**Covid-19 Vaccines and Public Health Efforts: A Brief Summary**

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**Mini-Review**

The road to Covid-19 vaccines has been a real challenge. The genetic sequence of SARS-CoV-2 was obtained in January, 2020: Earlier vaccinal studies began on Spring 2020 and in less than 12 months (December, 2020) the European Medicines Agency (EMA) could recommend the first conditional authorisation for a Covid-19 vaccine [1]. Immediately after (6th January, 2021) a second recommendation was given, for another Covid-19 vaccine [2].

Such a development in less than 1 year from the identification of the virus is unprecedented in the history of vaccinology [3]. Shortly after the discovery of that novel and extremely pathogenic Coronavirus (SARS-CoV-2), much effort was put into developing a vaccine. More than 150 companies and academic institutions started working on COVID-19 vaccines [4], using DNA-based and RNA-based vaccines, Non-Replicating Viral Vectors (NRVV), Replicating Viral Vectors (RVV), Inactivated Vaccines (IACV), Live-Attenuated Vaccines (LAVs) and protein sub-units, among other strategies [1]. Other than the development strategy for the seasonal influenza flu vaccine, typical vaccine development for a novel pathogen was expected to take several years of research to fully understand the viral structure-function relationship and the critical protective host immunity pathways [2]. However, COVID-19 pandemic diffusion and the subsequent worldwide increase in mortality and severe pneumonia incidence rendered the development of an effective vaccine urgently relevant. A need was widely recognized to develop a safe vaccine that would save lives, time, and money [5]: Government cooperation was globally developed, in order to
give people a concrete option to receive the vaccine just when necessary [6]. Moreover, a tight collaboration between govern-
ments and pharmaceutical companies while adhering to regula-
tions to create safe and effective vaccines played a crucial role in
that way to develop an effective vaccine [7].

When analyzing vaccine development, it can be recognized
that any step was completed successfully, by mixing effective
main factors as [8]: Previous research about mRNA technol-
ogy; human Coronavirus studies, especially those about SARS
(Severe Acute Respiratory Syndrome) and MERS (Middle East
Respiratory Syndrome); huge economic resources and scientific
and technological efforts as well; vaccine production starting in
parallel with the completion of the authorization process; re-
results evaluation by national/international regulatory agencies
by the way that those results were obtained (rolling review pro-
cess).

Usually, the typical time needed to develop a vaccine us-
ing conventional methods was 15 years [9]. That type of con-
ventional process could start with exploratory work on design
and evaluation in animal models, followed by a phase involv-
ing more extensive pre-clinical experiments: After those steps,
vaccine production process could be designed, towards clinical
trials construction [7]. Such a typical process could end by sub-
mitting a license application to appropriate regulatory agencies,
after obtaining final results applied to the appropriate end-
points; one or two more years could be needed for licensing
[10,11].

The scale of population impact of the Covid-19 pandemic
has driven a completely new strategy design, with the use of
next-generation vaccine technology platforms through novel
paradigms just to accelerate an effective and rapid vaccine de-
velopment [8]. Both standardized and innovative methods were
integrated in such a novel strategy, in order to successfully ob-
tain a vaccine in a short time, with a lot of effort and money [3].

One thing that was learned from Covid-19 pandemic first
phase was that previous pharmaceutical market’s financial and
regulatory mechanisms did not give enough incentive to sup-
port vaccine development before that catastrophic outbreak
occurred [5]. To compensate, academic institutions and enter-
prises all around the world started early to create an enormous
number of vaccine candidates [12], by using some different
methods: mRNA or DNA technology, or identification of specific
immunogenic epitopes and proteins [13]. Even more and more
research appeared to be needed, in order to find the most ef-
fective vaccine candidate that could start reducing the rising
number of Covid-19 cases [14].

Novel vaccine development paradigms were applied, in-
volving parallel and adaptive development phases, innovative
regulatory processes and scaling manufacturing capacity [15].
Besides, a strong international coordination and cooperation
between public health bodies and governments, regulators and
vaccine developers soon appeared as one of the key factors for
a successful end with several promising late-stage vaccine can-
didates [2].

The vaccine was recognized as a powerful tool to tackle the
pandemic: However, concern about the extraordinary low time-
line of its development was one of the main causes of people
hesitancy in accepting those new vaccines [3]. It must be recog-
nized that the real starting point of the timeline for SARS-CoV-2
vaccine development and discovery was not January 2020, date

for the publication of virus genetic sequence but almost more
than two decades earlier, with early studies about mRNA tech-
nology [8].

Another relevant contribution came from the pandemic
trend, which involved some unusual circumstances, as com-
pared to other public health crises in the past [16]. It can be rec-
ognized that SARS-CoV-2 genome was sequenced, assembled
and released very early in the course of the pandemic. That ge-
nomic information drove biomedical response studies against
this novel pathogen in several different ways [17]. In September
2020 over 180 vaccine candidates were in development, many
of which employed traditional vaccine technologies [9], where-
as public attention globally focused on vaccine development
platforms that used new technologies (mRNA vaccines). Since
then, the utilization of highly adaptable vaccine platforms (RNA)
in combination with the adaptation of structural biology tools
to design agents (immunogens) that could powerfully stimulate
the immune system [18] lead to a rapid success.

Despite these important efforts, more than three years since
the outbreak of Covid-19 it is well known that the causative
SARS-CoV-2 has been continuously evolving and generating
variants [19]. In some circumstances, existing vaccine-induced
antibodies could not fully neutralize the variants, especially
the newly isolated variants [20]. It can be highlighted that mutated
strains have brought new challenges to Covid-19 preventing
and controlling strategies [8], so that a request for vaccines that
could provide more effective and broad-spectrum protection
has appeared [7,21]. In the last more than three years, efforts
involving countries from all around the world, regardless of geo-
ographical characteristics and/or political orientation, have con-
tributed to a useful joined involvement [22] and collaboration
to obtain speedy and viable Covid-19 vaccines, whose research
and development has not ended yet.

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