

Preparation for the next pandemic-a plea for a nationalized approach

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This article is a translation and adaptation of an essay written in the Netherlands newspaper Trouw on March 28th 2020

When the original version of this article was written on March 28th 2020, the outbreak of infections by the SARS-Cov19 virus had just been declared a pandemic and the Netherlands had gone in lockdown. Now, more than a year later, some fortunate countries are looking at a recovery, but there is more fear, uncertainty and suffering to be expected for many.

The fact that we will emerge is to a certain extent a triumph for governments, health care systems and industries and the amount of collaboration has been unheard of. However, we need to question if what happened until now is the ideal situation. This is not an article to criticize what happened. No one was really prepared, and that errors and unwise choices were made was to be expected. Therefore, criticism with hindsight is less productive than planning for an even better response in the future.

The question is if we will remember the severity of the crisis when everything is back to normal. We may not, and our current privatized system of vaccine and drug development is not structurally able to cope with what we have experienced. This may seem so, but we have experienced a mild general rehearsal for something much worse. That will happen when a virus mutates in a form that is more deadly and more infectious than the current one. Sars-Cov and Mers-Cov were failed attempts from the viral point of view, but with some other characteristics the disaster would have been infinity larger.

We have seen excellent collaboration between all the different governmental bodies both international and national in limiting the damage and eventually winning the war against the virus. As the crisis went on the warlike rhetoric increased and it now looks as if we will win this war, or rather our immune system will win the war. The cost in casualties has been enormous and it is the question if that was inevitable.

What should be remembered?

Most if not all countries have an army. That is an expensive high technology system that luckily is rarely used to its full potential. The military must be ready, so they train on different scenarios, renew their procedures and equipment. Governments must buy expensive hardware like submarines, aircraft carriers or F35 planes (for about \$100M per unit). There is NATO in which the different national armies collaborate

and standardize so that they can fight together. Most countries spend considerable amounts of their national budgets on defense, without knowing against what. People understand that and there is no country in the world that even thinks about privatizing defense. In fact, any private involvement in defense is forbidden by law.

Now think about the defense against the much more well defined and sneakier adversaries that cause infections. We share the world with many of those and as they can evolve, they occasionally just acquire the right properties to multiply by hijacking a host, who becomes not too ill to spread the multiplied organisms to other hosts. The disruption and suffering this can generate needs no further explanation now. We have means to defend ourselves using our immune system, assuming we do not die. Other than that, there are vaccines and antiviral medicines. When an infectious agent attacks these are not always available and need to be developed fast. The question is how to do that.

Is there an incentive for private enterprise?

Traditionally only state vaccine producers made the traditional vaccines for diseases like tetanus, smallpox, whooping cough and diphtheria. From the 1990's research and production of new vaccines was privatized and fell in the hands of several large pharmaceutical firms. Although it is difficult to know if this transition speeded up the development of new vaccines it did happen, with measles, mumps, hepatitis, meningococcal disease, and HPV as the first vaccine preventing cancer. The hope of potential treatment of cancer by vaccines led to much activity by startups, but no current therapeutic success.

The national vaccine producers rapidly melted away. In the Netherlands the state vaccine factory needed an update of the facilities costing 3M euro and this was considered excessive by the ministry of health, after which the whole organization was sold to an Indian company. The national institutes have in many countries become purchase managers of vaccines and have lost expertise beyond negotiating skills about price and quality with foreign suppliers.

After a year of corona and extraordinary gains for the companies that made the vaccine, the enthusiasm of private enterprise appears unlimited and the willingness of investors to pump money in the field endless. In many ways we have been extraordinary lucky that the companies working on mRNA vaccines were funded to find vaccines against cancer antigens. However, we cannot call luck preparedness and although it worked this time by accident does not mean we are well prepared. Preparation for another, perhaps much worse attack requires a fundamentally different approach

To be prepared a military organizational mindset is necessary. This means an organization that develops scenarios practices them in all aspects even though they may never happen. A commercial organization driven by shareholder value, as currently all health care companies, is unable to cope with this. For instance, the problems with distribution of vaccines that were produced in one country in bulk, filled in another and distributed in a third was only a small rehearsal what may happen in a more serious epidemic, when infrastructure is collapsing. Manufacturing capacity with redundant facilities, that are kept up to date but remain unused perhaps (and hopefully!) for decades are expensive and will of course either be used for something else or slowly abandoned in some cost-cutting operation when everyone has forgotten 2021.

Why is there no antiviral army?

This question has been asked before by several, particularly Bill Gates in a TED talk in 2015 (https://www.ted.com/talks/bill_gates_the_next_outbreak_we_re_not_ready/transcript?language=nl). But this question must be asked again. We maintain complex technical gear like F35 JSF planes or Patriot anti-missile batteries. Military professionals practice with them, maintain them and most equipment (and the personnel) will reach the end of their technological life without ever having been used against an enemy. They are maintained by the state and paid by taxes. For antiviral defense we make use of existing commercial facilities and that has now been shown to be far from ideal.

Our viral defense is not under any central command. Governments cannot order the private partners to do certain research, only stimulate by grants. Companies can and will subsequently shield their know how on

production -perfectly acceptable in virological peace time but currently costing lives. Yet, the development of the vaccines has been phenomenally fast, and these developments have been for a large part been driven by private enterprises.

Can this be done better?

Countries have nationalized armies and should have national organizations for the management of infectious attack. Although they should not be run by the military, they should have a military mindset making use of the typical expertise in the army. This concerns scenario planning, and operational readiness for different scenarios including people and material. So pandemic preparedness is not an academic institute that write reports – as has been suggested in some countries – but an organization with a large budget, and actual material and staff.

Specifically, there must be testing laboratories and a factory to produce testing materials fast that can be operational within a week. Each country requires a modular vaccine factory that must be kept up to date with regard to manufacturing equipment and pre and postproduction facilities like filling lines. A chemical synthesis and production facility with formulation capacity for antivirals is essential because it is not known beforehand if vaccination will work. Finally clinical trial facilities, both for early and later phases should be kept at readiness with sufficient extra capacity to start testing vaccines and treatments immediately.

The required professionals may be difficult to find and motivated to spend their careers practicing something that may never happen-but there are examples how this can be solved. In the Netherlands surgeons in hospital practice get additional defense contracts and training and are partly paid by the government for military missions where they can be deployed immediately. The advantage is that a surgical team has additional capacity in peacetime and the staff member can be missed when deployed. This could also be done for virologists, biotechnology and pharmacy experts and clinical pharmacologists.

In virological peace time these facilities can collaborate and standardize (like the military in NATO) by sharing production protocols and participate in staff training and exercises.

Trials in virological wartime

The clinical pharmacologist will be essential in the planning and execution of clinical trials. In peacetime protocols for early studies with anti-infectious agents and vaccines can be set up and pre-approved by regulators. This approach has been describes earlier in BJCP. (1). Additionally we have recently shown that vaccine trials can be sped up considerably by mobile trial units setting up in hot-spot infection areas (2). Such approaches require trained staff and ready technology, and this can only be developed in virological peacetime-an ideal task for the clinical pharmacologist.

Financing the system

A system like this is expensive and can only be financed by governments. For a country like the Netherlands it would cost little more than a new guided missile frigate or a F35-JSF fighter plane. Private enterprise is unsuitable as there would be no return on investment in the classical financial sense. The systems will likely be unused for a very long time but would not be useless as they can pioneer new and flexible production or research methods. Just like a classical potential enemy can be spotted by intelligence services the antiviral army will use epidemiological intelligence to determine the next threat and prepare for it.

An antiviral defense like this cannot be established haphazardly and will require careful study of all different aspects. Our current pandemic may be only a weak prelude to the next one when public services may collapse. The Janssen Vaccines factory that produces vaccine for the USA is located about 1 m under sea level in Leiden. When the people who maintain the pumps are all disabled by a new illness the factory will flood. Considerations about the defense will therefore be wide ranging and go beyond what the scientific community can muster. Pandemic preparedness should start with a wide-ranging international study about what is required but should be operationalized in national levels with the aim to make all countries or regions

as self-sufficient as possible. The current inequalities in vaccination across the world are a shameful reminder of the lack of organized preparedness.

In 1953 the South-West of the Netherlands was flooded during a storm and about 2000 people died. This led to the Delta works- a nationally funded engineering project that goes on until today and protects the country against recurrence of this disaster. The enormous system of dams can be seen from space and requires continuous maintenance. (<http://www.deltawerken.com/English/10.html?setlanguage=en>) and costs about 2% of the GNP. Corona killed 18.000 people in the country and millions worldwide. To spend such amounts on viral defense appears reasonable and would make dealing with the next pandemic in a much more efficient manner feasible. A military mindset is required and there is no place for private enterprise, just like for the rest of our national defense. The testing of new health care interventions will be a large part of such preparedness organizations and the clinical pharmacologist has the right expertise to be an important contributor to the planning and execution of this new essential defense force.

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