

**Ministry of Healthcare of the Republic of Kazakhstan**

**NCJSC “Semey Medical University”**

**MSE on the right of EM “D. Kalmatayev Semey State Tertiary  
Medical College”**



**M. SYZDYKBAYEV, S. TANATAROV, Y. ZHUNUSSOV**

# **INTENSIVE THERAPY OF PATIENTS WITH CORONAVIRUS INFECTION**

Guidelines



**Semey, 2020**

**Ministry of Healthcare of the Republic of Kazakhstan**

**NCJSC “Semey Medical University”**

**MSE on the right of EM “D. Kalmatayev Semey State Tertiary  
Medical College”**



**M. Syzdykbayev, S. Tanatarov, Y. Zhunussov**

**INTENSIVE THERAPY OF PATIENTS WITH CORONAVIRUS  
INFECTION**

Guidelines

Semey, 2020

**UDC 616.085+578.834.1**

**LBC 55.142**

**C95**

**Developed by:** NCJSC “Semey Medical University” (Chairman of the Board – Rector, Dr. Yersin Zhunussov), MSE on the right of EM “D. Kalmatayev Semey State Tertiary Medical College” under the Health Administration of East Kazakhstan Region (Director Sayat Tanatarov).

**Prepared by:**

**Marat Syzdykbayev** – Doctor of Medical Sciences, Head of the Department of Anesthesiology, Resuscitation and Narcology of NCJSC “Semey Medical University”

**Sayat Tanatarov** – Doctor of Medical Sciences, Professor, Director of “D. Kalmatayev Semey State Tertiary Medical College” under the Health Administration of East Kazakhstan Region

**Yersin Zhunussov** - Doctor of Medical Sciences, Professor, Chairman of the Board – Rector of NCJSC “Semey Medical University”

**REVIEWERS:**

**Dmitriy Vasilyev** – Candidate of Medical Sciences, Associated Professor, Head of the Department of Anesthesiology and Resuscitation of NCJSC “Karaganda Medical University”

**Nurila Maltabarova** – Candidate of Medical Sciences, Professor, Head of the Department of Emergency Care, Anesthesiology and Intensive Therapy of NCJSC “Astana Medical University”

Intensive therapy of coronavirus infection / M. Syzdykbayev, S. Tanatarov, Y. Zhunussov.  
// Semey: NCJSC “Semey Medical University”, 2020. – 42 pages

The Guidelines include triage sorting in the emergency departments and in ARIT, taking into account the degree of severity, respiratory failure, sorting of patients at the hospital stage and in the department of anesthesiology, intensive care. The basics of intensive care for coronavirus infection and various complications, ARDS (acute respiratory distress syndrome), pneumonia, sepsis, septic shock, etc., the interaction of drugs and contraindications in the treatment of CVI (coronavirus infection), various modes of ALV, recruitment techniques. The Guidelines have been designed for anesthesiologists, anesthesiologists, resuscitators and emergency doctors who provide emergency care and treatment of CVI.

The Guidelines are temporary and can be used for the period of the pandemic and depend on the epidemiological situation in the country.

**UDC 616.085+578.834.1**

**LBC 55.142**

Approved and passed for press by the Decision of the Academic Committee of NCJSC “Semey Medical University”. Protocol No. 4 dated 22.04.2020

© M. Syzdykbayev, S. Tanatarov, Y. Zhunussov, 2020

## CONTENTS

|       |   |    |
|-------|---|----|
|       | List of abbreviations                                       | 3  |
| 1     | Introduction  | 4  |
| 2     | Triage of patients with CVI in ED                           | 6  |
| 3     | Triage criteria in ARIT                                     | 8  |
| 4     | Infection control measures                                  | 10 |
| 4.1   | PPC   | 10 |
| 4.2   | Implementation of infection prevention and control measures | 12 |
| 5     | Treatment of patients with severe COVID                     | 14 |
| 5.1   | Diagnostics in intensive therapy                            | 14 |
| 5.2   | Early supporting therapy and observation                    | 16 |
| 5.3   | Management of patients with RF and ARDS                     | 17 |
| 5.4   | Management of patients with septic shock                    | 18 |
| 5.5   | Prevention of complications                                 | 19 |
| 5.6   | Special recommendations for pregnant patients management    | 21 |
| 5.7   | Noninvasive oxygen support and inhaling                     | 21 |
| 5.8   | AVL   | 22 |
| 5.8.1 | AVL initial phase   | 25 |
| 5.8.2 | AVL stabilization phase                                     | 26 |
| 5.8.3 | AVL stopping  | 27 |
| 5.8.4 | Recruitment maneuver  | 27 |
| 5.9   | Surgical aspects in COVID 19                                | 28 |
| 5.10  | Prevention and resuscitation measures                       | 28 |
| 5.11  | Antibacterial therapy                                       | 29 |
| 5.12  | Steroids  | 30 |
| 5.13  | Surfactant  | 30 |
| 5.14  | Temperature regulation                                      | 30 |
| 5.15  | Sedation  | 30 |
| 5.16  | Muscle relaxation   | 31 |
| 5.17  | Nutrition   | 31 |
| 5.18  | Fluid therapy   | 31 |
| 5.19  | Inotropic support   | 31 |
| 5.20  | Incident atrial fibrillation                                | 32 |
| 5.21  | Example of COVID-19 patient management in ARIT              | 32 |
| 5.22  | Patient indicators control                                  | 33 |
|       | List of references  | 34 |
|       | Tear sheet  | 39 |

## List of abbreviations

ACA – acute cerebrovascular accident  
ARDS – acute respiratory distress syndrome  
ARI – acute respiratory infection  
ARM – alveolar recruitment maneuvers  
AVL – artificial ventilation of lungs  
COPD – chronic obstructive pulmonary disease  
CPAP/BiPAP – constant positive airway pressure / Bilevel positive airway pressure  
CR – cardiac rate  
CT – computer tomography  
DARIT – Department of Anesthesiology, Reanimation and Intensive Treatment  
EBW – estimated body weight  
ECLS – extracorporeal life support  
FiO<sub>2</sub> – fraction of inspired oxygen  
GC – glucocorticosteroids  
HFNOT – high-flow nasal oxygen therapy  
ICU – Intensive Care Unit  
IPC – infection prevention and control  
KDIGO – Kidney Disease Improving Global Outcomes  
LA – lower airways  
MD – mean deviation  
MERS – Middle East Respiratory Syndrome  
NIAVL – noninvasive AVL  
NYHA – New York Heart Association  
OI – Oxygenation index  
OIU – oxygenation index using SpO<sub>2</sub>  
PCR – polymerase chain reaction  
PPC – personal protective clothing  
PEEP – positive end-expiratory pressure  
RNA – ribonucleic acid  
RR – respiratory rate  
PRC – People's Republic of China  
SARS – severe acute respiratory syndrome  
SIRS – systemic inflammatory response syndrome  
SpO<sub>2</sub> – oxygen saturation  
SPAP – spontaneous positive airway pressure  
UA – upper airways  
USI – ultrasound investigation

## 1. INTRODUCTION

In November 2019, outbreak of novel coronavirus infection began in Wuhan, China, Hubei Province. The infectious agent was named 2019-nCoV [1-3].

On February 11, 2020, WHO officially named this infection as COVID-19. The International Committee on Taxonomy of Viruses officially named the viral agent as SARS-CoV-2 [4].

The rapid development of the COVID-19 epidemic has set new and complex challenges before health professionals related to the need for emergency diagnosis and adequate medical care to patients. Rapid changes in the epidemiological situation, a lot of conflicting information about the clinical features of the infection, and insufficient information about the possibilities of treatment determine the complexity and magnitude of the problem [5].

Bilateral pneumonia is considered to be a very common clinical manifestation of this coronavirus infection, and the development of acute respiratory distress syndrome with a very high risk of death is observed in a significant number of cases [6,7].

Own data on the management of patients with severe coronavirus-related conditions are limited to date, and these recommendations are largely based on data published by WHO, PRC, the USA and European countries.

## 1. ETIOLOGY AND PATHOGENESIS

Coronaviruses are a fairly large family of RNA-containing viruses. In humans, the viruses in this group are responsible for a number of diseases ranging from mild forms of ARI to SARS. There is a number of coronaviruses, which have tropicity to the upper respiratory tract epithelium and cause sporadic and seasonal morbidity of mild ARI and moderate severity SARS [8,9].

The family of coronaviruses is divided into four types:  $\alpha$ -coronavirus,  $\beta$ -coronavirus,  $\gamma$ -coronavirus, and  $\delta$ -coronavirus [10].

At the end of 2002, a coronavirus (SARS-CoV) was detected, which is atypical pneumonia pathogen associated with SARS [11,12]. This virus belongs to the genus  $\beta$ -coronavirus. Bats are a natural carrier of SARS-CoV; camels and Himalayan civets may be intermediate carriers. During the period of the outbreak in 2002-2003, more than 8000 cases were registered and the lethality was close to 10%. No SARS-CoV infection has been reported in humans since 2004 [13].

In 2012, there was a new outbreak of coronavirus infection MERS (MERS-CoV), Middle Eastern respiratory syndrome, also caused by the etiologic agent, belonging to  $\beta$ -coronavirus. The zoonotic reservoir of this pathogen is a single camel. At present, MERS-CoV continues to circulate and new cases occur. The lethality caused by MERS-CoV exceeds 30% [14,15].

Coronavirus SARS-CoV-2 is a single-stranded RNA-containing virus, belongs to the  $\beta$ -CoV B line. The virus belongs to the II pathogenicity group along with SARS-CoV, MERS-CoV [16].

The SARS-CoV-2 coronavirus is supposed to be a recombinant virus between the bat coronavirus and another virus of unknown origin (probably, pangoline) [17]. The genetic sequence of SARS CoV-2 consists with SARS-CoV by at least 79%.

The entrance gate of the pathogen is the epithelium of the upper respiratory tract as well as the stomach and intestines. Receptors of angiotensin converting enzyme II (ACE-2) are the ligand for SARS-CoV-2 on the surface of target cells [18]. They are mainly represented in the cells of respiratory tract, heart, CNS, kidney, esophagus, and bladder [19]. Taking into account the route of infection, the most easily achievable target is pulmonary alveolar cells of type II, which determines the predominant development and danger of pneumonia [20].

Rapid development of CNS lesion in a number of clinical cases can be explained by SARS-CoV-2 penetration from systemic blood flow or through the ethmoid bone plate. One of its manifestations is the changes in smell [21].

The epidemiological picture of the disease from its origin was characterized by the prevalence in China up to March 2020, but recently USA is the "leader" in the number of cases and mortality. There has been high mortality rate are in European countries (especially in Italy and Spain).

The main source of infection is the sick person, including those in the incubation period [22,23].

Transmission occurs primarily via respiratory droplets and contact. The main paths of infection are respiratory droplets from cough, sneezes and communication within a range of less than 80 cm - 2 m (according to different sources) [24,25]. The contact path of infection occurs via direct contact with the infected person and via foodstuffs, surfaces and objects contaminated with the virus. SARS-CoV-2 is believed to be capable of maintaining viability at various environmental mediums for up to 3 days at room temperature. At the same time, there are results of alternative studies showing that SARS-CoV-2 is not virulent when it is on the surface [26].

Fecal-oral transmission is potentially possible. SARS-CoV-2 RNA was detected in stool samples of patients. COVID-19 nucleocapside protein was found in cytoplasm of epithelial cells of the stomach, duodenum and rectum, but not in esophageal epithelium [27].

The role of COVID-19, as infection related to delivery of medical care, has been established [28,29].

State of emergency was imposed in our country by the Decree of the President of the Republic of Kazakhstan № 285 dated March 15, 2020.

The most difficult in clinical terms is the management of severe cases of infection, with a high risk of death and requiring intensive care. The present recommendations are devoted to this problem.

The recommendations given here are based on information from Chinese literature and experience in Lombardy, Italy and several other countries, and WHO recommendations,

and are temporary for the duration of a pandemic, state of emergency and coronavirus treatment.

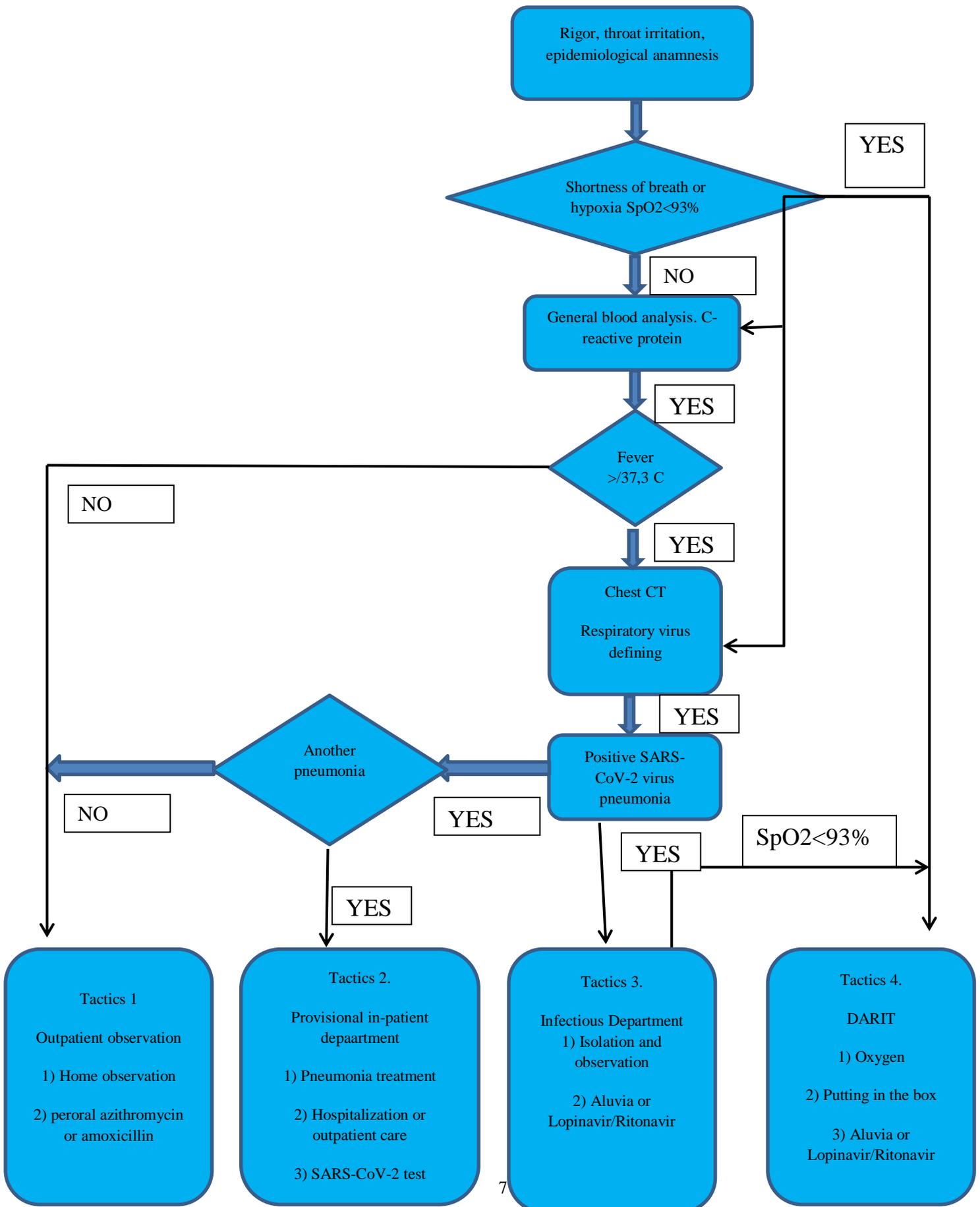
## **2. TRIAGE OF PATIENTS WITH CORONAVIRUS INFECTION IN EMERGENCY DEPARTMENT**

The presented algorithm of triage in emergency departments is based on the experience of doctors of Wuhan, China. Criteria: SARS CoV-2 test is required to decide what steps should be taken. Negative SARS CoV-2 test and respiratory symptoms in patient - taking to the provisional clinics; no symptoms and negative SARS CoV-2 test - home self-isolation; positive SARS CoV-2 test - taking to infection hospital. Obligatory conditions for all clinics: temperature measurement and general blood analysis; temperature is  $\geq 37.3$  C; in general blood analysis - reduction of lymphocytes [30].

If the patients has  $SpO_2 < 93\%$  saturation, they must be admitted to the intensive care unit [30].

The algorithm of triage sorting in intensive care units under different conditions is presented below (with free beds and without free beds in DARIT) [31].

## Triage of patients in emergency departments



### 3. CRITERIA OF SARS-CoV-2 PATIENTS IN DARIT

#### 3.1 Primary Triage: criteria for transfer to OIT

##### Stage 1

Does the patient have one of the following indications?

- Needs invasive respiratory support;
- Needs hemodynamic support with vasoactive agents (equivalent to noradrenaline >0.1 µg/kg/min).

If there is one of these criteria → Step 2

##### Step 2

**Does the patient have at least one exclusion criterion?**

Condition A: there are limited availability beds in ICU

- The desire of the patient (medical consent, etc.);
- cardiac arrest in anamnesis, repeated cardiac arrest, cardiac arrest without spontaneous circulation recovery;
- Malignant disease, with life expectancy of less than 12 months;
- The last stage of nervous-degenerative diseases;
- Severe and irreversible neurological condition;
- Chronic diseases:
  - Heart failure according to NYHA class IV;
  - COPD GOLD 4 (D);
  - Liver cirrhosis, CPT score >8;
  - Severe dementia;
  - Severe circulatory failure that does not respond to vasopressor therapy (hypotension and/or persistent inadequate organ perfusion);
- Poor survival prediction (less than 12 months).

**Condition B: There are no free beds in ICU**

Additional criteria:

- Severe injury;
- Extensive burns (>40% of body surface area) with damage to respiratory organs;
- Severe neurologic impairment after ACA;
- Chronic diseases:
  - Heart failure according to NYHA class III or IV;
  - COPD GOLD 4 (D) or COPD A-D with FEV1 <25% or cor pulmonale, or constant need for additional oxygen (prolonged oxygen therapy);
  - Liver cirrhosis with refractory ascites or 1st degree encephalopathy;
  - Stage 5 chronic renal failure according to KIDGO;
  - Moderate dementia (confirmed);
  - Age over 85;
  - Age over 75 years old with one of the criteria:
    - Liver cirrhosis;
    - Stage 3 chronic renal failure according to KIDGO;

- Heart failure according to NYHA class I;
- Poor survival prognosis (less than 24 months).

### **3.2 Secondary triage: stay in ICU**

#### **Stage 1**

Availability of criteria for transfer from ICU:

- The extubation has been performed or a patient on spontaneous breathing through the tracheostoma in stable condition. Clinical and laboratory parameters significantly improved.
- Patient is discharged from ICU.

#### **Step 2**

- Stabilization or improvement of oxygenation and ventilation, or the patient has concomitant organ failure;
- Stabilization or improvement of hemodynamics.

If there are both criteria:

→ Continue treatment in ICU

Further steps have been adopted in the recommendations emanating from the health systems of the countries with severe epidemics. They are currently unfeasible and ineffective, but if the epidemic worsens, they can be used to define target population to continue intensive care.

#### **Step 3**

Presence of one of the following criteria reflecting minimum or possible benefits of staying in ICU:

##### **Condition A: there are limited availability beds in ICU**

- Case of cardiac arrest with successful defibrillator resuscitation while in ICU, ;
- The patient has or develops multiple organ failure.

Condition B: There are no free beds in ICU.

- No improvement in respiratory or hemodynamic status or there is improvement in organ failure;
- The patient has or develops severe multiple organ failure.

If there is one of the criteria:

→ Patient is discharged from ICU and receives palliative care [31].

## 4. INFECTION CONTROL MEASURES

- The patient should be isolated in a special box, where low pressure is kept and there is a frequent change of air or system with negative ventilation pressure.
- If no such box is available, the patient should be placed in a separate room.
- Specialized boxes should also have a spacious enough sanitary inspection room for the staff to change into protective outerwear suit. If there is no, temporary sanitary inspection room can be built.

Risk! The air flow within a hospital department can dramatically increase the risk of in-hospital transport of some types of coronaviruses such as SARS [32].

Under these conditions, health professionals have to wear a full suit of protection against airborne and contact infections in wards, which are not provided with independent isolation system ("hot zones"). Medical staff must take these protective outerwear suits when leaving the "hot zone"!

- Medical workers should wear clean gowns, N95 respirators and gloves in low-pressure temporary sanitary inspection rooms built near wards without independent air-conditioning ("hot zones"), as infected air can be brought from such wards into common areas. Outside the ICU ("cold zones"), wearing protective suit is not required [33].

### 4.1 Infection control measures: PPE .

The recommended PPE kit (personal protective equipment) for contact with confirmed or suspected COVID-19 patients (Figure 1) in critical condition should include [34]:

- 1) a waterproof disposable scrub
- 2) gloves (long cuffed)
- 3) eye protection, full-face mask
- 4) suitable respirators, at least N95 standard (in Europe, N95 corresponds to EN 149, FFP2. and FFP3 protection classes). If there is no suitable respirator, a gas mask can be used, as there is 100% probability of infection during intubation.
- 5) cap or hood
- 6) impermeable shoes that can be disinfected. Risks! Boot covers can increase the risk of self-contamination of personnel when PPE is removed.
- 7) Personnel must wear operating suit or protective overall with hood under the PPE.

1) The use of PAPP (respiratory protection system) with hoods (Fig. 2) covering the head and neck may also provide additional protection compared to the standard PPE kit equipped with N95 mask. PAPP, respiratory protection system includes compressor combined with a filter at the waist (rear view on the left image), attached to the hose. Risks! Based on known cases of infection of health care workers using mask N95 during resuscitation of patients with SARS, the use of PAPP is justified in high-risk resuscitation of patients with 2019-nCoV infection (confirmed or not) [35].

Figure 1. PPE kit



Figure 2. PAPP use with hoods covering the head and neck



## 4.2 Implementation of IPC

IPC (Table1)

Standard preventive measures:

- hand hygiene;
- use of PPE to prevent direct contact with blood, physiological fluids and excreta of the patient (including excreta from the respiratory system) and damaged skin.
- measures to prevent cuts/punctures with needles or sharp objects;
- safe disposal of waste; cleaning and disinfection of equipment;
- cleaning of premises

**Table 1. Infection preventive and control measures for patients with suspected or confirmed COVID-19 [36, 37]**

|  |   |
|--|---|
| <b>During the sorting</b>                                | To give a medical mask to the COVID-19 suspected patient and refer to a special area - the isolation room, if available; to keep the distance of at least 1 meter between the patients with suspected COVID-19 and other patients. All patients should be instructed to cover their nose and mouth when coughing and sneezing with a tissue/screen or elbow fold to avoid endangering others. After contact with respiratory discharge, to disinfect hands using the soap or hand sanitizer.  |
| <b>To take measures to prevent airborne transmission</b> | To prevent the transmission of respiratory viruses, medical mask must be used when working within of 1-2 meters from the patient. Patients should be placed in wards one by one or together with patients with the same etiological diagnosis. If etiological diagnosis cannot be determined, patients should be placed with similar clinical diagnoses and epidemiological risk factors, ensuring spatial separation. When providing care in close contact with a patient with respiratory symptoms (e.g. cough or sneezing), use eye protection (face mask or goggles) because of the danger of aerosol formation and contact with excreta. Limit the movement of patients within the facility and ensure that patients use medical masks outside their wards.  |
| <b>To take measures to prevent contact transmission</b>  | The prophylaxis of airborne and contact transmission prevents direct and indirect transmission through contaminated surfaces and equipment (e.g. contact with bacterized oxygen hoses / oxygen delivery devices). It is necessary to wear PPE (medical mask, eye protection, gloves and suit) when entering the room and remove PPE when leaving it. If possible, use disposable or dedicated equipment (e.g. stethoscopes, cuffs of tonometers and thermometers). If the same equipment is to be used for several patients, it should be cleaned and disinfected after use and before use in the next patient. Medical personnel should not touch the eyes, nose and mouth with their hands if there is a possibility of contamination, whether they wear gloves or not. Objects that are not directly used in patient care (e.g. door handles and switches) should be kept free from contamination.<br>The wards should be well ventilated. Patients should not be moved or transported. Hand hygiene must be maintained. |
| <b>To take measures while</b>                            | All health workers who perform procedures involving risk of aerosol formation (aspiration or suction of airway contents through open  |

|  |   |
|--|---|
| <b>performing<br/>measures<br/>related to<br/>aerosols</b> | drainage, intubation, CPR, bronchoscopy) should wear PPE, including gloves, long-sleeved medical gowns, eye protection and a tight-fitting respirator (N95, equivalent or higher class of protection). The planned tightness check should not be confused with the tightness check carried out by the wearer each time he or she used the respirator. Wherever possible, procedures involving risk of aerosol formation, should be performed in well ventilated isolated rooms, i.e. rooms where the low pressure is kept, the air exchange rate should be at least 12 or the air flow rate should be at least 160 l/s per patient in rooms with natural ventilation. Access to these rooms by unauthorized persons must be prohibited. |
|--|---|

## 5. Treatment of patients with severe COVID-19

### 5.1. Diagnostics in intensive care

**Table 2. Clinical syndromes associated with COVID-19 [38]**

|                               |   |
|-------------------------------|---|
| <b>Noncomplicated disease</b> | Fever, cough, sore throat, nasal blockage, sickness, headache, muscle pain or muscle weakness. Older patients and patients with a weakened immune system may have atypical symptoms. Risks! These patients have no symptoms of dehydration, sepsis or respiratory failure.  |
| <b>Mild pneumonia</b>         | Pneumonia patient with no symptoms of severe pneumonia. A child with mild pneumonia has a cough or difficulty in breathing + rapid breathing: rapid breathing (in respiratory movements per minute): < 2 months. - $\geq 60$ ; 2-11 months. - $\geq 50$ ; 1-5 years - $\geq 40$ , no symptoms of severe pneumonia.  |
| <b>Severe pneumonia</b>       | <ul style="list-style-type: none"> <li>• Adolescents and adults: Fever or possible respiratory infection, and one of the following symptoms: Respiratory rate (RR) &gt; 30/min, severe respiratory distress, or SpO<sub>2</sub>&lt;90% in room air.</li> <li>• A child with a cough or difficulty in breathing and at least one of the following symptoms: central cyanosis or SpO<sub>2</sub>&lt;&lt;90%; severe respiratory distress (bubbling breathing, heavy chest indrawing); pneumonia symptoms generally indicating danger: inability to suck on breast milk or drink, atony or loss of consciousness or convulsion. Other pneumonia symptoms may be present: chest pulling, rapid breathing (respiratory movement per min): &lt;2 months - <math>\geq 60</math>; 2-11 months - <math>\geq 50</math>; 1-5 years - <math>\geq 40</math>.</li> </ul>  |
| <b>ARDS [39, 40, 41].</b>     | <p><b>Beginning:</b> deterioration of symptoms or onset of new respiratory symptoms within 1 week of infection.</p> <p><b>Visualization of the chest organs (X-ray, CT or ultrasound of the lungs):</b> shadows on both sides, not fully explained by the perspiration, the fall of the lung or its proportion, or the presence of nodules.</p> <p><b>NB:</b> Lung ultrasound and echocardiography are required to rule out cardiogenic cause of edema.</p> <p><b>Oxygenation (adults):</b></p> <ul style="list-style-type: none"> <li>• Mild ARDS 200 mm Hg &lt; PaO<sub>2</sub>/FiO<sub>2</sub> ≤ 300 mm Hg (PEEP positive end of exhalation pressure (PEEP) or constant positive pressure (CPAP) ≥ 5 cm water column or no AVL)</li> <li>• Moderate ARDS: 100 mm Hg &lt; PaO<sub>2</sub>/FiO<sub>2</sub> ≤ 200 mm Hg. (with PEEP ≥ 5 cm Hg or without AVL)</li> <li>• Heavy DDS: PaO<sub>2</sub>/FiO<sub>2</sub> ≤ 100 mm Hg. (with PEEP ≥ 5 cmHg or without AVL)</li> </ul> <p>• If the value of PaO<sub>2</sub> is unknown, SpO<sub>2</sub>/FiO<sub>2</sub> ≤ 315 indicates an ARDS (including in patients without AVL).</p> <p><b>Oxygenation (children; note: OI is an index of oxygenation, OSI is an index of oxygenation using SpO<sub>2</sub>):</b></p> <ul style="list-style-type: none"> <li>• Two-level non-invasive AVL (NIVL) or CPAP ≥ 5 cm water column through full-face mask: PaO<sub>2</sub>/FiO<sub>2</sub> ≤ 300 mmHg or SpO<sub>2</sub>/FiO<sub>2</sub> ≤ 264.</li> <li>• Mild ARDS (with invasive AVL): 4 ≤ OI &lt; 8 or 5 ≤ OSI &lt; 7.5.</li> <li>• Moderate ARDS (with invasive AVL): 8 ≤ OI &lt; 16 or 7.5 ≤ OSI &lt; 12.3</li> <li>• Heavy ARDS (with invasive AVL): OI ≥ 16 or OSI ≥ 12.3</li> </ul> |

|                                      |  |
|--------------------------------------|--|
| <p><b>Sepsis</b><br/>[42, 43].</p>   | <ul style="list-style-type: none"> <li>• Adults: life-threatening organ dysfunction: altered state of consciousness, difficulty or rapid breathing, low blood saturation, reduced diuresis, rapid heartbeat, weak pulse, cold limbs or low blood pressure, skin spotting or laboratory signs of coagulopathy, thrombocytopenia, acidosis, high lactate concentration or hyperbilirubinemia.</li> <li>• Children: possible or confirmed infection and <math>\geq 2</math> criteria for systemic inflammatory response syndrome (IRS), one of which should be an abnormal temperature or white blood cell count.</li> </ul>  |
| <p><b>Septic shock</b> [43, 44].</p> | <ul style="list-style-type: none"> <li>• Adults: persistent arterial hypotension against the background of replenishment of circulating blood volume, requiring the use of vasoconstrictor drugs to maintain mean BP <math>\geq 65</math> mm Hg and lactate concentration in the serum <math>&gt; 2</math> mmol/l.</li> <li>• Children: Hypotension (average BP <math>&lt; 5</math>th centnil or <math>&gt; 2</math> standard deviations (SD) less than the standard for this age) or 2-3 of the following symptoms: 1) altered state of consciousness; 2) tachycardia or bradycardia (heart rate (HR) <math>&lt; 90</math>/min or <math>&gt; 160</math>/min in infants, or HR <math>&lt; 70</math>/min or <math>&gt; 150</math>/min in children); 3) prolonged capillary filling time (<math>&gt; 2</math> s) or 4) warm vasodilation with high pulse pressure; 5) tachypnea; 6) marble skin or petechial or purple rash; 7) elevated lactate levels; 8) oliguria; 9) hyperthermia or hypothermia.</li> </ul> |

If the height of the oxygenation location exceeds 1000 m, it is necessary to calculate the correction factor using the following formula:  $\text{PaO}_2/\text{FiO}_2 \times \text{atmospheric pressure} / 760$ .

\* The SOFA scale index can be between 0 and 24 and takes into account the values associated with six systems: Respiratory (low  $\text{PaO}_2/\text{FiO}_2$  hypoxemia), blood clotting (low platelet count), liver (high bilirubin), cardiovascular system (hypotension), central nervous system (low Glasgow coma consciousness) and urinary system (low diuresis or high creatinine). Sepsis is determined by increasing the SOFA (Sequential [Sepsis-related] Organ Failure Assessment) score by  $\geq 2$  points. If no data are available, consider the initial value of the index as zero [38].

\* It is recommended to use the SOFA scale when determining polyorgan incompetence.

## 5.2. Early supporting therapy and observation

**Patients with SARS (severe acute respiratory syndrome) and respiratory distress, hypoxemia or shock should be immediately provided with additional oxygenation therapy.**

- Oxygenotherapy at 5 l/min and adjust the flow until  $SpO_2 \geq 90\%$  of non-pregnant adult patients and  $SpO_2 \geq 92-95\%$  in pregnant patients are reached [45, 46].
- Children with emergency symptoms (impaired airway patency, lack of breathing, severe respiratory distress, central cyanosis, shock, coma or seizures) should be provided with oxygen therapy during intensive care until  $SpO_2 \geq 94\%$  is achieved [47].

**NB:** Equipment - pulse oximeters, functional oxygen supply systems and disposable oxygen delivery devices (nasal cannulae, simple li-cele and respiratory bag masks).

**Infusion therapy for patients with SARS without signs of shock should be performed using a conservative approach [48].**

**Risks!** Massive infusion therapy can lead to impaired oxygenation.

**Prescribe empirical therapy with antimicrobial preparations for all probable bacterial agents of SARS. If sepsis is present, prescribe an antimicrobial therapy within one hour after the initial initial examination [49].**

**NB:** even if COVID-19 is possible, proper empirical antimicrobial therapy should be administered to the patient within one hour after the sepsis is detected.

Empirical therapy is cancelled based on microbiological analysis and medical opinion.

**Patients with SARS should be carefully monitored for timely detection of signs of worsening clinical condition (rapidly progressing respiratory insufficiency and sepsis), and if such signs appear, supportive therapy should be started immediately [38].**

Note: Timely adequate and safe supportive therapies are essential for the severe course of infection caused by COVID-19.

**It is important to be aware of the presence of concomitant pathology, as it affects the treatment and prognosis of patients in severe condition. Contact should be established with the patient and his or her relatives from the outset (38).**

Note: In the case of SARS intensive care, it is necessary to decide which treatment the patient continuously receives should be continued and which should be temporarily cancelled. Patients and their families should be informed on their own initiative, providing support and information about the prognosis.

## 5.3 Management of patients with RF and ARDS

Nasal high flow oxygen therapy (NHFOT) or non-invasive ventilation (NIV) should only be used in individual patients with hypoxemic respiratory failure. Patients receiving

NHFOT or NIVL should be closely monitored to detect signs of worsening symptoms [38].

*Note 1: NHFOT systems can provide gas flow rates up to 60 l/min and FiO<sub>2</sub> up to 1.0; loops for children typically provide only up to 15 l/min, and many children require an adult loop to provide sufficient flow.*

*Patients with hypercapnia (acute obstructive pulmonary disease, cardiogenic pulmonary oedema), unstable hemodynamics, polyorgan failure or altered consciousness should not be treated with NIV.*

**Endotracheal intubation should be carried out by qualified and experienced specialists observing measures of prophylaxis of airborne pathogen distribution [38].**

*Note: In patients with ARDS, especially small children, as well as obese and pregnant patients, saturation may rapidly decline during intubation. Pre-oxygenation at 100% FiO<sub>2</sub> should be performed for 5 minutes using a face mask with an airway bag, valve mask, NHFOT or NIV. Intubation in a rapid sequence is only recommended if no signs of intubation difficulties are apparent in the airway assessment.*

**Apply AVL at lower values of respiratory volume (4-8 ml/kg of calculated body weight, RMT) and lower pressure on inhalation (pressure of the ancient plateau <30 cm of water column) [38].**

*Notes: This is a strong recommendation from the guidelines for clinical management of patients with ARDS and is applicable to patients with respiratory depression in sepsis. The initial respiratory volume is 6 ml/kg RMT; in the presence of undesirable side effects (e.g., dissynchrony, pH < 7.15), respiration volume up to 8 ml/kg RMT is acceptable. Hypercapnia is acceptable if the target pH of 7.30-7.45 is achieved.*

**For patients with severe ARDS it is recommended to have an AVL in the left-hand position on the abdomen (pron position) for >12 hours per day.**

*Note: Lower abdominal AVL is strongly recommended for adults and children with severe acute respiratory infections, but requires sufficient human resources and co-worker experience for safe administration [50, 51].*

**A conservative approach should be adopted for infusion therapy in patients with ARDS without signs of hypoperfusion.**

*Note: This is a strong recommendation [49]; the main effect is to reduce the duration of infusion therapy [52].*

**For patients with severe ARDS, a higher PEEP rather than a lower PEEP is recommended (38).**

**In patients with moderately severe and severe ARDS (PaO<sub>2</sub>/FiO<sub>2</sub> < 150), neuromuscular blockage by continuous infusion should not be used continuously [38].**

*Continuous neuromuscular block may be considered for patients with ARDS in some situations: dissynchrony in sedation, due to which respiratory volume cannot be reliably limited, or refractory hypoxemia or hypercapnia.*

In the conditions of availability of specialists in extracorporeal membrane oxygenation (ECMO), consider the direction of patients with refractory hypoxemia on the background of a gentle AVL [38].

**Do not disconnect the patient from the TRS apparatus, which leads to PEEP and atelectasis loss.** Use installed catheters to suck out the contents of the airway tubes and, if necessary, cut off the endotracheal tube with a clamp [38].

#### 5.4. Management of patients with septic shock

In resuscitation measures against septic shock in adults, start infusion of crystalline solutions in the volume of at least 30 ml/kg within 3 hours. In resuscitation measures against septic shock in children under conditions of sufficient resources administer 20 ml/kg in a jet and up to 40-60 ml/kg in the first hour [38, 53].

Do not use hypotonic crystalloid solutions, solutions based on starch or gelatin for resuscitation measures.

Infusion therapy may lead to hypervolemia, including respiratory failure. If there is no effect of replenishing the circulating blood volume and if there are symptoms of hypervolemia (e.g. jugular vein dilation, wheezing with auscultation of the lung, imaging swelling or hepatomegaly in children), fluid administration should be reduced or cancelled. This step is especially important if AVL is not available. Alternative modes of infusion therapy are offered in the care of children in resource-limited settings [54, 55].

- *Crystalloid solutions - physiological solution and Ringer's solution. The need for additional jet injection of the liquid (250-1000 ml in adults or 10-20 ml/kg in children) is determined based on the clinical effect and improvement of perfusion targets.*
- *Perfusion targets are ADS (>65 mmHg or age-related values in children), diuresis (>0.5 ml/kg/h in adults, 1 ml/kg/h in children), reduced skin marbling, improved capillary filling time, state of consciousness and lactate concentration. At the end of primary resuscitation measures, fluid injection should be carried out taking into account the dynamic characteristics of the response to infusion therapy based on the availability of resources and experience [89].*
- **Risks!** *In comparison with crystalloid solutions, solutions based on starch lead to increased risk of death and acute kidney damage. The effect of gelatin-based solutions is less obvious, but they are more expensive than crystalloid solutions. Hypotonic solutions (as compared to isotonic solutions) are less effective at increasing intravascular volume maturity.*
- *It is recommended to use albumin.*

•If the shock does not go away during or after infusion therapy, vasoconstrictants should be used. The initial target value of average flowing pressure is  $\geq 65$  mmHg in adults and corresponds to the age values in children [38].

•If a central venous catheter is not possible to be used, vasoconstriction may be introduced through the peripheral catheter, but a large vein should be used and careful observation should be made to detect signs of extraction and local tissue necrosis. In case of extraction, infusion should be stopped. Vasoconstrictors may also be injected through intraosseous needles [38].

•If signs of poor perfusion and myocardial dysfunction persist despite the fact that the target value of average flowing pressure has been achieved due to the use of infusion therapy and vasoconstrictors, the use of inotropic drug, dobutamine should be considered [38].

*Note: vasoconstrictor drugs (including norepinephrine, epinephrine, vasopressin, and dopamine) are the safest to administer through a central venous catheter with strict control of injection rate, but they can also be safely administered through the peripheral vein [56] and intraosseous needle.*

Arterial medication should often be controlled and the vasoconstrictor dose adjusted to a minimum value necessary to maintain perfusion and prevent side effects. Norepinephrine is considered to be the first-line drug in adults; epinephrine and vasopressin can be used to achieve the target value of ADS. Because of the risk of tachyarrhythmia, dopamine should be administered in patients at low risk of tachyarrhythmia and in patients with bradycardia. In children with cold shock (more common), the first-line drug is epinephrine, while norepinephrine is used in warm shock patients (less common) [38].

### 5.5. Prevention of complications

The following interventions should be used to prevent complications (Table 3) related to critical illnesses. These interventions are based on the manual “Overcoming the effects of sepsis” and other guidelines and are generally limited to realistic recommendations based on high quality data [49, 57, 58, 59].

**Table 3. Preventing complications**

| Predicted outcome of the intervention                               | Presumed type of intervention  |
|---|--|
| Reduced number of days of invasive AVL                              | Use AVL cancellation protocols preferred daily assessment of readiness for self-sustaining breathing. Minimize continuous or periodic sedation by focusing on specific titration results (mild sedation if no other results are available) or daily stoppings in continuous sedation infusion.   |
| Reducing the incidence of ventilation pneumonia                     | In adolescents and adults, intubation through the mouth is preferable to intubation through the nose. Place the patient in a half-bed position (with bed backrest raised by 30-45°). Use a closed suction system; drain and remove condensation formed in hoses from time to time. Use a new ventilator circuit for each patient; replace the ventilator circuit if it is dirty or damaged, not according to a schedule. Replace the heat exchanger if it is faulty, dirty or every 5-7 days [32]. |
| Reducing the frequency of venous thromboembolism                    | Drug prophylaxis (subdermal heparin administration of 5000 IU twice a day or low-molecular weight heparin administration (preferable if available) for adolescents and adults without contraindications. If contraindicated, mechanical devices can be used to prevent venous thromboembolism, such as devices for intermittent pneumatic compression [33].  |
| Reduced incidence of blood flow infection following catheterization | Use a checklist of steps to ensure sterile manipulation, with real-time verification of compliance by an independent observer and a daily reminder function to remove the catheter if it is no longer needed [34].   |
| Reducing the frequency of bedsores formed                           | Patient should be rolled over every two hours.   |
| Reduced incidence of stress ulcers and gastrointestinal bleeding    | Early enteral feeding (in the first 24-48 hours after hospitalization)   |

|  |  |
|--|--|
|  | Prescription of H2-histamine prescription blockers or proton pump inhibitors for patients with gastrointestinal bleeding risk factors. Gastrointestinal bleeding risk factors include $\geq 48$ hours of AVL, coagulopathy, kidney replacement therapy, liver disease, multiple concomitant diseases, and high organ failure index [35]. |
| Reducing the frequency of acquired weakness in OIT | The patient should be mobilised early as soon as it is safe to do so [36].   |

## 5.6. Special recommendations for pregnant patients management

Pregnant patients with possible or confirmed COVID-19 infection should be prescribed supporting therapy taking into account physiological changes during pregnancy.

Decisions on emergency delivery and abortion are complex and based on many factors: the period of pregnancy, the condition of the mother and the stability of the fetus. Obstetrician-gynecologists, neonatologists and intensive caregivers (depending on the state of the mother) are to be consulted (60).

## 5.7. Noninvasive oxygen support and inhaling

Mild respiratory illnesses patients caused by COVID-19, oxygen therapy can be performed using conventional devices (Figures 3,4,5) [33].

### Risks!

- Wearing a surgical mask over the nasal cannulas is mandatory!
- Injecting medication through the nasal lasers should also be avoided!
- Inhalants should be used to administer bronchodilators.
- Do not use CPAP/BiPAP modes [33].

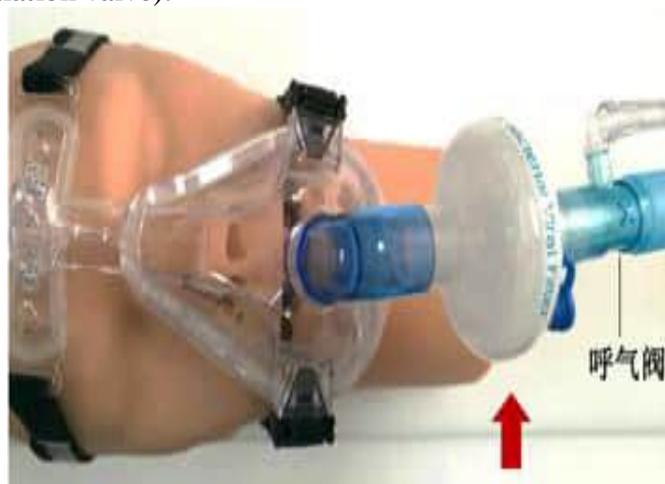
Picture 3. Transnasal high flow oxygen therapy  
A - not tight connection, B - correct connection



Picture 4. Non-invasive positive pressure ventilation, NPPV



Picture 5. Installation position of the bacterial/virus filter in a non-invasive positive pressure ventilation (between mask and exhalation valve).



## 5.8. AVL

- Intubation or resuscitation of patients requires special care and must be carried out in an air-insulated room! All staff members indoors must wear appropriate personal protective equipment against airway infections, including either N95 or PAPR mask tested for compliance [33].

- The intervention should be carefully planned. The procedure should be carried out by the person most experienced in the field of intubation using rapid sequential intubation.

- Movement of people bringing the equipment into the room may increase the risk of virus transmission [61].

- All necessary equipment and medications should be prepared in advance.

- The number of staff in the room during intubation should be kept to a minimum and include only the necessary members of the medical staff.

- AVL with an Ambu bag prior to intubation may cause airborne infection, as well as coughing up the patient during laryngoscopy.

- An exhalation filter, usually between the mask or endotracheal tube and the bag, should be attached to the intensive care bag.

- Inadequate sedation may also put the intubator at risk if the patient is panicking and the PPE is damaged.

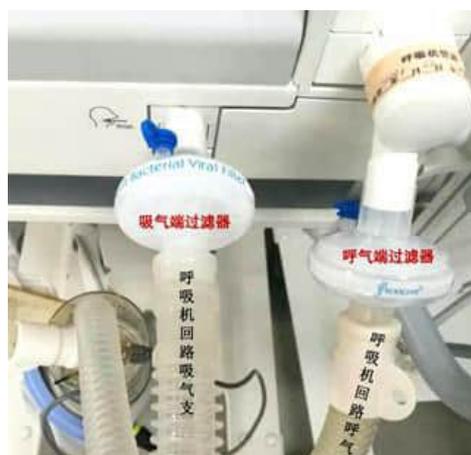
- With adequate pre-oxygenation, AVL can be avoided by using an Ambu bag before laryngoscopy.
- Video laryngoscopy should be performed with a screen separated from the blade (rather than placed, for example, on the handle), thus avoiding placing the intubator screen close to the patient.
- If the airways are difficult flexible bronchoscopic intubation can be performed using a video-bronchoscope with a screen remote from the patient.
- The location of the endotracheal tube should be confirmed by determining the partial carbon dioxide pressure in exhaled air at the end of exhalation. Personal protective equipment, especially PAPR, may interfere with auscultation to help confirm proper tube placement.
- After intubation, mechanical methods of artificial ventilation of the lungs should be used (target respiratory volume 6 ml/kg of calculated body weight, plateau pressure B 30 cm of water column, target SaO<sub>2</sub> level 88-95% and pH C 7,25) [62].
- All gas exhaled through the device must be filtered.
- Use a portable ultrasound device that allows you to quickly diagnose the pneumothorax (if suspected). Ultrasound is preferable to the patient's chest X-ray, taking into account time [33].

Pictures 6, 7, 8, and 9 demonstrate the peculiarities of connecting a bronchoscope, installing a bacterial filter, and connecting to a ventilator.

Picture 6. Circuit diagram for connection of the bronchoscope in case of invasive ventilation with positive pressure



Picture 7. Place of installation of bacterial / viral filter in invasive ventilation with positive pressure



Picture 8. Secure the endotracheal tube firmly before disconnecting the AVL invasive circuit



Picture 9. Position of the sieve sprayer with positive pressure invasive ventilation



### 5.8.1. AVL initial phase

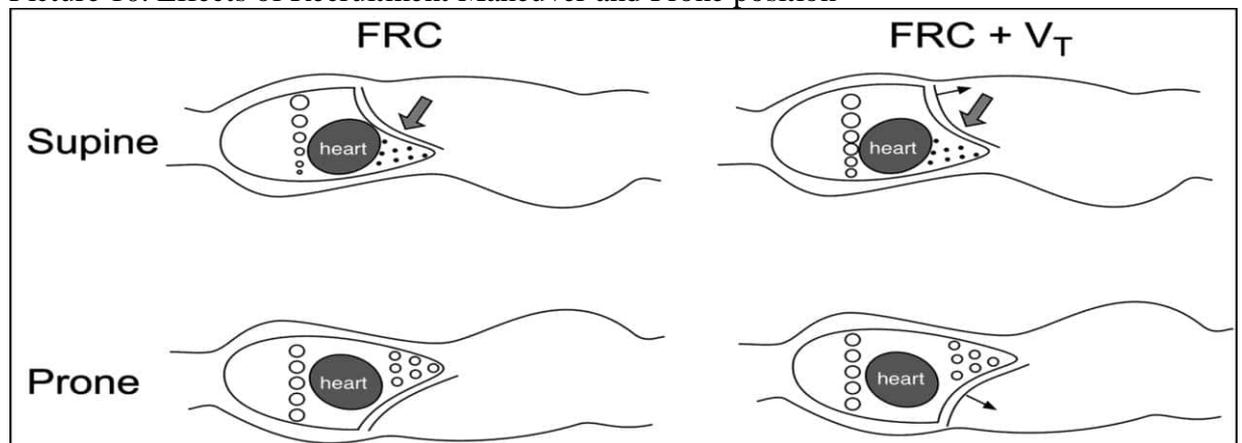
- At this stage, the patient is in deep sedation (e.g. propofol and opioids). Balanced or continuous myorelaxation may be required to ensure complete adaptation to the AVL machine [60].
- Perform the recruitment manoeuvre and adjust the AVL machine as follows:  
Start parameters: VCV mode, PEEP 14, VT 6-8 ml/kg BMT, respiration rate (RR) 15-25 min. Adjust FiO<sub>2</sub> to achieve SpO<sub>2</sub> of 92-95%. Adjust breathing rate with target pH 7.30 - 7.42. Avoid hypokapnia.

The aim of initial phase:

- SpO<sub>2</sub> 92-95%

- pH 7,30 - 7,42
- Pplat <28 cm H<sub>2</sub>O
- Driving pressure <12 cm H<sub>2</sub>O (Pplat-PEEP) - PaO<sub>2</sub>/FiO<sub>2</sub> > 120 [60].
- Pronation (prone position) should only be carried out by expert centres if there is a sufficient number of professionals in conditions of extremely serious gas exchange disruptions, despite the optimization of ventilation in the back position.
  - **Risks!** A prognostic manoeuvre performed by limited or inexperienced staff can in itself pose a great risk to the patient and therefore to the staff.
  - Patients should only be pronated if PaO<sub>2</sub>/FiO<sub>2</sub> remains <120 after optimization. The period of the abdominal position should be 12-16 hours. After that, the patient should be turned over to the back.
  - If severe hypoxemia persists after 8-10 hours and experienced staff are available, a second cycle may be considered.
  - **Risks!** The use of nitrogen oxide is NOT recommended. The positive effects on oxygenation are usually short-term, this therapy can be applied to very few patients and is not available at all prices.
  - Oxygenation improves rapidly with the start of AVL and its optimization. However, it is necessary to wait at least 48-72 hours before trying to switch to auxiliary ventilation.
  - For patients with severe ARDS, recruitment maneuver and prone position (Pictures 10, 11) is recommended to improve ventilation in unventilated areas of the lung and increase lung saturation [60].

Picture 10. Effects of Recruitment Maneuver and Prone position



Picture 11. Prone position



- minimum neck flexion
- face is on a soft ring, no pressure on eyes and nose
- elbow lining to avoid pressure on the elbow nerve
- no pressure on the armpit joint
- no pressure on the stomach
- shoulders in a small forward bend, retraction and external rotation position at an angle of less than 90 degrees

### 5.8.2. AVL stabilization phase

- After the initial phase of inflammation, lung instability lasts at least 48-72 hours, but often longer. [60].
- When the patient has a stable  $\text{PaO}_2/\text{FiO}_2 > 200$  with PEEP 12 cm of water column, it is possible to reduce the dose of sedatives until the RASS 0/-2 sedation level is reached and try to switch to a pressure assisted ventilation. Start ventilation in SIMV mode and gradually reduce the rate of forced inhalation. Consider setting the breathing rate to "Sigh" 1 act per minute, set the pressure assisted breathing (PS) to initially 8-10 cm of water column. [60].
- At this stage, the spontaneous breathing rate is allowed to be no more than 25 per minute, patients may make considerable effort to try to breathe; therefore, it is necessary to monitor the respiratory volume and  $\text{P.01}$ ,  $\text{P.01} < 3$  mbar and respiratory volume up to 10 ml / kg of calculated body weight are allowed [60].
- The transition to pressure-assisted ventilation can be problematic for two main reasons. First, even if gas exchange is stabilized and improved by invasive ventilation, the viral disease can still be in the acute phase, characterized by pneumonia. Secondly, the patient may wake up worried, jeopardizing the possibility of secondary ventilation. In both cases, it may be necessary to sedate the patient again in order to ventilate him in a protective, controlled manner. In some cases, the resumption of muscle relaxation may even be required [60].

Stabilization Phase Targets:

with SpO<sub>2</sub> 92-95%

with pH 7,35-7,42

with PaO<sub>2</sub>/FiO<sub>2</sub> > 200

- respiratory rate 10 - 25 per min
- P.01 <3 mbar
- spontaneous tidal volume of 6-10 ml/kg of the estimated body weight (anxiety with tidal volume > 800 ml) [60].

### 5.8.3. AVL stopping

- If PaO<sub>2</sub>/FiO<sub>2</sub> > 200 of the patient is stable on assisted ventilation, has good lung mechanics, reduce positive end-expiratory pressure by 2 cm H<sub>2</sub>O every 12 hours.

- When positive end-expiratory pressure ≤6 cm H<sub>2</sub>O with FiO<sub>2</sub> <0.4, PS <6 cm H<sub>2</sub>O, PaO<sub>2</sub>/FiO<sub>2</sub> > 200 and coordinated lung mechanics, make an attempt of extubation and breathing cycle with a constant positive airway pressure mask or non-invasive support [60].

### 5.8.4. Recruitment maneuver

Recruitment maneuver is performed to increase the saturation of patients with severe respiratory failure.

#### Mode 1

Carefully monitor blood pressure and be prepared to stop the recruitment maneuver in case of severe hypotension.

Set the ventilator to pressure monitoring mode: PEEP 15

Inflammatory pressure P<sub>insp</sub> + 20/25 cm of water column (In case of patients with body mass index > 30, consider using P<sub>insp</sub> 45 cm of water column).

Breathing rate: 10 in min I:E 1: 1

Continue for two minutes or 20 breathing acts, stop in case of hypotension.

#### Mode 2

Carefully monitor blood pressure and be prepared to stop the recruitment maneuver in case of severe hypotension (systolic pressure <70 mm Hg. Art.).

Set the ventilator to pressure monitoring mode: PEEP 14

P<sub>insp</sub> 15 cmH<sub>2</sub>O

Breath frequency 10 I:E 1: 1

Increase PEEP for 2 cmH<sub>2</sub>O every 30 seconds (5 actions) until PEEP 26.

At the end of the manoeuvre, adjust the fan according to the proposed layout.

#### Mode 3

Sustained inflation at P<sub>insp</sub> 40 cmH<sub>2</sub>O x 20 sec. [60].

## 5.9. Surgical aspects in COVID-19

- **Risks!** Excessive pressure maintained in the operating room may create a risk of virus spread when operating on a COVID-19-infected patient. It is advisable to create negative pressure with air exchange in the operating rooms if technically

possible. Procedures associated with a high risk of aerosol formation (e.g. intubation) should not be performed under overpressure [33].

- During the SARS outbreak, surgical procedures were performed in air-insulated areas in Department of Anesthesiology, Reanimation and Intensive Treatment (DARIT), eliminating the risk of hospital-acquired infection and helping to avoid the need to modify the operating rooms [33].

- In DARIT conditions, intravenous anesthesia is preferable to inhalation anesthesia, especially in those patients whose recovery and extubation is unlikely in the near future. [33, 63].

#### 5.10. Prevention and management of resuscitation / respiratory or cardiac arrest

**Table 4. Consideration of risks for resuscitation measures during coronavirus COVID-19 [33].**

|  |  |
|--|--|
| Reduced risk in resuscitation procedures                 | Increased risk in resuscitation procedures, mainly aerosol generators and/or increased risk of virus transmission to medical staff |
| Installation of an oropharyngeal duct                    | High-flow nasal cannula  |
| Application of an oxygen mask with an exhalation filter  | Ambu bag ventilation   |
| Compression of the chest                                 | CPAP/BIPAP   |
| Defibrillation, cardioversion, percutaneous stimulation  | Endotracheal intubation / airway surgery   |
| Obtaining venous or intraosseous access                  | Bronchoscopy   |
| Administration of intravenous gastro-resuscitation drugs | Endoscopy  |

- Patients infected with COVID-19 should be observed for early signs of respiratory deterioration and intubated routinely rather than urgently. [33].

- Isolated patients with COVID-19 should be placed in a critical care unit with air-insulated and permanently monitored physiological condition. By using insulation, it is possible to minimize the time spent by nursing staff in potentially harmful environments during exams and nursing care.

- Four people, each with his or her assigned responsibilities, may participate in intensive care.
- Use a specialized trolley with modular equipment stacking. In this case, the crew can take the required defibrillator and paving into the box instead of driving the entire trolley.
- After the resuscitation, the team members can leave the box at a suitable time and remove the PPE according to the checklist under the supervision of an instructor to avoid self-infection. [33, 64].

### **5.11. Antibiotic therapy**

- Empirical antibiotic therapy for outpatient pneumonia IS NOT ACCEPTED on admission to the intensive care unit in patients with interstitial pneumonia and positive SARS-COV-2 testing. [60, 65].
- Any antibiotics initiated in other departments should be discontinued unless there is clear evidence of co-infection of bacterial infection (purulent discharge, microbiological data). For patients with COPD exacerbation, the decision to continue antibiotic therapy should be made on an individual basis. [60].
- Patients with COVID-19 have low platelet count (PCT) in the absence of concomitant bacterial infection. This biomarker can be used as an indicator of bacterial infection in patients with COVID-19. [60, 66].
- In the Intensive Care Unit, it is useful, where possible, to perform bacterial sowing both on admission to the hospital and during patient monitoring. [60].
- When COVID-19 infection develops, it is likely to activate a fungal infection, which significantly worsens the prognosis against the background of lower immunity indices. We consider it advisable to include antimicrobial agents in the composition of complex intensive care in accordance with clinical indications in standard therapeutic dosages. [60, 67].

### **5.12. Steroids**

- Steroids are currently NOT recommended for treatment of patients with COVID-19, but are not contraindicated for any other indications other than COVID-19 [60, 68].
- Pulse therapy with corticosteroids is applicable as a component of septic shock treatment [60, 69].

### **5.13. Surfactant**

If possible, a surfactant preparation (e.g. Kurosulf) is used endotracheally in conjunction with AVL. The data obtained indicate a significant improvement of respiratory function indices in ARDS in the early period after administration. [70, 71].

#### 5.14. Temperature control

- If the fever is not accompanied by cardiovascular or respiratory disorders, it can be transferred by the patient, otherwise paracetamol 1 g intravenously is prescribed.
- Avoid using paracetamol at a fixed time so as not to mask the temperature curve dynamics.
- **Risks!** Ibuprofen and Voltaren should not be administered, there is evidence of virus activation and deterioration of the clinic. [60].

#### 5.15. Sedation

- **Risks!** Patients with COVID-19 receiving lopinavir/ritonavir or aluvia should avoid the prescription of benzodiazepines as far as possible, as lopinavir/ritonavir or aluvia unpredictably increases their effect and duration of their effects. [60].
- Lopinavir/ritonavir also enhances the effect of fentanyl [60].
- Sedation may be as follows: Propofol + opioid analgesic [60].
- It is possible to add a combination of ketamine to reduce sedative and opioid use [60].
- **Risks!** Avoid other sedatives, reserve antipsychotic drugs for documented cases of delirium, try to avoid Kvetiapin when using lopinavir/ritonavir because of the high level of interaction. [60].
- Every day after the initial phase of deep sedation, try to stop the infusion for at least 2 hours and resume it, if necessary, in half dose. [60].
- If immediate sedation is required (e.g. for the care of a patient who has been moved to a lying down position (pron position), etc.), administer 20-40 mg of propofol (bolus dose). [60, 72].

#### 5.16. Myorelaxation

- Painful or continuous infusion may be useful in the reverse-version phase of the disease to adapt to artificial lung ventilation. The duration of this phase seems to vary from 24 to 98 hours. If necessary, use Cisatracurium (0.1-0.2 mg / kg / hour) or Rocuronium (Esmeron) (0.2-0.6 mg / kg / hour) in continuous infusion [60].
- There are no contraindications to the use of arduan, tractorium and other myorelaxants [60].
- The earliest possible transfer to spontaneous respiration is recommended because of the higher risk of AVL complications [60].

#### 5.17. Nutrition

Both SARS-COV-2 and some antiviral drugs (retino-virus) can cause diarrhea. Despite this, the gastrointestinal tract seems to be functioning normally. Therefore, start with early enteral feeding, which should be maintained both lying on the back and lying on the stomach. Start at 20 ml/h, if well tolerated, increase to 40-60 ml/h in the first 24 hours. [60, 73].

### 5.18. Infusion therapy

- At early stages, balanced solutions (Ringer-Lactate or Rehydrating III) should be injected to ensure adequate perfusion (diuresis > 0.5 ml/kg/h and lactate < 2 mmol/l) [60].
- However, a positive water balance is often required in the first 48 hours. At this stage, it is inappropriate and possibly counterproductive (renal failure, electrolyte imbalance) to force diuresis and prescribe diuretics [60].
- Subsequently, when respiratory function is stabilized, stimulation of diuresis may be considered [60].

### 5.19. Inotropic support

- For vasodilation caused by medication or if required for other reasons, low doses of noradrenaline (0.05-0.1 µg/kg/min) should be preferred in order to achieve an average blood pressure > 65 mmHg. [60].
- Higher levels of Systolic blood pressure should be sought in patients with hypertension [60].
- If a high dose of noradrenaline is needed to achieve the values, in the absence of marked tachycardia, consider administering dopamine in an indicative dose of 4-10 µg/kg/min. [60].

### 5.20. Incident atrial fibrillation

- Certain precautions should be taken in case of first-time atrial fibrillation paroxysm and in patients with permanent atrial fibrillation. **Firstly, Risks!** Amiodarone should NOT be used due to its interaction with the ritonavir and the risk of serious arrhythmias. [60].
- Therefore, give preference to electric cardioversion (100-200 J). [60].

### 5.21. Example of patient management with COVID-19 in DARIT

**Table 5. Sample of therapy for a COVID-19 patient**

| Antiviral therapy   | Medicine  | Dosage                               | Way of entrance                                | Time of entrance                      |
|---------------------|---|--------------------------------------|--|---------------------------------------|
|                     | Lopinavir/Ritonavir [74]  | 400 mg 14 daily and 100 mg 14 daily  | Per os, including the nasogastric probe.       | in 12 h                               |
|                     | Chloroquine [75]  | 500 mg 14 daily                      | Per os, including the nasogastric probe.       | in 12 h                               |
|                     | Or  |                                      |  |                                       |
|                     | Hydroxychloroquine  | 200 mg 14 daily                      |  | in 12 h                               |
| Other               | Low molecular weight heparin [76, 77]                                 | As instructed, APPT, IHR control     | IV or s/c                                      | As instructed                         |
|                     | Proton Pump Blocker Drug  | therapeutically dosed                | As instructed                                  | As instructed                         |
|                     | Or  |                                      |  |                                       |
|                     | H2-Histamine receptor inhibitors                                      | therapeutically dosed                | As instructed                                  | As instructed                         |
|                     | Vitamin B1 supplement   | 200 mg                               | IV   | in 12 h                               |
|                     | Vitamin K1 supplement   | therapeutically dosed                | As instructed                                  | As instructed                         |
|                     | Vitamin C supplement [78]   | Up to 1,5 g daily                    | IV   | in 12 h                               |
|                     | Surfactant  | 120-200 mg                           | Endotracheal                                   | once                                  |
| Sedation            | Propofol  | 1-3 mg/kg/per hour                   | IV   | individually                          |
| Miorelaxation       | Suxametonium (lesthene, ditylene, succinylcholine)                    | Bolus according to body mass         | IV   | once for intubation                   |
|                     | Cisatracurium   | 0,1-0,2 mg/kg/per hour               | IV   | individually, depending on the course |
| <b>Vasopression</b> | Noradrenaline   | 0.05-0.1 mkg/kg/min                  | IV   | individually, depending on the course |
| Solutions           | Ringer's Solution   | according to body mass and condition | IV   | individually, depending on the course |
|                     | Physiological solution NaCl   | according to body mass and condition | IV   | individually, depending on the course |
| Feeding             | Any universal feed mixtures for probe feeding Or parenteral nutrition | according to body mass               | Per os, including the nasogastric probe.<br>IV | individually, depending on the course |

|               |                  |                           |    |   |
|---------------|------------------|---------------------------|----|---|
|               |                  | according to<br>body mass |    | individually,<br>depending on the<br>course |
| Antimicrotics | Fluconazole [79] | 150 mg                    | IV | in 48 h                                     |

## 5.22. Patient performance monitoring

- We are facing an increasingly limited number of medical personnel. Therefore, we have to accept a decline in the usual standards of care. It seems reasonable to us that in intensive care units where there is no electronic system for automatic collection of patients' indices, data (blood pressure, heart rate, urine, SpO<sub>2</sub>, respiration rate) can be recorded every 3-4 hours, and at night it may be sufficient to take these parameters off once every 4-6 hours [60].

- Obviously, it is the task of the medical personnel to set the alarms of the blood pressure monitor and the ventilator [60].

- Patient counseling by specialists and monitoring can be performed by means of telemedical systems, if technical capabilities are available [80].

## Bibliography

1. Stop the Wuhan virus. *Nature*. 2020 Jan;577(7791):450. doi:10.1038/d41586-020-00153-x.
2. Hui DS, I Azhar E, Madani TA, Ntoumi F, Kock R, Dar O, Ippolito G, Mchugh TD, Memish ZA, Drosten C, Zumla A, Petersen E. The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health - The latest 2019 novel coronavirus outbreak in Wuhan, China. *Int J Infect Dis*. 2020 Feb;91:264-266. doi: 10.1016/j.ijid.2020.01.009.
3. Biscayart C, Angeleri P, Lloveras S, Chaves TDSS, Schlagenhaut P, Rodríguez-Morales AJ. The next big threat to global health? 2019 novel coronavirus (2019-nCoV): What advice can we give to travellers? - Interim recommendations January 2020, from the Latin-American society for Travel Medicine (SLAMVI). *Travel Med Infect Dis*. 2020 Jan - Feb;33:101567. doi: 10.1016/j.tmaid.2020.101567.
4. Heymann DL, Shindo N; WHO Scientific and Technical Advisory Group for Infectious Hazards. COVID-19: what is next for public health? *Lancet*. 2020 Feb 22;395(10224):542-545. doi: 10.1016/S0140-6736(20)30374-3.
5. Lai CC, Shih TP, Ko WC, Tang HJ, Hsueh PR. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges. *Int J Antimicrob Agents*. 2020 Mar;55(3):105924. doi: 10.1016/j.ijantimicag.2020.105924.
6. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, Liu L, Shan H, Lei CL, Hui DSC, Du B, Li LJ, Zeng G, Yuen KY, Chen RC, Tang CL, Wang T, Chen PY, Xiang J, Li SY, Wang JL, Liang ZJ, Peng YX, Wei L, Liu Y, Hu YH, Peng P, Wang JM, Liu JY, Chen Z, Li G, Zheng ZJ, Qiu SQ, Luo J, Ye CJ, Zhu SY, Zhong NS; China Medical Treatment Expert Group for Covid-19. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med*. 2020 Feb 28. doi: 10.1056/NEJMoa2002032.
7. Kobayashi T, Jung SM, Linton NM, Kinoshita R, Hayashi K, Miyama T, Anzai A, Yang Y, Yuan B, Akhmetzhanov AR, Suzuki A, Nishiura H. Communicating the Risk of Death from Novel Coronavirus Disease (COVID-19). *J Clin Med*. 2020 Feb 21;9(2). pii: E580. doi: 10.3390/jcm9020580.
8. de Wilde AH, Snijder EJ, Kikkert M, van Hemert MJ. Host Factors in Coronavirus Replication. *Curr Top Microbiol Immunol*. 2018;419:1-42. doi: 10.1007/82\_2017\_25.
9. Aho LS, Simon I, Bour JB, Morales-Gineste L, Pothier P, Gouyon JB. Epidemiology of viral nosocomial infections in pediatrics. *Pathol Biol (Paris)*. 2000 Dec;48(10):885-92.
10. Su S, Wong G, Shi W, Liu J, Lai ACK, Zhou J, Liu W, Bi Y, Gao GF. Epidemiology, Genetic Recombination, and Pathogenesis of Coronaviruses. *Trends Microbiol*. 2016 Jun;24(6):490-502. doi: 10.1016/j.tim.2016.03.003.
11. Chan-Yeung M, Xu RH. SARS: epidemiology. *Respirology*. 2003 Nov;8 Suppl:S9-14.
12. Lam WK, Zhong NS, Tan WC. Overview on SARS in Asia and the world. *Respirology*. 2003 Nov;8 Suppl:S2-5.
13. Graham RL, Donaldson EF, Baric RS. A decade after SARS: strategies for controlling emerging coronaviruses. *Nat Rev Microbiol*. 2013 Dec;11(12):836-48. doi: 10.1038/nrmicro3143.
14. Hajjar SA, Memish ZA, McIntosh K. Middle East Respiratory Syndrome Coronavirus (MERS-CoV): a perpetual challenge. *Ann Saudi Med*. 2013 Sep-Oct;33(5):427-36. doi: 10.5144/0256-4947.2013.427.
15. Shapiro M, London B, Nigri D, Shoss A, Zilber E, Fogel I. Middle East respiratory syndrome coronavirus: review of the current situation in the world. *Disaster Mil Med*. 2016 May 4;2:9. doi: 10.1186/s40696-016-0019-2.
16. Zheng J SARS-CoV-2: an Emerging Coronavirus that Causes a Global Threat. *Int J Biol Sci*. 2020 Mar 15;16(10):1678-1685. doi: 10.7150/ijbs.45053. eCollection 2020.
17. Srinivasan S, Cui H, Gao Z, Liu M, Lu S, Mkandawire W, Narykov O, Sun M, Korkin D. Structural Genomics of SARS-CoV-2 Indicates Evolutionary Conserved Functional Regions of Viral Proteins. *Viruses*. 2020 Mar 25;12(4). pii: E360. doi: 10.3390/v12040360.

18. Gheblawi M, Wang K, Viveiros A, Nguyen Q, Zhong JC, Turner AJ, Raizada MK, Grant MB, Oudit GY. Angiotensin Converting Enzyme 2: SARS-CoV-2 Receptor and Regulator of the Renin-Angiotensin System. *Circ Res*. 2020 Apr 8. doi: 10.1161/CIRCRESAHA.120.317015.
19. Danser AH. Local renin-angiotensin systems: the unanswered questions. *Int J Biochem Cell Biol*. 2003 Jun;35(6):759-68.
20. Brojakowska A, Narula J, Shimony R, Bander J. Clinical Implications of SARS-Cov2 Interaction with Renin Angiotensin System. *J Am Coll Cardiol*. 2020 Apr 14. pii: S0735-1097(20)35001-4. doi: 10.1016/j.jacc.2020.04.028.
21. Asadi-Pooya AA, Simani L. Central nervous system manifestations of COVID-19: A systematic review. *J Neurol Sci*. 2020 Apr 11;413:116832. doi: 10.1016/j.jns.2020.116832.
22. Di Gennaro F, Pizzol D, Marotta C, Antunes M, Racalbutto V, Veronese N, Smith L. Coronavirus Diseases (COVID-19) Current Status and Future Perspectives: A Narrative Review. *Int J Environ Res Public Health*. 2020 Apr 14;17(8). pii: E2690. doi: 10.3390/ijerph17082690.
23. Siordia JA Jr. Epidemiology and clinical features of COVID-19: A review of current literature. *J Clin Virol*. 2020 Apr 10;127:104357. doi: 10.1016/j.jcv.2020.104357.
24. Cheng ZJ, Shan J. 2019 Novel coronavirus: where we are and what we know. *Infection*. 2020 Apr;48(2):155-163. doi: 10.1007/s15010-020-01401-y.
25. Kannan S, Shaik Syed Ali P, Sheeza A, Hemalatha K. COVID-19 (Novel Coronavirus 2019) - recent trends. *Eur Rev Med Pharmacol Sci*. 2020 Feb;24(4):2006-2011.
26. Gardner M. NRW launches COVID-19 research on disease prevention. *University World News* 07 April 2020 <https://www.universityworldnews.com/post.php?story=20200407113355442>.
27. Lin L, Jiang X, Zhang Z, Huang S, Zhang Z, Fang Z, Gu Z, Gao L, Shi H, Mai L, Liu Y, Lin X, Lai R, Yan Z, Li X, Shan H. Gastrointestinal symptoms of 95 cases with SARS-CoV-2 infection. *Gut*. 2020 Apr 2. pii: gutjnl-2020-321013. doi: 10.1136/gutjnl-2020-321013.
28. Heinzerling A, Stuckey MJ, Scheuer T, Xu K, Perkins KM, Resseger H, Magill S, Verani JR, Jain S, Acosta M, Epton E. Transmission of COVID-19 to Health Care Personnel During Exposures to a Hospitalized Patient - Solano County, California, February 2020. *MMWR Morb Mortal Wkly Rep*. 2020 Apr 17;69(15):472-476. doi: 10.15585/mmwr.mm6915e5.
29. Izzetti R, Nisi M, Gabriele M, Graziani F. COVID-19 Transmission in Dental Practice: Brief Review of Preventive Measures in Italy. *J Dent Res*. 2020 Apr 17:22034520920580. doi: 10.1177/0022034520920580.
30. Jinnong Zhang†, Luqian Zhou†, Yuqiong Yang†, Wei Peng, Wenjing Wang, Xuelin Chen Therapeutic and triage strategies for 2019 novel coronavirus disease in fever clinics Published Online February 13, 2020 [https://doi.org/10.1016/S2213-2600\(20\)30071-0](https://doi.org/10.1016/S2213-2600(20)30071-0).
31. COVID-19 pandemic: triage for intensive-care treatment under resource scarcity. *Swiss Med Weekly*. 2020;150:w20229.
32. Li Y, Huang X, Yu IT, Wong TW, Qian H. Role of air distribution in SARS transmission during the largest nosocomial outbreak in Hong Kong. *Indoor Air* 2005; 15: 83-95.
33. Randy S. Wax, Michael D. Christian Practical recommendations for critical care and anesthesiology teams caring for novel coronavirus (2019-nCoV) patients *Canadian Journal of Anesthesia/Journal canadien d'anesthésie* 2020 Feb 12. doi: 10.1007/s12630-020-01591-x.
34. Government of Canada. Interim national case definition: novel coronavirus (2019-nCoV). Available from URL: <https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirusinfection/health-professionals/national-case-definition.html> (accessed February 2020).
35. Novak D. Why, where, and how PAPRs are being used in health care. In: Institute of Medicine. The Use and Effectiveness of Powered Air Purifying Respirators in Health Care: Workshop Summary - 2015. Washington, DC: The National Academies Press.
36. Infection prevention and control of epidemic-and pandemic prone acute respiratory infections in health care [[http://www.who.int/csr/bioriskreduction/infection\\_control/publication/en/](http://www.who.int/csr/bioriskreduction/infection_control/publication/en/)]. Geneva: WHO; 2014.

37. Infection prevention and control during health care for probable or confirmed cases of Middle East respiratory syndrome coronavirus (MERS-CoV) infection: Interim guidance. Geneva: WHO; 2015.
38. Clinical Guidelines for the Management of Patients with Severe Acute Respiratory Infection in the Event of Suspicion of New Coronavirus (nCOV) Temporary recommendations 25 January 2020.
39. ARDS Definition Task Force, Ranieri VM, Rubenfeld GD, et al. Acute respiratory distress syndrome: the Berlin Definition. *JAMA* 2012;307:2526-33.
40. Khemani RG, Smith LS, Zimmerman JJ, Erickson S, Pediatric Acute Lung Injury Consensus Conference Group. Pediatric acute respiratory distress syndrome: definition, incidence, and epidemiology: proceedings from the Pediatric Acute Lung Injury Consensus Conference. *Pediatr Crit Care Med* 2015;16:S23-40.
41. Riviello ED, Kiviri W, Twagirumugabe T, et al. Hospital Incidence and Outcomes of the Acute Respiratory Distress Syndrome Using the Kigali Modification of the Berlin Definition. *Am J Respir Crit Care Med* 2016;193:52-9.
42. Goldstein B, Giroir B, Randolph A, International Consensus Conference on Pediatric Sepsis. International pediatric sepsis consensus conference: definitions for sepsis and organ dysfunction in pediatrics. *Pediatr Crit Care Med* 2005;6:2-8.
43. Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA* 2016;315:801-10.
44. 27 Davis AL, Carcillo JA, Aneja RK, et al. American College of Critical Care Medicine Clinical Practice Parameters for Hemodynamic Support of Pediatric and Neonatal Septic Shock. *Crit Care Med* 2017;45:1061-93.
45. Pocket book of hospital care for children: Guidelines for the management of common childhood illnesses [\[http://www.who.int/maternal\\_child\\_adolescent/documents/child\\_hospital\\_care/en/\]](http://www.who.int/maternal_child_adolescent/documents/child_hospital_care/en/). 2nd ed. Geneva: WHO; 2013.
46. Rosjo H, Varpula M, Hagve TA, et al. Circulating high sensitivity troponin T in severe sepsis and septic shock: distribution, associated factors, and relation to outcome. *Intensive Care Med* 2011;37:77-85.
47. Oxygen therapy for children: a manual for health workers [\[http://www.who.int/maternal\\_child\\_adolescent/documents/child](http://www.who.int/maternal_child_adolescent/documents/child)
48. Schultz MJ, Dunser MW, Dondorp AM, et al. Current challenges in the management of sepsis in ICUs in resource-poor settings and suggestions for the future. *Intensive Care Med* 2017;43:612-24.
49. Rhodes A, Evans LE, Alhazzani W, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. *Intensive Care Med* 2017;43:304-77.
50. Guerin C, Reignier J, Richard JC, et al. Prone positioning in severe acute respiratory distress syndrome. *N Engl J Med* 2013;368:2159-68.
51. Messerole E, Peine P, Wittkopp S, Marini JJ, Albert RK. The pragmatics of prone positioning. *Am J Respir Crit Care Med* 2002;165:1359-63.
52. National Heart L, and Blood Institute Acute Respiratory Distress Syndrome Clinical Trials Network,, Wiedemann HP, Wheeler AP, et al. Comparison of two fluid-management strategies in acute lung injury. *N Engl J Med* 2006;354:2564-75. 72 National Heart L, and Blood Institute Acute Respiratory Distress Syndrome Clinical Trials Network,, Wiedemann HP, Wheeler AP, et al. Comparison of two fluid-management strategies in acute lung injury. *N Engl J Med* 2006;354:2564-75.
53. Garcia PCR, Tonial CT, Piva JP. Septic shock in pediatrics: the state-of-the-art. *J Pediatr (Rio J)*. 2020 Mar - Apr;96 Suppl 1:87-98. doi: 10.1016/j.jpmed.2019.10.007.
54. Lamontagne F, Meade MO, Hebert PC, et al. Higher versus lower blood pressure targets for vasopressor therapy in shock: a multicentre pilot randomized controlled trial. *Intensive Care Med* 2016;42:542-50.

55. Musa N, Murthy S, Kissoon N, Lodha R, Ranjit S. Pediatric Sepsis and Septic Shock Management in Resource-Limited Settings. In: Dondorp AM, Dünser MW, Schultz MJ, editors. *Sepsis Management in Resource-limited Settings* [Internet]. Cham (CH): Springer; 2019. Chapter 10.
56. Loubani OM, Green RS. A systematic review of extravasation and local tissue injury from administration of vasopressors through peripheral intravenous catheters and central venous catheters. *J Crit Care* 2015;30:653 e9-17.
57. Klompas M, Branson R, Eichenwald EC, et al. Strategies to prevent ventilator-associated pneumonia in acute care hospitals: 2014 update. *Infect Control Hosp Epidemiol* 2014;35:915-36.
58. Muscedere J, Dodek P, Keenan S, et al. Comprehensive evidence-based clinical practice guidelines for ventilator-associated pneumonia: prevention. *J Crit Care* 2008;23:126-37.
59. Marschall J, Mermel LA, Fakih M, et al. Strategies to prevent central line-associated bloodstream infections in acute care hospitals: 2014 update. *Infect Control Hosp Epidemiol* 2014;35:753-71.
60. Treatment of patients with COVID-19 in critical condition. Research group on treatment of seriously ill patients at Covid-19 of Niguarda Ca 'Granda hospitals and IRCCS Ca' Granda Ospedale Maggiore Policlinico fund, Milano Niguarda 15/03/20.
61. Cocoros NM, Klompas M. Ventilator-Associated Events and Their Prevention. *Infect Dis Clin North Am.* 2016 Dec;30(4):887-908. doi: 10.1016/j.idc.2016.07.002.
62. Gottlieb M, Holladay D, Burns KM, Nakitende D, Bailitz J. Ultrasound for airway management: an evidence-based review for the emergency clinician. *Am J Emerg Med* 2019; DOI: <https://doi.org/10.1016/j.ajem.2019.12.019>.
63. Rupp ME, Karnatak R. Intravascular Catheter-Related Bloodstream Infections. *Infect Dis Clin North Am.* 2018 Dec;32(4):765-787. doi: 10.1016/j.idc.2018.06.002.
64. Barbateskovic M, Marker S, Jakobsen JC, Krag M, Granholm A, Anthon CT, Perner A, Wetterslev J, Møller MH. Stress ulcer prophylaxis in adult intensive care unit patients - a protocol for a systematic review. *Acta Anaesthesiol Scand.* 2018 Jul;62(6):744-755. doi: 10.1111/aas.13109.
65. Stam HJ, Stucki G, Bickenbach J. Covid-19 and Post Intensive Care Syndrome: A Call for Action. *J Rehabil Med.* 2020 Apr 15;52(4):jrm00044. doi: 10.2340/16501977-2677.
66. Kranke P, Weibel S, Sitter M, Meybohm P, Girard T. Obstetric Anesthesia During the SARS-CoV-2 Pandemic - a Brief Overview of Published Recommendations for Action by National and International Specialist Societies and Committees. *Anesthesiol Intensivmed Notfallmed Schmerzther.* 2020 Apr;55(4):266-274. doi: 10.1055/a-1144-5562.
67. Phua J, Weng L, Ling L, Egi M, Lim CM, Divatia JV, Shrestha BR, Arabi YM, Ng J, Gomersall CD, Nishimura M, Koh Y, Du B; Asian Critical Care Clinical Trials Group. Intensive care management of coronavirus disease 2019 (COVID-19): challenges and recommendations. *Lancet Respir Med.* 2020 Apr 6. pii: S2213-2600(20)30161-2. doi: 10.1016/S2213-2600(20)30161-2.
68. Thomas-Rüddel D, Winning J, Dickmann P, Quart D, Kortgen A, Janssens U, Bauer M. Coronavirus disease 2019 (COVID-19): update for anesthesiologists and intensivists March 2020. *Anaesthesist.* 2020 Mar 24. doi: 10.1007/s00101-020-00760-3.
69. Pandit A, Gupta N, Madan K, Bharti SJ, Kumar V. Anaesthetic considerations for whole lung lavage for pulmonary alveolar proteinosis. *Ghana Med J.* 2019 Sep;53(3):248-251. doi: 10.4314/gmj.v53i3.9.
70. Society of Pediatrics, China Medical Association, Editorial Board, Chinese Journal of Pediatrics. Recommendations for the diagnosis, prevention and control of new coronavirus infection in children in 2019 (first interim publication). *Chin J Pediatr.* 2020; 58 (3): 169 - 174.
71. Rosenberg O.A. Pulmonary surfactant preparations and surfactant therapy of ARDS in conditions of surgical resuscitation (literature review). *Creative Surgery and Oncology.* 2019. T9, №1. <https://doi.org/10.24060/2076-3093-2019-9-1-50-65>.
72. Eleveld DJ, Colin P, Absalom AR, Struys MMRF. Pharmacokinetic-pharmacodynamic model for propofol for broad application in anaesthesia and sedation. *Br J Anaesth.* 2018 May;120(5):942-959. doi: 10.1016/j.bja.2018.01.018.

73. Reintam Blaser A, Starkopf J, Alhazzani W, et al; ESICM Working Group on Gastrointestinal Function. Early enteral nutrition in critically ill patients: ESICM clinical practice guidelines. *Intensive Care Med.* 2017 Mar;43(3):380-398. doi: 10.1007/s00134-016-4665-0.
74. Zheng XW, Tao G, Zhang YW, Yang GN, Huang P. Drug interaction monitoring of lopinavir / ritonavir in COVID-19 patients with cancer. *Zhonghua Nei Ke Za Zhi.* 2020 Mar 1;59(0):E004. doi: 10.3760/cma.j.cn112138-20200219-00097.
75. Smit C, Peeters MYM, van den Anker JN, Knibbe CAJ. Chloroquine for SARS-CoV-2: Implications of Its Unique Pharmacokinetic and Safety Properties. *Clin Pharmacokinet.* 2020 Apr 18. doi: 10.1007/s40262-020-00891-1.
76. Testa S, Paoletti O, Giorgi-Pierfranceschi M, Pan A. Switch from oral anticoagulants to parenteral heparin in SARS-CoV-2 hospitalized patients. *Intern Emerg Med.* 2020 Apr 15. doi: 10.1007/s11739-020-02331-1.
77. Thachil J. The versatile heparin in COVID-19. *J Thromb Haemost.* 2020 Apr 2. doi: 10.1111/jth.14821.
78. Carr AC. A new clinical trial to test high-dose vitamin C in patients with COVID-19. *Crit Care.* 2020 Apr 7;24(1):133. doi: 10.1186/s13054-020-02851-4.
79. Gangneux JP, Bougnoux ME, Dannaoui E, Cornet M, Zahar JR. Invasive fungal diseases during COVID-19: We should be prepared. *J Mycol Med.* 2020 Apr 6:100971. doi: 10.1016/j.mycmed.2020.100971.
80. Chauhan V, Galwankar S, Arquilla B, Garg M, Somma SD, El-Menyar A, Krishnan V, Gerber J, Holland R, Stawicki SP. Novel Coronavirus (COVID-19): Leveraging Telemedicine to Optimize Care While Minimizing Exposures and Viral Transmission. *J Emerg Trauma Shock.* 2020 Jan-Mar;13(1):20-24. doi: 10.4103/JETS.JETS\_32\_20.

TEAR SHEET  
considering the effectiveness of the guidelines  
**"INTENSIVE THERAPY OF PATIENTS WITH CORONAVIRUS  
INFECTION"**

Should be sent to: 071400, East-Kazakhstan Region, Semey, 103 Abay Kunanbayev street, E-mail: smu@nao-mus.kz, to the Chairman of the Board-Rector Y.Zhunossov, MD

1. "Patient intensive care with a coronavirus infection"
2. Confirmed by the Academic Committee of HNCJSC "SMU"
3. Application outcomes:

- positive \_\_\_\_\_  
number of observations
- indefinite \_\_\_\_\_  
number of observations
- negative \_\_\_\_\_  
number of observations

Observation was held from "\_\_\_" \_\_\_ 2020 to "\_\_\_" \_\_\_ 202\_

4. Remarks and feedback (in words): \_\_\_\_\_
- 
- 

5. Person, responsible for implementation \_\_\_\_\_

Filling date

Signature

To be filled in by the institution applying the guidelines.

M.K.Syzdykbayev, S.Z.Tanatarov, Y.T.Zhunossov

**Methodological guidelines**

**INTENSIVE THERAPY OF PATIENTS WITH CORONAVIRUS  
INFECTION**

Link to access:

<https://semeymedicaluniversity.kz/koronavirus/#1585560446666-1c3e748c-ac8a>

Signed to print 22.04.2020

Format 60x84 1/16. Offset paper  
Circulation 100. Price: 1830 tenge.

Printed at the printing house of NCJSC “Semey Medical University”  
071400, Semey, 103 Abay street.