WEEKLY EPIDEMIOLOGICAL REPORT

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Vaccine trials on COVID 19 Part I

The origin, clinical picture and some adverse effects of COVID-19 disease caused by SARS-CoV-2 infection were well known. But the site of initial infection with SARS-CoV-2 is still not discovered and the pathogenesis of COVID-19 is still not fully understood.

Currently, the management of the patients is mainly supportive with limited antiviral and anti-malarial drugs. As prevention is a fundamental requirement in reducing the mortality and morbidity of the disease caused by infection, developing a vaccine has understood as the utmost importance to ensure primary prevention.

1. Steps in vaccine development

The decision to develop a new vaccine is based on the assessment of unmet public health needs. Once it is started with preclinical development in laboratory settings, the next clinical development procedures include animal and human trials. Clinical trials include three phases, Phase 1, Phase 2 and Phase 3 in which the number of testing individuals is gradually increased. Some rare adverse reactions may not be able to elicit even with phase 3 trials.

The success of the vaccine is determined by the efficacy and effectiveness of the vaccine. Efficacy is the percentage reduction of disease incidence by the vaccine under optimal conditions, such as in a randomized control trial, whereas effectiveness is the ability of the vaccine to prevent the disease in the real world. Outcome measures or the results of a clinical trial is designed at the beginning of the trial. Out of several outcome measures, the primary outcome measure is the variable that the investigator considered the most important among the many dependent variables. Usually, there is only one primary outcome but can have many of them. In vaccine trials, development of the immunity is considered as the main important result but some trials have considered side effects also as primary outcomes (Andrade, 2015). Development of the immunity by the vaccine is usually assessed by measuring Antigen-Specific Binding Antibody Titers and Antigen-Specific Interferon-Gamma (IFN-γ) Cellular Immune Response after a specific time interval following the vaccination.

The next step will be the World Health Organization (WHO) vaccine prequalification process. That includes pre-licensure vaccine evaluation review to ensure Good Manufacturing Practices (GMP) by reviewing efficacy and safety by expert groups, independent testing of samples and site visits to the manufacturer. Prequalification is not only a onetime procedure but also periodical reviews about the quality and safety issues. Normally it takes 5 to 15 years to develop a vaccine (World Health Organization, 2017). Even with WHO prequalification, no vaccine is allowed to use in Sri Lanka without prior registration at the National Drug Regulatory Authority, Ministry of Health.

2. Properties of the virus that should be considered in developing a vaccine

Immunotherapy is an efficient therapeutic intervention against COVID-19, mainly by immunoglobulin and plasma therapy. However, vaccines can also be successful because of the specific structure of the virus. One of the limiting factors for developing a successful vaccine is the degree of cross-protection rendered by these vaccines due to their extensive sequence diversity. Several outbreaks were caused by the members of the family *Coronaviridae* such as Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS). Multiple types of vaccine trials have been done for SARS based on inactivated SARS-CoV viruses, S proteins and fragments containing neutralizing epitopes but the majority has not proceeded above the animal studies (Shibo Jiang, Yuxian He, 2005)

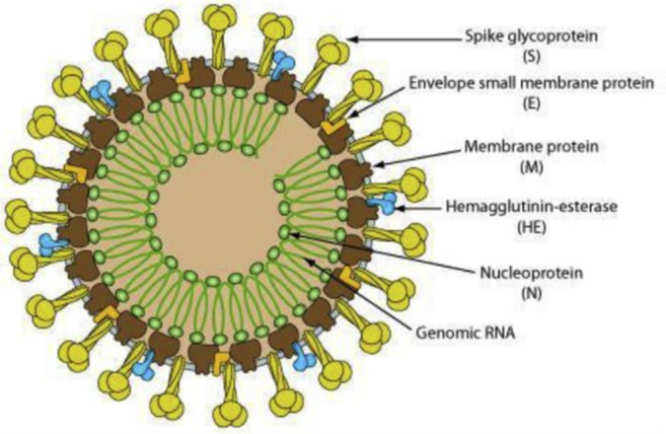
Coronaviruses are positive-sense, single-stranded, RNA viruses with multiple spike glycoprotein called S proteins on the envelope. S protein molecule has two subunits called S1 and S2. S1 has receptor-binding protein that inter-

Contents **Page**

Stages	Main Task	Sample size	Adverse reactions
Laboratory studies	Development of the vaccine		
Animal Studies	To gather information on efficiency, toxicity, and pharmacokinetics	Not restricted	may be concerned
Clinical Trials			
Phase 1	To gather more information on pharmacokinetics including dose-ranging	10-100	Common adverse reactions may occur
Phase 2	To assess the efficacy and side effects	100-1000	Common adverse reactions may occur
Phase 3	To assess efficacy, effectiveness, and safety	1000-10000	Common adverse reactions may occur
Phase 4 (Post marketing Surveillance)	Watching drug use in public		Rare adverse reactions can be detected

acts with its host cell receptor, Angiotensin-Converting enzyme 2 (ACE2), and S2 mediates fusion between the virus and host cell membranes for releasing viral RNA into the cytoplasm for replication.

(Mousavizadeh & Ghasemi, 2020).



Both SARS-CoV and SARS-CoV-2 use ACE2 as the entry receptor but MERS-CoV uses dipeptidyl peptidase (DPP)-4 as a specific receptor. C-terminal domain of the S1 subunit of porcine delta coronavirus has the immune dominant region and immune response to that region shows the most potent neutralizing effect. Thus, S protein has a major role in the induction of protective immunity by eliciting neutralizing antibodies and T cell responses. Therefore, S glycoprotein are believed to be the most promising candidate for the COVID vaccine. The vaccine should include antibodies that block not only viral receptor binding but also virus genome uncoating.

Among the viruses that cause respiratory diseases, only Influenza has a vaccine in use and no vaccines for other viruses such as parainfluenza and respiratory syncytial virus (Schmidt, 2011). Most of the developed countries have included influenza vaccine for their national immunization programmes. However, there is an evidence that, quadrivalent influenza vaccine has given improved patient outcomes than the trivalent influenza vaccine(McMahon, 2020). BCG vaccine also found to be protective for COVID-19 infection and it reduces both mortality and morbidity (Aaron Miller, Mac Josh Reandelar, Kimberly Fasciglione, Violeta Roumenova, Yan Li, 2020).

Compiled By;

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Table 1 : Water Quality Surveillance
Number of microbiological water samples Feb 2020

District	MOH areas	No: Expected *	No: Received
Colombo	15	90	NR
Gampaha	15	90	NR
Kalutara	12	72	NR
Kalutara NIHS	2	12	NR
Kandy	23	138	NR
Matale	13	78	NR
Nuwara Eliya	13	78	NR
Galle	20	120	NR
Matara	17	102	NR
Hambantota	12	72	NR
Jaffna	12	72	NR
Kilinochchi	4	24	NR
Manner	5	30	NR
Vavuniya	4	24	NR
Mullatvu	5	30	NR
Batticaloa	14	84	NR
Ampara	7	42	NR
Trincomalee	11	66	NR
Kurunegala	29	174	NR
Puttalam	13	78	NR
Anuradhapura	19	114	NR
Polonnaruwa	7	42	NR
Badulla	16	96	NR
Moneragala	11	66	NR
Rathnapura	18	108	NR
Kegalle	11	66	NR
Kalmunai	13	78	NR

* No of samples expected (6 / MOH area / Month)
NR = Return not received

... to be continued

Table 1: Selected notifiable diseases reported by Medical Officers of Health 11th– 17th April 2020 (16th Week)

RDHS Division	Dengue Fever		Dysentery		Encephalitis		Enteric Fever		Food Poisoning		Leptospirosis		Typhus Fever		Viral Hepatitis		Human Rabies		Chickenpox		Meningitis		Leishmaniasis		WRCD	
	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	T*	C**
Colombo	8	2704	0	13	0	4	0	4	0	14	5	62	0	0	0	2	0	0	7	153	2	16	0	0	**59**	**95**
Gampaha	2	1606	1	4	0	0	0	4	0	19	1	38	0	1	1	2	0	0	1	191	0	8	0	17	**53**	**85**
Kalutara	8	951	0	5	0	4	0	3	0	1	13	118	0	8	0	1	0	0	1	157	0	9	0	0	**54**	**91**
Kandy	14	1100	0	7	0	1	0	7	0	6	1	17	2	39	0	3	0	0	2	101	0	14	0	25	**62**	**99**
Matale	3	435	0	3	0	2	0	1	0	4	0	17	0	2	0	2	0	1	0	34	0	1	0	125	**60**	**100**
NuwaraEliya	0	129	0	11	0	0	0	0	0	0	0	15	0	40	0	2	0	0	1	46	1	7	0	0	**24**	**100**
Galle	1	942	0	11	0	8	0	2	0	12	0	159	0	21	0	1	0	0	2	189	0	15	0	2	**60**	**78**
Hambantota	4	259	0	4	0	0	0	1	0	37	0	53	1	14	0	2	0	0	2	104	0	8	0	231	**73**	**89**
Matara	0	351	0	7	0	3	0	0	0	0	0	81	0	4	0	6	0	0	0	68	0	5	0	117	**50**	**60**
Jaffna	4	1734	0	37	0	0	0	16	0	16	0	10	2	435	0	0	0	1	0	68	0	6	0	0	**33**	**93**
Kilinochchi	0	104	0	19	0	0	0	3	0	0	0	6	0	18	0	0	0	0	1	5	0	4	0	4	**67**	**100**
Mannar	0	117	0	0	0	0	0	1	0	0	0	3	0	1	0	0	0	0	0	1	0	3	0	0	**40**	**94**
Vavuniya	1	230	0	5	0	0	0	4	0	0	1	31	0	1	0	0	0	0	0	17	0	3	0	1	**61**	**100**
Mullaitivu	0	62	0	4	0	0	0	3	0	1	0	10	0	3	0	1	0	1	0	2	0	0	0	5	**42**	**75**
Batticaloa	23	2029	0	38	0	2	0	0	0	4	0	13	0	0	0	0	0	1	3	68	0	9	0	1	**59**	**98**
Ampara	1	282	0	8	0	1	0	0	0	0	4	26	0	0	0	1	0	0	3	67	2	10	0	4	**63**	**100**
Trincomalee	7	2148	0	4	0	0	0	0	0	1	0	11	0	2	0	0	0	0	0	64	0	5	0	0	**49**	**88**
Kurunegala	1	648	0	5	0	4	0	2	0	29	0	54	0	10	0	1	0	0	2	227	0	8	0	153	**56**	**86**
Puttalam	3	337	0	6	0	1	0	2	0	1	0	16	0	9	0	0	0	1	0	58	0	16	0	2	**64**	**93**
Anuradhapur	0	308	0	8	0	1	0	2	0	19	0	115	0	12	0	1	0	1	5	98	0	16	0	81	**55**	**83**
Polonnaruwa	1	183	0	4	0	0	0	0	0	0	0	55	0	0	0	12	1	1	1	70	0	8	8	95	**65**	**96**
Badulla	1	359	0	8	0	2	0	2	0	3	3	106	1	20	0	6	0	0	8	101	0	15	0	4	**59**	**100**
Monaragala	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
Ratnapura	0	583	0	29	0	11	0	1	0	13	3	273	0	9	0	10	0	0	0	106	0	35	0	38	**52**	**90**
Kegalle	3	357	0	5	0	3	0	1	0	12	0	68	0	16	1	5	0	0	7	108	0	11	0	9	**58**	**97**
Kalmune	6	817	0	25	0	2	0	0	0	1	2	4	0	2	0	0	0	0	11	167	0	12	0	0	**75**	**100**
SRILANKA	**91**	**18775**	**1**	**270**	**0**	**49**	**0**	**59**	**0**	**193**	**33**	**1361**	**6**	**667**	**2**	**58**	**1**	**7**	**57**	**2270**	**5**	**244**	**8**	**914**	**57**	**88**

Source: Weekly Returns of Communicable Diseases (WRCD).

*T=Timeliness refers to returns received on or before 17th April , 2020 Total number of reporting units 356 Number of reporting units data provided for the current week: 262 **C****-Completeness

A = Cases reported during the current week. **B** = Cumulative cases for the year.

Table 2: Vaccine-Preventable Diseases & AFP

11th– 17th April 2020 (16th Week)

Disease	No. of Cases by Province									Number of cases during current week in 2020	Number of cases during same week in 2019	Total number of cases to date in 2020	Total number of cases to date in 2019	Difference between the number of cases to date in 2020 & 2019
	W	C	S	N	E	NW	NC	U	Sab					
AFP*	00	00	01	00	00	00	00	00	00	01	02	11	30	- 63.3 %
Diphtheria	00	00	00	00	00	00	00	00	00	00	00	00	00	0 %
Mumps	00	00	00	00	00	00	00	00	00	00	06	55	118	- 53.3 %
Measles	00	02	00	00	00	00	00	00	00	02	02	24	66	- 63.6 %
Rubella	00	00	00	00	00	00	00	00	00	00	00	00	00	0 %
CRS**	00	00	00	00	00	00	00	00	00	00	00	00	00	0 %
Tetanus	00	00	00	00	00	00	00	00	00	00	01	03	04	0 %
Neonatal Tetanus	00	00	00	00	00	00	00	00	00	00	00	00	00	0 %
Japanese Encephalitis	00	00	00	00	00	00	00	00	00	00	01	06	08	- 14 %
Whooping Cough	00	00	00	00	01	00	00	00	00	00	02	03	25	- 25 %
Tuberculosis	00	00	00	00	00	00	00	00	00	00	51	1455	2521	- 42.2 %

Key to Table 1 & 2

Provinces: **W**: Western, **C**: Central, **S**: Southern, **N**: North, **E**: East, **NC**: North Central, **NW**: North Western, **U**: Uva, **Sab**: Sabaragamuwa.

RDHS Divisions: **CB**: Colombo, **GM**: Gampaha, **KL**: Kalutara, **KD**: Kandy, **ML**: Matale, **NE**: Nuwara Eliya, **GL**: Galle, **HB**: Hambantota, **MT**: Matara, **JF**: Jaffna, **KN**: Killinochchi, **MN**: Mannar, **VA**: Vavuniya, **MU**: Mullaitivu, **BT**: Batticaloa, **AM**: Ampara, **TR**: Trincomalee, **KM**: Kalmunai, **KR**: Kurunegala, **PU**: Puttalam, **AP**: Anuradhapura, **PO**: Polonnaruwa, **BD**: Badulla, **MO**: Moneragala, **RP**: Ratnapura, **KG**: Kegalle.

Data Sources:

Weekly Return of Communicable Diseases: Diphtheria, Measles, Tetanus, Neonatal Tetanus, Whooping Cough, Chickenpox, Meningitis, Mumps., Rubella, CRS,

Special Surveillance: AFP* (Acute Flaccid Paralysis), Japanese Encephalitis

CRS =**Congenital Rubella Syndrome

NA = Not Available

Influenza Surveillance in Sentinel Hospitals - ILI & SARI							
Month	Human				Animal		
	No Total	No Positive	Infl A	Infl B	Pooled samples	Serum Samples	Positives
April							

Source: Medical Research Institute & Veterinary Research Institute

Comments and contributions for publication in the WER Sri Lanka are welcome. However, the editor reserves the right to accept or reject items for publication. All correspondence should be mailed to The Editor, WER Sri Lanka, Epidemiological Unit, P.O. Box 1567, Colombo or sent by E-mail to **chepid@sltnet.lk. Prior approval should be obtained from the Epidemiology Unit before publishing data in this publication**

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