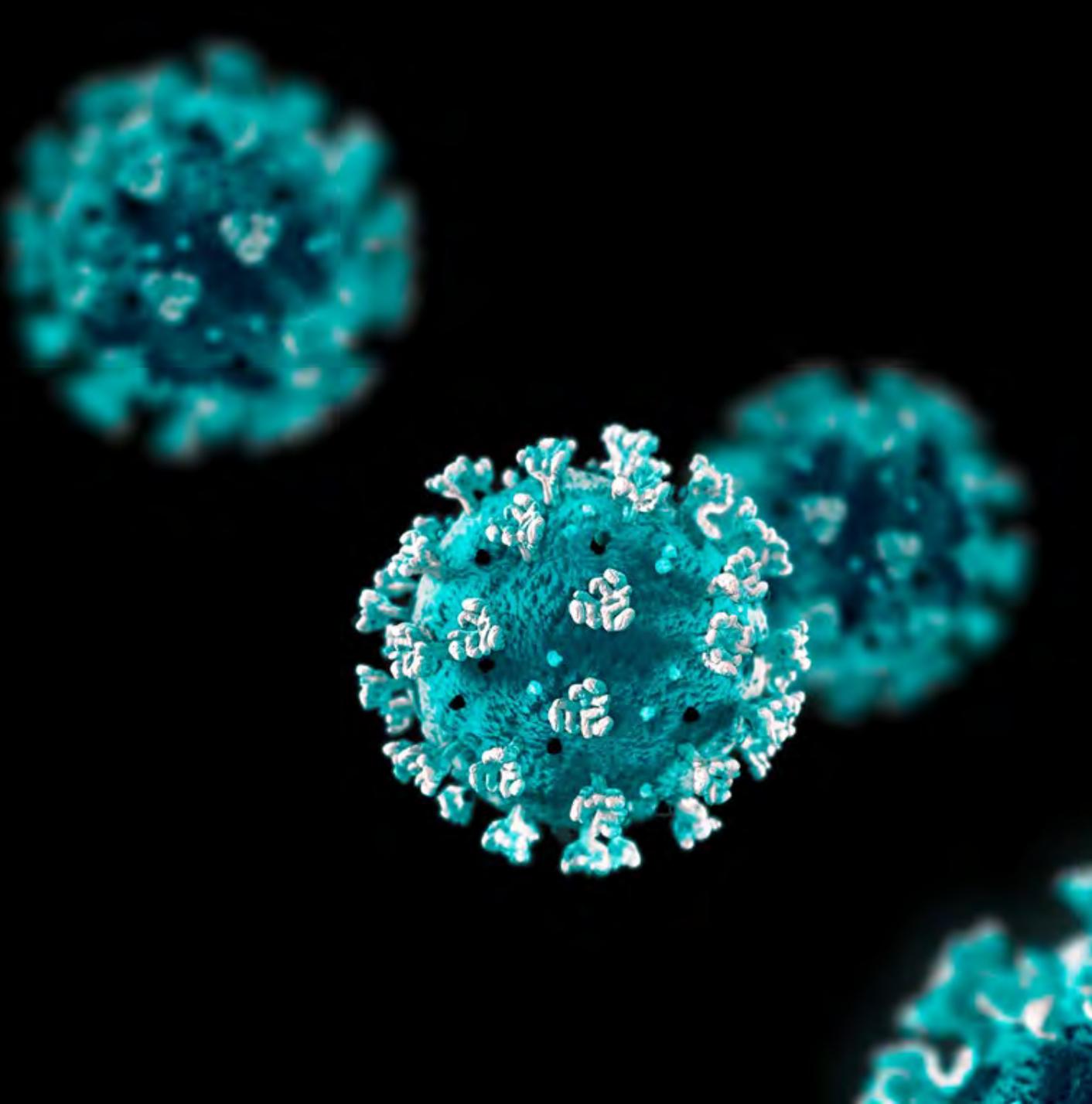


Diagnosis and Management of COVID-19: A Laboratory Medicine Perspective

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China Has Fought COVID-19, Winning a Decisive Victory

COVID-19 Cases	Confirmed	Dead	Recovered
China	84,271 +34	4,642	77,978 +183
<i>Wuhan (Hubei Province)</i>	68,128	4,512	63,514 +3
World	2,475,841 +73,765	170,261 +5,155	646,433 +22,522

Data source: CDC, WHO, China MOH as of local time April 20

Initial Outbreak and Identification in Wuhan, China



- Jan 10, 2020** ● Patients ramping up quickly, **5,417 confirmed cases** between Jan 11 and Jan 20; a total of 3,000 beds in 7 designated hospitals;
- Jan 5, 2020** ● Isolation and identification of novel coronavirus from patient samples by direct sequencing;
- Dec 29, 2019** ● Hubei Provincial Hospital of Integrated Chinese & Western Medicine reported to CDC of Wuhan City and Hubei Province respectively;
- Late Dec, 2019** ● Patients with pneumonia of unknown cause in **Wuhan** Central Hospital and other places; **symptoms similar to SARS.**

China's Experience

Quarantine



“A five-day delay in implementation would have increased epidemic size in mainland China three-fold.”

Modified SEIR and AI prediction of the epidemics trend of COVID-19 in China under public health interventions, J Thorac Dis 2020;12(3):165-174

Fangcang Shelter Hospitals



“By March 10, 2020, the 16 hospitals had provided care to about **12,000** patients and effectively supported China's COVID-19 policy of leaving no patient unattended or untreated. The Fangcang shelter hospitals inserted an additional level of care into the Chinese health system and thus served a **strategic triage function** for patients with COVID-19.”

Fangcang shelter hospitals: a novel concept for responding to public health emergencies, LANCET, April 2, 2020

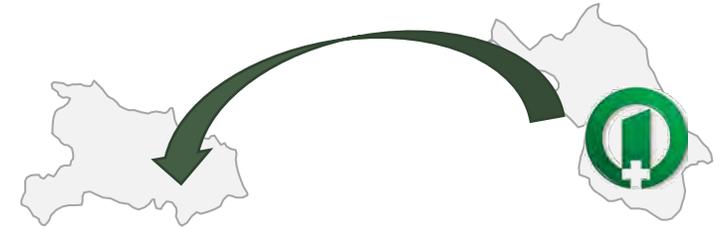
Support



“346 medical teams, 42,600+ medical staff from 29 provinces, 70+ days.”

CCTV News

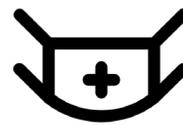
What NFH Has Done to Help Fight the Epidemic in Wuhan



2 medical teams of 60 doctors and nurses rushed to Wuhan to rescue the patients.



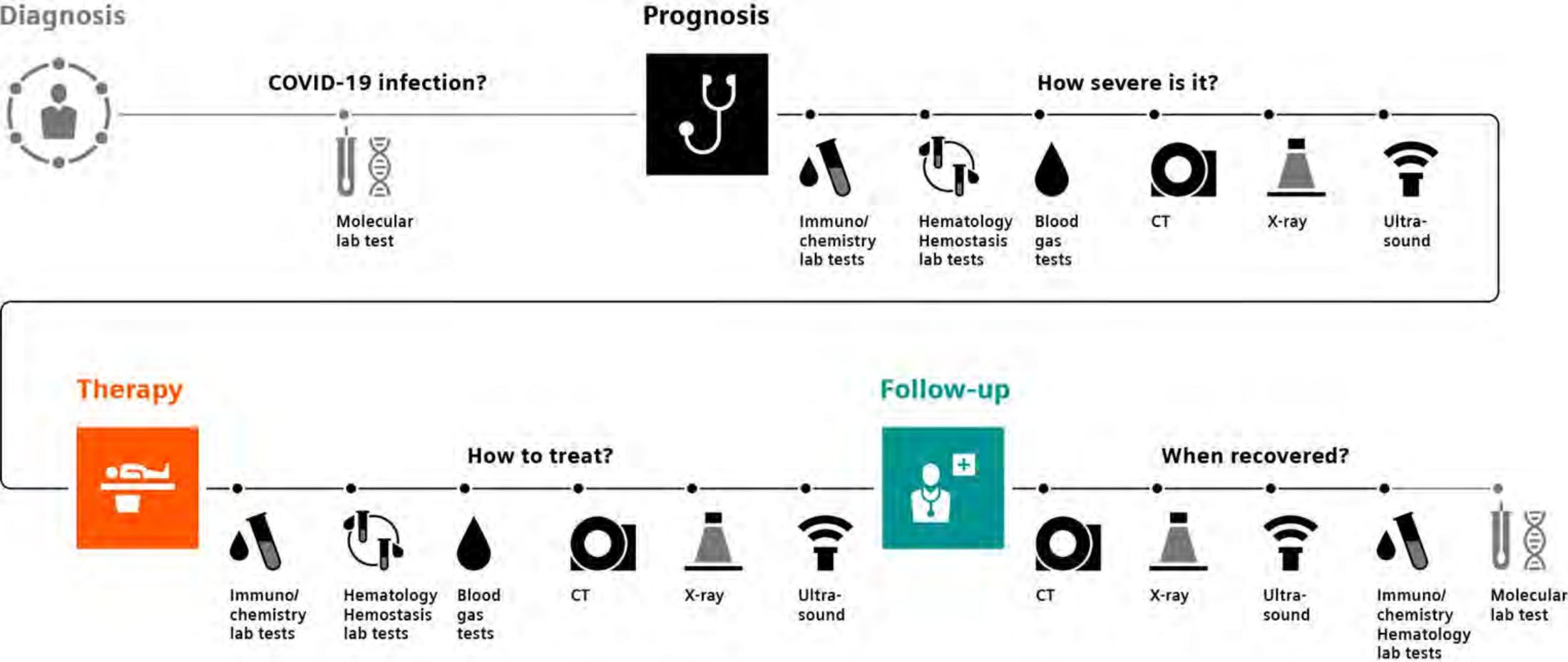
132 doctors and nurses were responsible for a ward of 48 beds in Tongji hospital.



Zero deaths out of the 88 patients, **zero infections** of the medical staff.

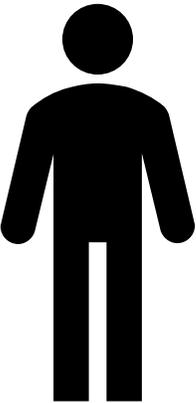


The Process of COVID-19 Patient Care



COVID-19-Positive qPCR Evidence is the Diagnostic Criteria, With an Antibody Assay Added in the 7th Edition of the National Guideline in China

Suspect

- 
- I. Travel/Living history to Wuhan within 14 days of onset;
 - II. Contact history with COVID-19 patient (qPCR+) within 14 days of onset;
 - III. Contact history with people from Wuhan with fever or respiratory symptoms within 14 days of onset;
 - IV. Group onset, 2+ fever and/or respiratory cases in family, office, school, etc.
 - V. Fever and/or respiratory symptoms;
 - VI. Pneumonia evidence from imaging;
 - VII. Normal or low **WBC count**, Normal or low **Lymphocytes**.

Meet any 1 of I~IV + 2 of V~VII or all of V~VII

Confirm

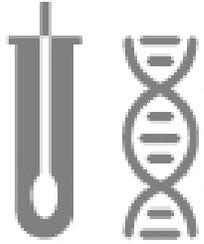
- 
- I. **qPCR** positive for SARS-COV-2;
 - II. **Genome sequencing** and mapped to SARS-COV-S reference genome;
 - III. Positive **SARS-COV-2 specific IgM and IgG antibody**; SARS-COV-2 specific IgG antibody turns from negative to positive or 4+ times elevation from acute phase;

Meet any 1 of I~III

Exclude

- I. 2 consecutive negative **qPCR results** for SARS-COV-2 (24h between sampling) and negative **SARS-COV-2 specific IgM and IgG antibody** 7 days after onset.

Role of in vitro and in vivo technology in diagnosis



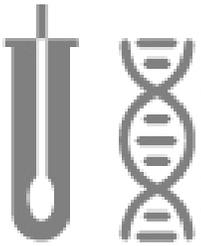
**Molecular
lab test**

- COVID-9 is caused by infection of 2019-nCoV; the presence of pathogen should be the “gold standard” for diagnosis;
- Nucleic Acid Testing (NAT) targets a specific sequence in the genome and serves as laboratory criteria of confirmation;
- CT scan is also important to aid the clinical understanding of infection and staging; however, CT scan cannot replace NAT due to its limitations in early diagnosis, differential diagnosis, and confirmation/exclusion.



CT

Determinants of SARS-COV-2 qPCR Testing



Molecular lab test

Several factors can impact NAT results :

- A course of COVID-19 illness and progression of the disease

COVID-19 patients may experience from none to severe symptoms, depending on disease progression, of which virus load varies at certain sampling sites;

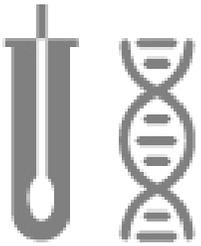


Caution on the window period;



A series of NAT should be performed to avoid mis-diagnosis ;

Determinants of SARS-COV-2 qPCR Testing



Molecular lab test

Several factors can impact NAT results :

- Sampling, transportation and storage

Multiple practice suggests NAT positive rate of NP Swab > Oral Swab; Sputum, BALF from lower respiratory tract > Oral/NP Swab from upper respiratory tract



Recommend sampling of multiple sites per patient and pool together for testing; i.e. combined oral and NP swabs in a single tube;

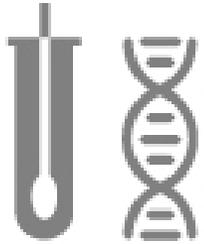


For patients with gastrointestinal tract symptoms, recommend to test feces sample or anal swab;



SARS-COV-2 is a RNA virus, susceptible to RNAase. Recommend to finish testing within 4 hours of sampling. If not, samples should be stored at 4°C for less than 24 hours; samples should be stored at -70 °C exceeding 24 hours.

Interpretation of SARS-COV-2 IgM and IgG Testing



Molecular lab test

From Feb 21, 2020, the SARS-COV-2-specific IgM and IgG antibodies have been included in the series update of China's MOH COVID-19 guidelines. Precautions should include:



Strictly follow testing kit IFU with good understanding of interference such as rheumatic factors, heterophilic antibodies, complement components, drugs, metabolites and other factors;



For testing kits requiring visual inspection, consistent training and evaluation should be done for operators;

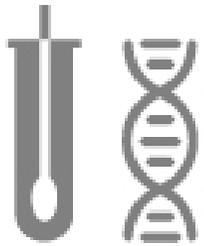


A series of monitoring would make sense; antibody results should not be interpreted alone for confirmation/exclusion; need to consider epidemiology, clinical symptoms, NAT, and CT scan in combination; with more caution on false-positive testing for large-scale population screening.



Immuno-chemistry lab tests

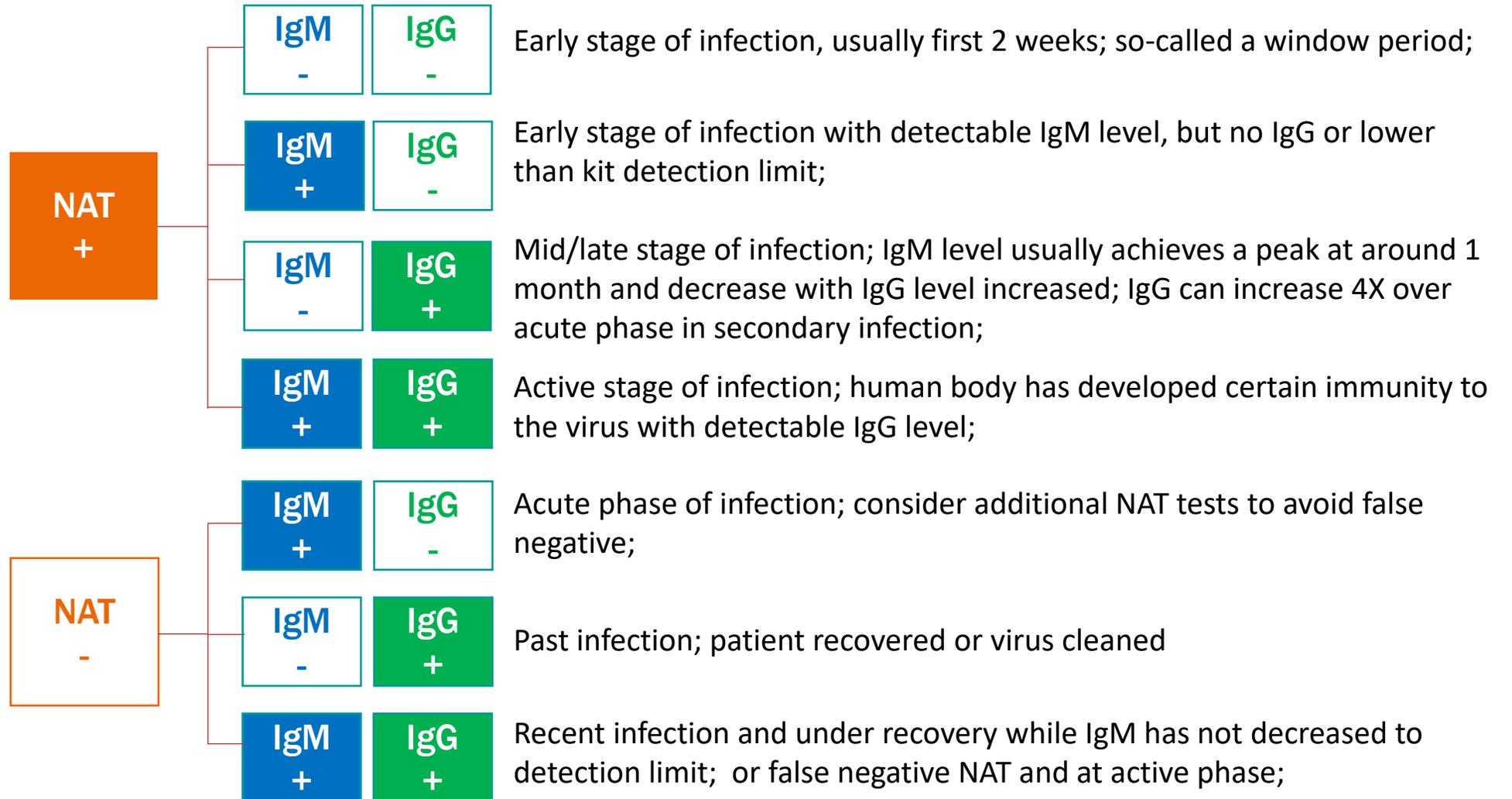
Interpretation of SARS-COV-2 IgM- and IgG-Positive



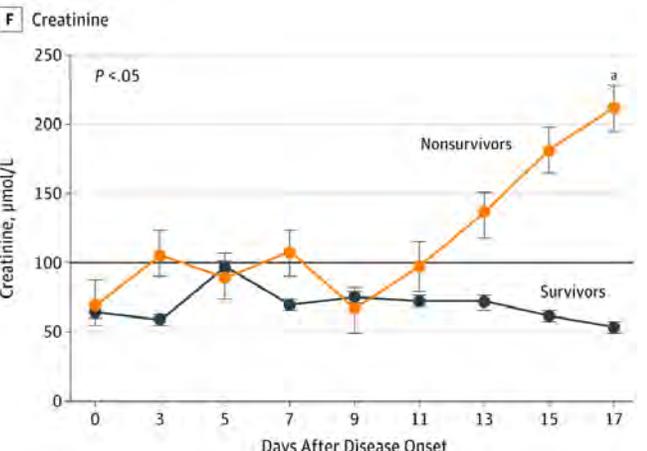
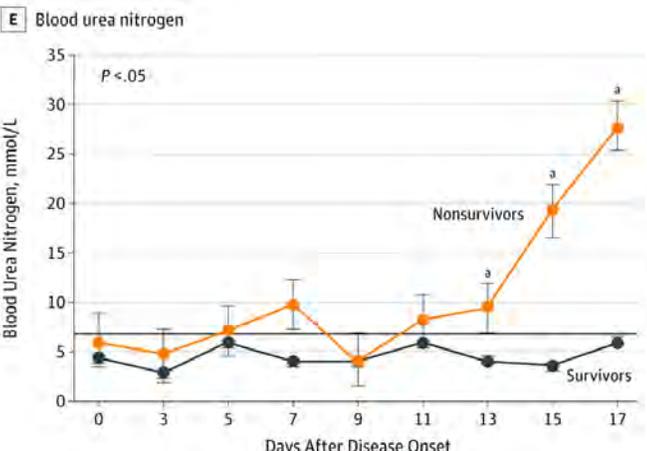
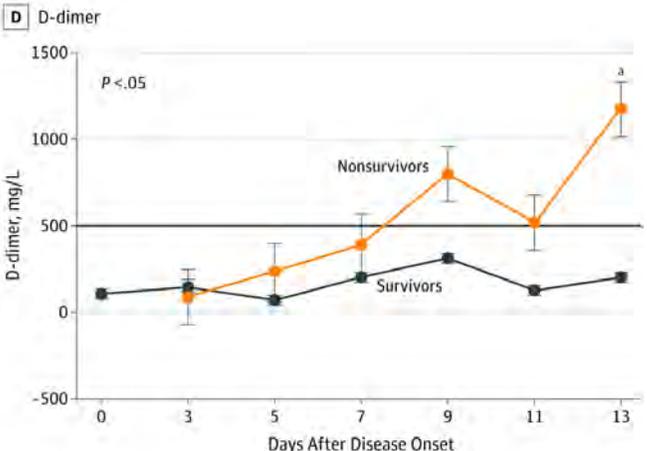
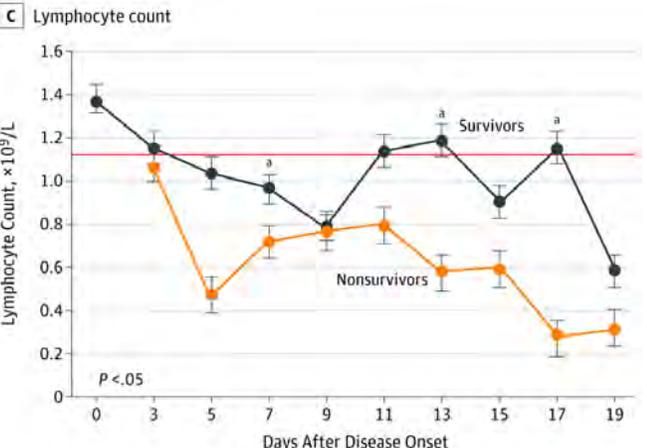
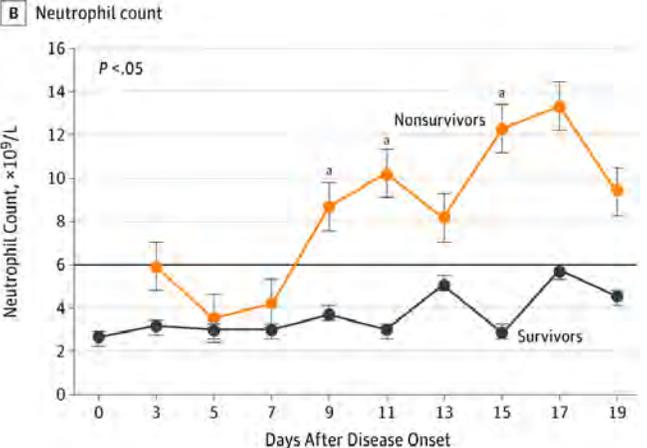
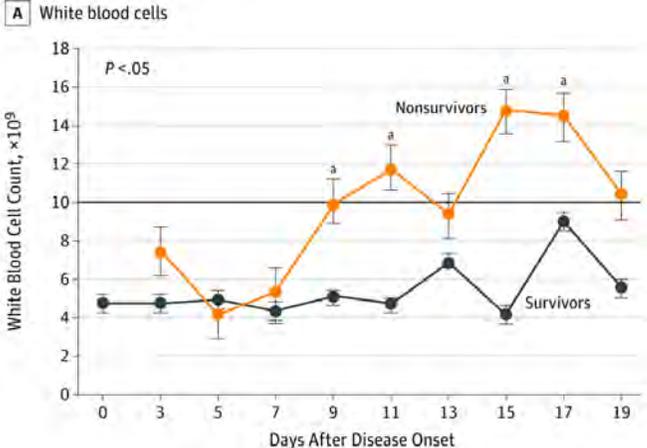
**Molecular
lab test**



**Immuno-
chemistry
lab tests**



Several Markers Associated With Disease Progression and Patient Outcomes



Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China, JAMA. 2020;323(11):1061-1069.

Several Markers Associated With Disease Progression and Patient Outcomes

Table 1. Characteristics of inflammatory biomarkers of patients infected with COVID-19

Laboratory Indicators	Mild Group	Severe Group	P Value	Reference
WBC, $10^9/L$	5.72 ± 2.93 , n=148	9.64 ± 10.63 , n=57	<0.01	3.5 ~ 9.5
NEU,%	66.45 ± 12.77 , n=148	80.37 ± 11.83 , n=57	0.446	40 ~ 75
LYM,%	23.88 ± 10.46 , n=148	12.79 ± 9.31 , n=57	0.158	20 ~ 50
hs-CRP, mg/L	20.81 ± 29.00 , n=134	51.32 ± 59.97 , n=47	<0.001	0 ~ 10
PCT, ng/mL	0.082 ± 0.116 , n=127	1.723 ± 4.291 , n=41	<0.001	0 ~ 0.046

*Patients in the severe group have higher white blood cell (WBC) counts, high-sensitivity C-reactive protein (hs-CRP) and procalcitonin (PCT) ($P < 0.01$) than common group.

Several Markers Associated With Disease Progression and Patient Outcomes

Table 2. Characteristics of cardiac markers of patients infected with COVID-19

Laboratory Indicators	Mild Group	Severe Group	P Value	Reference
LDH, U/L	255.18±110.10 , n=147	431.66±250.58 , n=53	<0.001	120 ~ 2500
hs-cTn, ng/mL	0.009±0.009 , n=106	0.149±0.455 , n=46	<0.001	
NT-proBNP, pg/mL	117.01±166.56 , n=47	9728.44±14368.25 , n=33	<0.001	

*Patients in the severe group have higher N-terminal B-type natriuretic peptide (NT-proBNP), high-sensitivity troponin T (hs-cTnT), and lactate dehydrogenase (LDH) ($P < 0.01$).

A Case Study

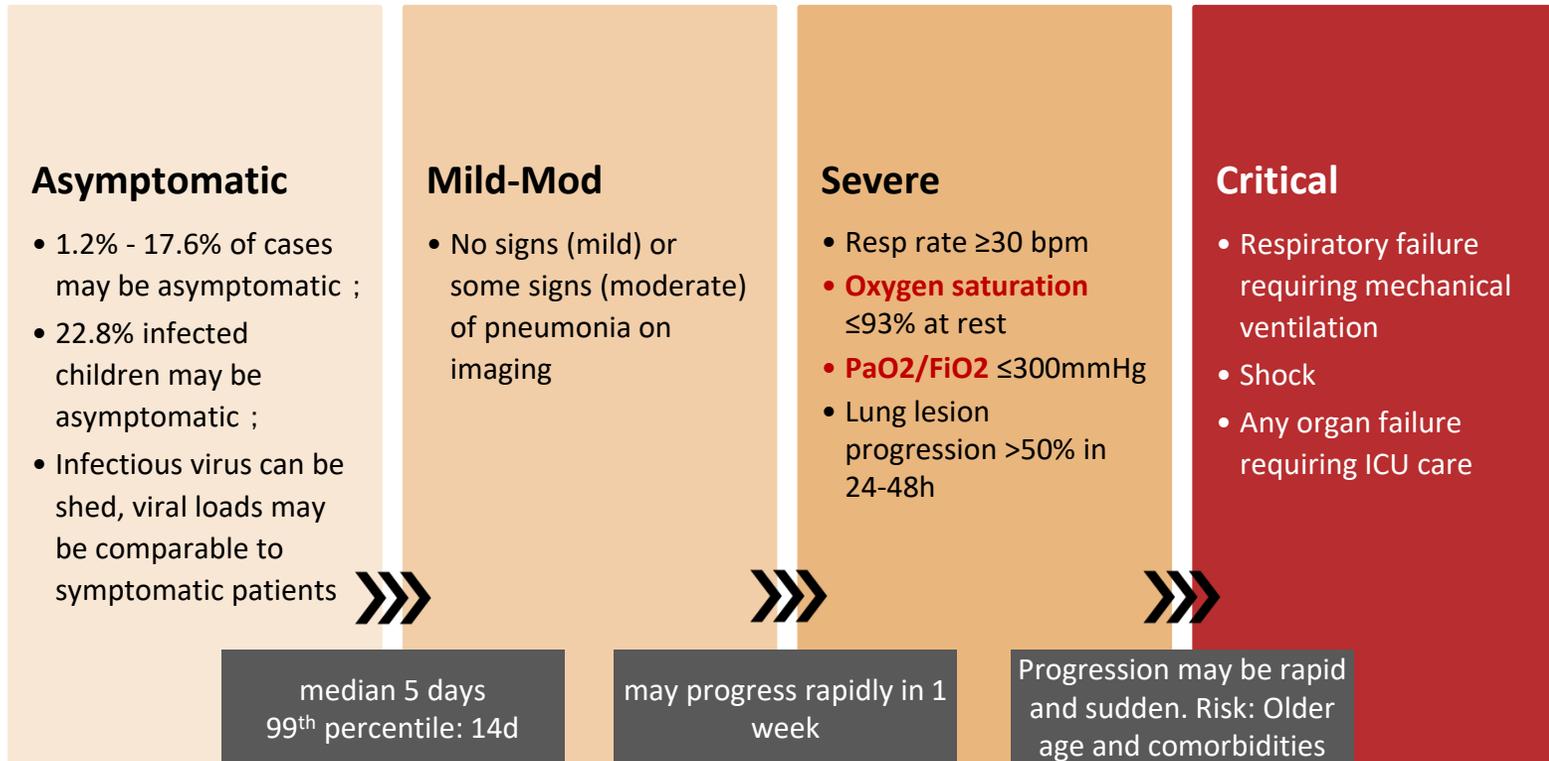


- **Chief complaint:** male, 81 years old, Feb.6, 2020 was admitted to the hospital due to "cough, chest tightness and gasping, for 4 days".
- **Past medical history:** Hypertension for 4 years, use of drugs and control conditions were unknown; gout for many years; no history of hepatitis, tuberculosis, kidney disease and heart disease.
- **Admission diagnosis:** viral pneumonia, cardiac insufficiency, renal insufficiency.
- **Outcomes:** Respiration was significantly better than before; vital signs were stable; COVID-19 NAT results were consecutively negative in 2 tests; transferred to a general ward.

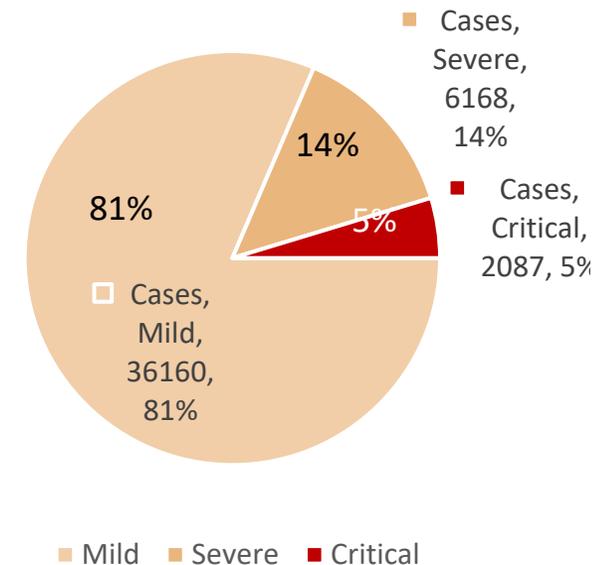
A Case Study

Laboratory Indicators		Results	Reference	Judgement	Clinical Significance
Heart function	hs-cTnT, ng/mL	0.096	<0.014	↑	Myocardial damage
	MYO, ng/ml	286.8	<58	↑↑	
	NT-proBNP, pg/mL	6338	<300	↑↑↑	heart failure
Renal function	GFR, ml/min	24.09	80-120	↓↓↓	renal failure
	BUN, umol/L	19.3	2.5-7.1	↑↑	
	Cr, umol/L	214.3	62-133	↑↑	
	UA, umol/L	497	149-416	↑	
	K, mmol/L	5.73	3.5-5.3	↑	
Infection markers	CRP, mg/L	190	<10	↑↑↑	infection
	PCT, ng/ml	0.68	<0.1	↑	

Blood Gas Results Serve Staging for Severe Patients



Disease spectrum of COVID-19 in China (n=44,672)



PaO₂/FiO₂: arterial partial pressure of oxygen/ fraction of inspired oxygen
[\[Chinese\] NHC. Diagnosis and treatment for the novel coronavirus pneumonia \(v7\)](#)
 Mizumoto et al. Euro Surveill. doi:10.2807/1560-7917.ES.2020.25.10.2000180
 Lu et al. N Engl J Med. doi: 10.1056/NEJMc2005073

<https://www.cdc.gov/coronavirus/2019-ncov/about/symptoms.html>
 Lauer et al. Ann Intern Med. doi: 10.7326/M20-0504
 Cascella et al. <https://www.ncbi.nlm.nih.gov/books/NBK554776/> [Updated 2020 Mar 20]
 China CDC report. JAMA. doi: 10.1001/jama.2020.2648

A Sub-Group of Severe COVID-19 Patients Experiencing Cytokine Storm

THE LANCET

ARTICLES | VOLUME 395, ISSUE 10223, P497-506, FEBRUARY 15, 2020

Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China

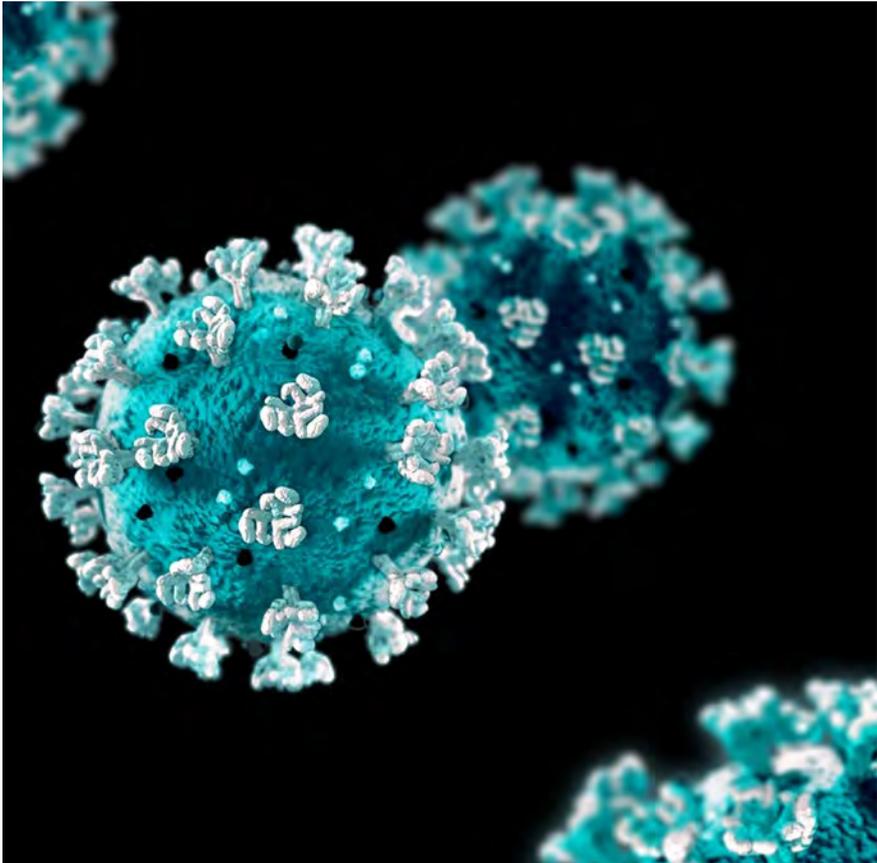
Prof Chaolin Huang, MD * • Yeming Wang, MD * • Prof Xingwang Li, MD * • Prof Lili Ren, PhD * • Prof Jianping Zhao, MD * • Yi Hu, MD * • et al. [Show all authors](#) • [Show footnotes](#)

Published: January 24, 2020 • DOI: [https://doi.org/10.1016/S0140-6736\(20\)30183-5](https://doi.org/10.1016/S0140-6736(20)30183-5) •  Check for updates

The research indicated that increased serum levels of proinflammatory cytokines were seen in NCP patients, leading to activated Th1 cell responses, and that higher plasma levels of multiple cytokines were also observed in ICU patients. This suggests that “cytokine storm” would be associated with disease severity. However, 2019-nCoV infection also initiated increased secretion of T-helper-2 (Th2) cytokines that suppress inflammation, which differs from SARS-CoV infection.

Our studies showed that COVID-19 patients have normal or higher levels of cytokines, including IL-2, IL-6, TNF- α , and IFN- γ , and that severe patients with organ failure manifested a significant increase in these cytokines.

Summary



- Overview of China's battle against COVID-19;
- Laboratory medicine plays key roles in diagnosis, staging, and monitoring of COVID-19 and prediction of its prognosis;
- Laboratory testing points to the right direction of caring for patients with COVID-19.

Thanks for your attention!

