



# ONE HEALTH **Knowledge-Café**

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## Diagnosis and Treatment of COVID-19 Cases: Practices, Evidences and Lessons Learned

Date: November 27, 2020 | Time (1:30PM-3:00 PM) GMT

7:15PM NPT | 2:30PM CET | 6:30AM PST



**Dr. Shravan Kumar Mishra**

Director  
Province Public Health Laboratory  
Ministry of Social Development, Province-2

**Nepal**



**Dr. Pem Chuki**

Deputy Medical Superintendent  
National Referral Hospital  
Thimphu

**Bhutan**



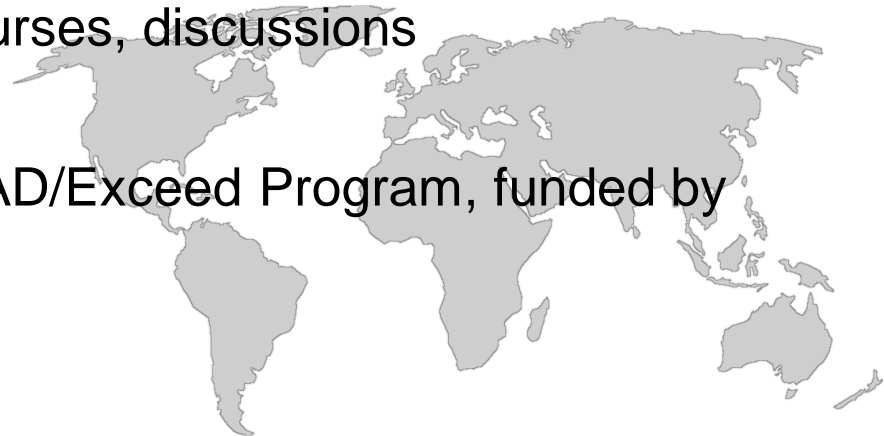
**Dr Karma Tenzin**

**Moderator**

# One Health Knowledge Café

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- A collaborative effort of more than 11 individuals representing CIH partners and alumni
- Represents Asia, Africa, Europe, South America and North America
- Brings together the expertise and network of researchers and professionals from various disciplines, countries and expertise to enable cross learning, sharing and network building
- Monthly talks, webinars, online courses, discussions
- Supported by LMU<sup>CIH</sup> through DAAD/Exceed Program, funded by BMZ





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## Diagnosis of COVID-19 cases: Practices, Evidence, Lessons Learned

**Dr. Shravan Kumar Mishra, Virologist**

Director at Provincial Public Health Laboratory

Province-2, MoSD, MoHP

Government of Nepal

# Corona Virus(family Coronaviridae)

- Enveloped, positive-stranded RNA viruses, **crow**n like in appearance, 100-160 nm in Diameter
- Infect various animals, including horses, cattle, pigs, cats, and goats, and humans
- Second only to rhinoviruses as a cause of the **common cold in humans**
- In 2003, an outbreak of severe acute respiratory syndrome (SARS), was shown to be caused **SARS-CoV**
- In 2012, an outbreak of a another Middle East respiratory syndrome (MERS), was caused by **MERS-CoV**
- In December 2019, **SARS CoV-2** from Wuhan, China, **still going on...Nov 2020**

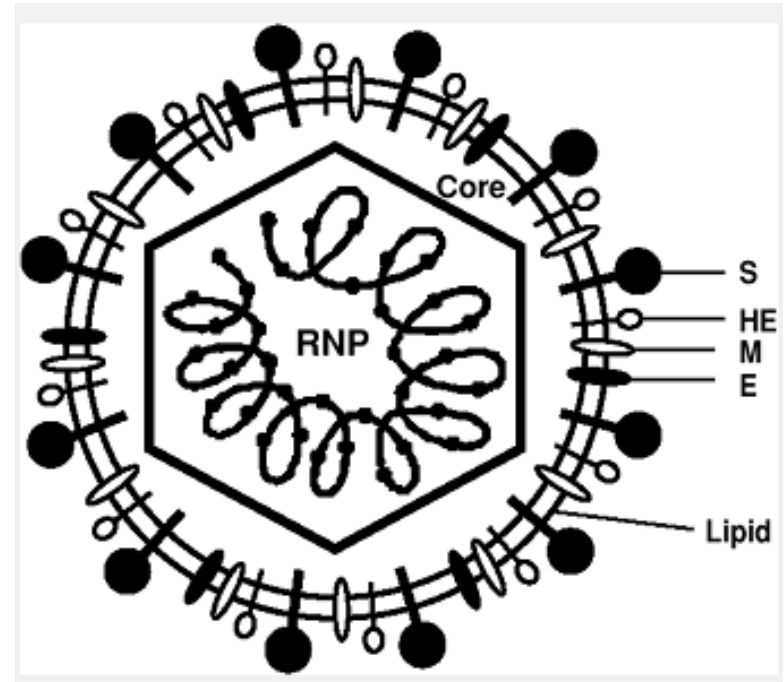
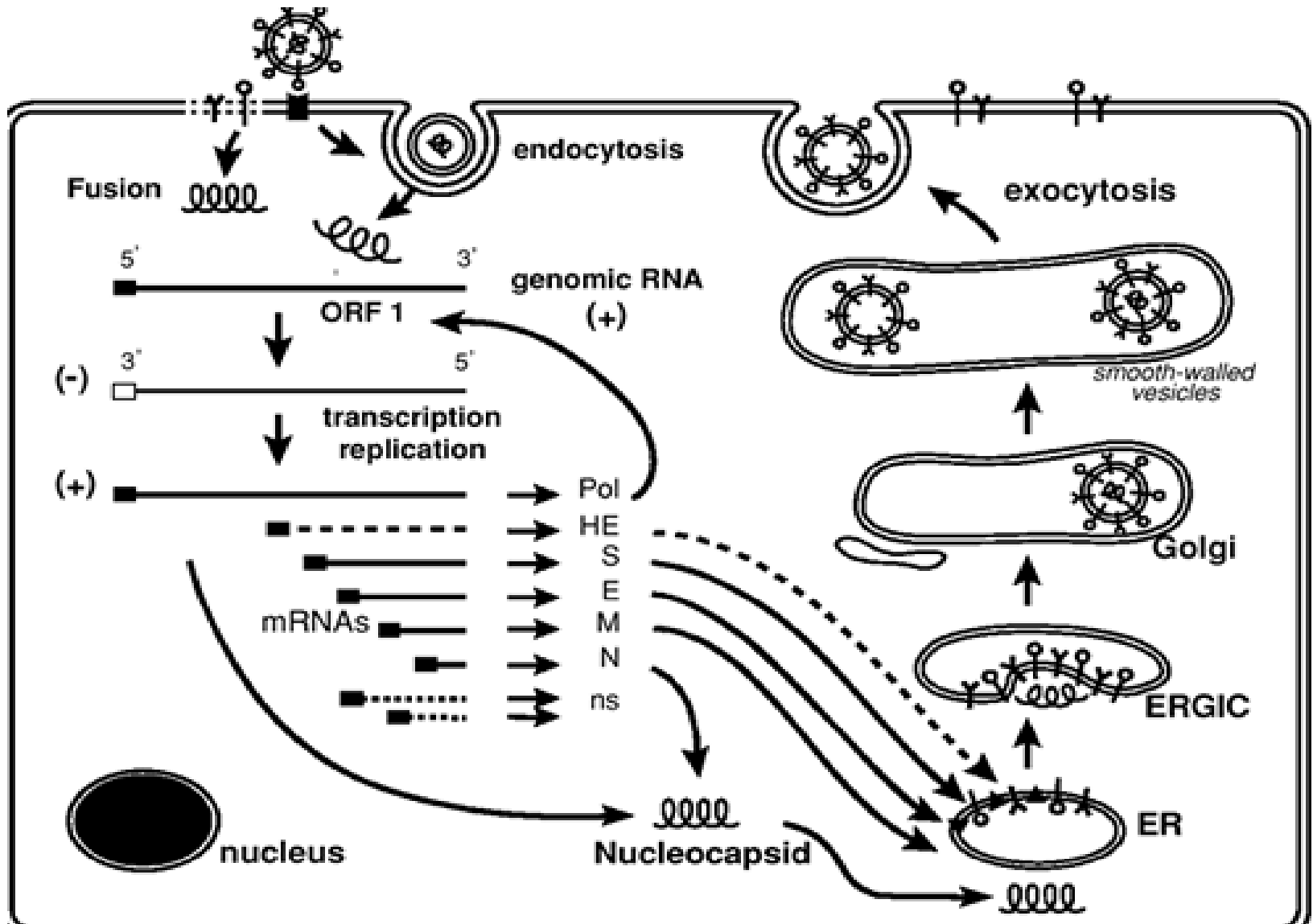


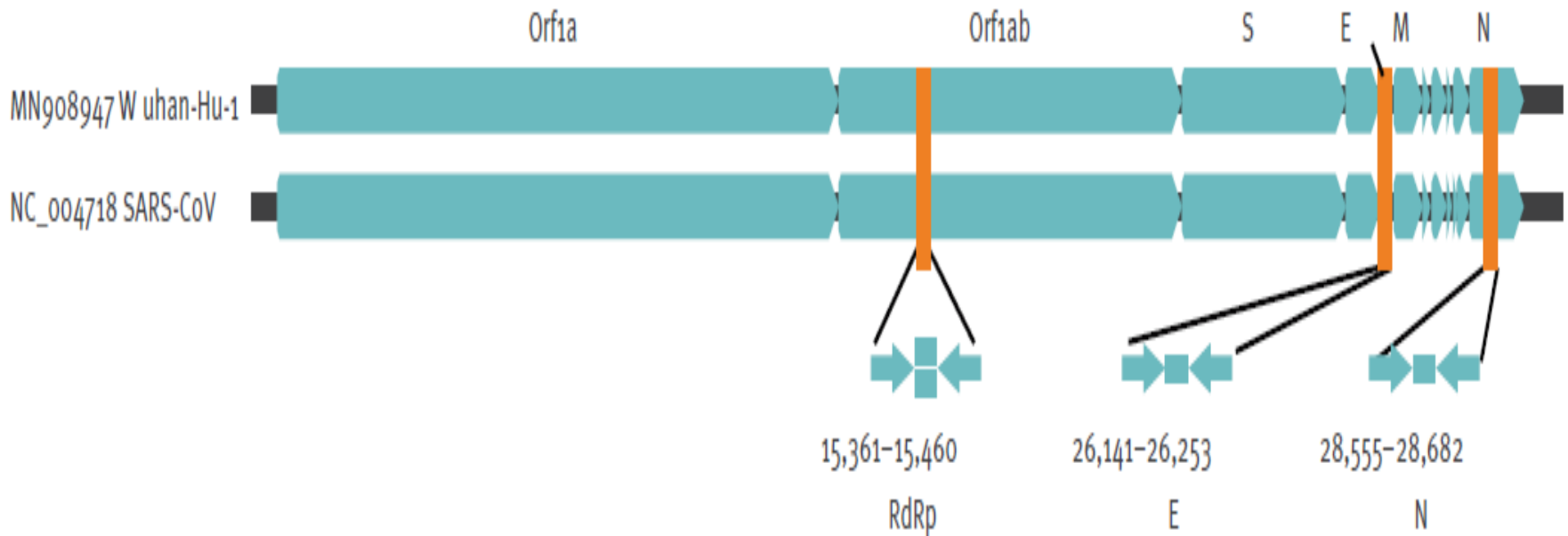
Figure1: Structure of Corona Virus (Fields Virology)

# Replication Cycle



# Genome organization of SARS CoV-2

Relative positions of amplicon targets on the SARS coronavirus and the 2019 novel coronavirus genome



E: envelope protein gene; M: membrane protein gene; N: nucleocapsid protein gene; ORF: open reading frame; RdRp: RNA-dependent RNA polymerase gene; S: spike protein gene.

# Diagnosis of COVID-19

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- Diagnostic test manufacturers have responded rapidly to the needs of countries, and over 700 products have been released onto the market to detect SARS-CoV-2 specific **nucleic acids, antigens (proteins) and antibodies**
- WHO currently recommends a single approach to clinical diagnostic testing for disease confirmation: the detection of unique sequences of SARS-CoV-2 RNA by **nucleic acid amplification testing (NAAT)**.

# Diagnosis of COVID-19....

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- Serological surveys of antibody responses to calculate **the attack rate** in different populations.
- In clinical situations where NAAT assays are negative in **symptomatic individuals** with a strong epidemiological link to a confirmed case, **paired serum samples** can support a retrospective diagnosis.
- In settings where RT-PCR is unavailable or TAT for results are slow (e.g., several days to weeks), **rapid antigen detecting tests** may facilitate earlier diagnosis and required actions.



# Specific Uses of NAAT, Ag, Ab, NA, Virus culture

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1. **Surveillance (detect acute or past exposure or infection):** Molecular detection eg . RT-PCR, **Antigen (Ag) and antibody (Ab) detection**
2. **Case management of suspects (detect active infection):** RT-PCR, **Ag Detection**
3. **Contact tracing (detect asymptomatic or symptomatic acute infection):** RT-PCR, **Ag Detection**
4. **Monitoring response or recovery:** RT-PCR, **Ag and Ab Detection**
5. **Prognosis:** Cytokine response (IL-1Beta, IL-6, TNF $\alpha$ , IL-8, IFN $\gamma$ , IL-10) and other biomarkers (Ferritin, CRP, Fibrinogen, ESR, LDH, procalcitonin, D-dimer)
6. **Vaccine Response:** Neutralization Assay, protein specific Ab response (BSL-3 Lab)
7. **Environmental monitoring:** RT-PCR and **Viral culture** (BSL-3 Lab)

# Uses of Serology (Abs) in COVID-19

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Surveillance of antibody seropositivity in a population can allow inferences to be made about the **extent of infection** and about the **cumulative incidence of infection** in the population.

The use of serology in epidemiology and public health research enables understanding of:

- the **occurrence of infection** among different populations;
- how many people have mild or asymptomatic infection
- the **proportion of fatal infections** among those infected;
- the proportion of the population who may be **protected against infection in the future**



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# TREATMENT OF COVID-19 CASES IN BHUTAN

Dr Pem Chuki

Jigme Dorji Wangchuck National Referral Hospital  
BHUTAN

# IMMEDIATE STRATEGY

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- National Technical Advisory Group formed (TAG)
  - One health Approach
    - Human Health expertise (Clinical Microbiologist, Virologist, Public Health experts)
    - Animal Health Expertise (Epidemiologist, Veterinary etc)
- Clinical Management Team (DOSA; Doctors on Special Assignment)
  - Medical Specialist, Intensivist, Pediatrician, Clinical Pharmacologist, Chest Physician
- Other National Task forces

# TARGET/ AIM

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- ZERO Mortality
- Protection of health care workers
- Training of COVID related protocols
- Generation of awareness on COVID and new norms among both staffs and public
- Immediate increase in both human resources and facilities for COVID

# PANDEMIC PREPARATION

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- Triage
  - FLU Clinics: Screening
  - Triage within the Emergency
- Dedicated COVID Hospital
  - 4 COVID Hospitals
- Critical care expertise
  - Mobilization and training of health care staffs
- Hospital Surge capacity
  - Worst case scenario preparation
- Uninterrupted Essential Care Services
  - Emergency services 24\*7
  - Cancer services
  - Mother and child health care services
  - Mental Health services

# STRATEGIES

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- All confirmed positive RT-PCR patients put into COVID hospital/ wards
  - 4 COVID Centers in the country (JDWNRH, CRRH,ERRH & Pling)
  - West/JDWNRH- National Eye hospital changed to COVID Center
  - South/Pling- RIGSS changed to COVID center,
  - East/ERRH- Royal Guest house changed to COVID Center and
  - Central/ CRRH- old CRR Hospital changed to COVID Center
  - All 4 centers have RT-PCR , Antigen & Antibodies testing facilities
  - JDWNRH – 100 ICU bed, Pling – 30 ICU beds, ERRH – 20 ICU bed, CRRH -2 ICU beds
  - Total 152 ICU beds
- All staffs trained on the National COVID guideline, ICP SOPs etc
- All staffs trained on Critical Care services and supports
- All staffs trained and routine Donning & Doffing training conducted

# CLINICAL MANAGEMENT

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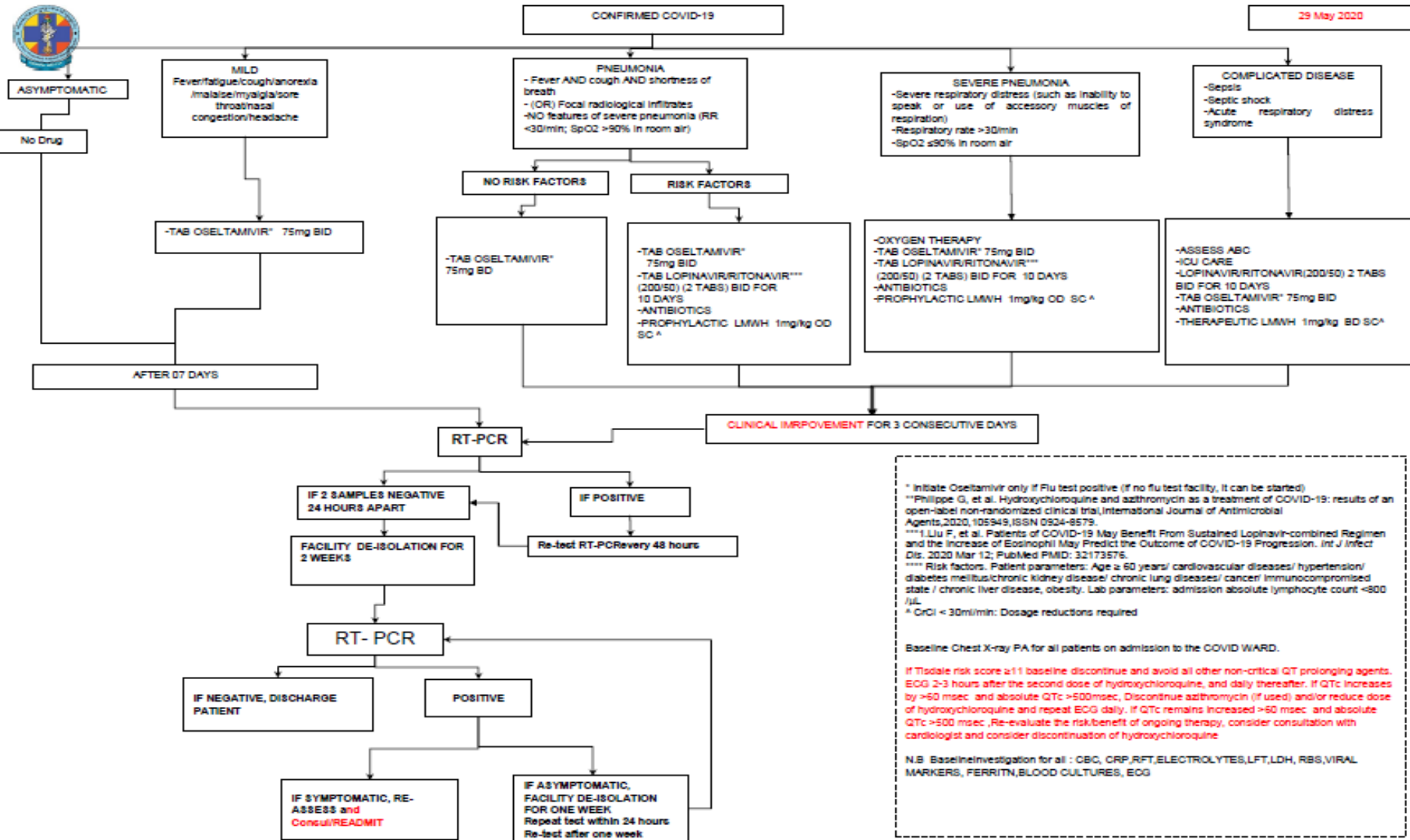
- Guideline developed after literature review and journal clubs
- Clinical syndrome classified as per WHO
  - Both symptomatic and asymptomatic confirmed cases admitted to COVID ward
- DOSA team and the active frontline team daily ZOOM on patient update and management
- Criteria for discharge
  - 2 consecutive RT-PCR Negative (24 hours apart) with clinical symptoms free for 3 consecutive days
  - Send for facility de-isolation
  - AT 14 days repeat RT-PCR, if negative send home
- Routine screening of all health care professionals (Low risk once a month and high risk once in 2 weeks)



# Clinical Management



29 May 2020



\* Initiate Osetamivir only if Flu test positive (if no flu test facility, it can be started)  
 \*\* Philippe G, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial, International Journal of Antimicrobial Agents, 2020, 105949, ISSN 0924-6460.  
 \*\*\* 1. Liu F, et al. Patients of COVID-19 May Benefit From Sustained Lopinavir-combined Regimen and the Increase of Eosinophil May Predict the Outcome of COVID-19 Progression. Int J Infect Dis. 2020 Mar 12; PubMed PMID: 32173576.  
 \*\*\*\* Risk factors: Patient parameters: Age ≥ 60 years/ cardiovascular diseases/ hypertension/ diabetes mellitus/ chronic kidney disease/ chronic lung diseases/ cancer/ immunocompromised state / chronic liver disease, obesity. Lab parameters: admission absolute lymphocyte count <800 /µL  
 ^ CrCl < 30ml/min: Dosage reductions required

Baseline Chest X-ray PA for all patients on admission to the COVID WARD.

If Tisdale risk score ≥ 11 baseline discontinue and avoid all other non-critical QT prolonging agents. ECG 2-3 hours after the second dose of hydroxychloroquine, and daily thereafter. If QTc increases by >60 msec and absolute QTc >500 msec, Discontinue azithromycin (if used) and/or reduce dose of hydroxychloroquine and repeat ECG daily. If QTc remains increased >60 msec and absolute QTc >500 msec, Re-evaluate the risk/benefit of ongoing therapy, consider consultation with cardiologist and consider discontinuation of hydroxychloroquine

N.B. Baseline investigation for all : CBC, CRP, RFT, ELECTROLYTES, LFT, LDH, RBS, VIRAL MARKERS, FERRITIN, BLOOD CULTURES, ECG

# COVID 19 TREATMENTS

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## Hydroxychloroquine (HCQ)

- Early Invitro some evidences
- Randomised Evaluation of COVID-19 thERapY (RECOVERY) Trial & WHO Solidarity Trial **no clinical benefits**
- Boulware DR, Pullen MF, Bangdiwala AS, Pastick KA, Lofgren SM, Okafor EC, et al. A Randomized Trial of Hydroxychloroquine as **Postexposure Prophylaxis** for Covid-19. N Engl J Med. 2020 Aug 6;383(6)
- Only the British RCT COPCOV continues, aiming to enroll 40 000 healthcare workers and other at-risk staff around the world to study the efficacy of HCQ as prophylaxis

## Lopinavir/ritonavir

- Both the WHO SOLIDARITY and the UK RECOVERY trials discontinued the lopinavir/ritonavir arms after interim analysis of the trial results

## Favipiravir

- A Japanese trial with 89 patients showed inconclusive results but the antiviral drug is still used in Russia

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## Remdesivir:














- Beigel JH, Tomashek KM, Dodd LE, Mehta AK, Zingman BS, Kalil AC, et al. Remdesivir for the Treatment of Covid-19 - Preliminary Report. N Engl J Med. 2020 May 22.
- Spinner CD, Gottlieb RL, Criner GJ, Arribas Lopez JR, Cattelan AM, Soriano Viladomiu A, et al. Effect of Remdesivir vs Standard Care on Clinical Status at 11 Days in Patients With Moderate COVID-19: A Randomized Clinical Trial. JAMA. 2020 Aug 21
- Uncertain clinical importance
- On 3 July 2020, the European Commission (with the recommendation of EMA) granted its conditional marketing authorization for the treatment of COVID-19 in adults and adolescents from 12 years of age with pneumonia who require supplemental oxygen making remdesivir the first authorized COVID-19 antiviral treatment in the EU.
- The U.S. Food and Drug Administration (FDA) has warned against use of remdesivir in combination with hydroxychloroquine

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## Dexamethasone

- Horby P, Lim WS, Emberson J, Mafham M, Bell J, Linsell L, et al. Effect of Dexamethasone in Hospitalized Patients with COVID-19: Preliminary Report. medRxiv. 2020:2020.06.22.20137273.
- Group RC, Horby P, Lim WS, Emberson JR, Mafham M, Bell JL, et al. Dexamethasone in Hospitalized Patients with Covid-19 - Preliminary Report. The New England journal of medicine. 2020 Jul 17.
  - showed that it significantly reduced the 28-day mortality, particularly among critically ill COVID-19 patients receiving mechanical ventilation. There was no evidence of benefit for patients not requiring oxygen
  - Based on these findings, the US National Institutes of Health (NIH) recommends the administration of dexamethasone for COVID-19 patients who are either mechanically ventilated or require supplemental oxygen
- RECOVERY Trial published findings concluding that the use of dexamethasone resulted in lower 28-day mortality among those who were receiving either invasive mechanical ventilation or oxygen alone at randomization, but not among those receiving no respiratory support
- Based on a systematic review and meta-analysis of the results of eight RCT, WHO published a strong recommendation of use of systemic corticosteroids in severely ill patients with COVID-19 and a conditional recommendation not to use systemic corticosteroids in patients with non-severe COVID-19

## How some of the Covid-19 vaccines compare

Company	Type	Doses	How effective*	Storage
 <b>Oxford Uni-AstraZeneca</b>	Viral vector (genetically modified virus)	 x2	62-90%	 Regular fridge temperature
 <b>Moderna</b>	RNA (part of virus genetic code)	 x2	95%	 -20C up to 6 months
  <b>Pfizer-BioNTech</b>	RNA	 x2	95%	 -70C
 <b>Gamaleya (Sputnik V)</b>	Viral vector	 x2	92%	 Regular fridge temperature

\*preliminary phase three results, not yet peer-reviewed

# ACHIEVEMENTS

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- No shortage of PPEs
- No mortality
- Motivated health care personnel's
- Behavioral change and acceptance of new norms
- Team, Multidisciplinary approach
- Uninterrupted essential health services in lockdown

# LESSONS LEARNED

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- Leadership is most crucial in such pandemics
- Multidisciplinary approach gives in success
- Decision based on evidences and not fear or peer pressure
- Team work between all categories of staffs
- Always best to prepare for the worst
- Keeping updated with the disease epidemiology, pathogenesis and management
- Strategies which can be implemented during lockdowns to provide essential care services



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# Thank you

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