COVID-19 epidemic in Europe: What have we learned? And does underlying HIV-infection make a difference?

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Conflict of Interest: JKR

• Honoraria for lectures and/or consultancies from Gilead, Janssen, Merck, Theratechnologies and Viiv.
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COVID-19

» Epidemiology
» Testing
» Clinical course
» Experimental treatments
» Patients with HIV-coinfection
» Learnings
COVID-19

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Distribution of laboratory confirmed cases of COVID-19 in the EU/EEA and the UK, as of 7th April 2020 (ECDC)
Situation update for the EU/EEA and the UK, as of 7th April 2020 (ECDC)

<table>
<thead>
<tr>
<th>EUEEA and the UK</th>
<th>Cases</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spain</td>
<td>130532</td>
<td>13055</td>
</tr>
<tr>
<td>Italy</td>
<td>122047</td>
<td>16135</td>
</tr>
<tr>
<td>Germany</td>
<td>95225</td>
<td>16027</td>
</tr>
<tr>
<td>France</td>
<td>74900</td>
<td>6911</td>
</tr>
<tr>
<td>United_Kingdom</td>
<td>51006</td>
<td>5373</td>
</tr>
<tr>
<td>Belgium</td>
<td>20614</td>
<td>1632</td>
</tr>
<tr>
<td>Netherlands</td>
<td>18002</td>
<td>1087</td>
</tr>
<tr>
<td>Austria</td>
<td>12297</td>
<td>220</td>
</tr>
<tr>
<td>Portugal</td>
<td>11700</td>
<td>311</td>
</tr>
<tr>
<td>Sweden</td>
<td>7206</td>
<td>477</td>
</tr>
<tr>
<td>Norway</td>
<td>8765</td>
<td>69</td>
</tr>
<tr>
<td>Ireland</td>
<td>5264</td>
<td>174</td>
</tr>
<tr>
<td>Czechia</td>
<td>4622</td>
<td>76</td>
</tr>
<tr>
<td>Denmark</td>
<td>4661</td>
<td>167</td>
</tr>
<tr>
<td>Poland</td>
<td>4413</td>
<td>107</td>
</tr>
<tr>
<td>Romania</td>
<td>4057</td>
<td>157</td>
</tr>
<tr>
<td>Luxembourg</td>
<td>2640</td>
<td>41</td>
</tr>
<tr>
<td>Finland</td>
<td>2176</td>
<td>27</td>
</tr>
<tr>
<td>Greece</td>
<td>1756</td>
<td>79</td>
</tr>
<tr>
<td>Iceland</td>
<td>1562</td>
<td>6</td>
</tr>
<tr>
<td>Guaatia</td>
<td>1222</td>
<td>16</td>
</tr>
<tr>
<td>Estonia</td>
<td>1100</td>
<td>19</td>
</tr>
<tr>
<td>Slovenia</td>
<td>1024</td>
<td>30</td>
</tr>
<tr>
<td>Lithuania</td>
<td>843</td>
<td>14</td>
</tr>
<tr>
<td>Hungary</td>
<td>811</td>
<td>47</td>
</tr>
<tr>
<td>Bulgaria</td>
<td>546</td>
<td>22</td>
</tr>
<tr>
<td>Latvia</td>
<td>542</td>
<td>1</td>
</tr>
<tr>
<td>Slovakia</td>
<td>634</td>
<td>2</td>
</tr>
<tr>
<td>Cyprus</td>
<td>465</td>
<td>14</td>
</tr>
<tr>
<td>Malta</td>
<td>241</td>
<td>0</td>
</tr>
<tr>
<td>Liechtenstein</td>
<td>78</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>608500</strong></td>
<td><strong>54009</strong></td>
</tr>
</tbody>
</table>
COVID-19 in Germany
7.4.2020

Germany:
• 103,375 confirmed cases
• 1,810 deaths
• 36,081 resolved infections
Why are there so big differences in the mortality rates by country?

» Different testing strategies (only testing in symptomatic disease patients versus early screening and self-isolation)
» Difference in median age (15 years difference between Italian COVID-19 patients and German COVID-19 patients)
» In Italy more “3 generation households”
» Differences in intensive care bed equipped with ventilators (In Germany 28,000 intensive care beds equipped with ventilators, or 34 per 100,000 people. By comparison, that rate is 12 in Italy and 7 in the Netherlands.)
COVID-19 in Norway

» The government in Norway introduced strict measures early in the Corona epidemic including lockdown, closing of borders for foreigners, 14 days quarantine for Norwegians coming back to Norway and closure of schools, churches, universities and more.

» Each Corona infected subject now infects on average 0.7 other persons, originally this number was 2-3.


» Initiation of general population testing including all asymptomatic individuals
COVID-19

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Testing

» Using real-time reverse transcription polymerase chain reaction (rRT-PCR) the test can be done on respiratory samples obtained by various methods, including nasopharyngeal swab or sputum sample.

» Results are generally available within a few hours to 2 days.

» Part of the immune response to infection is the production of antibodies including IgM and IgG. These can be used to detect infection in individuals starting 7 days or so after the onset of symptoms, to determine immunity, and in population surveillance.

» Assays can be performed in central laboratories (CLT) or by point-of-care testing (PoCT).

» Medical staff, at particular risk of contracting and spreading the virus, are regularly tested. To streamline the procedure, some hospitals have started doing block tests, using the swabs of 10 employees, and following up with individual tests only if there is a positive result.
Ad hoc laboratory-based surveillance of SARS-CoV-2 by 1 real-time RT-PCR using 2 minipools of RNA prepared from routine respiratory samples

Table 2: Number of minipools tested for SARS-CoV-2 RNA at five different sites, Germany, February – March 2020 (n=60).

<table>
<thead>
<tr>
<th>Laboratory site</th>
<th>Minipools tested (n=)</th>
<th>Individual samples (n=)</th>
<th>SARS-CoV-2 RT-PCR positive patients (n=)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (Freiburg)</td>
<td>42</td>
<td>420</td>
<td>1</td>
</tr>
<tr>
<td>B (Bonn)</td>
<td>6</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>C (Leipzig)</td>
<td>9</td>
<td>90</td>
<td>0</td>
</tr>
<tr>
<td>D (Regensburg)</td>
<td>8</td>
<td>80</td>
<td>0</td>
</tr>
<tr>
<td>E (Frankfurt)</td>
<td>5</td>
<td>70</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>70</td>
<td>700</td>
<td>0</td>
</tr>
</tbody>
</table>

Eis-Hübinger AM et al. MedRxiv 2020; doi: https://doi.org/10.1101/2020.03.30.20043513
Pharyngeal virus shedding was very high during the first week of symptoms (peak at $7.11 \times 10^8$ RNA copies per throat swab, day 4).

Infectious virus was readily isolated from throat- and lung-derived samples, but not from stool samples, in spite of high virus RNA concentration. Blood and urine never yielded virus.

Active replication in the throat was confirmed by viral replicative RNA intermediates in throat samples.

Shedding of viral RNA from sputum outlasted the end of symptoms. Seroconversion occurred after 7 days in 50% of patients (14 days in all), but was not followed by a rapid decline in viral load.
Hallmarks of viral shedding in aggregated samples.

Testing: remaining challenges

» With declining viral load pharyngeal PCR can become negative in later stages of disease whereas sputum is still positive.

» ELISA tests may have low specificity and sensitivity; more test evaluations need to happen

» Increasing testing capacities

» Different testing strategies: range from one center centrally to public health organized testing sites, drive-through testing and more…..
Testing: Covid-19 drive through testing site for employees

Testing of patients and HCW by real time PCR (n= currently 400/day)

Drive through and walk through in the parking garage of the hospital to test health care workers with clinical symptoms

Capacity: 228 HCW/day

Also open to employees of ambulance and other health care organisations

Reports by email to occupational physician and to authorities

⚠️ Drive through: one central place for Covid-19 testing for HCW
COVID-19

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Natural course of disease

There seem to be different stages of illness that patients may move through.

• (#1) Replicative stage – Viral replication occurs over a period of several days. An innate immune response occurs, but this response fails to contain the virus. Relatively mild symptoms may occur due to direct viral cytopathic effect and innate immune responses.

• (#2) Adaptive immunity stage – An adaptive immune response eventually kicks into gear. This leads to falling titers of virus. However, it may also increase levels of inflammatory cytokines and lead to tissue damage – causing clinical deterioration. There is a suggestion that this could lead to virus-induced hemophagocytic lymphohistiocytosis (HLH)

• Incubation is a median of ~4-5 days (interquartile range of 2-7 days), with a range up to 14 days

• Typical evolution of severe disease
  • Dyspnea ~ 6 days post exposure.
  • Admission after ~8 days post exposure.
  • ICU admission/intubation after ~10 days post exposure. However, this timing may be variable (some patients are stable for several days after admission, but subsequently deteriorate rapidly).
Symptoms of COVID-19

<table>
<thead>
<tr>
<th>Symptoms near the time of presentation in various cohorts</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Constitutional</strong></td>
</tr>
<tr>
<td>Fever</td>
</tr>
<tr>
<td>Mysalgia</td>
</tr>
<tr>
<td>Headache</td>
</tr>
<tr>
<td><strong>Upper respiratory</strong></td>
</tr>
<tr>
<td>Rhinorrhea</td>
</tr>
<tr>
<td>Sore throat</td>
</tr>
<tr>
<td><strong>Lower respiratory</strong></td>
</tr>
<tr>
<td>Dyspnea</td>
</tr>
<tr>
<td>Chest tightness</td>
</tr>
<tr>
<td>Cough</td>
</tr>
<tr>
<td>Sputum</td>
</tr>
<tr>
<td>Hemoptysis</td>
</tr>
<tr>
<td><strong>Gastrointestinal</strong></td>
</tr>
<tr>
<td>Nausea/Vomiting</td>
</tr>
<tr>
<td>Diarrhea</td>
</tr>
</tbody>
</table>
Global picture of severe cases

Fig. 1 Global picture of severe cases
The global case fatality rate for COVID-19 infected patients is estimated to be 2.3%* and disproportionately affects those of older age and those with comorbidities.

* Case fatality rate ranges from 1-3%; Infection is ongoing and additional research is needed

2. China CDC Weekly Feb 17, 2020 http://weekly.chinacdc.cn/en/article/id/e53946e2-c6c4-41e9-9a9b-fea8db1a8f51
Cardiovascular involvement

Potential Effects of Coronaviruses on the Cardiovascular System

A Review

Mohammad Madjid, MD, MS; Payam Safavi-Naeini, MD; Scott D. Solomon, MD; Orly Vardany, PharmD

**IMPORTANCE** Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes coronavirus disease 2019 (COVID-19) has reached a pandemic level. Coronaviruses are known to affect the cardiovascular system. We review the basics of coronaviruses, with a focus on COVID-19, along with their effects on the cardiovascular system.

**OBSERVATIONS** Coronavirus disease 2019 can cause a viral pneumonia with additional extrapulmonary manifestations and complications. A large proportion of patients have underlying cardiovascular disease and/or cardiac risk factors. Factors associated with mortality include male sex, advanced age, and presence of comorbidities including hypertension, diabetes mellitus, cardiovascular diseases, and cerebrovascular diseases. Acute cardiac injury determined by elevated high-sensitivity troponin levels is commonly observed in severe cases and is strongly associated with mortality. Acute respiratory distress syndrome is also strongly associated with mortality.

**CONCLUSIONS AND RELEVANCE** Coronavirus disease 2019 is associated with a high inflammatory burden that can induce vascular inflammation, myocarditis, and cardiac arrhythmias. Extensive efforts are underway to find specific vaccines and antivirals against SARS-CoV-2. Meanwhile, cardiovascular risk factors and conditions should be judiciously controlled per evidence-based guidelines.

JAMA Cardiol. doi:10.1001/jamacardio.2020.286
Published online March 27, 2020.
Key Points Related to the Interplay between Covid-19 and the Renin–Angiotensin–Aldosterone System

- ACE2, an enzyme that physiologically counters RAAS activation, is the functional receptor to SARS-CoV-2, the virus responsible for the Covid-19 pandemic.
- Select preclinical studies have suggested that RAAS inhibitors may increase ACE2 expression, raising concerns regarding their safety in patients with Covid-19.
- Insufficient data are available to determine whether these observations readily translate to humans, and no studies have evaluated the effects of RAAS inhibitors in Covid-19.
- Clinical trials are under way to test the safety and efficacy of RAAS modulators, including recombinant human ACE2 and the ARB losartan in Covid-19.
- Abrupt withdrawal of RAAS inhibitors in high-risk patients, including those who have heart failure or have had myocardial infarction, may result in clinical instability and adverse health outcomes.
- Until further data are available, we think that RAAS inhibitors should be continued in patients in otherwise stable condition who are at risk for, being evaluated for, or with Covid-19.
Coagulopathy Associated with COVID-19

» • Upon presentation of COVID-19, the measurements advised, in order of importance, are of d-dimer, prothrombin time, and platelet counts.
» • Increased d-dimers are commonly reported in patients with severe illness and may predict mortality.
» • Prolongation in prothrombin times and degree of thrombocytopenia (100–150 × 10⁹/L) have been modest.
» • In addition to the above parameters, fibrinogen should be monitored; nonsurvivors with severe illness have developed disseminated intravascular coagulation around day 4; significant worsening in these parameters at days 10 and 14 was also reported.
» • The panel advises use of prophylactic dose low-molecular-weight heparin unless there is active bleeding or a platelet count of <25 × 10⁹/L; it is hoped that this strategy will impact septic-like coagulopathy and protect against venous thromboembolism.
» • Bleeding has been rare, but if present, panelists advise keeping platelet counts >50 × 10⁹/L (and >20 × 10⁹/L goal in nonbleeding patients), fibrinogen >2.0 g/L, and the prothrombin ratio <1.5.

Stein B. NEJM Journal watch 2020
COVID-19
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Treatment: lopinavir/r

- After the emergence of severe acute respiratory syndrome (SARS) in 2003, screening of approved drugs identified lopinavir, a HIV aspartate protease inhibitor, as having in vitro inhibitory activity against SARS-CoV, the virus that causes SARS in humans.
- Lopinavir showed in vitro antiviral activity against SARS at concentration of 4 ug/ml. However, when combined with ribavirin, lopinavir appears considerably more effective (with an inhibitory concentration of 1 ug/mL (Chu et al. 2004).
- Up-front treatment in SARS with lopinavir/ritonavir combined with ribavirin correlated with reduced mortality (2.3% versus 16%). However, rescue therapy with lopinavir/ritonavir (often without concomitant ribavirin) didn't seem to make any difference (Chan 2003)
A Trial of Lopinavir–Ritonavir in Adults Hospitalized with Severe Covid-19

No therapies have yet been proven effective for the treatment of severe illness caused by SARS-CoV-2.

**METHODS**

We conducted a randomized, controlled, open-label trial involving hospitalized adult patients with confirmed SARS-CoV-2 infection, which causes the respiratory illness Covid-19, and an oxygen saturation (SpO₂) of 94% or less while they were breathing ambient air or a ratio of the partial pressure of oxygen (PaO₂) to the fraction of inspired oxygen (FiO₂) of less than 300 mm Hg. Patients were randomly assigned in a 1:1 ratio to receive either lopinavir–ritonavir (400 mg and 100 mg, respectively) twice a day for 14 days, in addition to standard care, or standard care alone. The primary end point was the time to clinical improvement, defined as the time from randomization to either an improvement of two points on a seven-category
Systematic review of the efficacy and safety of antiretroviral drugs against SARS, MERS, or COVID-19: initial assessment

Nathan Ford¹, Marco Vitoria¹, Ajay Rangaraj¹, Susan L Norris² Alexandra Calmy,³* Meg Doherty¹*

1. Department of HIV, Hepatitis and Sexually Transmitted Infections, World Health Organization, Geneva, Switzerland.

Conclusions

On the basis of the available evidence it is uncertain whether LPV/r and other antiretrovirals improve clinical outcomes or prevent infection among patients at high risk of acquiring COVID-19.
Treatment: hydroxychloroquin/chloroquin

• Chloroquine appears to work via multiple mechanisms, including:
  Interference with the cellular receptor ACE2 (potentially making it particularly effective against SARS and COVID-19).
• Impairment of acidification of endosomes, which interferes with virus trafficking within cells.
• Chloroquine also has immunosuppressive activities. It's unknown whether such immunosuppressive action could be beneficial or harmful (analogous to steroid therapy).
• In vitro data using cell lines shows that chloroquine can inhibit COVID-19 with an 50% inhibitory concentration of 1 uM, implying that therapeutic levels could be achieved in humans (Wang 2020)
• The 50% inhibitory concentration of chloroquine for SARS is closer to 9 uM, suggesting that chloroquine could be more effective against COVID-19 than SARS (Al-Bari 2017)
Treatment: hydroxychloroquin/chloroquin

Figure 1. Percentage of patients with PCR-positive nasopharyngeal samples from inclusion to day 6 post-inclusion in COVID-19 patients treated with hydroxychloroquine and in COVID-19 control patients.

### Treatment: hydroxychloroquin/chloroquin

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Male gender</th>
<th>Clinical status</th>
<th>Time between onset of symptoms and inclusion (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>t</td>
<td>p-value</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>Hydroxychloroquine treated patients (N=20)</td>
<td>51.2 ± 18.7</td>
<td>-1.95</td>
<td>9 (45.0)</td>
</tr>
<tr>
<td>Control patients (N=16)</td>
<td>37.3 ± 24.0</td>
<td></td>
<td>6 (37.5)</td>
</tr>
<tr>
<td>All patients (36)</td>
<td>45.1 ± 22.0</td>
<td></td>
<td>15 (41.7)</td>
</tr>
</tbody>
</table>

URTI: upper tract respiratory infection, LRTI: lower tract respiratory infection

Journal Pre-proof

No Evidence of Rapid Antiviral Clearance or Clinical Benefit with the Combination of Hydroxychloroquine and Azithromycin in Patients with Severe COVID-19 Infection

Jean Michel Molina Dr Constance Delaugarre Jerome Le Goff Breno Mela-Lima Diane Ponscarme Lauriane Goldwirt Nathalie de Castro

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Key words: Severe acute respiratory syndrome coronavirus 2 | Novel coronavirus pneumonia | Hydroxychloroquine | treatment outcomes | Safety
Treatment: remdesivir

- Remdesivir might be an excellent antiviral, based on a study involving in vitro and animal data with MERS (e.g. Sheahan 2020).
- Unfortunately, remdesivir is not commercially available. Remdesivir was used on the basis of "compassionate use" for one of the first patients with COVID-19 in the United States (Holshue 2020).
- Remdesvirus is currently evaluated in various clinical trials.
Antiviral therapy in asymptomatic or mild disease

» Limited data
Treatment: Empiric antimicrobial therapy?

- COVID-19 is no indication for prophylactic antibiotic treatment
- In case of suspected bacterial superinfection
  - Blood cultures and PCT prior to empiric antimicrobial therapy
  - Discontinue < 48h if bacterial superinfection not confirmed
- Diagnostics and treatment similar to ventilator or hospital acquired pneumonia
Treatment for severe acute respiratory distress syndrome

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Implementation</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-flow nasal oxygen</td>
<td>Might prevent or delay the need for intubation</td>
</tr>
<tr>
<td>Tidal volume</td>
<td>Use 5 mL/kg per predicted bodyweight (can reduce to 4 mL/kg per predicted bodyweight)</td>
</tr>
<tr>
<td>Plateau airway pressure</td>
<td>Maintain at &lt;30 cm H₂O if possible</td>
</tr>
<tr>
<td>Positive end-expiratory pressure</td>
<td>Consider moderate to high levels if needed</td>
</tr>
<tr>
<td>Recruitment manoeuvres</td>
<td>Little value</td>
</tr>
<tr>
<td>Neuromuscular blockade</td>
<td>For ventilator dyssynchrony, increased airway pressure, hypoxaemia</td>
</tr>
<tr>
<td>Prone positioning</td>
<td>For worsening hypoxaemia, PaO₂:FiO₂ &lt;100-159 mm Hg</td>
</tr>
<tr>
<td>Inhaled NO</td>
<td>Use 5-20 ppm</td>
</tr>
<tr>
<td>Fluid management</td>
<td>Aim for negative fluid balance of 0.5-1.0 L per day</td>
</tr>
<tr>
<td>Renal replacement therapy</td>
<td>For oliguric renal failure, acid-base management, negative fluid balance</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>For secondary bacterial infections</td>
</tr>
<tr>
<td>Glucocorticoids</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Extracorporeal membrane oxygenation</td>
<td>Use EOLIA trial criteria³</td>
</tr>
</tbody>
</table>

Figure: Therapeutic options for severe acute respiratory distress syndrome related to coronavirus disease 2019
ppm=parts per million.
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EACS/BHIVA Statement on risk of COVID-19 for PLWH

» So far there is no evidence for a higher COVID-19 infection rate or different disease course in people with HIV than in HIV-negative people.

» Current evidence indicates that the risk of severe illness increases with age, male sex and with certain chronic medical problems such as cardiovascular disease, chronic lung disease and diabetes.

» Although people with HIV who are on treatment with a normal CD4 T-cell count and suppressed viral load may not be at an increased risk of serious illness, many people with HIV have other conditions that increase their risk. Indeed, almost half of people living with HIV in Europe are older than 50 years and chronic medical problems, such as cardiovascular and chronic lung disease, are more common in people living with HIV.

» It has to be assumed that immune suppression, indicated by a low CD4 T-cell count (<200/µl), or not receiving antiretroviral treatment, will also be associated with an increased risk of serious disease presentation.

In Spain, we have sadly surpassed 100,000 cases of COVID-19 at the time of this writing (April 1, 2020), with a mortality rate of 8.9% among those diagnosed. Quite unexpectedly, we have seen that PLWH are not at increased risk of acquiring COVID-19 or of progressing to acute respiratory distress syndrome (ARDS) once infected, across the 3 risk classes defined above. For reasons that are as yet unknown, it appears that their risk may even be lower than that of the general population.

Josep M. Llibre CCO
Reduction and Functional Exhaustion of T Cells in Patients with Coronavirus Disease 2019 (COVID-19)

Bo Dao, Chenhui Wang, Yingyan Tan, Xiewen Chen, Ying Liu, Lifen Nie, Li Chen, Min Li, Yongping Liu, Gang Wang, Zhen Yuan, Zeqing Feng, Yuzhong Wu, Yongwen Chen
doi: https://doi.org/10.1101/2020.02.18.30024964
This article is a preprint and has not been peer-reviewed [what does this mean?]. It reports new medical research that has yet to be evaluated and should not be used to guide clinical practice.

Abstract

BACKGROUND The outbreak of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has posed great threat to human health, which has been declared a public health emergency of international concern (PHEIC) by the WHO. T cells play a critical role in antiviral immunity but their numbers and functional state in COVID-19 patients remain largely unclear. METHODS We retrospectively reviewed the counts of total T cells, CD4+, CD8+ T cell subsets, and serum cytokine concentration from inpatient data of 522 patients with laboratory-confirmed COVID-19, admitted into two hospitals in Wuhan from December 2019 to January 2020, and 40 healthy controls, who came to the hospitals for routine physical examination. In addition, the expression of T cell exhaustion markers PD-1 and Tim-3 were measured by flow cytometry in the peripheral blood of 14 COVID-19 cases.

RESULTS The number of total T cells, CD4+, and CD8+ T cells were dramatically...
EACS/BHIVA Statement on risk of COVID-19 for PLWH: Recommendations

» For patients with low CD4-counts (<200/ml), or who experience a CD4-decline during a COVID-19 infection, remember to initiate opportunistic infection (OI) prophylaxis.

» More information regarding recommendations for prophylaxis and treatment of specific opportunistic infections can be found in the BHIVA or EACS guidelines for HIV/AIDS.

» Smoking is a risk factor for respiratory infections; smoking cessation should therefore be encouraged for all patients.

» Influenza and pneumococcal vaccinations should be kept up to date.
Cohort/Observational studies in HIV-coinfected patients with COVID-19

- The NEAT ID Foundation has developed a ‘data dashboard’ to monitor COVID-19 case numbers, hospitalisations and mortality in people with HIV at European and country level. The data will be available for public viewing via www.NEAT-ID.org and if your centre has not signed up, you can do so via this link.

- The Lean European Open Survey on SARS-CoV-2 Infected Patients (LEOSS) launched by the German Society for Infectious Diseases (DGI) and ESCMID’s Emerging Infections Task Force (EITaF) an open register based on anonymous questionnaires and they’re keen to collaborate with other registries. See https://leoss.net, contact them by email at info@leoss.net and the register can be accessed here https://leoss.net/statistics
Maintaining HIV care during the COVID-19 pandemic

Coronavirus disease 2019 (COVID-19) has spread rapidly around the world since the first reports from Wuhan in China in December 2019, and the continent was characterised as a pandemic by WHO on March 11, 2020. Approximately 37.9 million people living with HIV are at risk of infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes COVID-19. Although some international institutions, in collaboration with governments and community partners, are working to sustain HIV service provision for people living with HIV, the COVID-19 pandemic presents several barriers and challenges to the HIV care continuum.1

First, implementation of quarantine, social distancing, and community containment measures have reduced access to routine HIV testing, which challenges completion of UNAIDS’ first 30-90 targets globally, that 50% of all people living with HIV will know their HIV status. HIV testing is the vital first step towards initiation into the HIV care continuum.2 Even with availability of HIV self-testing kits in some areas,3 testing remains a big challenge in settings with wide access to these kits. Therefore, increased efforts are needed to augment access and to facilitate testing.

Second, timely linkage to HIV care could be hindered during the COVID-19 pandemic. People living with HIV who should have initiated antiretroviral therapy (ART) in hospital might be deterred or delayed because hospitals are busy treating patients with COVID-19. Furthermore, because many public health authorities globally are focused on COVID-19 control, allocation of resources for HIV care could be diminished, and only could undergo physical health deterioration but also might suffer great psychological pressure.

In response to these challenges, WHO, UNAIDS, and the Global Network of People Living With HIV are working together to ensure continued provision of HIV prevention, testing, and treatment services.4 The Chinese National Center for AIDS/STD Control and Prevention issued a notice guaranteeing free antiretroviral drugs for selected treatment management agencies in China, and released a list of ART clinics.5 People living with HIV can refill antiretroviral drugs either at the nearest local Center for Disease Control and Prevention or by post, to maintain enrolment in treatment programmes and to continue ART.6 Hospitals in Thailand are to dispense antiretroviral drugs in 6-month doses to meet the needs of people living with HIV and reduce facility visits.7 The US Department of Health and Human Services released interim guidance for COVID-19 and people living with HIV on March 30, 2020,8 which emphasized that people living with HIV should maintain at least a 30-day supply and ideally a 90-day supply of ART and all other drugs, by mail-order delivery if possible.

Community-based organisations have also played an important part in maintaining HIV services. UNAIDS is working with the Bapsi in alliance of people living with HIV and other community partners to reach and help those who will run out of antiretroviral drugs in the near future.9 Since the lock down of Wuhan on January 23, 2020, a community-based organisation (Wuhan TongShi Center) has dedicated resources to ensure the supply of antiretroviral drugs and opened a hotline to provide consultations. As of March 31, 2020, this...
Liverpool Website on drug-drug interactions

» http://www.covid19-druginteractions.org/

Prescribing Resources

The Liverpool Drug Interaction Group (based at the University of Liverpool, UK), in collaboration with the University Hospital of Basel (Switzerland) and Radboud UMC (Netherlands), have produced various materials in PDF format to aid the use of experimental agents in the treatment of COVID-19.

Please check this site regularly for updates and additional information.

Detailed recommendations for interactions with experimental COVID-19 therapies.

Updated: Atazanavir and tocilizumab added as new COVID-19 therapies, anticonvulsants and antifungals added as new comedications.

Details of the nature of drug interactions with experimental COVID-19 therapies (atazanavir, lopinavir/ritonavir, remdesivir, favipiravir, chloroquine, hydroxychloroquine, nitazoxanide, ribavirin, tocilizumab) and many comedication classes are given in the PDF below. Please use your browser’s “Find” function to search for drug names. (Note: Darunavir/ritonavir has been removed from the PDF following a statement by Janssen regarding lack of evidence to support the use of darunavir-based treatments for COVID-19.)

Click here to view PDF.

Updated 20 March 2020

At-a-glance summary of interactions with experimental COVID-19 therapies.

Updated: Atazanavir and tocilizumab added as new COVID-19 therapies, anticonvulsants and antifungals added as new comedications.

A summary of interactions with experimental COVID-19 therapies (atazanavir, lopinavir/ritonavir, remdesivir, favipiravir, chloroquine, hydroxychloroquine, nitazoxanide, ribavirin, tocilizumab) and over 400 comedications are shown. The nature of the 

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Learnings

» Testing availability and roll-out as well as time-point of implementing lockdown and social distancing measures, determines exponential growth in new infection numbers.

» Mortality rates again depend on who is tested and affected predominant populations.

» Implementation of infection prevention and control (IPC) strategies are essential.

» Experimental therapies at best should be studied in controlled clinical trials.
COVID-19 epidemic in Switzerland: on the importance of testing, contact tracing and isolation

Testing, followed by contact tracing and isolation of those with positive test results has been applied by all countries that have managed to keep the SARS-CoV-2 virus in check. The epidemiological reasoning is straightforward. Current estimates of the basic reproduction number $R_0$ of COVID-19 are around 2–3. To bend the epidemic curve downwards (which will only happen once the effective reproduction number $R < 1$), we must prevent 50–70% of possible transmissions. Isolation of cases and precautionary self-isolation of contacts are key measures to do that, and the COVID-19 experience from other countries demonstrates that forcefully. Following a positive test result, that person should be isolated to prevent onward transmission. The person’s close contacts should be followed up and advised to go into precautionary self-isolation, unless a risk/benefit analysis deems this counterproductive. These measures can prevent a large fraction of possible transmission chains.
2. The Republic of South Korea has had a large epidemic of COVID-19, the cumulative number of cases exceeded 1000 on 26 February. A central part of the control strategy was widespread and easily accessible SARS-CoV-2 testing, linked to contact tracing, and self-isolation. The epidemic curve suggests that the control strategy in South Korea has curtailed the epidemic. The number of new cases peaked on 29 February and had fallen to 84 by 17 March.
6. A system for antibody testing (serology) will also need to be implemented at large-scale as soon as possible. Antibody testing provides additional information to that obtained from polymerase chain-reaction (PCR) detection of active infection. Antibody testing is the only way to reliably establish the fraction of the population that was infected by the virus – albeit with a delay of a few weeks. A cohort of people with documented infection should be monitored to determine the time to seroconversion, providing crucial input for large-scale testing. People with suspected exposure, healthcare workers in particular, should be tested as high antibody titres likely mean that they are no longer at risk of contracting or spreading the disease and can be preferentially employed in high-risk areas.
Coronavirus: Kurz für erweiterte Maskenpflicht und „Containment“

Für das nach Österreich empfohlene vorübergehende Ende des „Containment“-Verfahrens überantwortete die Regierung die Ausführung der Maskenpflicht. „Was im Supermarkt Sinn macht, macht natürlich auch in anderen Bereichen des Lebens Sinn“, so Kanzler Sebastian Kurz (ÖVP) am Samstag.
THANK YOU

“‘You cannot fight a fire blindfolded. And we cannot stop this pandemic if we don’t know who is infected.’” (World Health Organization Director-General, 16 March 2020).