The World Assciation of Societies of Pathology and Laboratory Medicine (WASPaLM) is present in the complex world of information on COVID-19, and specifically trying to give the correct information to stakeholders and public concerning the actual real power of diagnostics.

The main questions concerning the laboratory diagnosis of COVID-19 disease to which we should answer are:

1) RT-PCR is the main method to detect the presence of the virus. Is it possible to measure the number of virus copies by RT-PCR or it is only a qualitative assay? If yes, did someone correlate the number of copies with the seriousness of the disease?

2) Antibodies anti COVID-19 have been isolated. Do we know the time of appearance of IgM and IgG after the infection and how long they last? IgG antibodies are neutralizing and give immunity? For how long?

3) Have the levels of IL-6 been measured in COVID-19 patients? If yes, are the levels related to the gravity?

Additional questions:

4) How many different kits for RT-PCR are present in the world and what is their accountability and their cost.

5) How many diagnostic kits to detect antibodies are actually available?

6) What is the cost of the molecular test and what is the cost of the antibodies detection? Are there differences in the various Nations?

Thanks to Professor Stelios Chatzipanagiotou, and to Professor Beili Wang, some of the questions can be answered by means of useful articles on COVID-19 Laboratory Diagnosis.

Our task is not concluded, many questions are still unresolved, but this can be a good basis to start.

a) Is it possible to measure the number of virus copies by RT-PCR or it is only a qualitative assay? If yes, did someone correlate the number of copies with the seriousness of the disease?

Novel, Highly Sensitive and Specific COVID-19-RdRp/Hel Real-Time Reverse Transcription-Polymerase Chain Reaction Assay Validated *in vitro* and With Clinical Specimens

Jasper Fuk-Woo Chan [1 2 3 4 5], Cyril Chik-Yan Yip [6], Kelvin Kai-Wang To [1 2 3 4], Tommy Hing-Cheung Tang [7], Sally Cheuk-Ying Wong [8], Kit-Hang Leung [3], Agnes Yim-Fong Fung [3], Anthony Chin-Ki Ng [3], Zijiao Zou [3], Hoi-Wah Tsoi [3], Garnet Kwan-Yue Choi [6], Anthony Raymond Tam [9], Vincent Chi-Chung Cheng [6], Kwok-Hung Chan [1 3 4], Owen Tak-Yin Tsang [10], Kwok-Yung Yuen [11 3 4 5]

On 31st December 2019, the World Health Organization was informed of a cluster of cases of pneumonia of unknown etiology in Wuhan, China. Subsequent investigations identified a novel coronavirus, now named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), from the affected patients. Highly sensitive and specific laboratory diagnostics are important for controlling the rapidly evolving SARS-CoV-2-associated Coronavirus Disease 2019 (COVID-19) epidemic. In this study, we developed and compared the performance of three novel real-time RT-PCR assays targeting the RNA-dependent RNA polymerase (RdRp)/helicase (Hel), spike (S), and nucleocapsid (N) genes of SARS-CoV-2 with that of the reported RdRp-P2 assay which is used in >30 European laboratories. Among the three novel assays, the COVID-19-RdRp/Hel assay had the lowest limit of detection *in vitro* (1.8 $TCID_{50}$/ml with genomic RNA and 11.2 RNA copies/reaction with *in vitro* RNA transcripts). Among 273 specimens from 15 patients with laboratory-confirmed COVID-19 in Hong Kong, 77 (28.2%) were positive by both the COVID-19-RdRp/Hel and RdRp-P2 assays. The COVID-19-RdRp/Hel assay was positive for an additional 42 RdRd-P2-negative specimens [119/273 (43.6%) vs 77/273 (28.2%), P<0.001], including 29/120 (24.2%) respiratory tract specimens and 13/153 (8.5%) non-respiratory tract specimens. The mean viral load of these specimens was 3.21×10^4 RNA copies/ml (range, 2.21×10^2 to 4.71×10^5 RNA copies/ml). The COVID-19-RdRp/Hel assay did not cross-react with other human-pathogenic coronaviruses and respiratory pathogens in cell culture and clinical specimens, whereas the RdRp-P2 assay cross-reacted with SARS-CoV in cell culture. The highly sensitive and specific COVID-19-RdRp/Hel assay may help to improve the laboratory diagnosis of COVID-19.

Detection of 2019 Novel Coronavirus (2019-nCoV) by Real-Time RT-PCR

Victor M Corman [1], Olfert Landt [2], Marco Kaiser [2], Richard Molenkamp [3], Adam Meijer [4], Daniel K W Chu [5], Tobias Bleicker [1], Sebastian Brünink [1], Julia Schneider [1], Marie Luisa Schmidt [1], Daphne G J C Mulders [3], Bart L Haagmans [3], Bas van der Veer [4], Sharon van den Brink [4], Lisa Wijsman [4], Gabriel Goderski [4], Jean-Louis Romette [6], Joanna Ellis [7], Maria Zambon [7], Malik Peiris [5], Herman Goossens [8], Chantal Reusken [4], Marion P G Koopmans [3], Christian Drosten [1]

The ongoing outbreak of the recently emerged novel coronavirus (2019-nCoV) poses a challenge for public health laboratories as virus isolates are unavailable while there is growing evidence that the outbreak is more widespread than initially thought, and international spread through travellers does already occur.

Aim: We aimed to develop and deploy robust diagnostic methodology for use in public health laboratory settings without having virus material available.

Methods: Here we present a validated diagnostic workflow for 2019-nCoV, its design relying on close genetic relatedness of 2019-nCoV with SARS coronavirus, making use of synthetic nucleic acid technology.

Results: The workflow reliably detects 2019-nCoV, and further discriminates 2019-nCoV from SARS-CoV. Through coordination between academic and public laboratories, we confirmed assay exclusivity based on 297 original clinical specimens containing a full spectrum of human respiratory viruses. Control material is made available through European Virus Archive - Global (EVAg), a European Union infrastructure project.

Conclusion: The present study demonstrates the enormous response capacity achieved through coordination of academic and public laboratories in national and European research networks.

b) Antibodies anti COVID-19 have been isolated. Do we know the time of appearance of IgM and IgG after the infection and how long they last? IgG antibodies are neutralizing and give immunity? For how long?

Profiling Early Humoral Response to Diagnose Novel Coronavirus Disease (COVID-19)

Li Guo [1], Lili Ren [1], Siyuan Yang [2], Meng Xiao [3], De Chang [4], Fan Yang [5], Charles S Dela Cruz [6], Yingying Wang [1], Chao Wu [1], Yan Xiao [1], Lulu Zhang [1], Lianlian Han [1], Shengyuan Dang [1], Yan Xu [7], Qiwen Yang [3], Shengyong Xu [8], Huadong Zhu [8], Yingchun Xu [3], Qi Jin [5], Lokesh Sharma [6], Linghang Wang [9], Jianwei Wang [1]

Background: Emergence of coronavirus disease 2019 (COVID-19) is a major healthcare threat. Current method of detection involves qPCR-based technique, which identifies the viral nucleic acids when present in sufficient quantity. False negative results can be achieved and failure to quarantine the infected patient would be a major setback in containing the viral transmission. We here aim to describe the time kinetics of various antibodies produced against the 2019 novel coronavirus (SARS-CoV-2) and evaluate the potential of antibody testing to diagnose COVID-19.

Methods: The host humoral response against SARS-CoV-2 including IgA, IgM and IgG response were examined by using an ELISA based assay on the recombinant viral nucleocapsid protein. Total 208 plasma samples were collected from 82 confirmed and 58 probable cases (qPCR negative but had typical manifestation). The diagnostic value of IgM was evaluated in this cohort.

Results: The median duration of IgM and IgA antibody detection were 5 days (IQR 3-6), while IgG was detected on 14 days (IQR 10-18) after symptom onset, with a positive rate of 85.4%, 92.7% and 77.9% respectively. In confirmed and probable cases, the positive rates of IgM antibodies were 75.6% and 93.1%, respectively. The detection efficiency by IgM ELISA is higher than that of qPCR method after 5.5 days of symptom onset. The positive detection rate is significantly increased (98.6%) when combined IgM ELISA assay with PCR for each patient compare with a single qPCR test (51.9%).

Conclusions: Humoral response to SARS-CoV-2 can aid to the diagnosis of COVID-19, including subclinical cases.

c) Have the levels of IL-6 been measured in COVID-19 patients? If yes, are the levels related to the gravity?

Diagnostic Utility of Clinical Laboratory Data Determinations for Patients With the Severe COVID-19

Yong Gao [1], Tuantuan Li [1], Mingfeng Han [1], Xiuyong Li [1], Dong Wu [2], Yuanhong Xu [3], Yulin Zhu [4], Yan Liu [5], Xiaowu Wang [1], Linding Wang [5]

Abstract

The role of clinical laboratory data in the differential diagnosis of the severe forms of COVID-19 has not been definitely established. The aim of this study was to look for the warning index in severe COVID-19 patients. We investigated forty-three adult patients with COVID-19. The patients were classified into mild group (28 patients) and severe group (15 patients). Comparison of the haematological parameters between the mild and severe groups showed significant differences in IL-6, D-Dimer, GLU, TT, FIB and CRP ($P < 0.05$). The optimal threshold and area under the ROC curve of IL-6 were 24.3 pg/mL and 0.795 respectively, while those of D-Dimer were 0.28 μg/L and 0.750, respectively. The area under the ROC curve (AUC) of IL-6 combined with D-Dimer was 0.840. The specificity of predicting the severity of COVID-19 during IL-6 and D-Dimer tandem testing was up to 93.3%, while the sensitivity of IL-6 and D-Dimer by parallel test in the severe COVID-19 was 96.4%. IL-6 and D-Dimer were closely related to the occurrence of severe COVID-19 in the adult patients, and their combined detection had the highest specificity and sensitivity for early prediction of the severity of COVID-19 patients, which has important clinical value.

ECDC Novel coronavirus disease 2019 (COVID-19) pandemic: increased transmission in the EU/EEA and the UK – sixth update 12 March 2020

Viral shedding: Over the course of the infection, the virus has been identified in respiratory tract specimens 1-2 days before the onset of symptoms and it can persist for 7-12 days in moderate cases and up to 2 weeks in severe cases [22]. In faeces, viral RNA has been detected from day 5 after onset and up to 4 to 5 weeks in moderate cases. The virus has been detected also in whole blood [23], serum [24,25] saliva [26] and urine [27]. Prolonged viral RNA shedding has been reported from nasopharyngeal swabs, up to 37 days among adult patients [28] and in faeces, for more than one month after infection in paediatric patients [29]. It should be noted that viral RNA shedding does not directly equate with infectivity.

Testing and surveillance strategy Laboratory testing Timely and accurate laboratory testing of specimens from cases under investigation is an essential part of the management of COVID-19 and emerging infections in general. However, any shortage of laboratory diagnostic capacity at national or local level will hamper epidemic response. If countries need help in testing, a pool of specialised referral laboratories have offered support within the EU/EEA [82]. Member States should monitor the changes in the epidemic situation and be prepared to adjust the laboratory diagnostic capacity to the changing needs. Anticipating a rapid increase in the demand, countries

should continue rolling out primary diagnostic testing capacity to local clinical and diagnostic laboratories. The specimen types to be collected are listed in the WHO laboratory guidance [83]. When the diagnostic laboratories have established their SARS-CoV-2 detection assays and confirmed their first five positive and ten negative detection results with the national SARS-CoV-2 reference or international referral laboratories [83], the diagnostic laboratories can confirm the test results by the secondary target gene in their own laboratory. In countries with limited transmission or local clusters, positive specimens should be subjected to confirmation by targeting a second gene of SARS-CoV-2 in an RT-PCR assay. In areas with local community transmission of COVID-19, detection by RT-PCR of a single discriminatory target is considered sufficient [83]. Confirmatory testing should be performed only for specimens where the first result is technically not interpretable or the RT-PCR cycle threshold value is above 35. In such a case, additional sampling or repeated testing and confirmation is advised. Serological assays are under development, and collecting serum specimens iat symptom onset, or at admission and at convalescent stage, or at discharge, will be useful for later seroepidemiological studies and should be done for hospitalised patients and during specific outbreaks such as in schools or confined facilities. Several commercial assays for SARS-CoV-2 are on the market, however, information on their clinical performance is still limited. Validation of the commercial assays is an urgent priority that some laboratories have started to address. Influenza testing at least of hospitalised patients with severe acute respiratory infections (SARI) should be continued as long as local circulation of influenza continues in order to initiate early antiviral treatment of influenza-infected patients. The differential diagnostics are also key for isolation and contact tracing of COVID-19 cases. Sentinel virological surveillance of outpatients with acute respiratory infections/influenza-like illness (ARI/ILI) for the monitoring of COVID-19 is recommended, based on the existing surveillance of influenza (see Surveillance section). A subset of patients should be swabbed based on geographical and population distribution. At regular intervals, a representative batch of positive specimens should be sent to a reference/referral laboratory for confirmation and further characterisation in order to identify and follow up the evolutionary changes of the virus. Testing specimens from sentinel outpatient surveillance sites for COVID-19 should be continued for as long as possible. In case of any shortages of sampling materials, oropharyngeal and nasopharyngeal swabbing can be performed with one swab and combined for one diagnostic test. As per WHO biosafety guideline, non-propagative diagnostic laboratory work (for example, sequencing, nucleic acid amplification test [NAAT]) should be conducted at a facility using procedures equivalent to Biosafety Level 2 (BSL-2) and propagative work (for example, virus culture, isolation or neutralization assays) should be conducted at a containment laboratory with inward directional airflow (BSL-3). Patient specimens from suspected or confirmed cases should be transported as UN3373, 'Biological Substance Category B'. Viral cultures or isolates should be transported as Category A, UN2814, 'infectious substance, affecting humans' [84]. Countries should provide training to laboratory staff in laboratory diagnosis of SARS-CoV-2 as rapid expansion of laboratory diagnostic capacity is needed. Shortages for laboratory testing for COVID-19 Based on a rapid, 24-hour turnaround survey on 4-5 March, to which 15 EU/EEA countries responded, the countries reported shortages on deliveries of swabbing material, plastic consumables, RNA extraction and RT-PCR reagents such as enzymes, primers, probes and positive control material. In addition, shortages of PPE such as respirators, surgical masks, gloves and disinfectants for laboratory use were reported. The primary reasons for shortages were production bottlenecks. Based on the information available and modelling of expected cases in

Europe, laboratories should prepare themselves for critically increasing their testing volume. Shortages are not affecting only diagnostics of SARS-CoV-2 but also have an impact on other critical diagnostic testing for infectious diseases including screening for infectious pathogens for transplantation and beyond. Optimising testing for COVID-19 Countries across the EU/EEA might be in different scenarios, even within the same country, and testing approaches need to be adapted to the situation at national and local level. In scenarios 0 and 1, the strategy for testing should be in accordance with the ECDC case identification [85]. In addition, all patients with SARI requiring hospitalisation should be considered as suspected cases on admission and tested. As long as influenza is still circulating in the population, hospitalised patients with SARI should also be tested for influenza to initiate early antiviral treatment and separate them from other patients. RAPID RISK ASSESSMENT Novel coronavirus disease 2019 (COVID-2019) pandemic: increased transmission in the EU/EEA – sixth update 16 Once local transmission has been reported in the country or area (scenarios 2-4), as is the situation for most EU/EEA countries already or very soon, all patients presenting with symptoms of acute respiratory infection in primary care or the accident and emergency department of a hospital (first contact with the healthcare system) should be considered as suspected cases (considering also local influenza epidemiology). This may imply that a very large number of tests would need to be performed overwhelming testing capacity and priority groups will need to be established. As a rational approach, the following should be considered for priority testing (in decreasing order of importance): 1. Testing of hospitalised patients with SARI in order to inform appropriate clinical management, including isolation and PPE measures; 2. Testing any cases of acute respiratory infection in hospitals or long-term care facilities (LTCF) in order to guide infection control and PPE use to protect both vulnerable persons and healthcare staff; testing of symptomatic healthcare staff to guide decisions on exclusion from and return to work; the aim is to protect health and social care services; 3. Testing of patients with ARI/ILI in sentinel outpatient clinics and among patients admitted to hospitals with SARI in order to assess virus circulation in the population. 4. Elderly people with underlying chronic medical conditions such as lung disease, cancer, heart failure, cerebrovascular disease, renal disease, liver disease, diabetes, and immunocompromising conditions exhibiting signs of acute respiratory illness should be prioritised for testing, given that they may more rapidly need respiratory support. Healthcare workers should apply strict IPC measures when dealing with suspected cases (see below). During triage, suspected cases should be given a surgical mask and be directed to a separate area. Organising separate triaging areas or facilities in order to minimise contact between suspect cases and other patient groups should be considered. Such cohorting will also decrease the needs for PPE for staff. In South Korea and some EU/EEA countries, drive-in facilities for testing have been established. For antibodies there are some references in the literature and based on them I composed a kind of evaluation strategy. All commercial antibody tests with CE-IVD have a 100% specificity but a variable sensitivity which depends on the time after initial exposure. They are helpful for those asymptomatic persons at the end of the quarantine because of suspected previous contact, in order to ascertain if the were sensitized by the virus. Fourteen days after initial contact if the person contracted the virus, then antibody test sensitivity is almost 100%.

Manual or automated immunoassays

- Beijing Abace Biology Co., Ltd., Contact
  - *COVID-19 Viral Antigen Test Kit* (ELISA) (RUO)
  - *COVID-19 IgG Antibody Test Kit* (ELISA) (RUO)
  - *COVID-19 IgM Antibody Test Kit* (ELISA) (RUO)
- BluSense Diagnostics ApS, *ViroTrack COVID IgA+IgM/IgG/Total Ig Ab* (RUO) Contact
- Boditech Med, Inc. Contact
  - *AFIAS COVID-19, Viral Antigen* (automated; RUO)
  - *AFIAS COVID-19 Ab, IgM/IgG* (automated; RUO)
  - *Ichroma COVID-19, viral antigen* (manual; RUO)
  - *Ichromia COVID-19 Ab, IgM/IgG* (manual; RUO)
- Creative Diagnostics, Contact
  - SARS-CoV-2 IgG ELISA Kit (RUO)
  - SARS-CoV-2 IgM ELISA Kit (RUO)
  - SARS-CoV-2 Antigen ELISA Kit (RUO)
- Eagle Biosciences, Inc. Contact
  - *COVID-19 IgG ELISA Assay* (RUO)
  - *COVID-19 IgM ELISA Assay* (RUO)
- Epitope Diagnostics, Inc. Contact
  - *EDI™ Novel Coronavirus COVID-19 IgG ELISA Kit* (CE-IVD)
  - *EDI™ Novel Coronavirus COVID-19 IgM ELISA Kit* (CE-IVD)
- EUROIMMUN AG Contact
  - *Anti-SARS-CoV-2 ELISA (IgA)* (manual; automated; RUO)
  - *Anti-SARS-CoV-2 ELISA (IgG)* (manual; automated; RUO)
- GenBody, Inc. *GenBody FIA COVID-19 IgM/IgG* (manual; RUO) Contact
- Guangzhou Darui Biotechnology Co.,Ltd Contact
  - *2019 Novel Coronavirus (2019-nCoV) IgM Antibody Detection Kit (ELISA Method)* (RUO)
  - *2019 Novel Coronavirus (2019-nCoV) IgG Antibody Detection Kit (ELISA Method)* (RUO)
  - *Novel Coronavirus 2019-nCoV IgM Antibody Detection Kit (Colloidal Gold Method)* (RUO)
  - *Novel Coronavirus 2019-nCoV IgG Antibody Detection Kit (Colloidal Gold Method)* (RUO)
- Guangzhou Wondfo Biotech Co., Ltd, *Finecare SARS-CoV-2 Antibody Test* (manual; RUO) Contact
- Liming Bio-Products Co., Ltd, *COVID-19 Antigen Rapid Test Device* (CE-IVD) Contact
- SD BIOSENSOR, Inc., *STANDARD F COVID-19 Ag FIA* (manual; CE-IVD) Contact
- Shenzhen Yhlo Biotech Co. Ltd Contact
  - *iFlash-SARS-CoV-2 IgM* (CE-IVD)
  - *iFlash-SARS-CoV-2 IgG* (CE-IVD)
- Snibe Co., Ltd. (Shenzhen New Industries Biomedical Engineering Co., Ltd) Contact
  - *MAGLUMI 2019-nCoV IgG (CLIA)* (automated IA, CE-IVD)
  - *MAGLUMI 2019-nCoV IgM (CLIA)* (automated IA, CE-IVD)
- Taizhou ZECEN Biotech Co., Ltd., Contact
  - *SARS-CoV-2 IgM* (CE-IVD)
  - *SARS-CoV-2 IgG* (CE-IVD)
- Sugentech, Inc. Contact
  - *SGTi-flex COVID-19 IgM/IgG* (manual, CE-IVD)
  - *SGTi-flex COVID-19 IgM* (manual, CE-IVD)
  - *SGTi-flex COVID-19 IgG* (manual, CE-IVD)

Rapid diagnostic tests

- AmonMed Biotechnology Co., Ltd. Contact
  - *COVID-19 IgM/IgG test kit* (Rare Earth Nano Fluorescence Immunochromatography) (CE-IVD
  - *COVID-19 IgM/IgG test kit* (Colloidal Gold) (CE-IVD)
  - *COVID-19/Influenza A virus/Influenza B virus IgM combo test kit* (Rare Earth Nano Fluoresce
  - *COVID-19/Influenza A virus/Influenza B virus test kit* (Rare Earth Nano Fluorescence Immun
  - *COVID-19 Antigen Test Kit* (Rare Earth Nano Fluorescence Immunochromatography) (CE-IVD
- Anhui Deep Blue Medical Technology Co., Ltd., *Colloidal gold strip for SARS-CoV-2 IgG & IgM* (RUO) Con
- Avioq Bio-Tech Co.,Ltd., *Novel Coronavirus (2019-nCov) Antibody IgG/IgM Assay Kit* (Colloidal Gold) (RU
- Beijing Abace Biology Co., Ltd., Contact
  - *COVID-19 Viral Antigen Test Kit* (Colloidal Gold Immunochromatography) (RUO)
  - *COVID-19 Antibody (IgG/IgM)Test Kit* (Colloidal Gold Immunochromatography) (CE-IVD)
- Beijing Diagreat Biotechnologies Co., Ltd., Contact
  - *2019-nCoV IgG Antibody Determination Kit* (CE-IVD)
  - *2019-nCoV IgM Antibody Determination Kit* (CE-IVD)
- Beijing Kewei Clinical Diagnostic Reagent Inc. Contact
  - *Kewei COVID-19 IgM ELISA Test Kit* (CE-IVD)
  - *Kewei COVID-19 IgG ELISA Test Kit* (CE-IVD)
  - *Kewei COVID-19 IgG/IgM Fluorescence Rapid Test Kit* (CE-IVD)
  - *Kewei COVID-19 Antigen ELISA Test Kit* (Nasal/Throat Swab) (CE-IVD)
  - *Kewei COVID-19 Antigen Fluorescence Rapid Test Kit* (Nasal/Throat Swab) (CE-IVD)
- BioMedomics, Inc. *COVID-19 IgM-IgG Dual Antibody Rapid Test* (CE-IVD) Contact
- Core Technology Co., Ltd., *COVID-19 IgM/IgG Ab Test* (CE-IVD) Contact-1 Contact-2
- Coris BioConcept, *COVID-19 Respi-Strip* (RUO) Contact
- CTK Biotech, Inc., *OnSite COVID-19 IgG/IgM Rapid Test* (CE-IVD) Contact
- Dynamiker Biotechnology (Tianjin) Co., Ltd., *2019 nCOV IgG/IgM Rapid Test* (CE-IVD) Contact
- GenBody, Inc., Contact
  - *GenBody COVID-19 IgM/IgG* (CE-IVD)
  - *GenBody COVID-19 IgM/IgG DUO* (RUO)
- Getein Biotech, Inc., *One Step Test for Novel Coronavirus (2019-nCoV) IgM/IgG antibody (Colloidal Gold*
- Guangzhou Fenghua Bioengineering , Co. LTD, *Combined Detection Kit for Novel Coronavirus (2019-nCo*
- Hanghzhou AllTest Biotech Co., Ltd, *2019-nCoV Antigen Rapid Test Cassette* (Swab/Sputum) (CE-IVD) Co
- Hangzhou Biotest Biotech Co.,Ltd., *COVID-19 IgG/IgM Rapid Test Cassette* (Whole Blood/Serum/Plasma
- Humasis, *Humasis COVID-19 IgG/IgM Test* (RUO) Contact
- Innovita Biological Technology Co. Ltd, *2019-nCoV Ab Test (Colloidal Gold)* (IgM/IgG Whole Blood/Serur
- InTec Products, Inc., Contact-1; Contact-2
  - *Rapid SARS-CoV-2 Antibody (IgM/IgG) Test* (CE-IVD)
  - *Rapid SARS-CoV-2 Antibody Test* (CE-IVD)
- Jiangsu Bioperfectus Technologies Co. Ltd, Contact
  - *PerfectPOC Novel Corona Virus (SARS-CoV-2) Ag Rapid Test Kit* (RUO)
  - *PerfectPOC Novel Corona Virus (SARS-CoV-2) IgM/IgG Rapid Test Kit* (RUO)
- Liming Bio-Products Co., Ltd, *COVID-19 IgG/IgM Combo Rapid Test Device* (CE-IVD) Contact
- MedicalSystem Biotechnology Co., Ltd., *COVID-19 IgM/IgG Rapid Test Cassette* (CE-IVD) Contact
- Mei Ning Kang Cheng China Biotechnology R&D Center, Inc., *Corona Virus Disease 2019 (COVID-19) IgM*
- Nantong Egens Biotechnology Co., LTD, *EGENS COVID-19 IgG/IgM Rapid Test Kit* (CE-IVD; RUO) Contact
- SD BIOSENSOR, Inc., Contact

    - *STANDARD Q COVID-19 IgM/IgG Duo* Test (CE-IVD)
    - *STANDARD Q COVID-19 Ag Test* (CE-IVD)
- SensingSelf, Pte, Ltd, Singapore, *EDR COVID 19 Rapid Test Kit* (IgM/IgG) (CE-IVD) Contact
- servoprax GmbH, *Cleartest Corona, Covid-19* (CE-IVD) Contact-1; Contact-2
- Shenzhen Bioeasy Biotechnology Co., Ltd., Contact
    - *Novel Coronavirus (2019-nCoV) Fluorescence Antigen Rapid Test* (CE-IVD)
    - *Novel Coronavirus (2019-nCov) Colloidal Gold Antigen Rapid Test* (CE-IVD)
    - *Novel Coronavirus (2019-nCoV) IgG/IgM detection kit (colloidal gold immunochromatograp*
    - *BIOEASY 2019-nCoV Ag Fluorescence Rapid Test Kit (Time-Resolved Fluorescence)* (CE-IVD)
- Sugentech, Inc., Contact
    - *SGTi-flex COVID-19 IgM/IgG* (CE-IVD)
    - *SGTi-flex COVID-19 IgM* (CE-IVD)
    - *SGTi-flex COVID-19 IgG* (CE-IVD)
- Sure Bio-Tech (USA) Co., Ltd. Contact
    - *SARS-CoV-2 IgM Ab Rapid Test* (CE-IVD)
    - *SARS-CoV-2 IgG Ab Rapid Test* (CE-IVD)
    - *SARS-CoV-2 IgM/IgG Ab Rapid Test* (CE-IVD)
- Tianjin MNCHIP Technologies Co., Ltd., *Anti-COVID-19 virus IgM/IgG rapid test kit (Colloidal gold assay)*
- VivaChek Biotech (Hangzhou) Co., Ltd, *VivaDiag COVID-19 IgM/IgG Rapid Test* (CE-IVD) Contact
- Wuhan EasyDiagnosis Biomedicine Co.,Ltd Contact
    - *Novel Coronavirus IgM antibody test kit* (colloidal gold method) (CE-IVD)
    - *Novel Coronavirus IgG antibody test kit* (colloidal gold method) (CE-IVD)
- Xiamen Biotime Biotechnology Co., Ltd., *SARS-CoV-2 IgG/IgM Rapid Qualitative Test Kit* (CE-IVD) Contac

Additional important contribute by Professor Beili Wang, from Shanghai, China

1. So far, we don't have any quantitative assays in China.

2. 2. The reported time of appearance of IgM and IgG after symptom onset was significantly different and individual immunity dependent, generally, IgM 5~10 days, IgG 10~20 days, but one paper in *Lancet Infect Dis* reported that in quite a lot of cases, IgG turns positive even earlier than IgM. Theoretically, the anti-spike antibodies are neutralizing.

[1] Wang KK, Tsang OT, Leung WS, et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. Lancet Infect Dis, 2020. DOI: https://doi.org/10.1016/S1473-3099(20)30196-1

[2] Long QX, Deng HJ, Chen J, et al. Antibody responses to SARS-CoV-2 in COVID-19 patients: the perspective application of serological tests in clinical practice. medRxiv, 2020. https://doi.org/10.1101/2020.03.18.20038018.

[3] Guo L, Ren L, Yang S, et al. Profiling Early Humoral Response to Diagnose Novel Coronavirus Disease (COVID-19). Clin Infect Dis, 2020. DOI:10.1093/cid/ciaa310

[4] Zhao J, Yuan Q, Wang H, et al. Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019. medRxiv, 2020. https://doi.org/10.1101/2020.03.02.20030189.

[5] Thevarajan I, Nguyen T.H.O, Koutsakos M, et al. Breadth of concomitant immune responses prior to patient recovery: a case report of non-severe COVID-19. Nat Med, 2020. DOI: 10.1038/s41591-020-0819-2.

[6] Zhou P, Yang XL, Wang XG, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature, 2020, 579 (7798): 270-273. DOI: 10.1038/s41586-020-2012-7.

3. IL-6 was reported sustained increases in the severe group compared to the mild group, but the neutrophil-to-CD8+ T cell ratio achieved the best performance of predicting severe cases.

[1] Jing Liu et al. Longitudinal Characteristics of Lymphocyte Responses and Cytokine Profiles in the Peripheral Blood of SARS-CoV-2 Infected Patients (2/16/2020). Available at SSRN: https://ssrn.com/abstract=3539682