manaus even in the first wave. On the one hand, this led to excess mortality and, on the other, to an infestation in which herd immunity was to be expected. Nevertheless, the rate of new cases and deaths increased exponentially and again with COVID-19 in December, as if the first wave had not occurred. This was caused by mutant P1.

Mutants are formed in the bodies of infected individuals, as explained above. These individuals can thus pass on mutants other than those with which they themselves were infected. They thus become the starting point of the next generation of an epidemic. Herd immunity to the wild form of SARS-CoV-2 has not protected people in Manaus. Vaccines can be adjusted to the specific structures of the mutant. This is now happening at an encouraging pace. Nevertheless, this requires time. Time is also needed for production, distribution and inoculation to the entire population, as well as another 3 weeks for vaccine protection to kick in. That's several months, requiring appropriate measures (lockdowns, school closures...?). Then the danger of serious diseases and deaths is largely averted, although no vaccination is 100% effective. The question of the potential importance of vaccinated people as carriers of the germs that give rise to the prevention of the disease remains open.

The situation in Manaus only makes clear what is to be expected in principle: that infected persons can become the starting point of mutants. This applies irrespective of whether they are ill with classical or atypical symptoms. And even more so for asymptomatic diseases. Persons with latent viral load would be particularly critical: viruses then have a long time to develop increased plasticity.

The 2nd generation of the epidemic with P 1 will probably not be the last. One must be aware of the danger of an arbitrarily long succession of generations of epidemics with mutants of SARS-CoV-2. This requires further preventive measures. It is not enough to prevent the transmission of the virus. Efforts must be made to destroy the virus before it reaches humans and, in particular, the indoor respiratory tract. Thus, for example, the air in

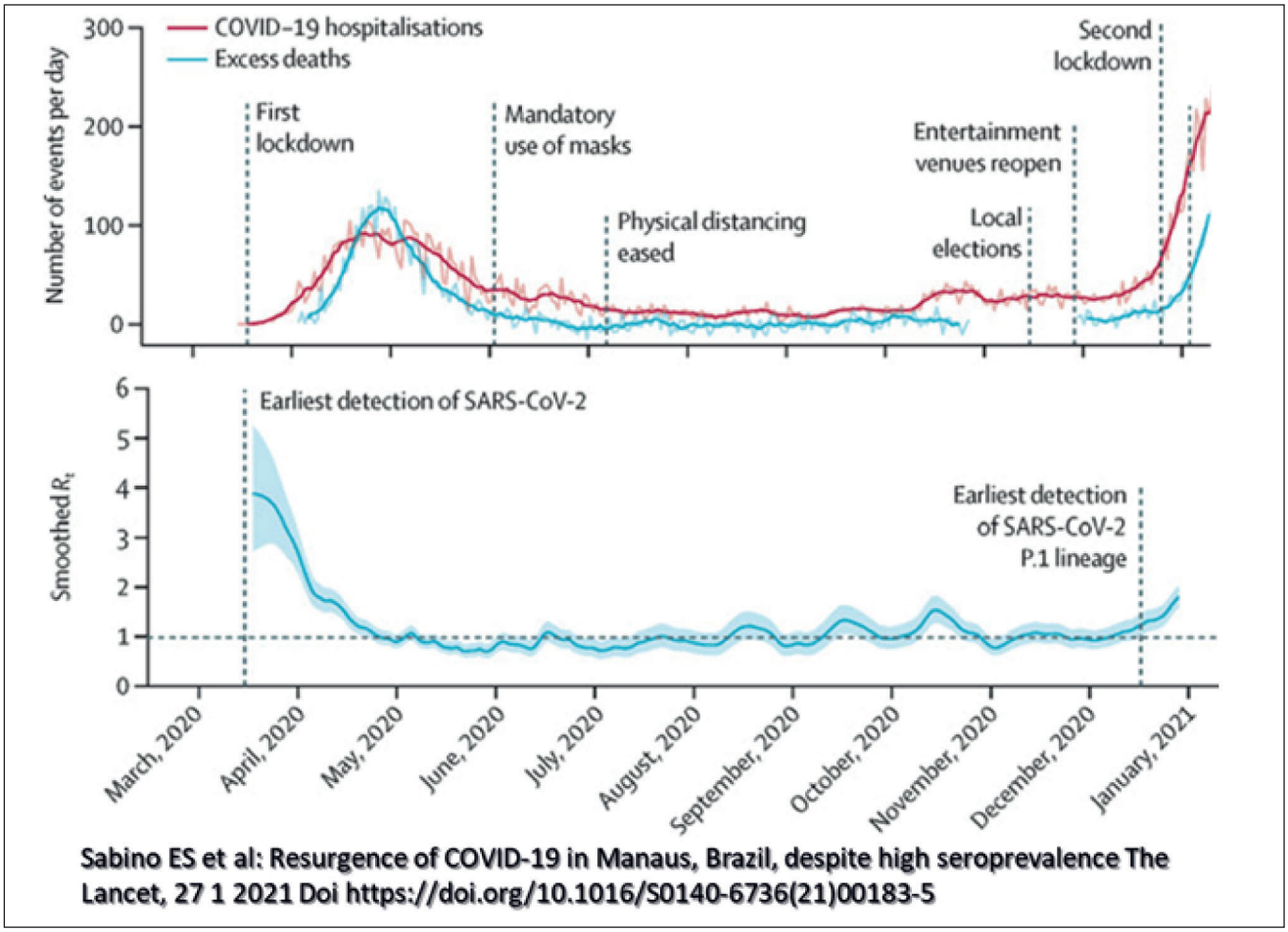

Fig. 10. Wave 1 (wild form of SARS-CoV-2) and Wave 2 (with P.1.) in Manaus

schools, ships, department stores, hotels must not only be exchanged, but filtered or inactivated with UV, ozone, etc.. But especially to prevent contamination or infection by antiseptic measures preventively during an epidemic or cluster: Without wild form in the host cells, no mutant that can be spread by the host cell.

c. Inferences: (at least) three stages of epidemics.

In any case, global experience to date suggests that different stages have occurred in the course of pandemics in different countries. This makes it necessary to adjust the strategy. But these adjustments have not been made.

a. The initial stage is characterized by the fact that the germ carriers can be confined spatially with sufficient precision to as small an area as possible. These are the cases described, for example, by Cori et. al. [84]. The processes can be focused in the short term on the control of one pathogen, i.e., SARS-CoV-2. The goal is to prevent spread, but also to prevent mutants from forming. As long as the virus is not under control worldwide, permanent precautionary measures must be taken.

b. If the spread of the virus could not be contained locally, the strategy should be fundamentally reconsidered and metrics sought that are meaningful for the new situation. The conventional calculation methods will be used for the possible and expected clusters. Their application to second-stage epidemics suggests misalignment. After all, they do not allow the assessment of all the reasons that may have prompted the transition from stage 1 to stage 2.

c. The less it has been possible to prevent persons — even if only temporarily — from becoming carriers of wild forms or already existing mutants, the greater the risk that they will become the cause for the spread of new mutants. In principle, it must be expected that the plasticity of SARS-CoV-2 can lead to mutants that are much more pathogenic and virulent, but also more successful against the use of vaccines. Therefore, it is not enough to prevent contact with the viruses, as essential as these techniques are. The viruses must be inactivated as far as possible in the immediate vicinity of everyday life (school, shopping....). Techniques are already available for this purpose. They can be used at short notice, e.g., in large-scale test series, not only to detect germ carriers at an early stage, but also to

reduce their viruses preventively thanks to antiseptic. The expansion of the range of possibilities justifies international cooperation comparable to that achieved in the development of vaccines.

d. The history of mankind shows that the possibilities were used to obtain own advantages, even if others were harmed against better knowledge («Semmelweis effect»). Even more frightening is the experience that existing possibilities are used for criminal purposes and to harm the «enemies». Therefore, it should be expected that a new global threat may emerge because knowledge is now widespread on how to create pathogenic and virulent mutants

4) International analyses of the strategies

In addition to the studies that examined the effectiveness of individual pandemic response operational measures, comprehensive analyses are now available that analyzed, from a variety of positions, the principles that must be followed if COVID-19 is to be successfully addressed and be the «last pandemic». Only three key contributions can be addressed here. Detailed conclusions will be addressed in Part 2. For an understanding of the necessary operational procedures, which are indeed the focus of Part 1, it is sufficient to address key messages.

The IPBES started in October 2020 with its report: The starting point of most pandemics are pathogens that have jumped from animals to humans due to deficiencies in the consideration of the Necessary Biodiversity. The main reason is that animals and humans live too close together. The number of potentially threatening viruses alone is estimated at 650,000 to 800,000. If we want to end the era of pandemics, we need comprehensive and fundamental measures that are closely linked to, for example, climate change, food habits, spatial planning, mobility, respect for cultural identity, and so on. Therefore, IPBES invites experts from a wide range of disciplines to support its biodiversity efforts. This invitation is not or only very generally addressed by the following conceptual analyses [1].

The paper prepared for the meeting of the G20 countries in Saudi Arabia by the presidents of the National Academies of these 20 countries is oriented practically exclusively to economically relevant research developments, such as the development of further vaccines and therapeutics, the worldwide use of modern internet networking, the expansion of the circular economy (reduce, reuse, recycle). This is probably in line with the expectations of the representatives in the G20 meetings [1].

The World Health Council has mandated the Director General of WHOI to establish an independent panel to analyze the strengths and weaknesses of the measures taken by member states and to make proposals for optimization. This «Independent Panel for pandemics preparedness & response» concluded that the pandemic could have been prevented if international coordination had been more effective under the direction of an adequately resourced WHO. It also points to other limitations in international cooperation, e.g., the use of urgency in aid for profit maximization. The concrete implementation at the local level is left out — probably in line with the mandate — as well as the connectivity to the demands of IPBES and the S20 [2, 4].

Already in May 2020, A. F. Pilon had presented a philosophical analysis of the complex problems that existed in principle after the first COVID-19 wave and that would have to be expected to develop. Based on Binswanger`s dimensions of being-in-the-world, the key problems of our time, such as crime, pollution, injustice, but also epidemics and the way they are managed, are only the manifest expression of political, cultural and economic interdependencies of persons. But this would remain largely unnoticed. These interdependencies and the relevance of individual interests must be recognized and taken into account. This is because mutual respect, a sense of responsibility, etc., are also an expression of the processes of balancing the interests of individuals. This is because mutual respect, sense of responsibility etc. is an expression of the weighing processes between value patterns of the individual as a member of communities. A change in value patterns would then also lead to the expectation of changed actions [97]. Such considerations are connected to Darwin's largely neglected assumptions about the essential further development of Homo Sapiens from the primate to the recent person: In the further development of «sympathy independent of (sexual) love» until «thanks to his intellectual power.... his sympathies were further extended so that they extended to all men of all races, to the weak, infirm and other useless members of society, at last even to the lower animals». [98].

C) Analysis of the application-oriented implementation

We have distinguished above five different principles on how to theoretically make SARS-CoV-2 or COVID-19 disappear. Current policies in EU countries and many other countries are based only on the following two principles:

1) Principle Nr 2: Without transmission, no contact with germ carriers of SARS-CoV-2.

To this end, policy makers have implemented the methods described in the graphic above. If these measures could be implemented ideally, all secondary infections would indeed be prevented. The person who brought the virus into the country would be isolated, could be cured and therefore released immune. Or he would die. SARS-CoV-2 would be destroyed. COVID-19 could not reoccur unless a germ carrier brought SARS-CoV-2 in again from the outside.

This is obviously pure theory. In the meantime, SARS-CoV-2 has spread worldwide. Everywhere there are infected persons with and without symptoms. Island states do prove that it is possible to be SARS-CoV-2-free if

they succeed in preventing the spread and subsequently implement extremely strict controls against the introduction. But this is also fraught with consequences: in Australia and New Zealand, the borders are virtually closed to entrants for the entire year 2021. Therefore, even this path does not lead to a «normal state» as it has been in 2019. After all, it must always be expected that an epidemic can occur as soon as even one infected person enters the country: after all, no one is immune as long as vaccinations are not carried out.

Normality has also been achieved in China, but a different one than in 2019. The epidemic was achieved through extremely consistent contact prevention and tracking measures. The lockdown in Wuhan lasted 60 days, much longer than would have been necessary according to model calculations. The segregation measures, even of suspects, were extremely restrictive. Since then, everyone has had to carry a cell phone so that every step can be centrally monitored. Nevertheless, there were sporadic occurrences of SARS-CoV-2 cases. They were again met with extreme restrictions. However, China is probably the only country that had economic growth in 2020.

Basically, successfully stopping contact with infectious individuals will not change the proportion of infectious BARES in the short term or permanently. Therefore, the risk of being infected with SARS-CoV-2 is only postponed. Therefore, the risk remains unchanged that one can also become manifestly ill and at best die from or with COVID.

The risk of a severe disease or of dying from COVID can so far only be decisively reduced by vaccination. The chance of being cured despite severe disease will also be increased by the currently so hopeful developments of specific drugs. However, their widespread use is still a long way off.

2) Principle 5a: Full protection through artificial herd immunity

If all persons were permanently immunized, e.g. thanks to a vaccine, so that no one could infect a third person and not fall ill again, no one could fall ill with COVID-19 and therefore no one could die of or with COVID. This also seems logically compelling and is also communicated worldwide in this or a similar way.

Not only that the vaccination alone would theoretically still take many months, it is obvious that these assumptions are also only pure theory: There is no vaccination that is 100% effective. There are large groups of people who should not be vaccinated (e.g. pregnant women) or are not allowed to be vaccinated (currently no vaccine for children). In addition, there are those who refuse to be vaccinated. And how often must vaccinations be given? The question is still open, to what extent the vaccination leads to the fact that the vaccinated person is eliminated as a potential carrier in principle — and therefore also permanently. The question here is whether the vaccinated person not only does not become ill himself in the event of subsequent contact with an infected person thanks to the existing or newly formed antibodies, but is not able to pass on viruses in any phase (including the phase until the pathogen enters the body and triggers the booster effect there for his own protection). The question of vaccine protection against mutants is also open. Good: Today, vaccines can be adjusted relatively quickly. But what if a fundamental change occurs tomorrow, the day after tomorrow or in three years' time and again completely unpredictably? Then not only will the vaccine need to be modified, but it will also have to be distributed worldwide? And what about in this phase in between? The next «post-war analog» collapse?

What is indisputable is that vaccination coverage is a crucial step in enabling the transition from an epidemic to an endemic course associated with low numbers of cases, with sporadic clusters at best. The risk of recurrence of epidemics with new mutants remains. The emergence of the current determinant mutants (from Brazil, England, India) shows: SARS-CoV-2 is only under control when the pathogen with all its mutants is under control worldwide. In addition, SARS-CoV-2 is only the current pathogen from the countless possibilities of the emergence of human pathogenic viruses. Therefore, it could be crucial to reduce the conditions for new emergence of pathogenic viruses (e.g., concept of IPBES).

Therefore, a new epidemic must be expected at any time, even with full vaccination coverage. The pharmaceutical industry has made encouraging progress, so that adjusted specific vaccines can be expected relatively quickly. However, during the phase leading up to their use, non-specific tools are needed to temporarily reduce susceptibility to pathogens that are not yet known. In principle, this can be achieved by methods that target the non-specific defense system. So far, these possibilities have been dispensed with.

D) Expanded possibilities thanks to all sub-steps of the causal chai

No one will deny that interrupting contact between germ carriers and infectious persons can effectively intervene in an epidemic. But why not use all the other possibilities that are available? This question should be at the top of the list when one sees that the measures taken so far have not brought the desired success. And this despite the fact that efforts are being made «with all available means» — i.e., using 100% of the available resources — to implement a single principle against the spread of SARS-CoV-2 and a single one against COVID-19, without achieving any lasting success. Here, borrowings from Reason and Pareto might be helpful.

The point, then, is not to abandon contact interruption options. It is about using available resources in a way that balances all available opportunities. If Reason and Paretto are right, this should lead to an improvement in the situation.

Strictly speaking, the dangerous thing is not the contact between people. It is the fact that a person carries the pathogen with him and therefore the germ can be transmitted from him to others. So if this carrier had not been exposed to the virus himself, because the pathogen no longer existed or was not currently present, he would not have been in danger of infection. Then his contact with others would be insignificant. But this is not the beginning of the causal chain that can ultimately lead to death from COVID-19: It all starts with the appearance of the new pathogenic mutant from the large variety of CORONA viruses.

But SARS-CoV-2 is now airborne because infected and sick people exhale the viruses. Why should there not be environmental factors, for example, that influence whether SARS-CoV-2 can reach another person at all. Can these also be used purposefully? Is there more than airing and hand disinfection? With these measures one is already at the transition from principle 1 (without SARS-CoV-2 no transmission) to principle 2 (without transmission no contact with an infected person) and thus to the methods, which determine at present the fight against SARS-CoV-2. After all, everyone knows from their own experience that you don't have to get sick right away if you are infected. This is true for a minor abrasion, which can heal without problems but can also become festering, just as it is for respiratory infections.

a. Every mother knows when the sweater protects the child from the respiratory infection

And every athlete knows that it is easy to catch a cold when standing exhausted and sweaty in the draft. And even more so, mothers know this: as the saying goes, «A sweater is a garment that the child must put on when the mother is too cold». The germ density does not become smaller, because one puts the anorak, the sweater or the rain cape over it. The non-specific defense can be artificially increased. The right clothing is just one example! Shouldn't all this also apply to SARS-CoV-2? This concerns the principles No. 2 and No. 3: Without contact no infection as well as without infection no manifest illness. Possibly not every schoolboy knows this (as Gregory Batson underpins the validity of his core statements). But every medical student had to know this at least during the examinations from hygiene, social medicine and probably also physiology. Nevertheless, so far the possibilities offered here remain unused by the political decision makers, although one can influence the unspecific defense with it. Remarkably, there is no reference to these possibilities in the resolutions of the National Academies of Sciences of the 20 CIS countries, although the various networks are discussed in detail there. With their help, it is possible to achieve non-specific immunity for a limited period of time and to reduce the risk of spreading germs. This is exactly what is urgently needed to bridge the period with a lower risk of disease until the vaccination date is finally reached or until the adjustment of the vaccines to new mutants is completed and the vaccines are distributed.

One can put it even more clearly: without non-specific defenses, humans would probably already be extinct. Since we are so often exposed to infections and the specific defense only sets in with a time lag, without the non-specific defense we would be at the mercy of the pathogens without protection in this phase.

Of course, the specific defense is often ultimately decisive for one's own fate, since the nonspecific defense is not ideally effective. But are there not other possibilities to use it specifically than vaccinations applied with injections? For example, the use of artificially produced antibodies against SARS-CoV-2, which are used as a nasal spray, is also being tested today. Thus, Principle 5 may also offer further untapped options. And special attention should be paid to vaccines that can be applied intranasally.

However, it is crucial to refrain from believing that one single principle can solve the current situation. Therefore, it is important to integrate the available options into an overall approach. These partial steps will now be dealt with.

1. Principle No. 1: No SARS-CoV-2 — No Transmission of SARS-CoV-2

a. Viruses and virions

This is probably where some clarification is needed: when one speaks of the SARS-CoV-2 virus, one imagines a spherical something with a rounded crown that is the carrier of the specific docking sites for the antibodies. But, strictly speaking, this is the virion. The «actual» virus, which imposes its own reproduction including all the specific and non-specific protein structures on the host cell, is only the associated RNA. This RNA is considered to be capable of stimulating the host cell to produce the viral RNA and the effects determined by it, e.g. the formation of the structures of the virion of SARS-CoV-2 (in particular four different protein structures as well as a lipid double structure). In this way the virus creates a protection against chemical-physical influences and at the same time the conditions for it to penetrate into the organism. In addition, the virus is granted plasticity. This means that it is capable of modifying and thus improving its own effectiveness against the host structures. This leads to the formation of mutants.

Mutants pose a particular challenge to strategies for managing the COVID-19 pandemic. Mutants can be more infectious than the wild form, lead to more severe courses, and cause the protection of immunity once acquired to be weakened or completely ineffective. This is illustrated by the course of the epidemic in Manaus in 2020: after the first wave, population infestation was reported to be about 70% [99]. This corresponds to the extent assumed at the time for effective herd immunity. Nevertheless, the second wave occurred with mutant P 1. It claimed even more victims than the first wave.

The nature of the processes leading to plasticity has not been adequately elucidated. However, only processes within the infected host cell can be practically relevant for the emergence of new mutants: If there were mutations in

the virion, e.g. in the air, this would only affect individual viruses. These would probably have no relevant chance to give rise to their multiplication. For this, the virion must enter the host cell. However, it obviously needs considerable loads of viruses to achieve the necessary penetration. So why should just the single mutated one be among them? Penetration is usually achieved only after several days of effective contact of the virion with the cells of the outer boundary of the organism (e.g. the nasal mucosa). Therefore, mutant formation can occur practically only in the host cell. Current studies show that mostly 1 or 2 mutants can be detected in diseased individuals [100]. However, the authors point out the importance of individuals in whom a large number of mutants have been detected. They see in the dynamics given thereby a reason for the formation and spread of new mutants. Be that as it may, if one wants to prevent the appearance and spread of new mutants, one must prevent their formation from becoming possible in the host cell. This is most efficiently achieved by inactivating the wild-type mutants before they can become the starting point of plasticity modifications. This can be achieved by inactivating the virion before penetration. There are possibilities for this during their stay in the outside environment, e.g. by special filtration, UV or ozone application in climatic plants. Or in the nose or throat area as well as in the lungs by natural or artificially applied antiseptic effects (sprays, inhalation). This will be discussed in more detail in Principle 3.

The chemical nature of the virion provides conditions for this, e.g. in the nose as the «anteroom» of the organism, which could no longer be so easily ensured in the areas affected by the blood in the organism. Thus, chemical processes can be used in the nose under sufficiently controllable conditions, which lead to denaturation of chemical compounds of the virion. This This is about the decomposition of chemical compounds by oxidative processes. Oak logs burn (= oxidize) as well as a gothic statue made of oak wood with a crown is! However, the exact structure of a certain part of the crown wreath would determine the antigen-antibody effect. involves the decomposition of chemical compounds by oxidative processes. Oak logs burn just as well as a gothic statue made of oak wood! Therefore, the efficacy of an antiseptic is independent of whether the chemical compound also has specific structures that are relevant for specific interactions, for example, when penetrating the cellular protective barrier or as a contact site for antibodies. The control of these processes in the nose is possible because the general conditions are locally largely constant. The physiologically active substances in this process could and had to prove themselves in the evolutionary process insofar as they had to be effective against the pathogens on the one hand and tolerable for their own cell structures on the other. Only mild and specially structured antiseptics are compatible with the cells' own structures of the «outer boundary», but cannot themselves overcome this boundary. For example, N-chlorotaurine does not enter the body. Antiviral disinfectants are also effective against viruses, but would attack the cells. Therefore, they can only be used on dead material. They are incompatible for use on respiratory interfaces. Neither antiseptics nor disinfectants may be injected into the body.

If the virion has succeeded in overcoming the external barrier, it can reach a wide variety of areas with the bloodstream. Therefore, it cannot be assumed that the general conditions will remain the same. Also, how should a mild antiseptic be developed in evolution that is compatible with all these systems but can inactivate viruses. How should it be possible to apply such a substance only to the «right» place, moreover in an appropriate concentration and long enough? Once the virions have overcome the cell barrier, another defense principle is obviously required. And this has gradually developed in the evolutionary process up to the vertebrates. In them, antigen-antibody reactions appear for the first time. These are not based on the «aggressive» decomposition of chemical compounds of the virion, as is the case with denaturation, for example, thanks to NCT. On the contrary. It comes to the «harmless» formation of larger structures by coupling in each case specific structures of selected proteins of the virion (epitope) with equivalents with the antibody (paratope) to an AG-AK complex together with virion. Under physiological conditions, this effect can only occur if the specific structures fit together, wherever the AKs go. The AG-AK structures can then be recognized as such by specialists, taken up into the phagocytes, and there — again under locally defined conditions — be fed to denaturation, e.g. by NO.

It is understandable that the modification of the protein structures has an influence on the antibodies required, but not on the efficacy of the antiseptics. To remain with the comparison with the log and the wooden statue: Whether it is a Gothic Madonna or log makes no difference to the combustion process.

b. Pathogenic viruses arise by mutation

The majority of scientists currently believe that SARS-CoV-2 naturally modified in an animal infected with a corona virus precursor from that precursor and was able to cause host cells to reproduce. This mutant was able to jump to humans because of their proximity to the host. Comparable things can happen again and again as long as, for example, humans live so closely with domestic and wild animals. If one wants to tackle the problem at its root, one must minimize this risk. IPBES has made proposals to do just that. IPBES (Intergovernmental science-policy Platform on Biodiversity and Ecosystem Services) is an international advisory body affiliated with the UN that currently includes over 130 countries. Its blueprint for ending the era of pandemics is available digitally in English, Spanish and French [101]. The greatly simplified connection between health and sustainable, including sociocultural, management of the environment is addressed in Part 2.

However, the discussion on the emergence of SARS CoV-2 exposed to everyone that it is possible to artificial-

ly modify such mutants and also viruses of other species to become human pathogenic. Recently, it has been published where SARS CoV-2 would have to be altered so that conventional vaccines would be ineffective [102]. Arguably, all institutions that can design appropriate vaccines would also need to be able to construct new mutants and new pathogenic viruses. This leads to an unprecedented threat potential. Against this threatening era of pandemics, only non-specific instruments of a «biological» but also legal nature are likely to help. The current concepts against SARS-CoiV-2 do not take this into account. This shows that it is not enough to provide measures that address the current situation. There is also a need for medium- and long-term strategies and their implementation.

Of practical significance is the possibility of making artificial changes to a virus to reduce its virulence. This is a classical way to produce live vaccines.

c. Two key questions: Why do pathogenic viruses disappear and why don't they?

SARS-CoV-2 has suddenly appeared by mutation of apathogenic forms. Why should it not disappear exactly quickly? What are the theoretical possibilities that SARS-CoV-2 could disappear again? How is it that SARS-CoV-2 becomes inactivated in the first place. Surely it needs a host to replicate this virus? And how relevant are the processes involved in this process for the persistence of SARS-CoV-2 according to previous experience?

Why do pathogenic viruses disappear?

- The pathogenic form can change into an apathogenic form by mutation: We have no control over this. However, mutations have occurred so far that are more pathogenic and virulent than the initial form.
- They lead to the death of the host/all hosts and are therefore no longer reproduced and are buried or incinerated with it. This is taken into account by the models of Kermack & McKendrick and the SEIR models, among others.
- Viruses outside their hosts are denatured by UV light, ozone, desiccation, heat, and chemical interactions: This is of practical relevance to SARS-CoV-2: contact transmissions are virtually negligible [103].
- Viruses are denatured by the microbiome: Therefore, COVID-19 is not a smear infection.
- Viruses are denatured in the course of nonspecific defense. This is where antiseptics, especially N-chlorotaurine as an acute measure, non-specific health promotion (e.g. hyper-hypooxia, sports, nutrition..) and strengthening of non-specific defenses through social measures that are effective in the medium term, come in.
- They will disappear if all viruses that entered the organism are/would be neutralized, phagocytized and denatured in the cell (natural and artificial specific immunity) thanks to antibodies as antigen-antibody complex. But it is an open question whether this can really be assumed in an ideal way. Is there latency of SARS-CoV-2 viruses?
- Immunity is «classically» achieved by successfully passing the disease. Therefore the therapy gets also epidemic-hygienic meaning. Immunity reduces the relevance of the non-infected person as a carrier. The extent to which this person can still be significant as a carrier at times has not yet been adequately clarified.
- Immunity can also be acquired through asymptomatic courses. Here, too, immunity is only temporary. This raises the question of the dynamics of relevance as potential vectors.
- Viruses are inactivated in contaminated persons when they are immune to such an extent that they are neither re-infected nor become ill again and therefore cannot infect anyone else. Kermack & McKendrick and e.g. the SEIR models optimistically assume this ideal variant. It is not tenable.

Why, for example, does SARS-CoV-2 not disappear as a health threat? E.g..

- Because susceptible hosts continue to exist: Lockdown does not make one immune or insusceptible! Acute support of a deficient non-specific defense (e.g. by NCT) leads only temporarily to insusceptibility, but inactivates pathogens and thus reduces the epidemic hygienic danger of potential germ carriers, e.g. also within families.
- Because asymptomatic germ carriers could transmit the pathogen to others unnoticed and therefore unhindered during the phase of their illness.
- If viruses can remain latent in the body (e.g. herpes, virological dark net of SARS-CoV-2?), they can later become effective and spread.
- If immunity is not permanent
- If the vaccination is not 100% effective
- If not all can be immunized (vaccination of children? tourists, incompatibility) or want to (refusers),
- When, due to mutation of viruses, the acquired specific defense does not protect anymore
- Because they can switch to other hosts (pets, ferrets, mink...).
- Because no process can be ideally implemented in a non-ideal world.

Only a few processes are open to us, which lead to a reduction of the viral load. However, viral load reduction is only one approach in dealing with the epidemic.

An essential variable for planning is to be able to make predictions about the spread of the pathogens and their effects, and to be able to derive conclusions for setting measures.

d. On the influenceability of the persistence of SARS-CoV-2.

Numerous respiratory infections show a seasonal dependence. The findings so far show that during the sum-

mer months the rate of new cases and thus also the number of deaths has decreased sharply in very many countries. This is not only true for Austria (see graph 4) and the other European countries, but also for Manaus (graph 5), i.e. on the other side of the equator. The reasons for this are not sufficiently clear. Important is certainly the increased stay in the open air. However, the World Meteorological Association is very cautious: «At this time, the evidence does not support the use of meteorological and air quality factors as a basis for governments to relax their transmission reduction measures» [104]. Still, if only because of the number of people vaccinated, it probably would not be a surprise to see a very significant decline in new cases, even in the summer of 2021.

As a rule of thumb, the infectivity of viruses is lost after 72 hours in the environment. But this is a very rough indication. If SARS-CoV-2 is experimentally exposed to full sunlight, 90% is no longer infectious after a few minutes, but indoors only after about 260 minutes [105]. UV radiation, heat, desiccation, the chemical nature of the surface on which the virus rests, etc. are considered to be influencing factors that accelerate deactivation. Their intensity is subject to strong fluctuations. This is used in the application of disinfectants. This is a bridge to principle No. 2 (interruption of contact): Contact with viruses on dead surfaces can also become the cause of infection. However, this route of infection is not considered to be very significant. Why do we not think about the fact that it is only one step to move from the special case of «disinfection» to antisepsis? Inactivation of viruses can also be achieved by mild chemical substances that are compatible with the mucous membrane. Then one would use a method that is also part of non-specific immunity. This also produces more natural antiseptic substances.

Are there really no other possibilities than airing and disinfection esp. of the hands? Department stores reduce the viral load by using UV or ozone in their air conditioning systems. Cruise ships and airplanes have used filtration techniques formerly used only in operating rooms. Temperature can also benefit an: Studies show the health benefits of saunas [106].

e. Conclusions:

We — in the first world — are in stage 2 or already in stage three. The chance to limit SARS CoV-2 locally and to eradicate it there is therefore no longer given. Obviously, SARS-CoV-2 will not disappear by itself. However, the natural and technical external environment obviously represents an effective sink for the persistence of the viruses. Exposures are to be expected in the vicinity of spreaders and in premises without adequate air exchange. Measures should be considered with respect to two problem areas: First, to reduce exposure of individuals, and second, as a preventive measure to reduce viral loads.

Air exchange is difficult to achieve to a desirable degree by simply opening windows. Filtering devices (e.g. in schools, department stores...) are therefore much more useful.

- Mutants are formed in the host cell. The risk of mutant formation is reduced by preventing the wild form from penetrating. The opportunity to do this can be by inactivation in the external environment (filtering systems...) and by inactivation in the «anterooms» of the organism (nose, lungs, throat).
- Substantially altered mutants can result in situations as if a new epidemic had begun. Therefore, inactivation is a primary goal — not just separating potential germ carriers from infectious individuals.
- The options available to individuals for themselves, their family and friends deserve to be

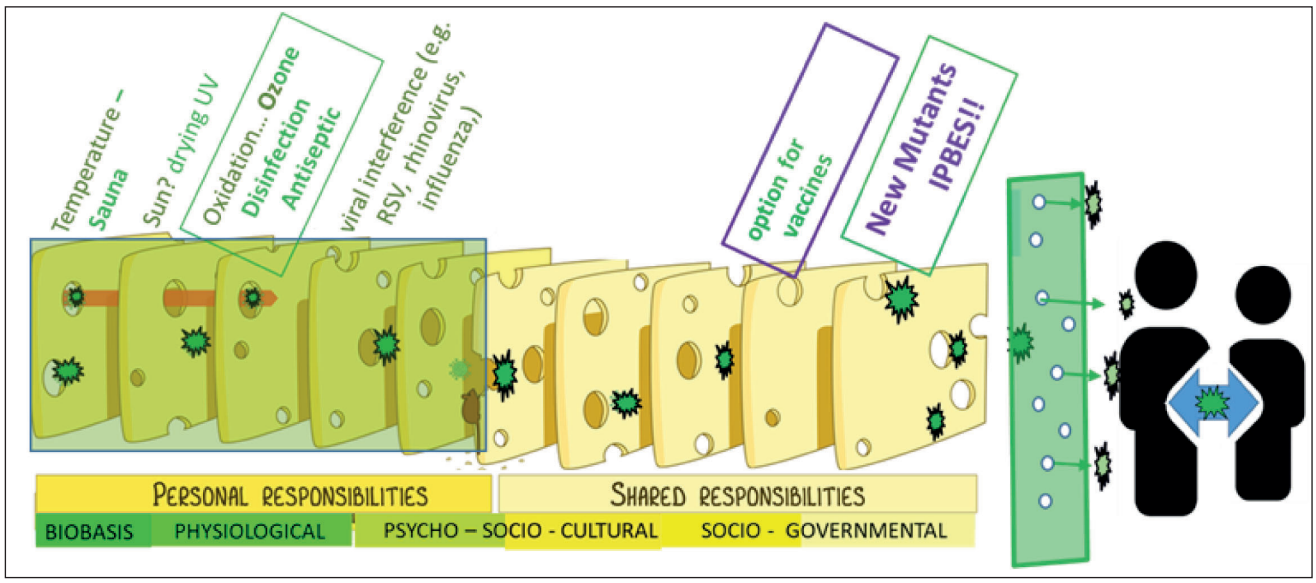

Fig. 11. Measures against the COVID-19 pandemic and its consequences
THE TOOLS FOR RISK — MANAGEMENT ON BASIS
PRINCIPLE 1: NO SARS-CoV-2 — NO TRANSMISSION OF SARS-CoV-2

appropriately indicated by government information systems.

- So far, personal initiative, such as the installation of high-efficiency filtration systems in air-conditioning units, has not gained any advantage over other facilities without them. Does it have to be this way?
- The most effective way to contribute to the disappearance of SARS-CoV-2 is to strengthen the non-specific defenses (see principles 3 and 4)
- Acute shoring up of nonspecific defenses against infection reduces the relevance of those so supported as potential vectors and sufferers by denaturing the pathogens, but does not cause permanent insusceptibility.

The occurrence of human pathogenic viruses cannot be avoided in principle. What can be avoided, however, are structures and behaviors that facilitate the spread of viruses from wild animals directly or via domestic animals to humans. Again, reference should be made to the concept of IPBES:

- Measures are needed to reduce the formation of spontaneously occurring human pathogenic mutants. This requires changes in land use planning toward ecosociocultural sustainability.
- This will probably not succeed without adjustments also in the direction of the production and use of energy, the water balance, climate change and the advancing impoverishment of species and the interconnectedness of natural and near-natural ecosystems.
- There is a threat of a new wave of terrorism from artificially created pathogens. This can be countered at the individual level, but especially by societal measures with the promotion and development of non-specific defenses.
- The resulting requirements presuppose strategies that are staggered in terms of time and success. They will only be successful if they take into account not only small-scale and regional aspects, but also global responsibility. Without taking into account the economically weak — whether individuals, groups or states — one should not expect any advantage for the prosperous even in the medium term.

But we should not overlook: Very many countries in the world have not yet reached the level of vaccine coverage. It is possible that large areas there are still at level 1 and could be saved from the occurrence of an epidemic by targeted and methodically balanced measures until they can be offered lasting protection via vaccination. Since the planned funding is targeted for the end of 2022, the time period to be bridged is very long. And with it the danger that pathogens — at best as new mutants — will be introduced from these countries into the so-called First World.

2. Basics of forecasting models based on Kermack & McKendrick [9]

At the center of public discussions are figures used to infer the current situation and what needs to be done to protect the population. Therefore, everyone should be interested in what these numbers really say — other than that so and so many people within the state borders have been found to be carriers of germs or have died from or with COVID. For this, it is useful to look very roughly at two papers: that of Kermack & McKendrick from 1927 and that of Cori et al from 2013 [84]. For this, please refer to Part 2.

But a few things in advance: Kermack & McKendrick wanted to prove that there was another way to fight epidemics beyond the methods commonly used in 1927: The usual practice at that time was to lock away lepers, for example, and to isolate everyone for 40 days (hence «quarantine») with the closing of the city gates. Therefore, during this phase, no one could get out and no one could get in. This set of instruments was extended by Pasteur and Koch. They developed special procedures to influence the pathogens. Kermack and McKendrick proved that the close contact between the individual germ carrier and the specifically infected person is another prerequisite that can be used to slow down the epidemic. In fact, if the germ carrier meets the next infectee late enough, then the chain of infection is slowed down without the need to change the properties of the viruses or to sequester them all permanently. In addition, the number of infectious persons is reduced because the infected persons either die or become immune after recovery. The reduction in contacts therefore leads to a flattening of the curve of newly infected people, with all the consequences this has for relieving the burden on the health care system. But the threat of the pathogen may not end until the viruses can no longer infect anyone. The reasons for this may be that everyone has either died or become immune in the meantime, or that the period between the next contact is so long that the viruses have been inactivated in the body of the infected person or in the environment.

To prove their approach, Kermack and McKendrick had to make simplifying assumptions for the effectiveness of the previously recognized methods (locking away, influence on the pathogenicity and virulence of the pathogen) for methodological reasons: they assumed a constant dangerousness of the pathogen and a constancy of the defensive power of all persons. In addition, they assumed that all persons live so close that everyone has the same probability of hitting everyone else. This is the only way to prove that their method of changing the frequency of contact is influential. They also assumed that the infectiousness of a person is lost in any case with his recovery, the cured do not get sick again for life and they cannot infect anyone else. Therefore, the number of infectious people is permanently reduced by the number of the deceased and the cured. However, you have pointed out that these simplifications should not be assumed in reality. Not only that: they have even emphasized as point 1 of

their results that even small changes in infectivity can lead to significant changes in the course of the epidemic: «Thus a small increase in the infectivity rate may cause a very marked epidemic in a population which would otherwise be free from epidemic». However, these simplifications are necessary for methodological reasons, since Kermack & McKendrick wanted to prove that their approach is effective on its own. It follows that Kermack & McKendrick assume that for the description of a real existing epidemic, of course, all variables must also be considered as variable.

For the dynamics of an epidemic it will therefore also be necessary to consider, for example, how long viruses can persist in the environment without losing their infectivity. Kermack McKendrick also take this into account only indirectly: with the insinuation that cured persons cannot pass on the germs and that there are no other sources of infection than infected persons, whose effectiveness formula massively can be sufficiently characterized by contact and time interval. In any «real» case, one must be aware that in the approach of Kermack & McKendrick and all models derived from them, all these indisputably variable aspects of the factor «virus» are included together with all aspects of the factor «human» in the one quantity «infectivity. In their model, only the contact between persons is variable. This obviously does not correspond to reality. Nevertheless, various forecasts are based on this approach, without pointing out the limits of the predictive power.

- Kermack & McKendrick also assume that individual data are available, i.e., information that is precisely and individually attributable to each individual person in the collective. Currently, calculations are made on the basis of aggregate data. These are the «aggregated» data that are reported, for example, by the district headquarters to the central office. This is usually based on the method developed by Cori et al. This is also discussed in more detail in H.
- It is essential for the appropriate use of both techniques that the persons can meet them reciprocally and with approximately equal probability. Therefore, they must live in a correspondingly close spatial relationship, for example. Otherwise they could not pass on their germs. This is not the case with the data for states and federal states.

If a person is exposed to a relevant viral load, a confrontation occurs between the viruses and the cells of the outer boundary of the organism — with an open outcome. Viruses can penetrate individual cells and be reproduced by them and released back into the nasal cavity, for example. This increases the viral load in the nose and increases the risk of penetration into the interior of the body. At the same time, the amount of virus introduced to the outside world through sneezing, etc., increases with the risk of transmission to other people [107]. Therefore, depending on the individual circumstances, the time interval

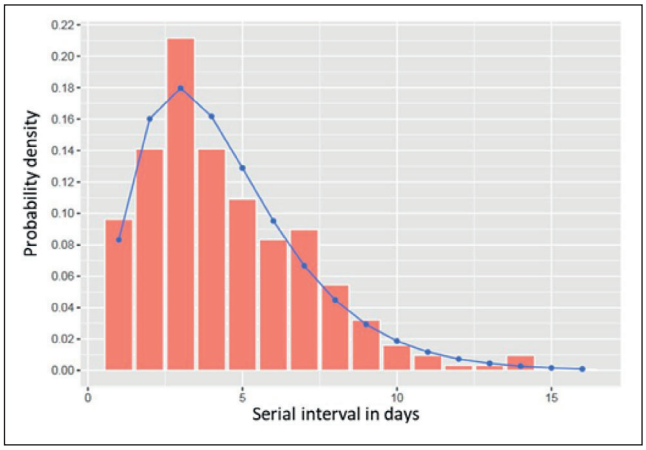

Fig. 12. Distribution of time between disease of a COVID-19 case and its subsequent case (312 transition pairs) and estimated gamma distribution (blue), 2/23 — 4/1/2000, Austria, Richter L et al, 2020

between the contact of the spreader and the manifestation can vary greatly.

Conventional model calculations neglect this range, which is important for the nature of an infection and the dynamics of an epidemic. They assume mean values and calculate with so-called «serial intervals». In doing so, they build on the determinations of the incubation period.

The mean value of the serial interval determined here for Austria on 312 transition couples in spring 2020 was 3.96 days (standard deviation 4.75 days) [108].

3. Principle 3: Without successful contact with SARS-CoV-2 — no infection with SARS-CoV-2.

The presentation of the possibilities to reduce the risk by measures based on principle 2 (Without transmission — no contamination) can be omitted here. The corresponding measures have already been referred to under «current situation».

If the risk management measures based on principles 1 (Without SARS-CoV-2 no transmission) and 2 (Without transmission no infection) have not led to success, a relevant viral load can reach the interior of e.g. the nose. Then the mucosal cells of the mucosa with their nonspecific defense come into play. This is a direct follow-up to the introduction to the Kermack & McKendrick model.

a. Again: Contagion index and serial interval

Efficacy against the same pathogen can vary greatly between different groups in the same country, but also in individuals depending on their current situation of contact with the virus. Physicians express these differences with the help of changes in the contact index. As explained above, the contagion index indicates how many people who have never contracted the infection in question and have not been vaccinated become contaminated, i.e. infected, when they come into contact with the pathogen. How much this value can change and even — in connection with the manifestation index — lead to a radical decrease

in mortality without the use of vaccination and antibiotics can be seen in the example of tuberculosis. Tuberculosis is the most significant infectious disease in the history of mankind. The number of people who died from it was recently estimated at 2 billion people [109]. In Part 2 it is shown that in Austria it was possible to reduce the mortality from tuberculosis from about 500 per 100,000 inhabitants in 1900 to 50 in 1950, without this being attributable to vaccination or the use of antibiotics. It was societal measures to raise nonspecific defenses and thus lower the contagion and manifestation index. (See Part 2 for more on this). Such time spans are not currently available, of course. But the contagion index and manifestation index can be changed at the individual level, even in the short term. But the computational models based on Kermack and McKendrick and Cori et al. do not provide for this. Therefore, it is an extreme simplification to assume constant «serial intervals» even over time in the model calculations [107]. Assuming that the «virus factor» and contact frequency are constant, the average incubation time determines its level. In the spread calculations, one assumes that the «virus» and «human» factors are constant. The only factor that can be changed is the frequency with which infectious persons encounter infectious agents. This is used to calculate the reproduction rate, i.e. the average number of newly infected persons that a diseased person infects. Since the contact index and also the manifestation index can even vary greatly, but this is not included in the spread calculations, they cannot be included in the considerations of why the reproduction number has not changed according to the forecasts.

The experience with tuberculosis emphasizes the importance of starting or strengthening social measures as soon as possible, which will permanently improve the contact index, i.e. reduce it. However, during the epidemic, short-term effects on the contact index are paramount. These will occur whether one is aware of them or not. However, the changes can be both desirable and detrimental.

Therefore, one must assume that the contagion index has changed and will continue to change as a result of experiencing, for example, a lockdown. These shifts can lead to an — undesirable — increase in the contagion index. However, there are also possibilities of influence that lead to a — desirable — lowering. Once again, we are reminded of the mathematically based prognosis of Kermack & McKendrick: They emphasize that the pathogen-person relationships must not be underestimated. Even small increases in infectivity — i.e., even as a result of a small increase in the contagion index — would lead to severe epidemics.

Policy makers should proceed according to the precautionary principle and anticipate that there will be increasing increases in the contagion index as the pandemic progresses. In considering how to counter this, one can draw on the findings of physiology and, for example, the work of Nobel laureate Blackburn which was referred to under A) 2 d (the holistic answer to COVID-19). Biological processes always occur at the level of the individual cell, from whatever evolutionarily young level the processes are initiated. Infection is a biological process. Therefore, the effects, but also the possibilities of influence against the undesirable effects such as a deficient non-specific immune defense, will take place at the cellular level. Therefore, as a precaution, one should assume that one has three possibilities to improve a current — and therefore possibly only temporary — weakness of the non-specific immunity, however caused.

a. One can remedy the deficient natural antiseptic effect due to insufficient production of the corresponding substance by administering the same but synthetically produced substance.

b. A — related to the place of application — foreign antiseptic may be used, provided that tolerance is demonstrated.

c. One can counteract a possible deficit in the efficiency of the cells as a result of a lack of e.g. oxygen by anticipatory training of the intake of oxygen even from oxygen-deficient air.

b. The use of N-chlorotaurine (NCT).

The only viable non-specific defense substance that can currently be manufactured on a large scale and used at the site where it physiologically occurs is N-chlorotaurin. It is a safe, well-tolerated, endogenous, mild antiseptic with anti-inflammatory properties. NCT can be administered as a nasal spray or via inhalation. It does not enter the body, so in the strict sense of the word it is not a drug, but a medical device. More than 200 scientific articles are listed in PubMed. The tolerability of NCT has been confirmed several times in humans, e.g. in 2010 [110] and 2018 [111]. Its broad efficacy against bacteria, fungi, viruses and protozoa has also been demonstrated in numerous studies in animals and humans. In contrast to HOCl, for example, which is only present instantaneously due to its high reactivity and therefore does not persist, NCT belongs to the cloramines. In contrast, these are also referred to as «long-lived oxidants» because it is assumed that they persist for a longer period of time. Lackner, Nagl et al. also recently confirmed virucidal activity against SARS-CoV-2, influenza A virus, and respiratory syncytial virus (RSV) [74]. This broad efficacy is not surprising, given the reasoning of Nobel laureate Burnett, elaborated in H: According to this, interactions between chemical structures require that they be connectable to each other. NCT is an amine and not a globulin. It has a «simple» chemical structure: Cl-NH-CH2-CH2-SO3 NCT leads to denaturation, i.e. a degradation of the protein of SARS-CoV-2 by oxidation. The combustion of oak wood is also based on oxidation: in the case of a log, just as in the case of an artistically carved statue with a crown. NCT attacks somewhere else than e.g. antibodies. Antibodies combine with a very specific area of the crown of the pathogen to form an antigen-antibody complex. This is thus a «building up» process, which only leads to denaturation after phagocytosis (uptake into the phagocytic cell). The differ-

ence between the mutants lies precisely in these characteristic structures in the crown, not in the basic structure of the virus. Therefore, there would need to be good reasons why mutants of SARS-CoV-2 should NOT be inactivated by NCT. The use of an artificially produced but natural substance at exactly the point where it is physiologically used explains why NCT has such good tolerability: After all, the fight against viruses is probably part of the everyday life of the cells of the mucosa. Therefore, only those substances could prove themselves in the evolutionary process that were on the one hand antiviral, but on the other hand well tolerated by the cells of the mucosa.

i. «It would be great and a super idea to have a cure..».

Not many comments can be found from virologists on the topic of «prevention». But recently the topic was basically addressed in a Prodcast of the Norddeutscher Rundfunk with Prof. Drosten (Charitee, Berlin) and Prof. Ciesek (Uni, Frankfurt), but not on the example of the unspecific defense, but the possibility to use a nasal spray with antibodies preventively [112]. In the Proadcast Nr 77 (27.2.2021) is stated [113]: «...it would also be great if you had a means that can reduce the transmission, if someone is infected... For... virus entry into the cells, a fusion between the membrane of the host cell and the virus is necessary. And that fusion of the membrane can be inhibited.... And the idea is that you can offer such a... agent for prophylaxis before and after exposure..... But it would also be interesting in the context of certain areas of life. For example, if someone who is infected needs medical treatment quite urgently to minimize the risk for the practitioner, if you think of a dentist for example. Or sometimes, if someone is infected and still needs treatment or needs to have contact in order to protect fellow humans, such an application would of course be conceivable..... And I think if that works, that's a super idea».

It has now been demonstrated that such agents exist, in particular NCT, the natural antiviral substance of the natural nonspecific defense, which can also be produced on a large scale. Its efficacy against SARS-CoV-2 has been demonstrated in collaboration with Charitee, Berlin (Carsten Schwarz) and Robert Koch Institute (Thorsten Wolf), 360 biolabs Melbourne in December 2020 and the Section of Virology (V. Laer) and the Section of Hygiene of the Medical University of Innsbruck under the leadership of M Nagl. (M.Lackner, M. Nagl et al.) [74].

So far, the permissibility of the use as a preventive medical device is missing. This could be achieved — as has been done for NO in Israel — in the short term via an emergency regulation. Even without CE marking and emergency regulation, a nasal spray could be prescribed by any physician to his patient and manufactured by a pharmacy, provided that the raw substance would be made available to pharmacies. This step could help to ease the current debate in many countries about the unequal treatment of vaccinated and recovered persons and open up v3equal relief to persons with negative tests and nasal spray without accepting a significant additional risk. Why not allow those people with evidence of a negative AG test and the application of 1% NCT in front of the eyes of the owner to visit a restaurant, by following all the other now «classic» precautions (distance...)? The effectiveness would be higher than by testing. This only helps to recognize asymptomatic carriers of germs in advance and to separate them as potential carriers. The additional administration of the antiviral nasal spray would reduce the risk of illness and infection, even if this person were to provide a positive AG test on the subsequent day. In addition, this would be an effective measure to reduce the viruses and thus a step toward reducing the risk of creating more mutants.

Why not offer regular inhalations with NCT to all patients with COVID-19 on normal wards?

c. Support of the nonspecific defense with substances foreign to the stock.

i. Nitric monoxide

NO can also be used successfully. Extensive studies are available for this substance on its function inside the organism or in and between cells, but no information is available on whether it is released in the course of excretion, e.g. into the nasal cavity. But the studies on its preventive efficacy as a nasal spray were so convincing to the Israeli health minister that he issued an emergency decree making the use of the Israeli-Canadian product available even to children over the age of 12. In doing so, Israel set a precedent: The first emergency order for an antiseptic against SARS-CoV-2 [114].

Nitric oxide is a poison, namely an irritant gas and methaemoglobin former. Therefore, it has no place in the respiratory tract (car exhaust!). But the dose determines whether something is a poison or not (Paracelsus). In the body, small traces of NO serve as messenger substances. In immune cells, NO is used as part of the non-specific defense against pathogens to denature them by oxidation. Thanks to its small size, NO can easily pass through cell walls. NO has been approved for years as a drug, e.g., for severe pulmonary dysfunction.

In March 2021, NO was approved as a preventive nasal spray («Endovid» by SaNOfice) by way of an emergency regulation probably as a medical device [no studies level 3 available] also for children over 12 years of age [115]. (Up to now — summer 2021 — there is no vaccination for young children. From an epidemic hygiene point of view, it is essential to reduce their importance as spreaders).

ii. Various other potential antiseptics

Recently, various proposals have been published for the use of artificial substances as antiseptics for inhalation or as nasal-mouth sprays. (e.g., Cegolon L., M. Javanbakhit, G. Mastrangelo [116]) They offer the use of antiseptics based on substances not commonly found on the mucosa, e.g., iodine, copper, carragelose from red algae. Therefore, clarification of tolerability is particularly significant.

Other research is being conducted to prevent direct contact of SARS-CoV-2 with mucosa thanks to a nasal spray based on lipopeptides. (e.g. V.K. Outlaw et al. [117], R.D.de Vries et al. [118]) Others offer prophylactics based on nanoparticles (e.g. P.A.Koenig et al. [119]) and antibodies. These, too, can be applied with a nasal spray. Drugs are also being developed [120]. Unfortunately, evidence of tolerance is lacking for these substances as well.

It is obvious: specific immunity is not the only indispensable tool in the fight against infection! Everyone agrees: the use of antiseptics does not replace the methods of inhibiting person-to-person transmission through contacts, nor the need to treat the disease thanks to specific therapies or prevention thanks to vaccines. However, nonspecific defense seems to be the only way to achieve temporary immunity so far. Moreover, it leads to a reduction in the risk of infection of others. This is important to bridge the phase until vaccines are developed, adapted to mutants at best, and also distributed population-wide. They are irreplaceable in the fight against terrorist threats from artificial yet unknown pathogens.

d. Further nonspecific defense of the organism

NCT is only one example of the efficiency of the non-specific defense in the fight against virus penetration. In principle, we must reckon with the possibility that other ecophysiological processes may also be at work here. The term «ecophysiological» here is meant to express that, for example, the nasal mucosa interacts with a network of interacting microbiome including virobiome. Far too little is known about their efficacy, just as in general the non-specific defense of non-vertebrate organisms is of incomprehensibly little interest, although there are well-documented reasons why they are relevant as precursors of the «specific immunity of vertebrates» for the understanding of the entire defense process. Reference is made only to the standard work of the Academy of Sciences of New York [121].

If a virus has entered the organism of an unvaccinated person for the first time, this person does not yet have antibodies. Only after about 4 days can the first antibodies be detected in the blood, a very long time when one considers that, for example, Escherichia coli takes about 20 minutes to reproduce. Even at this stage, the infected person relies on the nonspecific defense to keep them alive until the specific defense becomes fully effective. Here, NCT no longer plays a role because it cannot enter the organism. But this does not mean that innate immunity is not effective. Again, only a few examples can be pointed out, e.g. the work of F. Gaudet et al.: A human apolipoprotein L with detergent-like activity kills intracellular pathogens [122], or of C.Nathan, who logically calls for an expansion of the field of interest of current immunologists [123]. Significant also the native function of B cells in this phase before the appearance of specific antibodies to form convergent clones to SARS-CoV-2 with weak cross-reactivity to other coronaviruses. They are thought to contribute to the mild course of the disease in children by supporting the defense in the phase leading up to the formation of specific antibodies [124].

However, this work does not currently allow any concrete measures to be taken.

It may be possible to provide preventive support through the use of trace substances and vitamins that are thought to be effective in blocking viral replication intracellularly, particularly in individuals who are deficient in this regard. Experience in this regard is available, for example, from the USA [125].

e. Bridge to specific immunity

The type of vaccination also appears to have an impact on both virus penetration and the potential of the vaccinated individual to be effective as a carrier in the event of subsequent contamination by SARS-CoV-2. In principle, intranasal vaccination methods are particularly suitable against respiratory infections. They suggest a stronger mucosal immune response than vaccines administered intramuscularly [126]. The graph below, taken from this work by F. R. Lund and T. D. Randall, illustrates this. Lund and Rendal explain the graph and thus the difference as follows: Immunglobuilin A (IgA) and resident memory B and T cells in the nasal passages and upper airways are elicited by intranasal vaccination and prevent infection and reduce virus shedding. Serum IgG elicited by intramuscular vaccination transudates into the lungs and prevents pulmonary infection but allows infection in the nasal passage and virus shedding. The advantages of intranasal vaccines include needle-free administration, delivery of antigen to the site of infection, and triggering mucosal immunity in the respiratory tract. This makes their surprise of Lund and Rendal understandable that only seven of the nearly 100 vaccines against SARS-CoV-2 currently in clinical trials are administered intranasally, including one project in Oxford [127].

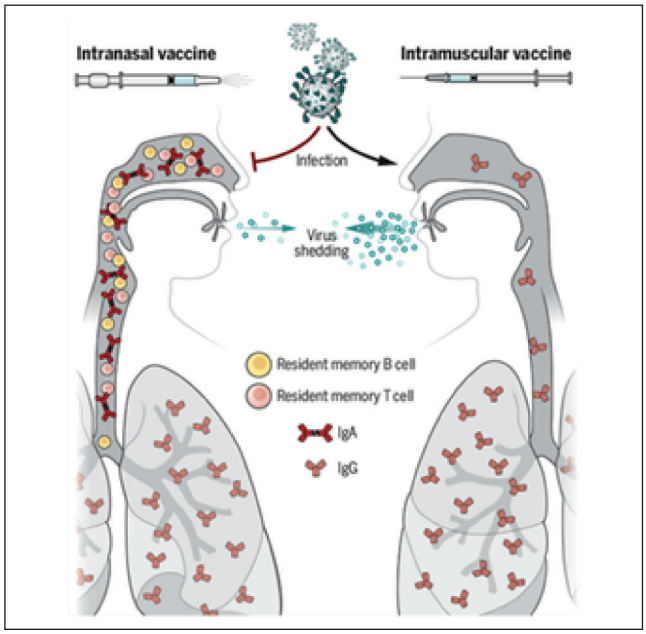

Fig. 13. Routes of vaccination. Lund F. E., Randall T. R. Science, 10.1126/science.abg9857

f. Linkage of contact index with manifestation index.

Epidemiological studies mostly do not distinguish between the influence of the contact index and that of the manifestation index on the evidence of the effects studied. Therefore, the influencing variables used in risk management for effect principle No 3 (Without successful contact with SARS-CoV-2, no infection with SARS-CoV-2) and effect principle No 4 (Without infection with SARS-CoV-2, no manifestation of COVID-19) are presented in the joint graph No 7.

4. Principle No 4: Without infection with SARS-CoV-2 — no manifestation of COVID-19.

However, this does not mean that the phase between infection and manifestation is not worthy of consideration from a health perspective. Quite the contrary. This is the phase in which it is decided whether and when disease will occur. This phase, in turn, is determined by the performance of nonspecific immunity. Now no longer at the level of the mucosa cells, but of the organism.

a. The variability of the incubation period as an indicator

The more efficient the non-specific defense is, the longer the incubation period will be. In the optimal case, the disease will be prevented despite contamination and thus infection. There is also the remarkable case of a permanently asymptomatic form of disease, which is unnoticed by the person, but leads to the formation of antibodies. How frequent this pathway to the formation of immunity is an open question: It seems to be subject to strong fluctuations, which is not surprising in view of the possibilities of influence on the contagion and manifestation index. The Robert Koch Institute suggests that transmission from asymptomatic individuals would play a «minor role» [128]. As early as April 2020, the German National Academy expressed the opinion that «a substantial portion of the infected population has little to no disease even for the entire duration of infection» [51]. H. Zhenyu et al's elaborate study, which is informative for Wuhan, demonstrates that although only about 7% of the population in Wuhan was immune at the end of 2020 [129]. Of these, however, 82% of those with antibodies never had symptoms.

If there are no symptoms, the question of the length of the incubation period no longer arises, but the question of whether these persons may have been carriers does. However, if nonspecific immunity is weakened, the incubation period becomes shorter. Nonspecific immunity to the same pathogen can vary widely between individuals for the reasons listed in the graph. The extent of the variation in incubation time for COVID-19 within a group of people considered representative of a population at a given time in practice is evidenced by the graph below for Austria. It shows the distribution of time spans between the infectious contact of an Austrian infected with COVID-19 (primary) and the appearance of COVID-19 symptoms in the person infected by him (secondary) [108]. Quite a few showed COVID-19 symptoms after only one day, the last ones after 14 days. Nevertheless, this distribution makes a statement about a very specific situation in which the secondarily infected person was during the incubation period. If one takes into account the considerations made under «The interdependence of organism and person», it becomes conceivable that the symptoms could have appeared earlier in every secondarily infected person, if he or she had had to cope with e.g. a heavy physical or psychological burden, or also that the incubation period would have lasted longer, if such burdens had

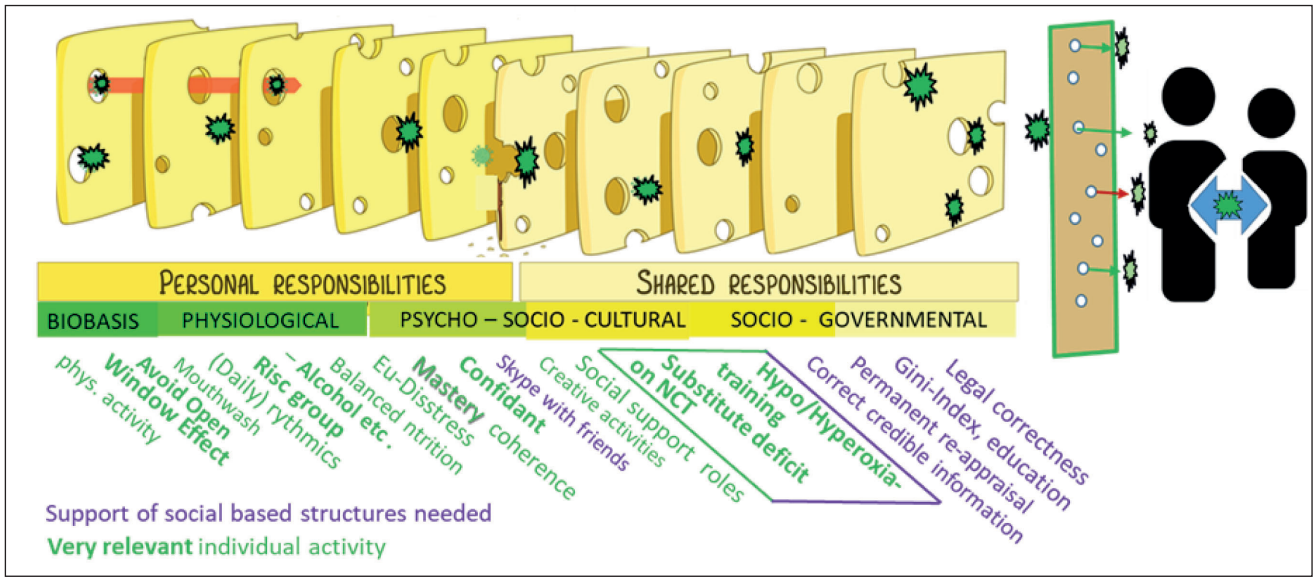

Fig. 14. Measures against the COVID 19 pandemic and its consequences
THE TOOLS FOR RISK — MANAGEMENT ON BASIS
PRINCIPLE 3: WITHOUT CONTACT WITH SARS-CoV-2 NO CONTACT/INFECTION
PRINCIPLE 4: WITHOUT INFECTION WITH SARS-CoV-2 NO MANIFESTATION OF COVID 19

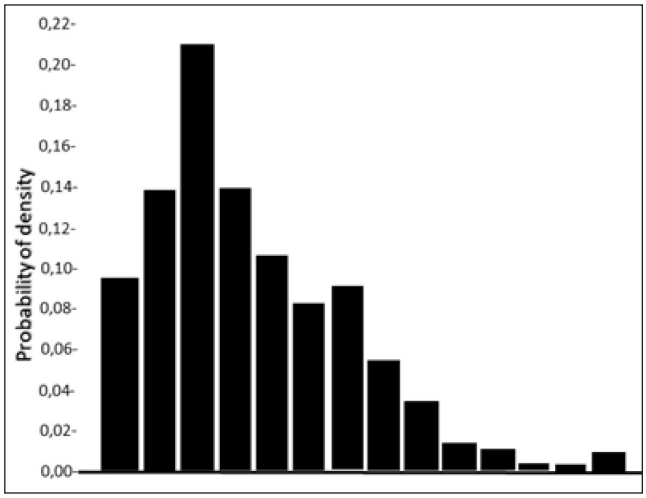

Fig. 15. Distribution of COVID-19 incubation times per day; 312 individuals collected between 2/23 and 4/1/2020, Austria Data: Richter et al, AGES 2020, https://www.ages.at/download

not had to be coped with. Ultimately, it must even be kept open whether, under particularly favorable conditions, one or the other would not have fallen ill at all.

The survey of the AGES served primarily to determine the so-called «serial interval». Methodologically, this was done in such a way that at the time of analysis (=07.04.2020) 312 source-case-follow-up pairs with reliable information on disease onset were available. From each of these pairs, the time between the days of disease onset was calculated [108]. Therefore, this experimental design also meets the requirements to determine the time interval between first contact and disease onset, i.e., the incubation period [as stated in A 2 b). With serial intervals based on laboratory-confirmed cases, the curve would probably be shifted somewhat to the right]. The value averaged from the values of the 312 pairs is needed by calculators of models to determine the dynamics of the epidemic according to Cori et al. The smaller the serial interval, the greater is what Cori et al call the «power of the epidemic» [84]. The «force of the epidemic» includes not only the «human factor» with its nonspecific immunity to infection and manifestation and the «pathogen factor» with its infectivity and virulence, but also the frequency of contact between an infected person and an infectious person. In the calculations of dynamics, the factors «infectious person» and «pathogen» are assumed to be invariant. The figure must also include the influence «modifiability of virus excretion». Therefore, the «force of the epidemic» in a model based on Cori et al. can be influenced by only one of the diverse variables: by the influence on contacts with infectables. And this is far from reality from a medical point of view. The medical considerations are obviously quite different from those that model calculators have to make. They must neglect individual behavior. Otherwise, they will not arrive at any calculability.

From a medical point of view, the goal must be to prolong the incubation period, if it is already not possible to prevent the spread of germs per se and also not to prevent the contact of the infectious with the infectious. Here it is a matter of bringing «the power to resist the epidemic» to the center.

b. Possibilities of influence

In graphic 12 a distinction is made between the ways in which the risk can be reduced individually or collectively or socially. Biological and physiological processes can be used as a starting point. However, this may also require upfront efforts on the part of society. For example, NCT can only be purchased if it is available in pharmacies. Devices for training oxygen uptake by means of hyper-hypo-oxia training will also not be available for everyone to buy privately (see also chapter H). However, they could be made generally available, e.g., in day care centers for seniors. Physical activity with respect to the Open Window Effect, on the other hand, is much more within the individual's own sphere of decision, as is the effort to keep to a daily rhythm. Details about this are also given in chapter H. More difficult to classify is the question of alcohol consumption. Here, influences from the pandemic are to be expected. Some people may be surprised that Eu- and Disstress are listed in the graph. COVID-19 is an infectious disease after all. To be sure, the pandemic and the measures taken provide classic examples of the various forms of stress and the associated challenge of dealing with them appropriately. Therefore, reference should be made to the corresponding chapter in the special section. This reference to special chapters also applies to all other aspects of the evaluation processes. The psychosociocultural specifications, for example, flow into these. They lead to individual emotional, cognitive and intellectual assignments of meaning. The classic statement «A chimpanzee is not a chimpanzee» is not only true for chimpanzees, but at least for all primates: They need contact to their own kind. How much more important is this for humans as social beings.

In the graphic 12 also influencing factors on the risk to fall ill with COVID-19 or on the various consequences of the unintended, but inevitably occurred effects of the struggle to secure the health care system are listed. In Graph No. 5, some of the most important ones have been listed. These are related to the influencing variables indicated, such as the credibility of the information transmitted, the compliance with the legal bases, but also to the effects expressed by the Gini index. This index indicates how the distribution of wealth is in a population. It is noteworthy that, thanks to studies that can already be classified as classical, there is evidence that not only the poor are healthier when the gap between rich and poor is not too wide, but also the wealthy [130].

c. Asymptomatic — atypical — symptomatic — disease — being sick — Long COVID et al.

From a medical perspective, considerations of the importance of asymptomatic individuals with positive antibodies, as well as those with atypical symptoms, take on special weight. Can preventive action be taken to

reduce Long COVID: Already estimated to affect millions of people (Hayday Adrina, Francis Crick Institute): «It affects people in the most productive phase of life». (A. Nath, NINDS in NIH). «COVID-19 is a new disease that is pushing the research community and the world at large into «uncharted territory» (Jean Laurent Casanova, Rockefeller University). Thus, researchers are embarking on a quest to determine whether «viral reservoirs or residual segments of viral RNA contribute to the ominous findings [131]. A lot of unanswered questions. But one thing is already clear. If the viruses can be inactivated before they can penetrate and if the organism manages, primarily thanks to its non-specific defense and secondarily through the specific defense mechanisms, to prevent the disease from developing, the risk of the classic lung infection disease developing into a systemic form of progression is reduced, but also the risk of Long COVID, PIMS, etc. is reduced. The «discarded stone» would have to become the cornerstone: The possibilities of strengthening fundamental biological processes (example hyper-hypo-oxia training) and supporting currently reduced capacities of nonspecific defenses by NCT, NO or any other compatible antiseptic cannot be replaced by testing, testing testing, as significant as they are. The success in the fight against tuberculosis shows how effective it is to build up permanent improvement of nonspecific defenses without changing the pathogenicity and virulence of the pathogens. The urgency of such measures, especially for dealing with COVID-19, has been compiled for the WHO by Maxmen [132] and Wilkinson and Marmot [133], for example.

The battle against Long COVID is still ahead of us: given the estimated 1 million plus people — accounting for one in six — in the UK suffering from the long-term symptoms of Covid, Chief Medical Officer England Professor Chris Whitty reckons we are still «in the early days of our understanding of the long-term effects of Covid» [134].

d. Conclusions to reduce the risk of SARS-CoV-2 infection and COVID-19 manifestation.

- COVID-19 is an infectious disease. Therefore, the interaction of the virus with mucosal cells is the starting point of the health-related biological process.
- At the heart of the options to reduce the risk of infection with SARS-CoV-2 despite contact with germ carriers and the likelihood of contracting COVID-19 are nonspecific processes. Currently, the near-term options that society could provide are very limited: N-chlorotaurine could be made available worldwide in the short term, for an NO preparation there is an approval in Israel on the basis of an emergency regulation. Technology for enhancing oxygen uptake is available but limited during the pandemic.
- Several promising proposals for antiseptic agents are available. To date, there appears to be a lack of public interest in supporting this approach even to the extent that it has been done for vaccination. Options for the use of e.g. nasally applicable antibodies also deserve attention.
- So far, the possibilities opened up by principles 3 and 4 to influence the epidemic have not only remained unused. It must be feared that the pandemic has been adversely affected by the way things are currently done. At least, this is what the mathematical arguments of Kermack & McKendrick suggest.
- This is all the more incomprehensible since the legal situation in various states has endowed decision-makers with special rights in the event of pandemics to take effect in this area as well, e.g., to make a medical product available even by emergency prescription. Non-use of delegated rights must also be accounted for.
- The risks associated with the use of assistive devices, which may contribute to temporary immunity, are balanced against the reduction of direct and indirect consequences of COVID-19. The appropriateness of their use must therefore be reviewed. Arguably, the same principles should be applied as when assessing the appropriateness of restrictions on personal liberties, etc., against the risk of health care collapse.
- It is also likely to be relevant to consider whether measures leading to the restriction of fundamental constitutional rights are permissible if the possibilities conferred by the legislature for epidemics have not been used.
- In the present case, however, it also seems essential to consider that it is obvious that, as a result of the restrictions that have now lasted so long, serious damage to health has also occurred that might not have occurred, or not to the same extent, had other methods been used earlier to influence the spread of SARS-CoV-2.
- In evaluating NCT, it seems significant that the synthetically produced product has been tested for compatibility. It is chemically the same substance that is regularly produced in nature at the same location — e.g. in the nose, for protection against e.g. viruses.
- The health risks of COVID-19 must be weighed against other health risks that are unintended consequences of the fight against the collapse of the health care system.
- Individuals may be at increased risk for health reasons or because of their occupation. In addition, the protection of individuals with system-maintaining jobs is particularly significant. People over the age of 65 are generally considered to be a high-risk group (about one-quarter in Western countries). Asthmatics, the severely overweight, diabetics, HKH patients, etc. also belong to the group of persons with particularly severe courses. Thus, in Germany,

36.5 mi. of the 83 million are classified as high-risk individuals and 21.6% as a high-risk group [135]. Taking into account the system maintainers and those exposed particularly often, about half of the population is in need of special protection.

- Individuals with low socioeconomic status are at higher risk for severe COVID-19 courses.
- Many states failed to control the pandemic at the time it occurred. In the meantime, it must be assumed that germ carriers are widely dispersed and will remain so. It seems to be only a question of time until particularly effective mutants determine the course of infection, which at best cannot be combated by the current vaccines.
- It seems foreseeable that delayed effects of infections with SARS CoV-2 will result in unexpected and so far not adequately explained consequences (such as PIMS, Long COVID) in increasing proportions. The best measure currently available is to strengthen nonspecific preventive capabilities. («The discarded stone should become a cornerstone»)
- Successful use of nonspecific defenses does not cause specific immunity. Therefore, Principles 3 and 4 alone are also unable to eliminate SARS-CoV-2 in a situation where infected individuals are spread throughout the country. But both principles can help move the epidemic from epidemic to endemic and sporadic.
- The use of artificial agents to support nonspecific defenses against infection (e.g., NCT, NO) suggests a temporary reduction in both the likelihood of becoming infected oneself and of infecting others. This should significantly improve the very limited temporary possibilities to reduce the risk by e.g. antigen testing, as the viral load will be reduced.

5. Principle 5:

a) Immunization: No need for hospitalization without contracting COVID-19.

b) Thanks to successful therapy, no overload of the intensive care system.

The measures that can be taken on the basis of principles 1 to 4 therefore lead to a reduction in the risk of disease in the current situation. However, they make little difference to the number of individuals who remain susceptible to infection with SARS-CoV-2 the more successful their intervention. At best, temporary immunity can be achieved in all, but only temporarily! This is not sufficient in the long run.

a. Possibilities and limits of artificial immunization

Therefore, the presence of SARS-CoV-2 wherever in the world represents a sword of Damocles for the health threat of every single citizen. This risk can be addressed through sustained and global immunization. However, even the use of vaccines does not guarantee that no one will fall ill with COVID-19 or die from it. This is due to the fact that no vaccine is 100% effective and not everyone is allowed to be vaccinated or wants to be vaccinated. In addition, it takes a considerable amount of time to develop and produce the required vaccines. Then they have to be distributed to the entire population and develop their effect. During this time, there remains a considerable risk of disease and death.

The emergence of new mutants is particularly problematic: Their occurrence — in contrast to influenza, for example — cannot be predicted in terms of time. Therefore, the precautionary production of effective vaccines is not possible. Vaccines may then have to be adjusted during an epidemic. This may mean that the population has to be vaccinated again, even though it has just been successfully vaccinated against the «old pathogen».

Therefore, while vaccination is essential, it alone cannot ensure a return to life as it was in 2019. This is not true even if one accepts morbidity and mortality rates as with influenza. COVID-19 is not really comparable to influenza (see Part 2).

b. Specific therapy and rehabilitation

Therefore, the development of specific therapy methods will become increasingly important in the future. It is gratifying to note that considerable successes have been reported in this regard, e.g., in the development of new drugs.

However, cures are not enough to solve the health problems resulting from COVID-19. The late effects after COVID-19 mean that many of those who have recovered are «no longer the same» [136]. Months of rehabilitation are often required. A new «English term» is currently being used for this: Long COVID. Many people first have to learn to breathe again with their own muscles. Possibly this phase can be shortened by using the possibilities of intermittent hypoxia training (IHT) passively, sitting in a chair, actively — combined with intervallic moderate exercise, or another option is individually adjusted intermittent hypoxic-hyperoxic exposures based on biofeedback principles [137].

c. Implementation of measures based on principle 5 against COVID-19

Those who are being vaccinated, are in the hospital or for rehabilitation should be able to be neglected as spreaders at least during this period: After all, the relevant institutions can be organized and appropriately staffed and equipped so that the risk of transmission is extremely low. It would make sense to use a suitable antiseptic both to support the therapy by reducing the relevance of re-infection with the germs released by the patient's own cells in the nose and especially in the lungs, and also as a measure to safeguard the workplace.

Since many diseased persons are thus already eliminated as causative agents of secondary infections, the question arises, among other things, with what justification one actually always speaks of «effective reproduction rate». The starting point is the number of manifestly ill

persons. Therefore, the pre- and asymptomatic carriers are not taken into account. Moreover, the models assume that everyone can contract the disease with the same probability. But this does not apply at all to those who have been detected and suspected, i.e. who are at least in home quarantine. Of course, it is important to know how many people have been newly infected, hospitalized, etc., and where. But why just these persons, who were recorded numerically, should give information about the further course of the disease, can be questioned. Are not completely different persons the carriers of the today freshly infected ones than those «under control»? And where were the people infected who brought the germs into the families?

Regardless of such questions, it remains obvious: In all measures based on Principle 5, the infrastructure, the creativity of the actors and the logistics are in the foreground and not the persons threatened by COVID-19.

This is also reflected in the graphical representation:

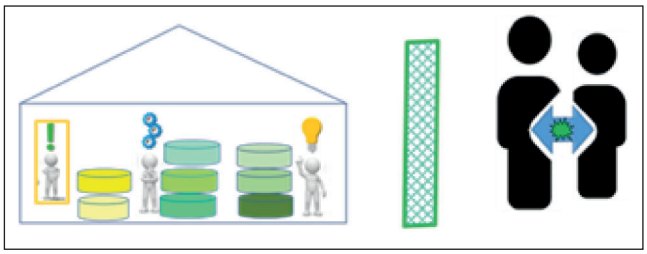

Fig. 16. Principle No.5: Increasing the proportion of immune patients and the survival rate through vaccination, therapy and rehabilitation thanks to appropriate structures, logistics, etc.

6) No single principle alone leads to achievable risk reduction.

The present chain of reasoning proves: Each of the principles presented suggests a reduction in the risks associated with COVID-19. This is illustrated by the graph no. 10 below. But it is not to be expected that even one of the 5 principles can be implemented in an ideal way. In our world, nothing is ideal. Moreover, errors cannot be excluded in principle. Therefore, risk cannot be eliminated in principle: Life is always life — threatening. One can only strive to reduce risks. Since our resources are limited, it must be expected that another risk will be increased if one focuses one's resources on only one approach to a solution. This is also true when using a single principle of action, when multiple techniques can be used to achieve the same goal (e.g., preventing the collapse of the health care system). The Pareto Principle 80:20 suggests that greater success can be expected when not one method is used using all available resources, but when there is a balanced distribution of resources.

This is illustrated by the graph below. It is also clear that the 5 principles are linked to each other in a dynamic way.

a. How sure can we be that vaccinated and recovered people are not contributing to the dark net?

There is consensus that freshly and first-time contaminated unvaccinated individuals become infectious first and only then become symptomatic themselves. Therefore, this brief period of asymptomatic transmission of germs is important in terms of epidemic hygiene. There is also consensus that the first symptoms appear before the antibodies appear and that the infectivity of the persons who now have antibodies decreases sharply.

The following two graphs should clarify the situation. The first shows the average change in viral load, e.g. in the nose, determined from many individual values, and the appearance of antibodies after initial contamination. The time from which the contaminated person is on average contagious is also entered: i.e. approximately 1—2 days before the onset of symptoms in the contaminated person.

The second graph shows again the distribution of days after contact of the contaminated person with the person who infected them and the onset of symptoms (incubation period). Shown are the values collected from 312 couples in Austria in April 2020. On average, 4.6 days pass until the onset of symptoms. If we transfer the conclusions roughly adopted from the first graph, infectivity begins around day 3 after contact. However, a considerable number of persons become symptomatic only after 5 days and quite a few already days before day 5. Therefore, the times from when and until when asymptomatic individuals may be carriers may differ significantly from the «planned value» of one day before one's symptoms.

A person who has been fully successfully vaccinated or has full immune protection following illness can be expected to have a different epidemic hygiene event than an unvaccinated person or a person whose vaccination or cure was long ago. This is to be expected depending on whether and how long the vaccination and or the immunity acquired by the disease has a protection against the contamination or not and how strong this protective effect is.

Negligible is the case should and as long as the specific immunity by vaccination and disease also protects 100% against the contamination.

In all other cases it should be expected that e.g. in the nose of the contaminated immunized asymptomatic person there will be an increase of the viral load, which will become so high that the transmission of the viruses can occur, although the penetration of the pathogens into the organism can be sufficiently prevented. Only when this penetration can no longer be prevented and the build-up of specific immunity would begin in the unvaccinated first infected person, can it also be expected in the vaccinated or recovered person that the existing antibodies can protect the contaminated and immunized person from a new disease. At the same time, a booster effect should be expected.

In terms of epidemic hygiene, this would mean that vaccinated and recovered persons would cause a — depending on the degree of their immunity — more or less high or low share in the transmission of the germs.

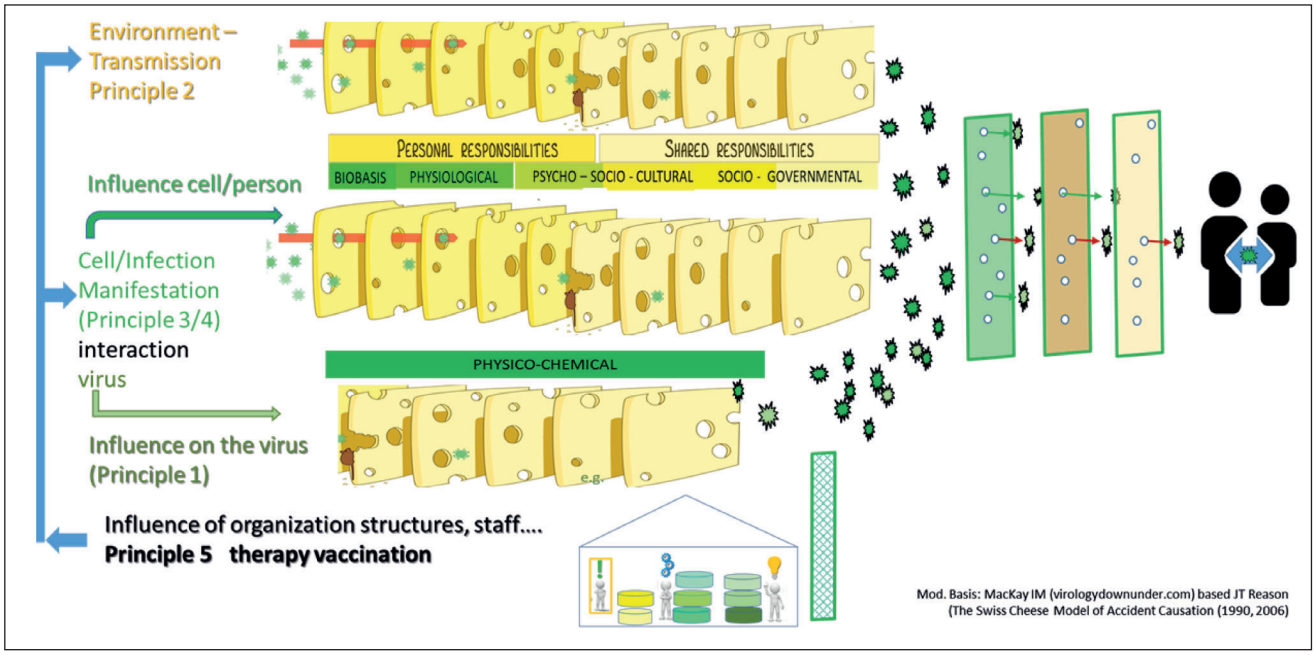

Fig. 17. Measures against the COVID-19 pandemic THE CONNECTION OF THE VARIOUS PRINCIPLES TO REDUCE THE RISK OF COVID 19 ON THE BASIS OF FOLLOWING THE CAUSE RESPONSE from the occurrence of SARS-CoV-2 to possible death from COVID-19.

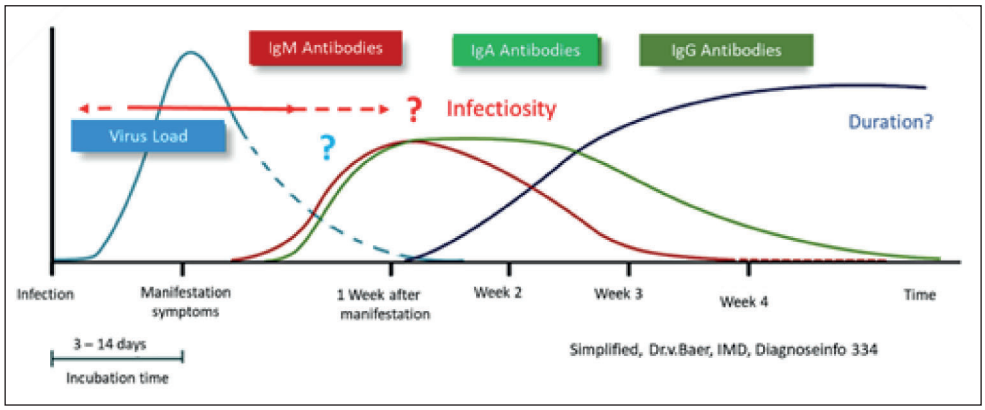

Fig. 18. Viral load (smear, nose), selected antibodies (blood) over time after infection (symbol plot) and infectivity at first illness and before booster in case of lack of protection against contamination or infection.

The effectiveness of specific immunity would reduce the relevance of the now secondarily infected vaccinated and recovered to the possibility of new mutants forming, but would not completely eliminate their relevance. Mutants arise naturally almost exclusively in the bodies of infected individuals. Full protection against the further development of mutants would only be achieved if it were possible to prevent contamination or at least penetration. This is probably best achieved by the application of compatible antiseptics or, at best, by artificially produced antibodies, especially into the upper respiratory tract.

All this is to be feared only if the recovered and vaccinated should not be able to prevent renewed contamination in addition to the specific intracorporeal efficacy against their own disease. So far, however, there is no evidence of this. Moreover, the goal of vaccination is «only» to protect against severe disease and death. This goal is achieved in up to 90% of those vaccinated, but not permanently. Therefore, even in the optimal case, vaccinated persons remain as potentially self-threatened.

For reasons of the precautionary principle, one should thus currently assume that vaccinated and recovered persons also make a contribution worthy of consideration to the spread of the epidemic as well as to the appearance of new mutants. In terms of epidemic hygiene, it is not the quantity of illnesses that is the focus of concern, as is understandable for clinicians: a single person, especially one who spreads germs inconspicuously, is enough to be the starting point of an epidemic — as evidenced, for example, by the bartender in Ischgl.

If this chain of reasoning is correct, the indispensable option is the WORLDWIDE use of well-tolerated antiseptics. This measure is seen as a necessary complement to, if possible, worldwide vaccination of all those willing to be vaccinated.

E) Is this fight against COVID-19 enough?

1. The new priority: fight against the mutants — or fighting Long COVID after all?

Obviously, the current approach is not enough. Important measures are also needed with regard to the infrastructure if one turns to the pandemic within the pandemic, as Long COVID. If one wants to work consistently against the new emergence of mutants, one will have to turn to a greater extent to the supply of LMIC as well as to the underprivileged groups in one's own countries. Lasting success can only be expected if the experience gained in the fight against tuberculosis in Austria between 1900 and 1950 is utilized.

2. Linking the fight against SARS-CoV-2 and the collapse of the health system in the comprehensive COVID-19 crisis.

The fight against SARS-CoV-2 was lost in many countries in the early summer of 2020: the opportunity to eradicate the virus with a combined strategy was missed. The situation at the beginning of 2021 is characterized by the fight against the collapse of the health system and the efforts against the unintended consequences of this fight on the economy, society, culture, international connectivity and last but not least against the threat to internal and external peace. The following diagram symbolizes the comprehensive options in the current situation. From the point of view of health, it should be borne in mind that the measures to be used in this context have a reciprocal effect on each other. It is not without reason that both the WHO and the EU, for example, take the view that the development of health levels is an essential measure of the success of the policy as a whole [138].

The effect of indirect impacts on COVID-19 represents only the tip of the iceberg. This is demonstrated by the changes in life expectancy in the U.S. demonstrated between January and June 2020 [139]. The life expectancy of all Americans decreases by a whole year, that of the black population by 2.7 years within this half year! The difference between white and black Americans thus widened to 6 years. It thus dropped to the 1998 level [140]! The last time such changes occurred was after the Spanish flu of 1917/1916.

a) «Three times three and three»

Consideration of the optimal course of action in the event of an epidemic with a novel pathogen can be expressed by the catchphrase «three times three and three».

1. from a temporal point of view, one can distinguish the need to act immediately, in the medium term and in the long term.
2. the course of an epidemic begins when carriers who are known or can be detected at a precisely definable location introduce the pathogen into a

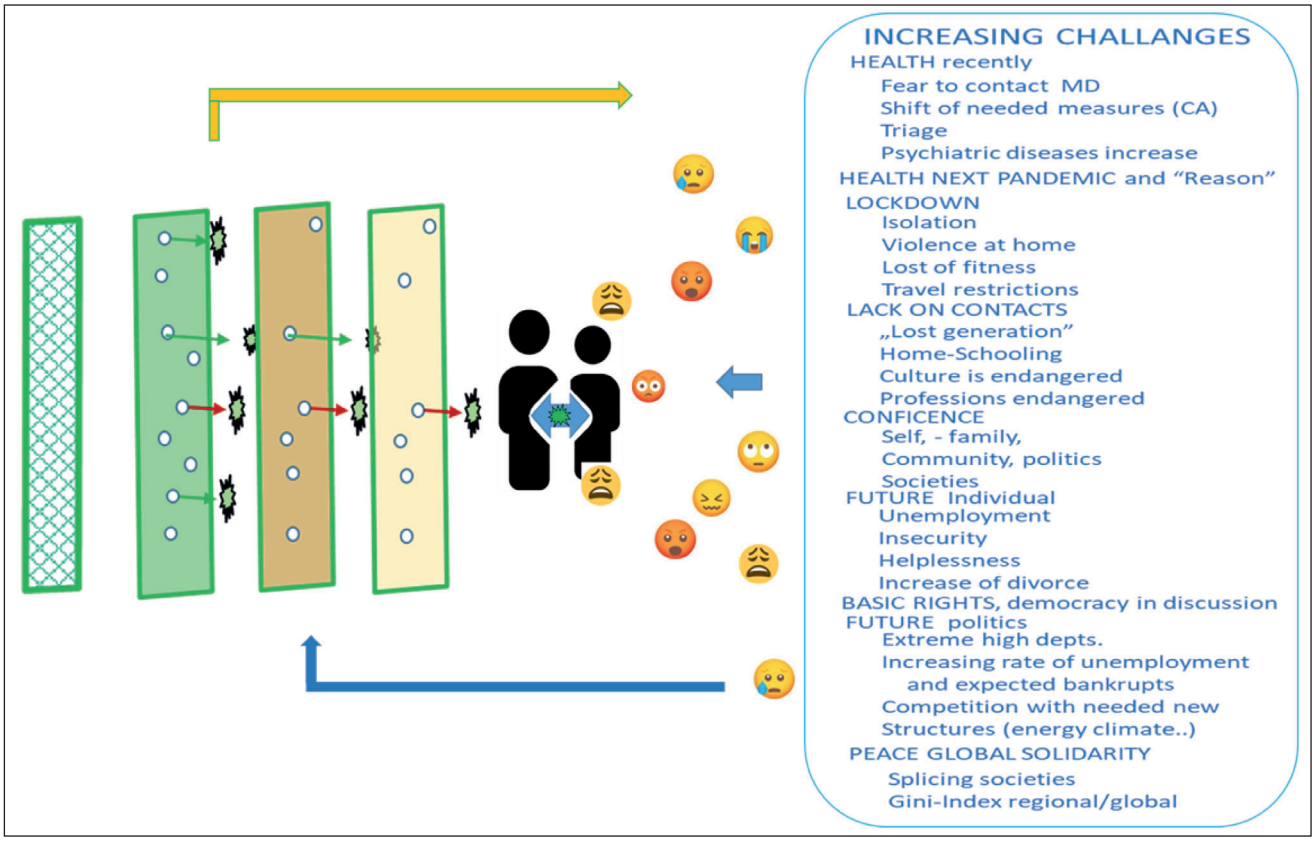

Fig. 19. The current situation — dominated by the unintended effects of the intended measures based on simplified theoretical assumptions about the nature of the COVID-19 pandemic

population that has never come into contact with it. If it is not possible to destroy the germ in this phase, the germ is spread via areas and persons that can no longer be precisely defined. In the third phase, delayed health effects are in the foreground.

3. an epidemic and especially a pandemic not only have medium and immediate health effects that have to be considered individually, locally, regionally and globally. The epidemic and the measures taken and not taken also have ecological, economic, sociocultural and solidarity-related effects.

The resulting requirements can only be considered in a weighted evaluative manner.

Science can offer valuable assistance in this regard. It can base its reasoning on three foundations:

1. the entire available state of knowledge
2. epistemologically available techniques to make different scientific disciplines, which so far seem to be incompatible on a causal level, compatible with each other (e.g. Einstein's «theories of principles»)
3. «The application of the laws of thought and the experiences of daily life».

b) «Never let a good crisis go to waste (Churchill)»

Crises require of profound changes. Under these conditions, the population is also ready to accept interventions that under «normal conditions» would lead to massive resistance. Responsible politics can and should use this willingness to set the course for the future: As a yardstick for the success of overall policy, WHO and the EU refer to the development of health and well-being. It is thus about the possibility of each individual as a sociocultural and responsible being to be able to develop in a future-oriented way [141].

MULTI-INTENTIONALITY

Churchill's quotation directs our interest to an almost shamefully omitted topic, which is therefore also here only a few explanations, but which is rightly to be seen as a counterpart to the extensive chapters on multicausality: That the reasons for actions and omissions are not determined by objective needs, but by the justifiability with the personally and in a community enforceable desires.

Churchill thus extends the scientifically proven fact for the field of research and developments to everyday circumstances: Th. Kuhn has proved in his groundbreaking work «The Structure of Scientific Revolutions» that not that is in the center of scientific interest, where the greatest need for knowledge would be, but that which fits with the achievement and safeguarding of private personal desires. And woe to him who goes beyond the gray area of the border between the pragmatic normal science and the so-called paradigmatic science. He is persecuted by all legal and illegal means by the community of normal scientists: Kuhn proves the range from «not even ignoring» and therefore keeping away from all resources to social and physical annihilation.

a. Evolution and the struggle for physical, psychological and social survival

From an evolutionary point of view, this approach should not be surprising: The focus is now on preserving one's own physical, psychological and social survival, coupled with the effort to increase one's own advantage. After all, one does not accuse the baker of packing bread not to satisfy world hunger, but to be able to finance his daughter's studies and, at best, his girlfriend on Lake Garda. It is therefore not surprising that researchers prefer to focus their interest on the open questions, for which personnel, established funding and high impact points beckon. This then leads to the fact that objectively urgent questions are practically excluded from normal science. This is the case even though their urgency — indeed, their indispensability for solving the problem — is obvious to anyone who approaches the problem with an open mind. This becomes especially clear in connection with the nature of defense mechanisms against infections and the area covered by a very large number of researchers: as early as 1978, Micklem pointed out in the still remarkable «Encyclopedia of Ignorance,» written with the participation of numerous Nobel Prize winners, that immunology, as it is understood today, begins with the evolutionary level of vertebrates. Only vertebrates have antibodies. Vertebrates, however, make up only single percent of all living things that need to protect their selves against potential invaders and apparently have been able to do so successfully. Therefore, each cell seems to be able to defend itself against infections to a certain extent, even in the vertebrate organism network, and not by antibodies. At least this is what the studies of Gaudet et al suggest [122]. C. Nathan goes one step further: In the light of his own studies, he calls on the scientific community to finally reconsider its much too narrow focus in immunology [123]. Here it is about the extension to non-specific aspects, i.e. to what has been emphasized in the book published by the NY Academy of Science in 1994 and again in 2006: The evolutionary precursors of the infection defense are indispensable for understanding the success or failure of the infection defense in humans. At the same time, the very complex adaptive system of vertebrates is the result of a gradual development of primordial systems, whose effectiveness has therefore not been lost in principle [142]. Why this was abandoned — to the detriment of patients and as a voluntary relinquishment of an inhibitory influence on pandemic events, e.g. of COVID-19 — was not apparent to the editor of this standard work. The same applies to N-chlorotaurine. Over 20 years of research with over 200 publications in PubMed remain unconsidered. And no Minister of Health has followed the lead of Israel, which approved the use of NO as a nonspecific antiseptic nasal spray

even for children over 12 years of age by emergency prescription.

b. Personal primacy and the Semmelweis phenomenon.

Thus, it is not professional reasons but personal decisions that may be made in anticipation of collective approval and possibly promotion. Einstein put it so aptly, «Whoever wants to be a recognized member of a flock of sheep must first of all be a sheep». And who wants to follow the realization of Max Planck, according to which the deepest motive of everyone is «the preservation of the peace of mind», has a proven possibility: The Three Monkeys: «Hear nothing, see nothing, say nothing». There is otherwise enough to do! In the doubt then an old Arab wisdom helps further: Rather 1000 whip strokes on the back of/the other, than a whip stroke on the own back. And who wants to mess with the authorities and admit that one was wrong: Thus, the empirical evidence of antisepsis, which Semmelweis had presented in 1847/48 as a highly successful weapon against puerperal fever, was deliberately suppressed by the universities, including Virchow, and the ministries. For more than 20 years, mothers had to give up their lives because of non-scientific reasons. COVID-19 is probably about other dimensions. Is COVID-19 the next example of a «Semmelweis phenomenon», as such misappropriations of expert knowledge for non-scientific motives are called in professional circles.

c. The «left» hand of Adam Smith

In a limited, non-ideal world, one has to choose between the different options, advantages and disadvantages, if one wants to solve critically at problem. Then one can consciously choose a certain solution and consciously accept that this or that undesirable consequence will occur. But who is able to estimate what the consequences of these consequences are? These inevitabilities are not changed even if decisions are made automatically and without deliberation.

Adam Smith started from these considerations and thus created an essential basis for economic liberalism: Even through the orders of the rich for lavish luxury goods, a cascade of service providers receives an order and thus also income, which secures their livelihood as long as enough orders are placed. However, these are only placed because the clients expect personal benefits from them — regardless of the unintended and unthinking benefit of the contractors.

The COVID-19 example shows a second side of coercion that is unobserved and unintended, but inevitably to be expected from the same thought process. The different methods used to fight COVID-19 also provide benefits to selected groups. And the more expensive measures are, the greater the potential benefits associated with them. Taking advantage of these is to be expected, if only for the reasons explained above. It is also to be expected that rivalries will arise among potential users and that attempts will be made to overcome competitors. One could get this impression from the arguments that have been put forward against Astra Zeneka and spread with the help of the mass media. It is not even necessary to assume that the use of cheap antiseptics is being deliberately opposed. The lack of interest in the comparatively small private benefits is enough.

It is easier to shift one's interest to the area where a lot of profit can be expected in the shortest possible time: Supply and demand, for example, for such mundane things as masks, gloves, etc. (see Fig. 5)

We are talking about average increases of over 1000 percent and maximum prices of close to 4000%. These differences are not even remotely matched by a corresponding increase in employment for service workers. However, this was the idea underlying «invisible hand» by Adam Smith. Moreover, face masks are not luxury goods, but essential purchases that everyone, including service employees, has to make. Thus, it is not surprising that the gap between rich and poor has widened in the pandemic, and thus all the adverse health effects evidenced in the context of the Gini index (i.e., the measure of this gap) are to be expected. Thus, it makes sense to point out that the approach of classical national economics of the 19th century may no longer be transferred 1:1 under the given conditions: one must also reckon with an invisible «left» hand.

It is a fact that despite the massive economic losses of very large parts of the population in the Western countries, the total disposable wealth has increased in the wake of the pandemic as rarely in the period since the end of the Second World War. The impact is even more extreme in the developing countries: Many have had to accept setbacks in their development of many years.

The various cases of corruption of leading politicians in the context of the acquisitions, for example, also seem to point to an unfortunate close link between politics and business. But also quite legal lobbying activity contributes to the overall situation, which prompts Churchill to advise using the changed assessment situation during and after disasters for future-oriented long-term measures.

SUMMARY

Remember in advance: The issue is the appropriate course of action during a state of emergency. Therefore, it must not be demanded that every measure is covered by the state of knowledge. On the contrary, the challenge lies precisely in finding the most forward-looking solution, despite a lack of knowledge, which can be justified «by applying the laws of reasoning and the experiences of everyday life» in a weighted manner. It is therefore to be expected that, as knowledge increases, previously assumed threats can and must be repeatedly withdrawn as unjustified. This special situation in the understanding of risk management in the case of previously unknown pathogens must also be communicated to the population accordingly.

1. Create free space at the moment

- The decision maker is responsible according to his position to act NOW or to refrain from certain possibilities. Refraining from using delegated authority also requires the same justification as acting.
- Experts are selected because they can be expected to provide evaluative advice beyond the state of established knowledge. A reference that something is not yet certain and therefore cannot be taken into account is not justifiable in a pandemic — in the case of imminent danger. This also applies to the neglect of — as is well known after a preliminary review by an expert — publications that have been put online but have not yet been peer-reviewed.
- Individual contribution: Adherence to the various regulations for avoiding contact with contagious material should in itself be indisputable. However, interrupting contact will not increase the number of those no longer susceptible. Therefore, everyone should be shown and given the opportunity to reduce his or her threat in a self-determined way until successful immunization, and without having to accept unreasonable restrictions.
  - For example, in the course of an AG or PCR test, the test person could be given a nasal spray containing a compatible and effective antiseptic. This could be done, for example, in the course of preventive measures for returnees from abroad. This would potentially protect those testing positive from the disease and reduce the likelihood of transmitting the viruses to others, for a longer period of time if the spray were used regularly.
  - Individuals with a current negative AG or PCR test could be given additional options for action, given the appropriate framework: They could, for example, be allowed to visit a restaurant — while complying with all other currently necessary regulations — by applying a 1% NCT solution to their left and right noses in addition to presenting the test result in front of the restaurant owner. This measure would be effective both in terms of epidemic hygiene and individual hygiene.
  - In the light of the new mutants and the rather limited effectiveness of the vaccinations, consideration should also be given to suggesting that those who have already been vaccinated and those who have recovered should protect themselves — and possibly others — by using an antiseptic nasal spray when visiting a restaurant or soccer match, for example.
  - So far, such possibilities have been withheld from citizens in Austria. Therefore, it makes sense to first read through the examples of how one can reduce one's own risk of contracting COVID-19 beyond the regulations (see e.g. open window effect, green plants, maintain daily structure, maintain confidant relationship, gargle with an antiseptic- but do not inject into the nose, into vessels or even eat or drink! For details see Part 2)

This should create the room for maneuver that allows one to approach the situation at hand with a mental distance. Conclusions can also be summarized for this.

2. On the nature of the disease

- COVID-19 is a very dangerous disease with many faces that can lead to a horrible death and threaten the stability of the health care system and not only that of intensive care.
- SARS-COV-2 is an «insidious» pathogen with high «plasticity» (= adaptability).
  - This plasticity occurs especially in the host cell and despite «resistance» [143]: One more reason to prevent, if possible and unspecific measures (e.g. NCT), or new vaccination offers (administered intranasally) to influence that viruses cannot penetrate
  - The temporal occurrence of its health-relevant mutations cannot yet be predicted — as in pragmatic influenza.
  - It must be expected that the germ can infect inconspicuously and can be present in the body for a very long time even without symptoms. Therefore, for precautionary reasons, a «viral dark net» should be expected.
  - It can cause clinical pictures that are not yet sufficiently understood.
  - It can lead to various long-term damages.
- There is no reason to deny COVID-19 or the danger of SARS-CoV-2!
- But there is also no reason to ignore the current possibilities that antiseptics would be against: So no reason for antiseptic deniers and preventers either! A comprehensive approach to the disease and strategy is needed.
- Nevertheless, SARS-CoV-2 is not particularly contagious. For the majority of individuals, contact with SARS-CoV-2 does not result in contamination or manifestation of the disease. This does not mean that SARS-CoV-2 is harmless. Neither are polio viruses, although only about 1% of susceptible individuals become ill after contact with the virus.
- The persons do not get sick if their mucosal cells can prevent the penetration of the viruses into the body and the necessary multiplication, so that the disease can be prevented. The person owes this to their non-specific defenses.
- The risk of the disease therefore increases for four reasons in particular

1. That a correspondingly high viral load cannot be prevented from reaching the person.
2. That the viruses increase in infectivity (mutants) and can penetrate more effectively.
3. if the current non-specific defense of the cells cannot prevent the susceptibility and thus the contamination, even if this could be expected under normal conditions, supported by individual hygienic measures («open window effect»).
4. If the non-specific defense of the organism cannot prevent the disease with manifest symptoms.
5. The risk increase in groups of persons with a permanently reduced immune status for sociocultural reasons and as a result of previous damage, but also as a result of acute multiple exposures, among other things as a result of measures against the spread of SARS-CoV-2.

- Against 1) measures like testing, checking, secreting, filter systems .... help.
- Against 2) the measures of the IPBES and all steps, which lead to an early inactivation of the viruses and thus shorten the duration, in which it can come to the mutant formation, help
- Against 3, 4 and 5 the preventive strengthening and the substitution of the currently deficient non-specific defenses.
- We have to fight SARS-CoV-2 and COVID-19 with ALL means, but really with ALL and in a balanced way

3. About the current situation

But what can one do or refrain from doing in one's own area to be able to take appropriate steps oneself. Or how would one act if one were a political decision maker? What would be the very first starting point to end the current restriction of measures? This would probably require putting up for discussion one of the fundamental pillars on which the founders of the measures are built: The dominance of forecasts based on the calculation of the dynamics of the epidemic. But this should actually be easy to do if only decision makers were aware of the limitations that Kermack & McKendrick (1927) placed on the applicability of their model. Interested parties are referred to the papers in chapter H (Fundamentals): But everyone should at least be aware of the following: The fathers of the experimental epidemiology of epidemics recall that in their model they assume the infection process itself to be constant in order to demonstrate evidence of an independent effect of contact reduction. It should be obvious to everyone that these simplifications are of course not given in practice. This was clear to Kermack & Kendrick especially for the factor «human». They also summarized this unmistakably as follows in the characterization of their «infectivity concept»:

a. The pathogenicity of the virus, which enables it to penetrate the mucosal wall in the nose, mouth and lungs
b. The ability of the nonspecific defenses of the cells of the mucosa to inhibit infection; and
c. the non-specific ability of the organism to fight against the manifestation of the disease in order to inhibit the symptoms.

They therefore arrive at point 3 of the abstract: «Small increases in the rate of infectivity can lead to large epidemics» (p. 720)

However, every mother already takes this into account at the individual level. She urges her child to wear a sweater when it's cold and a raincoat when it's raining: Clothing does not change the viral load that is inhaled or the number of contacts. It also does not replace vaccination. But the risk of catching a cold does. This is just one example of the possibility of individual improvement of non-specific defenses. But such influences cannot be uncovered by the predictive models used. On the contrary. All adverse influences on infectivity via the «human factor» both as a living being and as a psycho-socio-cultural being can only be interpreted as consequences of inadequate compliance with contact avoidance regulations. A method can only do what it can do. And this is what Kermack & Kendrick pointed out: «Small increases of the infection rate — e.g. also by evaluation processes — can lead to large epidemics» -or «Small reductions of the infection rate — e.g. by targeted use of NCT- can be expected to have relevant braking effects on large epidemics.

4. Further conclusions.

Important further conclusions are already listed in the individual chapters. Additional rationales are addressed in the chapters of Part 2.

- Risks can only be reduced, not eliminated, in our less than ideal world. If you use your resources to reduce one risk, you must expect that other risks will be increased because you lack the resources to reduce the risk there as well.
  - People make mistakes. This is ultimately unavoidable. In order to reduce risks, one can start with the acting persons as well as with the system. The key is to constantly check for overlooked opportunities instead of «looking for the culprit» and just implementing «the same thing, only with greater severity». (Reason)
  - The efficiency of one and the same effect principle decreases with the increasing demand on the success to be achieved: Pareto states as a rule of thumb that with 20% effort 80% of the possible effects can be achieved, the remaining 80% are needed to achieve the remaining 20%.
  - Therefore, the allocation of resources (Follmer) should be aimed for a comprehensive approach (Comprehensive Care). This is consistent with Reason's model of risk management («Swiss cheese model»). But this assumes — in contrast to the current widespread approach — the use of different principles of action rather than different techniques of the same principle

of action, e.g. to stop the epidemic by interrupting contact.

- Contact with infected persons is a necessary but not a sufficient explanation for either infection with SARS-CoV-2 or manifest disease with COVID-19. Without penetration of the virus, e.g., through the mucosa of the nose, there is no infection. This step is influenced by the nonspecific defense of the mucosal cells. Current weaknesses of the defense can be compensated by antiseptics. The principle of antisepsis has been known since 1847 (Semmelweis: savior of mothers from puerperal fever). Striving for authority in the university and the ministry prevented its Europe-wide use until 1865. («Semmelweis effect»). Then Lister rediscovered it.
  - The development of specific protection against pathogens (antibodies...) usually requires the penetration of the pathogens and thus the overcoming of the non-specific defense. It then takes days for the first antibodies to become available. In this phase, non-specific possibilities (e.g. improved oxygen supply after successful training) are still significant.
  - Legally significant in the classification of antiseptics is whether they are to be classified as medical devices or as drugs. Medical devices may not be absorbed into the body, but medications may. Their general use (CE marking) can therefore be achieved with less experimental effort.
  - In Europe, during epidemics, the government/the responsible minister is authorized to approve both drugs and medical devices by emergency prescription, and if necessary, to prescribe their production and distribution.
  - Action and inaction must be justified equally with regard to the precautionary principle.
  - Doctors in Europe are entitled to issue prescriptions for their patients that are to be produced according to the individual prescription of a medical doctor by pharmacies. However, they can only do so if the raw products are delivered. Patent holders can prohibit this.
- Currently, there is only one synthetic, industrially produced, antiviral substance that has been tested for tolerability and can be used in the same place where it occurs naturally and for which extensive studies on its efficacy have been available for years: N-chlorotaurine.
  - The efficacy of NCT has been confirmed in vitro by researchers from the Hygiene and Microbiology and Virology sections of the Medical University of Innsbruck, the Robert Koch Institute, Charitee Berlin and 360biolabs Pty Melbourne. This work can be viewed online since December 2020 [74].
  - NCT could be used individual hygienically to reduce the risk of infection and disease. This opportunity is currently being withheld from citizens.
  - There would also be a desirable impact in terms of disease hygiene: the likelihood of transmission to others would decrease.
  - The effectiveness of antiseptics is based on the fact that the structures of the viruses are denatured, i.e. destroyed. Antigens act differently: first, there is not a «crushing» of structures, but an «enlargement»: the combination of antigen and antibody into one unit. This takes place at very special, mutant-specific spatial structures (epitope and paratope). This new unit is only broken down in the course of the next step (phagocytosis) in the corresponding cells. Therefore, efficient antiseptics against the parent form of SARS-CoV-2 are expected to be effective against mutants as well.
  - In addition, an NO preparation has been available in Israel since March 2021, and its use has been approved by way of emergency regulation even for children over 12 years of age. Thus, a medical product is available in Israel that can influence this group of spreaders.
- In the medium term, various hopeful methods are under discussion to compensate for current deficits in non-specific defenses by means of antiseptics or, for example, locally applicable antibodies. This will require the initiative of policy makers: it is they who are responsible for protecting the health of the population, not scientists or industry.
  - Arguably, the government/minister is also obliged to use the competences delegated by parliament in case of an epidemic or pandemics.
- Non-specific defenses are altered by physical, chemical, emotional, intellectual, cognitive, etc. Processes altered. This can lead to their short-term deterioration but also improvement of the defense situation. It is fundamentally wrong to assume that the defense situation remains constant and that the way the epidemic and its consequences are experienced is irrelevant in terms of health and the spread of pathogens. This should be considered by decision makers when dealing with those affected in order to better manage the epidemic and avoid preventable harm to citizens.
  - Therefore, the indirect health relevance of the measures as well as the epidemiological effect to be expected from them should be examined in the same way as their influence on the interruption of transmission.
  - The use of agents to temporarily lower the contagion index, e.g., by supporting nonspecific defenses, should be used to better protect health care workers, especially when mutants are likely to be encountered against which vaccines may not be fully effective.

- The early phase of COVID-19 is co-determined by reinfection of viruses that are released «back out» (into the nose, lungs, mouth) in the respiratory tract. It is expected that inhalation with a tolerable antiseptic will improve the healing processes of these patients and therefore reduce the proportion of individuals who require artificial respiration and thus have an increased risk of mortality.
- In addition, this will reduce the risk of transmission to nursing staff.
- In the medium term, the risk of infectious diseases can be reduced by raising the quality of life, strengthening precautions for risks that cannot be managed by the individual (illness, unemployment, old-age provision, care) and supporting hope for a better, foreseeable future (education), etc. o In the long term, the risk of infectious diseases can be reduced by improving the quality of life.

- It is essential to develop comprehensive strategies not only from an individual and epidemic hygiene point of view. Man as a social being needs personal contact with others. They have a right to transparent, verifiable explanations as to why which measures are taken, how they are justified (also mathematically), and how their basic rights and future opportunities are thereby curtailed. However, for medical reasons alone, this is essential.
  - Even if the measures are set, a residual risk cannot be ruled out.
  - Particularly where the persons concerned and their current risk of transmitting the germs are known, it is possible to increase individual freedom of action through accompanying measures: For example, in the presence of a current negative test, a visit to a pub could be made possible for those who apply a compatible antiseptic to the nose in front of a witness before entering the pub. This is intended as an additional measure to the other precautions required of pub operators and patrons
  - Such a measure could put individuals on an equal footing with those already vaccinated for selected situations.
- Since the beginning of January 2020, vaccines are available that are administered intramuscularly. Their task is to significantly reduce the individual risk for the vaccinated person to become seriously ill or to die from COVID-19. It is gratifying if, in addition, there are also advantages in terms of epidemic hygiene. In any case, effectiveness can be expected from the fact that the relevance of vaccinated persons as classical carriers is greatly reduced. They only fall ill much less frequently. Whether there will be any relevant effects on the epidemic beyond this cannot be definitively assessed at present.
- Greater efficacy is attributed to intranasally applied vaccines, also with regard to the relevance of the release of viruses to others and as protection against a new infection. Unfortunately, such vaccines are not yet available.
- It must be expected that mutants will suddenly appear that cannot be combated by the currently available vaccines. If we do not want to live with the constantly looming threat of new lockdowns, we must be prepared to combat them with non-specific measures as well.
- There are still many open questions about the nature of the interaction between SARS-CoV-2 and the organism
  - It is striking, for example, how often it is impossible to trace the chain of infection. Just blaming the infected persons for being unwilling or forgetful is obviously not enough: An epidemiologically excellently constructed study on the course of the effects of the epidemic in Wuhan recently came to the conclusion that 82% of all persons in whom antibodies and thus the disease were detected had no symptoms [129]. The assessment of the relevance of these so-called «asymptomatics» therefore ranges from «probably subordinate role» (Robert Koch Institute [144]) to «urgent need for further clarification» because of the broad differences (4 — 41%) [145] to with 82% probably no longer subordinate. The informative value of the persons conspicuous with symptoms or by PCR tests in the follow-up for the characterization of the situation and the estimation of the further course seems thus worth reviewing.
  - Regardless, it would be valuable to know which and how many individuals per day were shown to have been admitted to the hospital with COVID-19 and how long each lingered. However, this would require individual data.
  - What is the reason that in Carinthia, for example, during the summer of 2020, despite extreme tourist utilization and the associated increase in contacts, the reproduction number was not even calculable for quite some time (end of April to end of June)? The dead no. 13 was registered in Carinthia on May 3, 2020, the dead no. 14 only on October 23. Natural scientific characteristics of the climate cannot find the world organization of the meteorologists for it [146].
- The global significance of the pandemic deserves special attention. The effort to also provide the financially weak countries with the necessary aid is a priority, if only for self-protection. The

aid must come quickly: As honorable as it is to discuss releasing the patents for the vaccines, this will not achieve the necessary protection. It would make more sense to provide a free supply of vaccines throughout the country. These countries would be more helped by releasing the patents for the production of tolerable antiseptics. They could probably produce these themselves very quickly and thus bridge the phase so that the vaccines can be made available to them.

- An era of pandemics is looming. This has various consequences: They also affect internal and external peace in many ways. Anyone who can produce a modern vaccine could also construct a pathogenic virus with terrorist intent. A new form of threat has emerged. In terms of individual hygiene, only non-specific defenses can be used against it. For the e.g. legal solution and the corresponding monitoring the company is required.
- This also applies to the implementation of the demands of the IPBES: It estimates the number of different types of viruses for which animals are currently the hosts and are potential threats to humans at 700,000 to 825,000. It is high time to counter the danger of new human-pathogenic viruses forming and causing epidemics. This will require correspondingly comprehensive spatial planning measures and appropriate habitat disentanglement.
- The global confrontation with COVID-19 must not only take into account the ecological framework. The threat also affects cultural diversity. But it is also possible that the experience accumulated over millennia offers evidence-based medical options that have not yet been adequately considered.

«THE GAME ABOUT THE NEW NORMALITY» — ALMOST A THOUGTH EXPERIMENT

Nobody knows the future, everybody would like to know at least roughly how it could look like. With the information now available, it is possible to mentally derive one's own model of the future. A game is intended to help with this: Not as a classic scientific thought experiment, but rather as a playful exploration of «What if?». Hence «The game about the NEW NORMALITY». It is supposed to help everyone — whether private person or decision maker — to realize which «NEW normality» would expect us, if which measures are set or would have been set.

The game can be played alone, in pairs or with several people. It is only necessary to agree beforehand on what the content of the game should be this time. The game allows for many creative possibilities. The basics for the game are included in this handout.

Thus, one can think about how the situation might look today if one had not taken the measures actually realized in March 2020, but had also used this or that possibility. You are also free to try to determine, for example, what the consequences would be in the future if this or that measure were taken today. You can focus on the near or distant future of your personal life or think about global changes. One can also make it a goal to consider what measures would be appropriate so that next summer would again be the everyday normal as it was in the summer of 2019.

One can take into account what which concepts have yielded in practice so far, e.g., the actions of most Western countries with their effects that go far beyond health aspects. One can also consider how the current situation in China came about and how surprisingly little impact the models of experimental epidemiologists have had on Chinese policy. Decision makers in so many states, however, have gone by the model that was calculated for WUHAN in the spring. No SEIR model would likely have calculated 60 days of quarantine in Wuhan, linked to the range of other measures. What would the consequences have been if, for example, the South Korean approach had been adopted. This state showed only an approximate 1% decline in GDP for 2020, but requires considerable concessions from its citizens and visitors regarding the state's access to individual behavior.

1. Zero-sum game or WINWIN?

Intentionally, only a few suggestions are made as to how the game should be organized. Playing should stimulate one's own creativity. For many, it is essential to be able to defeat one's teammate in the game, as in soccer: in order to succeed, one must inflict a defeat on the other team. The gain of one is matched by the loss of the other: Hence «zero-sum game». But isn't there another way [147]? Computer games in particular show us: You can fight together against an anonymous enemy and win by the fact that the other player also wins. Such WINWIN situations are a prerequisite for evolutionary progress. Games have also become established in which one experiences success by successfully managing the processes in a city to the prosperity of its citizens. This does not necessarily mean that one has to cheat one's former partner in the end, as game theory teaches us with the example of the prisoner's dilemma: Here, both prisoners go home with a small penalty as long as both cover each other. Therefore, both would have an advantage as long as one assumes that the partner continues to be satisfied with the small advantage. After all, each has the chance to give the other a severe punishment and himself a greater advantage by betraying him. But why is it necessary to assume that both have something to hide and therefore, objectively, both are delinquent? Must the (economic, biological) maximization of success always be assumed as the determining control component, as leading economists (e.g. the Nobel Prize winner for economics Nash) and John Maynard Smith, a trendsetter in evolutionary game

theory, have assumed? Surely this «classical approach» rarely applies in the case of COVID-19, when the real issue is the successful fight against the pandemic. That one can draw personal advantage from the distress of others is indisputable. But this approach is rather counterproductive when it comes to the problem at hand, namely the fight against the direct and indirect consequences of COVID-19.

2. Risk Sharing and Functional Cooperation

The doctrine of profit maximization imposed on industry draws attention to a little-discussed but crucial change in COVID-19 strategies: the fact that vaccines could be developed and brought to market within a year. J.Inama-Sternegg attributes this to the fact that, for the first time, the steps in vaccine development that used to take place one after the other were carried out in parallel and in continuous coordination with the regulatory authorities [148]. In this way, the interests of those developing the vaccines as well as the naturally different, and therefore not competing, requirements of responsible inspection could be secured at the same time. The parallel processing of the previously successive steps could only be justified from an economic point of view because the institutions responsible for health security, namely the EU and the countries concerned, were prepared to share the cost risk of the development in advance. The prerequisite for this success was obviously a paradigm shift in self-image. Not only WINWIN can unite, but also the reduction of different risks. But for this to happen, it was necessary for both sides to abandon paradigms that had been out of discussion for decades. How difficult it is to abandon a position once held and long proven, as logically compelling as it may seem in retrospect, is probably known to everyone from their own experience. Because this is so difficult especially in science and usually only occurs with great sacrifices, Th. Kuhn felt compelled to distinguish between «paradigmatic science» and «normal science» [149].

3. Against the inner resistance — Max Planck and the peace of mind

The game opens up another possibility for success: In the game, one is «allowed» to think about things that would be completely out of the question «in real life». But often such considerations later turned out to be completely obviously correct, even if insignificant for everyday life. Let us only think which resistances Galilei, Copernicus, Darwin and Freud have caused with their logical deductions from facts, which are in themselves indisputable. Who cares today whether the earth revolves around the sun or the sun around the earth, that man is biologically a primate and that there are unconscious influences on behavior. But at that time this was obviously not a question of logical evaluation of newly available facts or conclusions. Here it was a question of the «canned stuff» and not only of mankind at that time, but of each individual in his self-conception as a person and member of his community. The resistance grew, so to speak, out of the necessity to protect oneself from the consequences of a new way of thinking against which no logical arguments could be put forward.

a. Who wants to question themselves?

Freuds saw in this a «narcissistic mortification» of mankind [150]. Perhaps Max Planck described such situations better when he speaks of the threat to the «peace of mind» which Max Planck classified as the most fundamental goal of every human being. Thereby he anticipates conclusions which are discussed in different versions in modern communication research: e.g. as «tragedy of risk perception»[151]. Investigations of the neuronal correlates show that the recognition of one's own basic misperceptions is answered with reactions that one would also expect when threatened, e.g., by a bear [152]. How profound such entrenched positions can be is proven by none other than Albert Einstein. He represented the revolutionary scientific opinion that the planets and all particles would move purposefully themselves according to the way most comfortable for them from technical point of view. His friend Bertrand Russel clarified the world view of Einstein with following example: «Just as the sea is not the cause that the water flows to it, the sun is not the cause that the planets orbit it. The planets move around the sun because this is the easiest possibility for them — in the technical sense of «smallest effect». It is the easiest of all possibilities because of the nature of the area in which they are, not because of any influence emanating from the Sun» [153]. But at the same time Einstein insisted that everything, even himself, had no free will. We would only imagine it. This was incompatible with a model of thought represented in particular by Heisenberg during his life. According to this, one could make the indeterminacy of the individual orientation, e.g. of a particle, understandable by granting them an individual arbitrariness within explorable and narrow limits [154] Heisenberg's proposal is scientifically correct and worth testing. Einstein could react to it — as an avowed follower of the religion view of Baruch Spinoza consequently — only more emotionally. And he did this in an extreme way [155]: «The thought that an electron exposed to a beam chooses by free decision the moment and the direction in which it wants to jump away is unbearable to me. If anything, I would rather be a cobbler or even an employee of a casino than a physicist» [156].

And Darwin wrote to his closest friend Hooker in 1844: I am almost convinced (quite contrary to opinion I started with) that species are not (it is like confessing a murder) immutable [157]. This scientifically correct conclusion inevitably had consequences for Darwin that went far beyond science: They forced Darwin to adopt attitudes that were no longer compatible with his requirements for himself. Therefore, in 1844, they prevented Darwin's peace of mind as murder would have done. Fourteen years later, when Darwin's ideas were first put forward in public, Darwin had ordered his world of thought to such an extent that the idea that species were

changeable was incompatible neither with his scientific ideas nor with his ideas about «God and the world». They corresponded — as the later Archbishop of Canterbury emphasized in his sermon before the world-famous confrontation between Bishop Wilberforce and «Darwin's bulldog» Huxley — very well to the view of religion held by the ultimately successful progressive clergy of the Anglican Church [158]. Einstein and Darwin thus prove two things: On the one hand, that religion-bound world views were significant for them also for the understanding of science and, on the other hand, that scientific correct arguments can be significant far beyond the principles of logic. Just the one who puts forward such fundamental positions in a logically compelling way puts one in the situation of having to question oneself. This must be prevented and the peace of mind must be restored. This is someone who fouls his own nest and must be fought therefore with all means. And the scientific argumentation brought forward is «not even ignored». Also this can be proved with Darwin: The Secretary General of the Line? Society, in which the world-changing contributions of Darwin and Wallace were presented on July 1, 1858, concludes in the report on the year 1858 that no really significant lecture had been given. A few months later, the first edition of the Origin of Species, which had been increased from 500 to 1250, was sold out within a week. As if nobody had recognized the importance of the lecture!

One will now object that the time is past — at least in Europe — when religion-related taboos were violated and the peace of mind of enlightened scientists could be threatened. Today, every argument would be discussed without prejudice, as long as it was logically correct. But is this really true? Or is not Newton's self-assessment confirmed, according to which his importance as a religious philosopher was greater than that as a physicist and mathematician. Einstein relativized Newton as a physicist and his mathematics. He proved mathematically and empirically that Newton's world view of the forces is appropriate only from the evolutionary level, in which there are solid bodies. Popper even tried to convince Einstein that he had thus falsified Newton's formulas. But Newton's world view of the cause of the movement of the solid bodies seems unbroken: The solid bodies are moved passively. To be able to justify this, he had to change the understanding of the being of God as the first mover. Since Aristotle and — for Christianity adjusted by — Thomas Aquinas it was valid that God motivates to the self-movement and every effectiveness and forces nothing and nobody. In this world view, God was the first mover, because he motivates to choose between alternatives the one that is advantageous in the long run, but also leaves other choices open. Newton changed this fundamentally. His God is the first mover because he forces the objects of his creation to act in an externally determined way through his physical omnipotence. Guilt and sin become possible only by the soul breathed into man.

b. Does Newton as a philosopher of religion still determine science today?

With Aristotle only God rests in himself and thus experiences his bliss in this ideal rest. The godlike stars and planets observe God and strive to move as exactly as possible around God, in order to attain thereby as similar bliss as possible. They themselves are empowered to effectively align themselves with self-chosen goals. There is no need for a passive, externally determined cause. Thus, Aristotle anticipated Einstein's world view of physical objects moving themselves constantly as conveniently as possible, but at the price of having to attribute divinity to the stars and planets. For Einstein the stars become inanimate earthly objects. But they remain part of the creation by an ideal God who is therefore himself limited to be able to create only ideal (Baruch Spinoza!). All objects must therefore ultimately come — consciously or unconsciously — to the decision for the ultimately ideal working. Einstein thus refutes not only Newton's machine model of physics. He refutes the being forced, replaces it by conscious or unconscious insight on the ideal. From the effect it comes out to the same: Whether one can be sure as a researcher that an effect will occur, because the objects must act in such a way determined by others (Newton), or because they will decide consciously or unconsciously for it (Einstein) or will probably act in such a way in the expectation of an own advantage (Darwin, extended evolutionary view), one does not even need to disclose: After all, the result corresponds to the prediction. It becomes really interesting when one has to justify why the predicted result does not always occur.

Thus it is well conceivable that also atheistic scientists assume to live in a world which functions so well only because inanimate objects can have only foreign-determined — therefor just passive — effects. It then remains open who ultimately determines. That these scientists carry on with it the inheritance of a religion-philosophical world view, which was invented only in the late 18th century, these researchers probably do not know at all. Nevertheless, one must reckon with the fact that this irrational position is represented just as consistently as at that time opposite Galilei, Kepler, Darwin, etc... however with reference to God as the causer. These questions will be discussed in more detail in Part 2.

c. Potential relevance to understanding mutations in SARS-CoV-2?

For the discussion of SARS-CoVB-2 and COVID-19, this discussion could become important, for example, when it comes to explaining why there is an increased occurrence of mutants. It is discussed e.g. in Oxford that in the probably rare cases of a simultaneous infection with two variants of the same or of different viruses it could come to an exchange or transfer of genetic material. It is in any case also remarkable that it is discussed whether the local coincidence of different mutants is conceded relevance for a combination of hereditary materials. Then the probability of the occurrence would depend nevertheless

also on other influencing variables, than the pure coincidence distribution with the spontaneous mutations for instance in the sense of a Lederberg constant. Remarkable the interpretation by Nels C. Elde of his own work on the significance of extensive recombination, i.e. the incorporation of whole gene segments into the genome without their origin being clear [159]: «In some cases it almost looks as if a sequence came from outer space, from coronaviruses, of whose existence we do not even know anything». But does it even have to be recombination? B. Choi et al. (Jinan University in Guangzhou) surmises, «It could simply be that they evolved themselves». [160]».

Thus, B.Choi et al. take a position that is very close to the proposed discussion that Burnet presented at the Nobel Prize ceremony as the central position of his work on the rationale for the interaction between the inanimate structures of antigens and antibodies. Recent studies of the distribution of mutations on the genome of SARS-CoV-2 confirm that the mutations were not randomly distributed: 38% were located on the 50th of the viral genome that encodes the antigen-binding domain of the spike protein [160]. Thus, the mutations were not normally distributed across the RNBA. This is also discussed in Part 2.

4. The playing field and the cloud

A thought game also needs a playing field: This can be imagined as in a game in which the game figure has given possibilities which the player can use according to his self-assessment in order to reach the evaluation point on a shorter or longer path. The shortest path corresponds to the assumption of having sufficient knowledge to solve the problem pragmatically. The longer way is chosen if one wants to proceed like an application-oriented scientist or if one believes to want to obtain additional information to individual questions. After all, the player is expected to be so critical that he will only move on to the next field if he has formed his own opinion about the previous procedure. Each character has the possibility to get information «from the cloud»: So, for example, to go the short way and get additional information «from the cloud» only to get more insight in a special aspect.

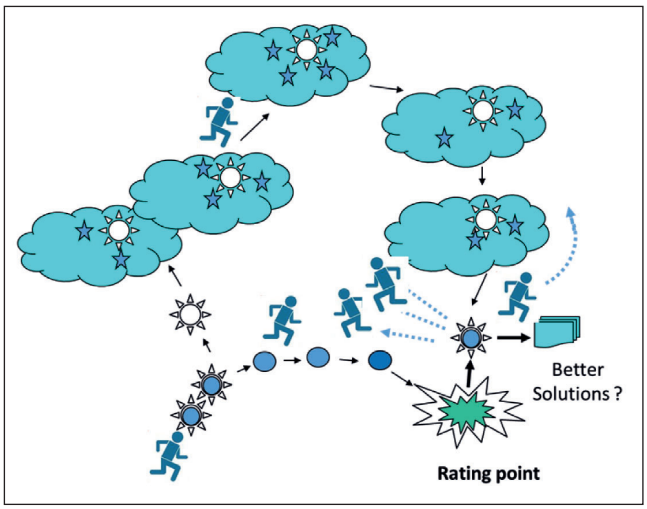

Fig. 20. THE «GAME OF NEW NORMALITY»

When playing the game with others, it makes sense to start a discussion with the other players on how they rate the situation. For this reason alone, it makes sense to view information from the cloud in order to be better equipped for this discussion.

In the end, one wants to be able to represent one's ideas about the «New Normal» well. In the cloud are all the positions that are passed through on the «long road». As with the cloud on the Internet, one can easily get to the targeted information from any point. Of course, one can also skip positions on both the pragmatic, short path and the «long» path oriented to application-oriented science or jump to a position via the cloud at any time.

Once you have reached the evaluation point, the next essential part of this game begins: using the knowledge you have gained in the meantime to form your own picture of the «New Normal. Now it is particularly informative to play the game together with others and discuss the positions. These will possibly suggest other solutions. In this way, all players are ultimately winners.

5. Weighting and linking the arguments

But this is only possible if the game instructions also offer methods for relating the different arguments to each other. One must then be able to weigh the advantages and disadvantages, goals and fears against each other. But these are by their nature much more different than the famous «apples and pears». To compare them would be scientifically inadmissible. But this incompatibility exists only if one assumes a two-value logic. Then apples are apples and not pears. But in everyday life it is self-evident that one must always decide between not comparing advantages and disadvantages according to these strict rules of Aristotelian logic. There are good reasons why someone prefers this kind of apples to those pears, although one actually prefers pears. It becomes even more difficult when one has to weigh up between duty and inclination, would it be better to play soccer now or do homework? And it becomes problematic with predictions about the epidemic with COVID-19 in a certain country, if one is to estimate how constants change, if they are not constant at all, but are dependent on several mutually independent influencing variables, e.g. the infectivity in the sense of Kermack and McKendrick: There variables of the viruses and innumerable influencing variables on the factor humans go into one and the same constant. The importance of the resulting uncertainties can be seen from the fact that the former CEO of SCIENCE recently called for the establishment of a new Federal Agency in the USA in an editorial in Science: The currently available models, he said, are too less informative and often arrive at extremely different forecasts. We do not need to wait for this Agency for our playbook. It must contain two different approaches to decision making:

And it would also be very significant to consider the trends in costs to be covered over the period in which

SARS-CoV-2 and its mutants achieve new waves or are replaced by new pathogens. Currently, we have to expect that, at any rate, after about half a year, the vaccination protection will no longer be sufficient to safely protect the vaccinated person from a serious illness. Therefore, this person must also be expected to be a spreader. How long can even a state that is currently still economically stable bear the costs of a strategy that is based almost exclusively on contact interruption and vaccines delivered by injection? What impact will the fact that very many states are unable to take these measures have on what happens at home? What impact can be expected on internal and external peace? Is there a threat of a wave of refugees for health reasons? What impact will this have on each individual citizen and his or her children and children's children? Will the decision ultimately come down to the question of solidarity with developing countries and the weakest members within each state?

Surprisingly, this future-oriented discussion is practically absent. This is reminiscent of the «law of triviality» described by Parkinson («The time spent on an agenda item is inversely proportional to its respective cost [161]) about the interest of board members in the projects presented for decision. Parkinson finds that projects above a certain amount are virtually waved through, while those below are discussed longer the cheaper, more foreseeable and more transparent they are. Changing the type of coffee would be discussed the longest. Does this also apply in everyday life? If so, we would be in a situation where we would behave like the famous «three monkeys» in view of the upcoming complex and extremely momentous decisions: See nothing, hear nothing, and talk nothing about it.

In the New Reality game, these considerations can also be thought through without risk and without attracting attention. But for this one needs insightful assumptions, no matter how rough they may be. We therefore offer the following approaches for decision-making:

Fig. 21. Three Monkeys: Hear Nothing, See Nothing, Say Nothing, Amazon, Leonardo Collection

First, a handout for weighting judgmental tradeoffs, namely the «crosshairs». It allows a semiquantitative and individual classification. The second access can be used for decision making on the level of a two-valued and thus generalizable logic. Some help can come also from the evaluation of special tools

a. The Crosshair

The name comes from the comparison with a telescopic sight that shooters use. Here, the selected target is in the center. The requirements that have to be taken into account are those that have to be coordinated with each other. In our case, the influencing variables and their effects in relation to the target in the center are to be matched. One can list the different effects on the vertical axis (ordinate) among themselves and on the horizontal axis (abscissa) the different measures to achieve these effects. The importance one attaches to the successful implementation of the measure for the central goal from the personal point of view can be indicated with semiquantitative symbols, e.g. one to three plus or minus points or a zero if no effect is to be expected...

In this way, even contexts that are not comparable in themselves, etc., are made comparable from the point of view of one's own assignment of meaning. Already the creation of the diagram is helpful: One must make clear what is to be brought into the center and which possibilities are given at all. Once the list of possibilities and the list of effects have been drawn up, one is reminded that measures can also have effects in areas that one had not even thought of before. Assigning semiquantitative ratings to each field of the «crosshairs» also helps to check oneself to see if one has «made a mountain out of a molehill» in one context, and «made a molehill out of an elephant in another».

And should one not recognize such misclassifications oneself, one's attention is drawn by a fellow player to the fact that one could, with more or less good reasons, do the weighting of meaning differently.

The procedure presented here is used in a similar form e.g. in environmental impact assessments to make the positions of experts from different disciplines transparent for a project.

The crosshairs can be created simply or very comprehensively. If you also want to convert these assignments of importance into a mathematizable form, you can calculate a score for each measure and each effect by summing up the evaluation points. This can be used, for example, to determine significance, which is useful for using the second technique.

b. A simple fault tree (following G. Fumarola [163])

There are questions for which weighting is not or no longer decisive. Let us just think of a chess tournament. For the chess players it is essential to be able to think oneself into the other in such a way, in order to guess which of the weighting evaluating decisions he will make and how one should prepare oneself accordingly. The partner can choose

between different pieces and then decide in which way he wants to move the chosen piece. But the referee is completely different: he only checks whether the rules have been correctly followed. Who wins and who loses is of no importance to him. Nevertheless, all three have a common goal, for which chess is a means: professional chess players and arbiters are paid. So when it comes to the question of securing a livelihood, the differences fall away. Then there is no longer any need for a weighted evaluation.

Whether behind physical and biological processes weighting evaluating weighing processes are to be assumed, as this e.g. Burnet in connection with the sensitization against potential allergens puts to the discussion [162], one can often ignore in practice: In the allergic person, the allergen will trigger the antibody response. Why the two inanimate substances can do this is not relevant for the patient. The same applies to the different interests and fears in the context, which one wants to take into account for one's own appropriate course of action. But once it has been clarified by weighting evaluative weighing how significant what is classified and which methods have been deemed useful for achieving it, then one can move on to a pragmatic yes-no decision. But this also requires a scheme. It is now necessary to consider what needs to be done and in what order, from whom one can get the best expert advice, what technology will perform the necessary service and how successfully, etc. If one proceeds haphazardly here, this can lead to mistakes with serious consequences. So it takes decision support to avoid these mistakes.

One way is to approach the pandemic phenomenon using logic trees. In doing so, one can start with the infection of the first person who has become the starting point of an epidemic and follow the chain that may or may not lead to the top event to be averted, i.e., a high number of deaths worldwide. The following logical decision tree is a strong simplification. It is intended to show only the key steps of the remedial actions to be taken immediately, the most critical conditions in the event of a pandemic risk, and the responsibilities of scientists, institutions, the health care system, and citizens [163].

Some brief comments may help to read the logic tree from bottom to top.

- A virus that has evolved as a human pathogen infects one or more individuals.
- If the individuals are not vaccinated and they do not have adequate nonspecific defenses, the infection can spread and affect additional individuals, either those who show symptoms or those who do not.
- In persons who do show symptoms, the disease may worsen and, if not properly isolated, they may uncontrollably infect other persons.
- Individuals who do not show symptoms and are not diagnosed and isolated in a timely manner may uncontrollably cause a chain of additional infected individuals.
- With a high number of severely ill patients, a relatively high number of deaths can be expected worldwide if no suitable therapy is available.

c. Assistance through evaluations of the different measures.

As described above, model calculations were and are used as the basis for the forecasts of the planned measures. The consistency of these forecasts with the phenomena that actually occurred has also been verified. It has led to the call for new federal authority in the United States. Studies have also been conducted on the effectiveness of the intervention measures used. The results vary widely. Of note is the dependence of the applied calculation method on the outcome. For example, in May 2021 in Salzburg, J. Ioannidis reported the contradictory results regarding the effectiveness of the same lockdown depending on the method used. Haug has pointed out one of the limitations that arises [164]: the assumption that the same mathematically tangible measure always leads to the same effect regardless of the state in which it is applied is too optimistic. But this is also true for the assumption that the same regulation leads to the identical reaction by the population at other periods of a longer lasting epidemic. After all, only the behavior of individuals is measured, not their assessment processes and their influence on the interaction between cell and virus: COVID-19 remains an infectious disease and not a behavioral disease.

Nevertheless, the data on the efficacy of prescribing e.g. wearing masks etc. in different collectives and time periods provide useful information. Therefore, this will be discussed in Part 2.

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