Swine flu: Is virus mutation dangereous ?

A study on the importance of the host as a determinant of a dangerous pandemic

Mac Heynar Ramos F. and Johannes G. Schmidt
Foundation Paracelsus today, CH-8840 Einsiedeln

This paper is dedicated to the Polish Ministry of Health.

Introduction

All have joined in the vaccination campaign – except Poland and a few other countries. The WHO pandemic alert on Swine flu and the recommendations to vaccinate, however, have now become a focus of criticism [1]. Critique is expressed about the manipulation of the pandemic criteria as well as about the close relationship of the WHO to the pharmaceutical industry. With this critique, however, the argument can not be refuted that the precautions recommended by the WHO have been necessary at that time to protect the population while every-one believed in the danger of virus mutations. We rather think that it was a misperception of global scale of the true determinants of health throughout institutions and the general population that has led to the global blunder. The medical community kept parroting the allegation of the possibility of dangerous virus mutations as thought to be seen during the Spanish flu in 1918 [2, 3].

We will examine the question to what extent dangerous virus mutations really exist or whether this is a potential myth which has ignored other plausible explanations. In this context, the clinical relevance and danger of virus mutation is not a question of virological methods and it cannot be resolved by laboratory science such as antigen studies or antigen theories. The clinical benefit, in the end, is a question of the clinical results put to epidemiological analysis. Clinical epidemiology and systematic reviews are needed to obtain sound and reliable answers to the question of the effectiveness and benefit of medical interventions.

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Praxiszentrum Meinradsberg, Ilgenweidstrasse 3, CH-8840 Einsiedeln/Schweiz
Tel. (+41) 055 418 81 95 Fax 055 418 81 96 e-mail: stiftung@paracelsus-heute.ch
Kto. 306020-0024, Kantonalbank Schwyz Einsiedeln (PC 60-2577-8 · BLZ KBSZ CH 228811)

Host and disease

The interplay between host and disease has long been an important medical issue [4, 5], but has lost proper attention in the modern medicalization boom. It is easy to propagate risk factors and disease factors and - viruses - as a threat to public health without examining the modification effect of the host and his resistance. We believe that this is scientifically wrong and has led medicine astray. If the (non-specific) host resistance would determine whether a disease progress is benign or rather malignant, "successful" interventions to change the (specific) disease manifestation, then, are not yet a true success. We need to know exactly if there is a sustainable improvement on overall morbidity and mortality, i.e. on the total suffering, before success and benefit is truly established.

It is known that the first successful vaccine ever – smallpox – has made disappear infant mortality from smallpox in Berlin of the 30s, but it is less well known that the overall infant mortality rate remained unchanged [6]. In the end, the susceptible host (malnourished children) was unable to resist competing infections and infants died at the same rate - whether vaccinated against smallpox or not. In his large epidemiological study Thomas McKeown has examined how mortality from infectious diseases has developed between 1860 and 1960. He found that the constant decline occurred almost linearly over the whole period, long before medical action was taken [7]. The introduction of vaccination (and antibiotics) made no change into this curve. He concluded that adequate nutrition and improved housing since the end of the 19th Century correlates best with this observation.

Another example is measles which was endemic in our country in virtually all children until the seventies, but rarely caused a death case. Measles in third world countries at the same time, however, often were a major contributor to child mortality. Thus, not the measle virus as such was the determinant of child mortality, but the compromised host resistance under precarious conditions.

The Spanish flu

Unlike smallpox and measles influenza viruses undergo constant mutations with the result that no general influenza immunity develops. The Spanish flu in 1918 is often regarded as the textbook case of a dangerous pandemic to which no specific immunity pre-existed in the population. The WHO and numerous health authorities have used the example of the Spanish flu to justify their Swine flu activism. This perception, however, entirely ignores the host situation at that time. Europe, in 1918, was behind a devastating war. Not only the

specific flue mortality was high, but also total mortality showed a noticeable increase. During the Honkong flue 1957 and the Asian flu 1968 there was no increase in total mortality [8].

If one puts these results into its proper perspective one may well conclude that the death toll of the Spanish flu was likely the result only of the precarious conditions at the end of world war I. Deprivation and weakness on the side of the host may sufficiently explain the high mortality due to the Spanish flue. It is arguable, therefore, whether the virus and its mutation had anything to do with the severity of the Spanish flu. It must not be overlooked that a high susceptibility to disease complications may be the cause of a bad outcome rather than the virulence of a disease.

The H1N1 flu

In accordance with these epidemiological observations also Swine flu shows this host pattern (the same as with SARS a few years earlier). The documented fatalities were mostly associated with pre-existing morbidity in the host [9]. H1N1, thus, shows again the same pattern: A weak host gets sick and may even die, if host resistance is in order the flu showed a very mild course.

In this context, however, we face a major problem in regard to the current ICD classification which lacks a taxonomy of the host condition, and thus, lacks a reasonable predictivity for the severity and the course of a specific disease in individual patients [10]. The ICD classification is the result of the limited modern medical perception that has no classification of host resistance. The ICD classification ignores patient characteristics that would be important for predicting the disease course, especially if the information is of anamnestic nature [10,14]. This gap is not easily filled, but it brings our attention to the fact that we do not yet truly know whether a patient has a benefit if we have improved or averted specific disease symptoms. Maybe his susceptibility to competing diseases remains unchanged and the measures taken compromise the host resistance in the end.

Effectiveness of influenza vaccination and the nature of vaccination

Because flu viruses undergo mutations they do not leave a general influenza immunity if the host has had flu. Vaccines, similarly, must be adapted from year to year in order to fit the specific antigenic properties of the virus to come. This makes flu vaccination even more difficult and more unlikely to hit the target, but on the other side it multiplies the prospects of selling vaccines, “needed” every year again.

In a systematic review in 2006, Jefferson et al. found a lack of good methodological evidence to show a beneficial effect of conventional flu vaccination because the relevant studies contain potential biases and errors [11]. Another study by the same group under the auspices of the Cochrane Collaboration [12] showed that also influenza vaccination in the elderly is of no proven value if adequate methodological standards are applied. It appears that weaker people also have a weaker immunological response even if a specific immune response is wanted. Jefferson as an immunologist has used the methods of clinical epidemiology for this analysis.

From a systematic point of view and using the methods of clinical epidemiology as well as careful clinical observation one can regard vaccination effects and the clinical nature of vaccination - at least hypothetically - as a gamble: A competent host with a good resistance does very well without vaccination and also does not need to fear adverse effects of vaccination. A host with a weakened defence, on the other side, can be affected by viruses as well as by vaccinations - to an extent similarly unknown in both cases. In the case of vaccination, weak host resistance is confronted with the stress to produce a specific immune response that my never be needed. That may compromise the resistance for competing infections or in rare cases even lead to a vaccination hazard if vaccination comes in an unfavourable moment. From this perspective vaccination is an unpredictable gambling. Vaccination may protect someone in the rare instance where the achieved specific immunity is just needed, but it may also be just an unnecessary burden for a host with a weak resistance and thereby increases the susceptibility to any other infection in an unfavourable moment. Because thousands of people need to be vaccinated to perhaps prevent one single specific complication or death the benefit is questionable a priori (the "number-needed-to-treat" NNT is too high).

Good studies that show a benefit of influenza vaccination in small groups (young pregnant women in Bangladesh) seem to confirm that a high "pre-treatment risk" with a correspondingly low NNT is necessary for a possible vaccination benefit. In this study population over 90% of newborns had febrile respiratory infection. If mothers were vaccinated against flu only 34% of the infants had seen a doctor compared to 59% in the control group - an NNT of only 6 [13]. An open question remains whether a clinically relevant benefit will persist. Although in itself interesting, this single study may also lack generalizability so far.

Conclusions

Using a systematic approach it can be seen that the death toll of virus epidemics or pandemics do not simply depend on the virus and its variation, but on the pre-existing health status of the host in the population. Viruses can mutate and thus survive. To survive, however, they must not decimate the host too much. It is a mere theory and probably a misinterpretation that viruses become dangerous by mutations. It is not the specific immunity, but "mutations" (or changes) in the non-specific resistance of the host that correlate with a complicated outcome of viral infections. While the specific immunity alone has become the subject of today's medical scholasticism it now appears to be largely without any real epidemiological relevance. Clinical epidemiologists or mathematician know that the maximization of the specificity is always at the cost of the sensitivity - at the cost of clinical relevance and generalizability [14].

In clinical practice, we can not measure host resistance with the methods of immunology (the few exceptions confirm the rule). Especially as flu-related deaths are not due to the viral effect, but are usually produced by super-infections that are perhaps predictable by a thorough history, but not by the use of immunological tests. The question of the eventual benefit of vaccination is further complicated by the possibility that a competent host could gain health by the successful coping with flu. Even a well-documented reduction of deaths due to a specific virus infection – in careful consideration – is only a potential benefit of vaccination, but not yet a certain benefit. In the end, we must know its effect on the overall morbidity and mortality. It is difficult to conduct proper controlled studies on this key question. The lack of such studies, however, shows that we do not truly know the overall benefit of influenza vaccination. The existing evidence beyond wishful thinking, in fact, rather suggests that even “successful” vaccination efforts lack any true benefit in the end because total mortality was never improved. Only a change of the specific cause of death – or a change of the name of the death cause – was achieved, but not a true reduction of the relevant clinical endpoints as a whole.

Because of this, even methodologically sound results showing an improvement of influenza statistics would not yet tell us much. The praise of progress and the apparently inevitable marketing efforts, based on methodologically unsound study results, exhibit only the extent of wishful thinking or the extent of the existing business sense, but are no serious medicine and science. It can easily be seen that the broad consensus among immunologists and physicians on the use of flu vaccination and on how to tackle the alleged Swine flu danger was not based on good empirical evidence

and on proper theoretical analysis.

On the basis of pre-existing knowledge, the Swine flu was never dangerous. Activism and business could happen because of the allegation that dangerous mutations may follow. We believe that we have a serious problem in medical science because the modern "medical community" has increasingly learnt to ignore the importance of the host-disease-interaction, and thus, has lost its sense of judgment. We believe that the false assumptions and conclusions of the WHO on the Swine flu pandemic is not the result of frank corruption, but the result of collective wishful thinking and unguarded science – of scholastic analysis with no sense of proportion. Our study is not challenging vaccinations in total, but the benefits and the importance of vaccination is certainly much smaller than usually believed and perhaps restricted to relatively small groups such as pregnant women in Third World countries. It is interesting to note that the host condition for other diseases - for example cancer, rheumatism, multiple sclerosis, etc. – may also be the crucial and scientifically neglected determinant of disease progression and mortality, not the alleged virulence or malignancy of the specific disease diagnosis [15].

Taking no specific measures and explaining well, such as the Polish Minister of Health has exemplified to all other countries in the case of Swine flu, is a good and increasingly needed option when medical scholasticism, selective facts and wishful thinking have become the basis of decisions rather than proper scientific evidence. Wishful thinking and the active hysterization in health issues, today, show such a militancy that the "reformatory stance" of the Polish Minister of Health should be well estimated. Unlike the WHO.

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