As China is getting close to declare victory over COVID-19 (only 10-20 new cases a day across the country), here are some important lessons learned from the Chinese experience:

**Chinese Guidelines for Diagnosis and Treatment of COVID-19 (7th Edition)**

**Virology and Epidemiology**

- SARS-CoV-2 $\rightarrow$ β genus, diameter 60-140 nm
- Shares 79% of nuclear identity of SARS-CoV-1 and 52% of that of MERS
- ACE-2 is the host cell receptor
- Affects alveolar type II cells primarily $\rightarrow$ lung pathology very similar to SARS and MERS (bilateral diffuse alveolar damage with cellular fibromyxoid exudates)
- Can also affect the heart, the liver, and the kidney
- Disinfection by Ethanol and UV light, not inactivated by Chlorhexidine
- Epidemic started in China, now Europe is the epicenter
- Mortality in China 2.3%, but ~5% in Italy
- Median incubation period 4 – 5.2 days (95% percentile is 12.5 days)
- Main source of infection is asymptomatic infected people
- Route of transmission is respiratory droplets, close contact with asymptomatic infected people, long-term environmental exposure to high viral aerosolized load, possibly fecal transmission too
- $R_0$ 2.2 – 2.95 (i.e. one infected person infects on average 2-3 healthy individuals)

**Clinical Findings**

- WHO diagnostic criteria (one epidemiological + 2 clinical findings OR 3 clinical findings)
  - Epidemiological criteria:
    - H/o travel to (or residence in) high risk areas
    - H/o contact with a confirmed or suspected case
    - Attendance of events where clusters of cases were reported
  - Clinical criteria:
    - Fever
    - Respiratory symptoms (e.g. cough and dyspnea)
    - Leucopenia/ Lymphopenia (unclear etiology but very characteristic with COVID-19)
- Frequency of symptoms and complications:
  - Fever 98%
  - Cough 76% (mostly dry)
  - Lymphopenia 63% - lowest at day 7, prolonged lymphopenia poor prognostic sign
  - Diarrhea 3%
  - Complications: ARDS 29%, acute cardiac injury 12%, AKI 7%, septic shock 7%, secondary bacterial infection 10%
- Average duration of dyspnea is 13 days, 45% of survivors still had cough on discharge
• Median duration of viral shedding is 20 days (up to 37 days)
• COVID vs Influenza
  o Similar constellation of symptoms – recommend evaluation with RVP
  o Clinically, onset of COVID is slower than influenza which tends to be more abrupt
  o Additionally there appears to be less sputum production in COVID as compared to influenza
• Important observations from the Chinese experience:
  o D-dimer > 1µg/ml → independent risk factor for in-hospital death
  o Very high D-dimer and FDP levels in severe cases → extensive intravascular microthrombi on autopsy (possibly related to high ACE-2 expression in vascular endothelial cells) → **Anticoagulation should be started in severe COVID-19 cases if no contraindication** (Chinese Expert opinion – no supporting evidence)
  o Red flags for severity:
    ▪ Progressive lymphopenia
    ▪ Progressive increase in inflammatory biomarkers (IL-6 and CRP)
    ▪ Progressive worsening infiltrates on CT scan
    ▪ Elevated troponin and D-dimer

**Diagnostic Tests**

- RNA detection (RT-PCR) from nasopharyngeal swab, sputum, lower respiratory tract samples (best yield), blood and feces
- Serum antibody detection (IgM and IgG)
  o RNA testing alone has high false negative
  o When RNA testing + serum Ab testing → 98% sensitivity
  o Some cases tested positive for RNA again after discharge with negative test (unclear significance for now)
- Chest CT
  o Bilateral lung involvement
  o Peripheral distribution
  o Diffuse distribution
  o Ground glass opacities (can appear before the clinical onset of illness)
  o No septal thickening

**Features of CT scan of COVID-19**

- **Common**: bilateral lung involvement (79%); peripheral distribution (54%); diffuse distribution (44%).
- **Less common**: nodules (6%), cystic changes (10%), bronchiectasis (11%), pleural effusion (5%).
- **Not observed**: Tree in bud signs, masses, caviation, and calcifications.

**Treatment**

- **Isolation**
  o All confirmed and suspected cases (did not specify but seems that they used airborne given use of N95 and mention of negative pressure rooms)
  o PPE for healthcare workers → N95 when taking care of suspected or confirmed cases / Surgical masks everywhere else in the hospital **(ALL THE TIME)**
- **Supportive therapy**
- Sufficient caloric intake (many patients had hypoproteinemia)
- Water and electrolytes

**Antiviral therapy**
- So far, no specific antiviral for SARS-CoV-2
- Clinically evaluated antivirals:
  - Remdesivir (CAP China Remdesivir 1 and 2, ongoing trials for mild-mod and severe pneumonia)
- Other antimicrobials without supportive clinical data:
  - Ribavirin
  - Chloroquine
  - Arbidol
  - Convalescent plasma therapy
  - Favipiravir (favitavir)

**Immune therapy**
- Targeting the host immune response to the virus
- Tocilizumab – IL-6 monoclonal antibody – for severe cases

**Steroids**
- Controversial
- Central role for inflammation has been determined in the pathophysiology of COVID-19
- Used for rapid deterioration in oxygenation and radiologic findings
- Low to moderate doses only – max 1-2 mg/kg/day of methylprednisone
- For 3-5 days only

**Discharge Criteria**
- Normal temperature for >3 days
- Improvement of respiratory symptoms
- 2 consecutive negative respiratory specimens at least 24 hours apart

**COVID-19 and Cardiovascular Disease**

COVID-19 patients with underlying cardiovascular disease have the highest fatality rate (10.5%)

**Pathology of Cardiac Damage**
- Mononuclear inflammatory infiltrate
- Endothelial shedding
- Intravascular thrombosis
- SARS-CoV-2 inclusions can be seen

**Mechanisms of Acute Cardiac Damage**
• ACE-2-mediated direct cellular damage
• Hypoxia-induced myocardial damage
• Microvascular damage
• SIRS

**Clinical Presentations and Complications**

• Arrhythmias (17%)
• Acute cardiac injury (elevated high-sensitivity troponin) (12%)
• Elevated regular troponin or CK-MB (7.2%) → occurs in severe cases (mostly negative in mild and moderate cases) → mortality 49%
• Fulminant myocarditis can occur (they presented a case with regional STE [inferior leads], negative coronary angiogram, initial drop in EF to 27%, and complete recovery with supportive therapy)
• STEMI can also occur as a complication
• Important observations:
  o ↓ pericardial adipose tissue correlates with COVID-19 severity
  o There may be evidence of chronic cardiovascular damage following COVID-19

**Management of Cardiac Medications**

• ACEI/ ARBs → dilemma:
  o The good: ACEI/ARBs → ↓ Angiotensin II activity → improvement of lung inflammatory response
  o The bad: ACEI/ARBs → ↑ ACE-2 activity → increase viral cellular bindings and facilitate infection
  o CV perspective:
    ▪ They are essential medications from a cardiovascular standpoint
    ▪ For COVID-19 mortality, HTN had an OR of 3.05
    → The current Chinese recommendation is NOT to stop them in COVID-19 patients
• Antiplatelets → continue
• Statins → continue and monitor liver functions closely
• BB → selective B1 blockers are recommended in the absence of airways spasm

**Important Considerations with Antiviral Medications**

• Antiviral interaction with cardiovascular drugs (......I missed the examples....)
• Lopinavir/ritonavir (the first-line antiviral therapy in China) can cause complete heart block and dilated cardiomyopathy

**Management of Acute MI and Protection of Cardiologists during COVID-19**

Important general rules:
• Nearby therapy (treat at the nearest medical center – avoid transfers as possible)
• Safe protection (if fever or suspicion of COVID-19 in AMI patients → test immediately → isolate)
• Travel and exposure history should be assessed in all STEMI patients
• Thrombolysis first (rather than primary PCI) in confirmed or suspected COVID-19 patients. Remember: PCI less widely available in China than in US, and thus thrombolysis remains a more standard therapy there.

• Coronary angiography for suspected or confirmed COVID-19 patients should be in designated Cath labs (with negative pressure if available)

• In suspected or confirmed COVID-19 cases who need cardiology input → use remote cardiology consultation as possible (virtual or telephone)

• Avoid unnecessary hospitalizations

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**Important Final Remarks**

• The most dangerous thing about this epidemic from the Chinese perspective is the transmission by asymptomatic or mildly symptomatic infected individuals.

• We learned from Wuhan and Italy that young healthy people can also get severe disease and die

• Many infections in healthcare professionals (in China → 3.8% of the cases are HC workers, of those, 15% were severe/critically ill, 5 deaths)

• Observation from Wuhan is that the rate of co-infection with other respiratory viruses especially influenza is high. Dr Bin Cao said “As if they always came together” when referring to influenza pneumonia and COVID-19. This has huge implications since many US hospital protocols now say that if RVP is +ve then no need to test for SARS-CoV-2.

• Best way to prepare from a hospital perspective is DIAGNOSIS (you need to know who’s infected and who’s not once they present to clinic or ED → RNA testing IMMEDIATELY) – to ensure proper isolation and admission to appropriate wards/ICU.

• Changes to hospitals workflow in Wuhan:
  o All outpatient clinics were closed during the epidemic surge
  o All outpatient visits were performed virtually or by telephone (if medical attention is needed → ED)
  o Marked increase in the use of thrombolysis (vs primary PCI) for STEMI

• Social isolation/distancing is EFFECTIVE → needs to be done for at least 2-4 weeks

• Best way to think about the situation now is: No more normal life, it’s COVID-19 pandemic life (things that are not normally acceptable or feasible should be now, to face the pandemic)