# Evidence Search Service Results of your search request

## HFNC as aerosol generating procedure

**ID of request:** 24344  
**Date of request:** 9th July, 2020  
**Date of completion:** 16th August, 2020

If you would like to request any articles or any further help, please contact:  Igor Brbre at [igor.brbre@nhs.net](mailto:igor.brbre@nhs.net)

Please acknowledge this work in any resulting paper or presentation as: Evidence search: HFNC as aerosol generating procedure. Igor Brbre. (16th August, 2020). BRIGHTON, UK: Brighton and Sussex Library and Knowledge Service.

**Sources searched**  
EMBASE (44)  
Europe PMC (11)  
Google (Advanced) (2)  
MEDLINE (26)  
PubMed (10)  
Scopus (58)  
TRIP Database (14)

**Date range used** (5 years, 10 years): no restrictions   
**Limits used** (gender, article/study type, etc.): none   
**Search terms and notes** (full search strategy for database searches below):

Relevant natural language terms were identified, selected and combined. Search strategies were adapted to the search facilities of the medical information resources used. Medline and Embase searched on OVID. Results were de-duplicated in EndNote. **No relevance screening done.** Full search strategy below.

Database search results pre-deduplication count:

MEDLINE 26

EMBASE 62

PUBMED 37

SCOPUS 93

Europe PMC 11 (pre-print)

De-duplicated = 149

TRIP Database search strategy: "hfnc aerosol"~10

Euro PMC search strategy:

((((TITLE:("Oxygen therapy") OR ABSTRACT:("Oxygen therapy")) OR (TITLE:(Respirat\* OR ventilat\*) AND (artificial OR mechanical) OR ABSTRACT:(Respirat\* OR ventilat\*) AND (artificial OR mechanical)) OR (TITLE:((Noninvasive OR "non invasive") AND ventilation) OR ABSTRACT:((Noninvasive OR "non invasive") AND ventilation))) AND ((TITLE:(("high flow" OR “high-flow” OR highflow OR nasal\*) AND (canula OR Cannula)) OR (nasal AND ("high flow" OR “high-flow” OR highflow OR prong)) OR (hfnc OR hnc OR HHHF OR HFNO OR HFNOT OR HHFNC) OR (Vapotherm OR Optiflow OR Airvo)) OR (ABSTRACT: (("high flow" OR “high-flow” OR highflow OR nasal\*) AND (canula OR Cannula)) OR (nasal AND ("high flow" OR “high-flow” OR highflow OR prong)) OR (hfnc OR hnc OR HHHF OR HFNO OR HFNOT OR HHFNC) OR (Vapotherm OR Optiflow OR Airvo)))) AND (TITLE:((aerosol\* OR “bio-aerosol” OR "bio aerosol" OR cough\* OR droplet\*) AND (generat\* OR induc\* OR disper\* OR stimulat\* OR produc\* OR spread\*)) OR ABSTRACT:((aerosol\* OR “bio-aerosol” OR "bio aerosol" OR cough\* OR droplet\*) AND (generat\* OR induc\* OR disper\* OR stimulat\* OR produc\* OR spread\*)))) AND (SRC:PPR)

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* PeerJ Preprints
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For more information about the resources please go to: <https://www.bsuh.nhs.uk/library/>.

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### [E. Search History](#SearchHistory)

## A. National and International Guidance

#### Canadian Anesthesiologists’ Society

**COVID-19 recommendations during airway manipulation** (2020)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=20aeee9beeea1262fe61a47e975a3f61)

#### Centre for Evidence-Based Practice, Penn Medicine

**COVID-19: High Flow Nasal Cannula** (2020)

Anon.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=688dcc01deda9e64a4464e269a79b231)

#### NSW Department of Health

**Covid-19: What is the evidence that continuous positive airway pressure (CPAP) and/or Bilevel Positive Airway Pressure (BiPAP) are aerosol generating?** (2020)

Anon.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=bf7970ed0582898e492ea3b1a9b70e50)

#### Paediatric Intensive Care Society (PICS)

**PICS Guidance on management of critically ill children with Covid-19 infection** (2020)

Anon.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=e4a4b779d7928565e99f60d8ef6fed2b)

## B. Synopses or Summaries

#### Justin Morgenstern

**Aerosol generating procedures [first10em.com blog]** (2020)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=dc90434a575b84cc89979e203109dd67)

Blog post by Justin Morgenstern|Published April 6, 2020-Updated May 17, 2020

## C. Systematic Reviews

#### SpringerLink

**High-flow nasal cannula for acute hypoxemic respiratory failure in patients with COVID-19: systematic reviews of effectiveness and its risks of aerosolization, dispersion, and infection transmission** (2020)

Agarwal A., Basmaji J., Muttalib F., Granton D., Chaudhuri D., Chetan D., Hu M., Fernando S. M., Honarmand K., Bakaa L., Brar S., Rochwerg B., Adhikari N. K., Lamontagne F., Murthy S., Hui D. S. C., Gomersall C., Mubareka S., Diaz J. V., Burns K. E. A., Couban R., Ibrahim Q., Guyatt G. H., Vandvik P. O.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=5dc696558584323d13a2702e025ee174)

Purpose: We conducted two World Health Organization-commissioned reviews to inform use of high-flow nasal cannula (HFNC) in patients with coronavirus disease (COVID-19). We synthesized the evidence regarding efficacy and safety (review 1), as well as risks of droplet dispersion, aerosol generation, and associated transmission (review 2) of viral products. Source: Literature searches were performed in Ovid MEDLINE, Embase, Web of Science, Chinese databases, and medRxiv. Review 1: we synthesized results from randomized-controlled trials (RCTs) comparing HFNC to conventional oxygen therapy (COT) in critically ill patients with acute hypoxemic respiratory failure. Review 2: we narratively summarized findings from studies evaluating droplet dispersion, aerosol generation, or infection transmission associated with HFNC. For both reviews, paired reviewers independently conducted screening, data extraction, and risk of bias assessment. We evaluated certainty of evidence using GRADE methodology. Principal findings: No eligible studies included COVID-19 patients. Review 1: 12 RCTs (n = 1,989 patients) provided low-certainty evidence that HFNC may reduce invasive ventilation (relative risk [RR], 0.85; 95% confidence interval [CI], 0.74 to 0.99) and escalation of oxygen therapy (RR, 0.71; 95% CI, 0.51 to 0.98) in patients with respiratory failure. Results provided no support for differences in mortality (moderate certainty), or in-hospital or intensive care length of stay (moderate and low certainty, respectively). Review 2: four studies evaluating droplet dispersion and three evaluating aerosol generation and dispersion provided very low certainty evidence. Two simulation studies and a crossover study showed mixed findings regarding the effect of HFNC on droplet dispersion. Although two simulation studies reported no associated increase in aerosol dispersion, one reported that higher flow rates were associated with increased regions of aerosol density. Conclusions: High-flow nasal cannula may reduce the need for invasive ventilation and escalation of therapy compared with COT in COVID-19 patients with acute hypoxemic respiratory failure. This benefit must be balanced against the unknown risk of airborne transmission. © 2020, Canadian Anesthesiologists' Society.

#### pre-print

**Clinical presentations, laboratory and radiological findings, and treatments for 11,028 COVID-19 patients: a systematic review and meta-analysis** (2020)

Wong Carlos K. H., Wong Janet, Tang Eric H. M., Au Chi Ho, Wai Abraham

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=999c6c0c878ef544aebf5abffb3aa97c)

## D. Original Research

1. **84-YEAR-OLD PATIENT WITH DENGUE INFECTION WITH ACUTE RESPIRATORY DISTRESS SYNDROME**  
   Sivakorn C. Chest 2020;157:A102.

TYPE: Abstract Publication TOPIC: Chest Infections PURPOSE: An 84-year-old Thai female retired officer presented with fever, myalgia, productive cough for five days which did not improve with antibiotic. She denied smoking or travel history. Her vital signs were febrile, pulse full and regular, mild tachypnea and normal blood pressure. Initial laboratories showed mild decrease leukocyte counts for 3800 x 103/uL with thrombocytopenia for 98000 x103/uL. Dengue NS1Ag, IgM and IgG were positive all and Dengue PCR was positive for Dengue virus serotype four. Chest radiograph showed cardiomegaly. On the second day, she developed dyspnea, desaturation. On physical examination, we found fine crepitation and wheezing on her lungs with flat jugular venous pressure. Convalescence rashes presented on her trunk, arms and legs.Her complete blood count showed improvements of leukocyte count for 5800 x 103/uL and thrombocytopenia for 107000 x 103/uL. Chest radiograph showed bilateral alveolar opacities with cardiomegaly. We sent for respiratory virus PCR and the result was positive for Human metapneumovirus. She was treated with HFNC with bronchodilators for 7 days and her symptoms were improved. METHOD(S): Not Applicable RESULTS: Not Applicable CONCLUSION(S): Not Applicable CLINICAL IMPLICATIONS: ARDS is not common among general dengue patients; however, it occurs among severe or fatal dengue cases. We describe an 84-year-old woman co-infecting with Human metapneumovirus. This patient developed ARDS during convalescence phase of dengue fever leading us to think of other causes of ARDS beside dengue itself. The patient was treated successfully with noninvasive ventilation along with other supportive measures. The possibility of concomitant dengue viral infection reducing the severity of Human metapneumovirus was considered. DISCLOSURE: No significant relationships. KEYWORDS: Dengue Infection, Human metapneumovirus, ARDSCopyright © 2020 American College of Chest Physicians

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=3f8bb3edb519e99ed2858423d0fc449d)

1. **A 55-year-old COVID-19-positive man managed with self-regulation of high-flow oxygen by high-velocity nasal insufflation therapy**  
   Ciment A. J. Respirology Case Reports 2020;8:No page numbers.

Management of critically ill coronavirus disease 2019 (COVID-19) patients remains both risky and technically challenging. A 55-year-old male COVID-19-positive patient with obstructive sleep apnoea (OSA), diabetes, and obesity presented with cough and shortness of breath, escalating to requiring high-flow oxygen therapy by high-velocity nasal insufflation. The patient's flow rate and oxygen fraction remained labile throughout much of the hospitalization. This lability required frequent clinician interactions and use of personal protective equipment. The patient was alert and oriented and was instructed on the operation of the high-flow system, specifically the adjustment of both flow rate and oxygen percentage. The patient was instructed to modify oxygen to maintain an SpO2 (peripheral capillary oxygen saturation) target range, and flow rate to address dyspnoea as well as reduction of flow as tolerated when other staff entered the room. The patient was successfully self-regulated for 10 days and was discharged on 2 L/min nasal cannula on day 14 of his illness. © 2020 The Authors. Respirology Case Reports published by John Wiley & Sons Australia, Ltd on behalf of The Asian Pacific Society of Respirology

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1. **A nationwide survey on the use of heated humidified high flow oxygen therapy on the paediatric wards in the UK: Current practice and research priorities**  
   Hosheh O. BMC Pediatrics 2020;20:No page numbers.

Background: Heated Humidified High Flow Nasal Cannula Oxygen Therapy (HHFNC) is increasingly used on the paediatric wards and High Dependency Units (HDU) for different types of pathologies and different age groups. We aimed to describe current practice related to the use of HHFNC on the paediatric wards and HDUs, weaning practices and preferred outcome measures for future research. Methods: We carried out a cross-sectional online survey of UK paediatric consultants or their delegates working on the paediatric wards. Descriptive analysis of their geographical, and organizational characteristics, their specialties, and their level of experience was investigated. Reasons for HHFNC initiation, weaning criteria, patients' characteristics and their primary pathologies were also analysed. Results: Participation of 218 paediatricians from 81 hospitals (Median: 2.7, Range: 1-11) was registered. HHFNC was provided in most of the surveyed hospitals (93%, 75/81). A High Dependency Unit (HDU) was available in 47 hospitals (58%); less than a third of those have a dedicated paediatrician. Decisions around HHFNC were made solely by paediatricians in (75%) of the cases, mostly at hospitals with no HDU compared to those with dedicated HDUs (70.3% VS 36.6, 95%CI:22.6-50.4%, P <.001). HHFNC was reported by nearly two-thirds (68%) of the practitioners who used it on the wards to be as effective or superior to CPAP (Continuous Positive Airway Pressure) with fewer complications. Failure rate while on HHFNC was identified as the most important outcome measure in any future research followed by the length of need for HHFNC support (37.1, and 28% respectively). Conclusion: This survey showed support for developing paediatric-specific national guidance on the use of HHFNC on the wards. Our list of defined research priorities may help guide further collaborative research efforts in this field. © 2020 The Author(s).

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1. **Aerosol filtering efficiency of respiratory face masks used during the COVID-19 pandemic**  
   Loupa Glykeria 2020;:No page numbers.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=1d599e9fbbce86ae0ebb5753757b97ed)

1. **Aerosol generation related to respiratory interventions and the effectiveness of a personal ventilation hood**  
   McGain F. Critical care and resuscitation : journal of the Australasian Academy of Critical Care Medicine 2020;:No page numbers.

Objective: To quantify aerosol generation from respiratory interventions and the effectiveness of their removal by a personal ventilation hood. Design and setting: Determination of the aerosol particle generation (in a single, healthy volunteer in a clean room) associated with breathing, speaking, wet coughing, oxygen (O2) 15 L/min via face mask, O2 60 L/min via nasal prongs, bilevel non-invasive positive-pressure ventilation (BiPAP) and nebulisation with O2 10 L/min. Intervention(s): Aerosol generation was measured with two particle sizer and counter devices, focusing on aerosols 0.5-5 mum (human-generated aerosols), with and without the hood. An increase from baseline of less than 0.3 particles per mL was considered a low level of generation. Main Outcome Measure(s): Comparisons of aerosol generation between different respiratory interventions. Effectiveness of aerosol reduction by a personal ventilation hood. Result(s): Results for the 0.5-5 mum aerosol range. Quiet breathing and talking demonstrated very low increase in aerosols (< 0.1 particles/mL). Aerosol generation was low for wet coughing (0.1 particles/mL), O2 15 L/min via face mask (0.18 particles/mL), and high flow nasal O2 60 L/min (0.24 particles/mL). Non-invasive ventilation generated moderate aerosols (29.7 particles/mL) and nebulisation very high aerosols (1086 particles/mL); the personal ventilation hood reduced the aerosol counts by 98% to 0.5 particles/mL and 8.9 particles/mL respectively. Conclusion(s): In this human volunteer study, the administration of O2 15 L/min by face mask and 60 L/min nasal therapy did not increase aerosol generation beyond low levels. Non-invasive ventilation caused moderate aerosol generation and nebulisation therapy very high aerosol generation. The personal ventilation hood reduced the aerosol counts by at least 98%.

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1. **Aerosolization - HFNC Simulation [video]**  
   Clyde Matava 2020;:online.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=2e8235e47c7071c5b0982c8489818631)

1. **All India difficult airway association (AIDAA) consensus guidelines for airway management in the operating room during the COVID-19 pandemic**  
   Patwa A. Indian Journal of Anaesthesia 2020;64:S107-S115.

Severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) which causes coronavirus disease (COVID-19) is a highly contagious virus. The closed environment of the operation room (OR) with aerosol generating airway management procedures increases the risk of transmission of infection among the anaesthesiologists and other OR personnel. Wearing complete, fluid impermeable personal protective equipment (PPE) for airway related procedures is recommended. Team preparation, clear methods of communication and appropriate donning and doffing of PPEs are essential to prevent spread of the infection. Optimal pre oxygenation, rapid sequence induction and video laryngoscope aided tracheal intubation (TI) are recommended. Supraglottic airways (SGA) and surgical cricothyroidotomy should be preferred for airway rescue. High flow nasal oxygen, face mask ventilation, nebulisation, small bore cannula cricothyroidotomy with jet ventilation should be avoided. Tracheal extubation should be conducted with the same levels of precaution as TI. The All India Difficult Airway Association (AIDAA) aims to provide consensus guidelines for safe airway management in the OR, while attempting to prevent transmission of infection to the OR personnel during the COVID-19 pandemic. © 2020 Indian Journal of Anaesthesia | Published by Wolters Kluwer - Medknow.

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1. **Arnold-Chiari malformation type i and the posterior dislocation of the odontoid process aggravate prolonged weaning in a patient with severe viral pneumonia: A case report**  
   Ding R. BMC Pulmonary Medicine 2020;20:No page numbers.

Background: Prolonged and difficult weaning is associated with higher rates of complications and mortality. Therefore, it is important to identify the associated factors. Case presentation: We describe our experience with a 37-year-old man diagnosed with severe viral pneumonia (influenza A). He presented with acute respiratory failure type I on admission. During intubation, his blood pressure and heart rate decreased, and epinephrine and norepinephrine were administered. Although his clinical condition improved 8 days after intensive care unit (ICU) admission, he experienced difficulty weaning. He remained conscious but had a poor spontaneous cough with sputum production and weak limb muscle strength. His cough reflex was absent during bronchoscopic sputum suction, and he used abdominal breathing during the T-tube test. Magnetic resonance imaging revealed an Arnold-Chiari malformation type I, posterior dislocation of the odontoid process, and syringomyelia, with compression and deformation of the medulla and high cervical cord. The patient was successfully weaned from the ventilator at 20 days after ICU admission. Conclusions: Arnold-Chiari malformation type I and posterior dislocation of the odontoid process, which aggravate medullary compression and increase the risk of cervical nerve injury, might be a rare factor affecting prolonged weaning in critical illness. © 2020 The Author(s).

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1. **Clinical and Radiographic Characteristics, Management and Short-term Outcomes of Patients with COVID-19 in Wenzhou, China**  
   Hong Liang 2020;:No page numbers.

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1. **Clinical characteristics of 51 patients discharged from hospital with COVID-19 in Chongqing，China**  
   lei liu 2020;:No page numbers.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=005b6b5c061fe86a3401def7bc685ce9)

1. **Clinical Consensus Recommendations Regarding Non-Invasive Respiratory Support in the Adult Patient with Acute Respiratory Failure Secondary to SARS-CoV-2 infection**  
   Cinesi G.ómez C. Archivos de Bronconeumologia 2020;56:11-18.

Coronavirus disease 2019 (COVID-19) is a respiratory tract infection caused by a newly emergent coronavirus, that was first recognized in Wuhan, China, in December 2019. Currently, the World Health Organization (WHO) has defined the infection as a global pandemic and there is a health and social emergency for the management of this new infection. While most people with COVID-19 develop only mild or uncomplicated illness, approximately 14% develop severe disease that requires hospitalization and oxygen support, and 5% require admission to an intensive care unit. In severe cases, COVID-19 can be complicated by the acute respiratory distress syndrome (ARDS), sepsis and septic shock, and multiorgan failure. This consensus document has been prepared on evidence-informed guidelines developed by a multidisciplinary panel of health care providers from four Spanish scientific societies (Spanish Society of Intensive Care Medicine [SEMICYUC], Spanish Society of Pulmonologists [SEPAR], Spanish Society of Emergency [SEMES], Spanish Society of Anesthesiology, Reanimation, and Pain [SEDAR]) with experience in the clinical management of patients with COVID-19 and other viral infections, including SARS, as well as sepsis and ARDS. The document provides clinical recommendations for the noninvasive respiratory support (noninvasive ventilation, high flow oxygen therapy with nasal cannula) in any patient with suspected or confirmed presentation of COVID-19 with acute respiratory failure. This consensus guidance should serve as a foundation for optimized supportive care to ensure the best possible chance for survival and to allow for reliable comparison of investigational therapeutic interventions as part of randomized controlled trials. © 2020

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1. **Comparative Analysis of Clinical Characteristics in Children and Adults with 2019 Novel Coronavirus Infection: A Descriptive Study**  
   Han Ya-nan 2020;:No page numbers.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=425696ad6353dfa025d9b3e5e6a961a5)

1. **Consensus guidelines for managing the airway in patients with COVID-19: Guidelines from the Difficult Airway Society, the Association of Anaesthetists the Intensive Care Society, the Faculty of Intensive Care Medicine and the Royal College of Anaesthetists**  
   Cook T. M. Anaesthesia 2020;75:785-799.

Severe acute respiratory syndrome-corona virus-2, which causes coronavirus disease 2019 (COVID-19), is highly contagious. Airway management of patients with COVID-19 is high risk to staff and patients. We aimed to develop principles for airway management of patients with COVID-19 to encourage safe, accurate and swift performance. This consensus statement has been brought together at short notice to advise on airway management for patients with COVID-19, drawing on published literature and immediately available information from clinicians and experts. Recommendations on the prevention of contamination of healthcare workers, the choice of staff involved in airway management, the training required and the selection of equipment are discussed. The fundamental principles of airway management in these settings are described for: emergency tracheal intubation; predicted or unexpected difficult tracheal intubation; cardiac arrest; anaesthetic care; and tracheal extubation. We provide figures to support clinicians in safe airway management of patients with COVID-19. The advice in this document is designed to be adapted in line with local workplace policies. © 2020 The Authors. Anaesthesia published by John Wiley & Sons Ltd on behalf of Association of Anaesthetists

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1. **COVID-19 challenge for modern medicine**  
   Dzieciatkowski T. Cardiology Journal 2020;27:175-183.

Coronaviruses cause disease in animals and people around the world. Human coronaviruses (HCoV) are mainly known to cause infections of the upper and lower respiratory tract but the symptoms may also involve the nervous and digestive systems. Since the beginning of December 2019, there has been an epidemic of SARS-CoV-2, which was originally referred to as 2019-nCoV. The most common symptoms are fever and cough, fatigue, sputum production, dyspnea, myalgia, arthralgia or sore throat, headache, nausea, vomiting or diarrhea (30%). The best prevention is to avoid exposure. In addition, contact persons should be subjected to mandatory quarantine. COVID-19 patients should be treated in specialist centers. A significant number of patients with pneumonia require passive oxygen therapy. Non-invasive ventilation and high-flow nasal oxygen therapy can be applied in mild and moderate non-hypercapnia cases. A lung-saving ventilation strategy must be implemented in acute respiratory distress syndrome and mechanically ventilated patients. Extracorporeal membrane oxygenation is a highly specialized method, available only in selected centers and not applicable to a significant number of cases. Specific pharmacological treatment for COVID-19 is not currently available. Modern medicine is gearing up to fight the new coronavirus pandemic. The key is a holistic approach to the patient including, primarily, the use of personal protective equipment to reduce the risk of further virus transmission, as well as patient management, which consists in both quarantine and, in the absence of specific pharmacological therapy, symptomatic treatment. © 2020 Via Medica.

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1. **COVID-19 in Children: Clinical Approach and Management**  
   Sankar J. Indian Journal of Pediatrics 2020;87:433-442.

COVID-19 pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a major public health crisis threatening humanity at this point in time. Transmission of the infection occurs by inhalation of infected droplets or direct contact with soiled surfaces and fomites. It should be suspected in all symptomatic children who have undertaken international travel in the last 14 d, all hospitalized children with severe acute respiratory illness, and asymptomatic direct and high-risk contacts of a confirmed case. Clinical symptoms are similar to any acute respiratory viral infection with less pronounced nasal symptoms. Disease seems to be milder in children, but situation appears to be changing. Infants and young children had relatively more severe illness than older children. The case fatality rate is low in children. Diagnosis can be confirmed by Reverse transcriptase – Polymerase chain reaction (RT-PCR) on respiratory specimen (commonly nasopharyngeal and oropharyngeal swab). Rapid progress is being made to develop rapid diagnostic tests, which will help ramp up the capacity to test and also reduce the time to getting test results. Management is mainly supportive care. In severe pneumonia and critically ill children, trial of hydroxychloroquine or lopinavir/ritonavir should be considered. As per current policy, children with mild disease also need to be hospitalized; if this is not feasible, these children may be managed on ambulatory basis with strict home isolation. Pneumonia, severe disease and critical illness require admission and aggressive management for acute lung injury and shock and/or multiorgan dysfunction, if present. An early intubation is preferred over non-invasive ventilation or heated, humidified, high flow nasal cannula oxygen, as these may generate aerosols increasing the risk of infection in health care personnel. To prevent post discharge dissemination of infection, home isolation for 1–2 wk may be advised. As of now, no vaccine or specific chemotherapeutic agents are approved for children. © 2020, Dr. K C Chaudhuri Foundation.

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1. **COVID-19 pandemic and non invasive respiratory management: Every Goliath needs a David. An evidence based evaluation of problems**  
   Winck J. C. Pulmonology 2020;26:213-220.

Background and aim: The war against Covid-19 is far from won. This narrative review attempts to describe some problems with the management of Covid-19 induced acute respiratory failure (ARF) by pulmonologists. Methods: We searched the following databases: MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials and reviewed the references of retrieved articles for additional studies. The search was limited to the terms: Covid-19 AND: acute respiratory distress syndrome (ARDS), SARS, MERS, non invasive ventilation (NIV), high flow nasal cannula (HFNC), pronation (PP), health care workers (HCW). Results: Protection of Health care workers should be paramount, so full Personal Protective Equipment and Negative pressure rooms are warranted. HFNC alone or with PP could be offered for mild cases (PaO2/FiO2 between 200–300); NIV alone or with PP may work in moderate cases (PaO2/FiO2 between 100–200). Rotation and coupled (HFNC/NIV) strategy can be beneficial. A window of opportunity of 1–2 h is advised. If PaO2/FIO2 significantly increases, Respiratory Rate decreases with a relatively low Exhaled Tidal Volume, the non-invasive strategy could be working and intubation delayed. Conclusion: Although there is a role for non-invasive respiratory therapies in the context of COVID-19 ARF, more research is still needed to define the balance of benefits and risks to patients and HCW. Indirectly, non invasive respiratory therapies may be of particular benefit in reducing the risks to healthcare workers by obviating the need for intubation, a potentially highly infectious procedure. © 2020 Sociedade Portuguesa de Pneumologia

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1. **COVID-19: minimising risk to healthcare workers during aerosol-producing respiratory therapy using an innovative constant flow canopy**  
   Adir Y. Eur Respir J 2020;55:No page numbers.

An innovative constant flow canopy enables noninvasive respiratory support with minimal risk of healthcare worker infection https://bit.ly/3eqgoVZ Noninvasive ventilation (NIV), continuous positive airway pressure (CPAP) and high-flow nasal cannula (HFNC) can be used as the first line of treatment in coronavirus disease 2019 (COVID-19) patients with respiratory failure, postponing and maybe even avoiding the need for intubation and mechanical ventilation [1]. Recent systematic review and meta-analysis demonstrated that HFNC reduces the need for intubation compared with conventional oxygen, with no change in the death risk or length of stay in the intensive care unit [2, 3]. No direct evidence supports the use of NIV, due to a high failure rate [4]. However, when resources become limited, with no option of invasive ventilation, the use of NIV may be justified. The major caveat of using noninvasive respiratory support in the face of the COVID-19 pandemic is the generation of aerosols, composed of small virus-containing particles, which may remain suspended in the air, with increased risk for healthcare workers [5, 6]. The risk of aerosolisation depends on many variables, including duration of use, flow velocity, mask leakage and patient coughing and cooperation. eng from Actelion, Boehringer Ingelheim, Teva, Bayer, GSK, Roche, Novartis, AstraZeneca, Kamada and UT Pharmaceuticals, and research grants from Actelion, Bayer, Boehringer Ingelheim and GSK. Conflict of interest: O. Segol has nothing to disclose. Conflict of interest: D. Kompaniets has nothing to disclose. Conflict of interest: H. Ziso reports that the Israeli innovation authority have granted funds to Tamar Robotics Ltd, such funds along with the funds allocated by our investors were used to develop the system presented in this paper; H. Ziso has a US Provisional Patent Application number 63/001,562, Israel Patent Application number 273616, entitled: “Portable Patient Hood System For Protection Of Medical Staff And Others From Infectious Disease Transmission” pending, and a US Provisional Patent Application number 62/994,614 entitled: “Portable Patient Hood System For Protection Of Medical Staff And Others From Infectious Disease Transmission” pending; and would like to state that: 1) the author is an employee of Tamar Robotics Ltd, that developed the system presented in the paper as a VP of R&D; 2) the author is co-founder of Tamar Robotics Ltd and has holdings in the company (less than 6%); 3) Tamar Niv Breathing Solutions Ltd may sell this product in the future and the author will be receiving dividend or royalties if such sales are made in the future. Conflict of interest: Y. Yaffe has nothing to disclose. Conflict of interest: I. Bergman has nothing to disclose. Conflict of interest: E. Hassidov reports that the Israeli innovation authority have granted funds to Tamar Robotics Ltd, such funds along with funds allocated by our investors were used to develop the system presented in this paper; E. Hassidov has a US Provisional Patent Application number 63/001,562, Israel Patent Application number 273616, entitled: “Portable Patient Hood System For Protection Of Medical Staff And Others From Infectious Disease Transmission” pending, and a US Provisional Patent Application number 62/994,614 entitled: “Portable Patient Hood System For Protection Of Medical Staff And Others From Infectious Disease Transmission” pending; and would like to state that: 1) the author is a part-time employee of Tamar Robotics Ltd that developed the system presented in the paper; 2) the author's brother is Noam Hassidov, CEO of Tamar Robotics Ltd; 3) the author is a fifth year student in the Bar Illan medical school in Israel; 4) the author works once a week in the ER of Carmel Medical Center as an assistant physician; 5) the author has no holdings in Tamar Robotics or any other companies related to the system presented in this paper; 6) Tamar Niv Breathing Solutions Ltd may sell this product in the future. Conflict of interest: A. Eden has nothing to disclose.

1. **Deposition of Aerosolized Lucinactant in Nonhuman Primates**  
   Gregory T. J. Journal of Aerosol Medicine and Pulmonary Drug Delivery 2020;33:21-33.

Background: Lucinactant for inhalation is an investigational noninvasive, aerosolized surfactant replacement therapy for treatment of preterm neonates with respiratory distress syndrome. Lucinactant for inhalation consists of lyophilized lucinactant and the Aerosurf® Delivery System (ADS). The objective of this study was to characterize the total and regional pulmonary deposition of lucinactant delivered by the ADS in nonhuman primates (NHPs). Methods: Lucinactant was radiolabeled by the addition of technetium-99m (99mTc)-sulfur colloid. The radiolabeled aerosol was characterized and validated using a Mercer cascade impactor. An in vivo deposition study was performed in three cynomolgus macaques. Radiolabeled lucinactant was aerosolized using the ADS and delivered via nasal cannula under 5 cm H2O nasal continuous positive airway pressure (nCPAP) for 5-9 minutes. A two-dimensional planar image was acquired immediately after aerosol administration, followed by a three-dimensional single-photon emission computed tomography (SPECT) image and a second planar image. The images were analyzed to determine the pulmonary (lungs) and extrapulmonary (nose + mouth, trachea, stomach) distribution. The SPECT data were used to determine regional deposition. Results: The radiolabed lucinactant aerosol had a mass median aerodynamic diameter = 2.91 μm, geometric standard deviation (GSD) = 1.81, and an activity median aerodynamic diameter = 2.92 μm, GSD = 2.06. Aerosolized lucinactant was observed to deposit in the lungs (11.4%), nose + mouth (79.9%), trachea (7.3%), and stomach (1.4%). Analysis of the SPECT image demonstrated that the regional deposition within the lung was generally homogeneous. Aerosolized lucinactant was deposited in both the central (52.8% ± 1.2%) and peripheral (47.2% ± 1.2%) regions of the lungs. Conclusion: Aerosolized lucinactant, delivered using the ADS via constant flow nCPAP, is deposited in all regions of the lungs demonstrating that surfactant can be aerosolized and delivered noninvasively to NHPs. © Timothy J. Gregory, et al., 2020. Published by Mary Ann Liebert, Inc. 2020.

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1. **Early and critical care in severe patients with COVID-19 infection in Jiangsu Province, China: a descriptive study**  
   Huang Mao 2020;:No page numbers.

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1. **ENVIRONMENTAL SAFETY EVALUATION OF THE PROTECTION AND ISOLATION SYSTEM FOR PATIENTS WITH COVID-19**  
   Quadros Claudio Almeida 2020;:No page numbers.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=2f7e5d8729d2eb77d46234bcb77b562f)

1. **Extended pharmacopeial characterization of surfactant aerosols generated by a customized eflow neos nebulizer delivered through neonatal nasal prongs**  
   Bianco F. Pharmaceutics 2020;12:No page numbers.

The delivery of nebulized medications to preterm infants during Non-Invasive Ventilation (NIV) remains an unmet clinical need. In this regard, the effective delivery of nebulized surfactant has been particularly investigated in preclinical and clinical studies. In this work, we investigated the feasibility of delivering nebulized surfactant through various commercially available nasal prong types. We first performed a compendial characterization of surfactant aerosols generated by the eFlow Neos nebulizer, customized to be used in neonates, determining the amount of surfactant delivered by the device as well as the aerodynamic characteristics of surfactant aerosols. Additionally, we extended the compendial characterization by testing the effect of different nasal prong types on the estimated lung dose using a realistic Continuous Positive Airway Pressure (CPAP) circuit that included a cast of the upper airways of a preterm neonate. The compendial characterization of surfactant aerosols delivered through different nasal prongs achieved relatively high delivered surfactant doses (in the range 63–74% of the nominal dose), with aerodynamic characteristics displaying mass median aerodynamic diameters ranging between 2.52 and 2.81 µm. Nevertheless, when using a representative in vitro setup mimicking NIV in a clinical setting, significant differences were observed in terms of the estimated lung dose accounting for up to two-fold differences (from 10% to 20% estimated lung deposition of the nominal dose) depending on the chosen nasal prong type. Considering that surfactant lung deposition rates are correlated with therapeutic efficacy, this study points out the relevance of choosing the appropriate NIV interface to maximize the lung dose of nebulized medications. © 2020 by the authors. Licensee MDPI, Basel, Switzerland. T.

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1. **Guideline for the management of COVID-19 patients during hospital admission in a non-intensive care setting**  
   Nielsen Jeschke K. European Clinical Respiratory Journal 2020;7:No page numbers.

Introduction: Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has presented health-care systems worldwide with novel challenges and experiences and evidence is emerging during the pandemic. Patients requiring hospitalization frequently suffer from respiratory failure of different severities. Aim: The aim of this guideline is the treatment of patients with SARS CoV-2 (COVID-19) in hospital; in particular, it addresses the treatment of respiratory failure treated in general Internal Medical- and Pulmonary Medical wards. Results: Elderly patients and patients with chronic disease are particularly vulnerable to COVID-19. Target oxygen saturation should be between 92% and 96% in patients without chronic lung diseases. Treatment with >5 L oxygen/min should be in close collaboration with intensive care colleagues and >15 l/min preferably in intensive care units. High-flow nasal canula (HFNC) and long-term Continuous Positive Airway Pressure (CPAP) are recommended for patients not responding to conventional oxygen therapy. Non-invasive ventilation (NIV) is only recommended for selected patients, such as those with a ceiling of treatment or patients presenting with hypercapnic failure. With the use of humidification protective equipment as FFP2-3 masks should be used. Nebulized medication should be avoided, and spacers should be used instead. Conclusion: Respiratory failure is frequently the cause of hospitalization in patients with COVID-19 and should be monitored closely. © 2020, © 2020 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group.

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1. **High flow nasal cannula in COVID-19: A literature review**  
   Gürün Kaya A. Tuberkuloz ve Toraks 2020;68:168-174.

In recent years, high flow nasal cannula (HFNC) is a respiratory support sys-tem that has become prominent in the treatment of respiratory failure. HFNC provides higher concentration and flow of oxygen, resulting in decreasing anatomic dead space by preventing rebreathing and ensure positive end-expi-ratory. However, in COVID-19, the usage of HFNC is much controversial due to concerns about the benefits and risk of aerosol-dispersion. Considering the debates about the use of HFNC, we reviewed the literature related to the usage of HFNC in COVID-19. The available reports suggest that HFNC provides high concentrations of oxygen to the patients, who can not reach with conventional devices. HFNC can reduce the requiring of intubation in patients with COVID-19, and it can decrease the length of intensive care unit stay, and complications related to mechanical ventilation. Also HFNC can in achieving apneic oxygenation in patients during airway management. Besides that, the use of high-flow oxygen cannulas can produce aerosols. So, HFNC treatment should be carried out in a negative pressure room; when it is not possible, devices should be undertaken in a single room. © 2020 by Tuberculosis and Thorax.

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1. **High-flow nasal cannula for COVID-19 patients: low risk of bio-aerosol dispersion**  
   Li J. Eur Respir J 2020;55:No page numbers.

Bio-aerosol dispersion via high-flow nasal cannula shows a similar risk to standard oxygen masks. High-flow nasal prongs with a surgical mask on the patient's face might benefit hypoxaemic COVID-19 patients without added risk for the environment. https://bit.ly/34p7Fyy

1. **High-flow nasal cannula may be no safer than non-invasive positive pressure ventilation for COVID-19 patients**  
   Remy K. E. Critical Care 2020;24:No page numbers.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=7318ec7167488f62907247f0abcb570e)

1. **High-flow nasal-oxygenation-assisted fibreoptic tracheal intubation in critically ill patients with COVID-19 pneumonia: a prospective randomised controlled trial**  
   Wu C. N. British Journal of Anaesthesia 2020;125:e166-e168.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=e345842aabafe137516205b7c46327dc)

1. **High-flow Oxygen Therapy - Step by Step**  
   Wachs C. C. wachs uke de Deutsche Medizinische Wochenschrift 2020;145:693-697.

In recent years, high-flow oxygen therapy (HFNC) has become established and proven as an oxygenation method for patients with severe respiratory restrictions in most intensive care units. Advantages of this method, which is used especially for patients with hypoxaemia, are the easy application and the compliance by the patient. Devices are used which enable individual oxygen therapy by means of humidification, warming up and gas flow regulation options. © 2020 BMJ Publishing Group. All rights reserved.

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1. **High-Flow, Noninvasive Ventilation and Awake (Nonintubation) Proning in Patients With COVID-2019 With Respiratory Failure**  
   Raoof Suhail Chest 2020;:No page numbers.

The coronavirus disease 2019 pandemic will be remembered for the rapidity with which it spread, the morbidity and mortality associated with it, and the paucity of evidence-based management guidelines. One of the major concerns of hospitals was to limit spread of infection to health-care workers. Because the virus is spread mainly by respiratory droplets and aerosolized particles, procedures that may potentially disperse viral particles, the so-called "aerosol-generating procedures" were avoided whenever possible. Included in this category were noninvasive ventilation (NIV), high-flow nasal cannula (HFNC), and awake (nonintubated) proning. Accordingly, at many health-care facilities, patients who had increasing oxygen requirements were emergently intubated and mechanically ventilated to avoid exposure to aerosol-generating procedures. With experience, physicians realized that mortality of invasively ventilated patients was high and it was not easy to extubate many of these patients. This raised the concern that HFNC and NIV were being underutilized to avoid intubation and to facilitate extubation. In this article, we attempt to separate fact from fiction and perception from reality pertaining to the aerosol dispersion with NIV, HFNC, and awake proning. We describe precautions that hospitals and health-care providers must take to mitigate risks with these devices. Finally, we take a practical approach in describing how we use the three techniques, including the common indications, contraindications, and practical aspects of application. Copyright © 2020. Published by Elsevier Inc.

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1. **In vitro comparison between inspiration synchronized and continuous vibrating mesh nebulizer during trans-nasal aerosol delivery**  
   Li Jie Intensive care medicine experimental 2020;8:6.

BACKGROUND: Compared to continuous vibrating mesh nebulizer (VMN), inspiration synchronized VMN has shown increased inhaled dose during noninvasive ventilation; however, its use during aerosol delivery via high-flow nasal cannula (HFNC) is still unknown., METHODS: An adult manikin was connected to a dual-chamber model lung, which was driven by a critical care ventilator to simulate spontaneous breathing. A HFNC system was utilized with temperature at 37 degree C while gas flow at 5, 10, 20, 40, and 60 L/min. Inspiration synchronized and continuous aerosol generation were compared at different positions (at the inlet of humidifier vs close to patient). One milliliter of albuterol (2.5 mg/mL) was used in each run (n = 3). Collection filter was placed at the trachea and was removed after each run. Drug was eluted from the filter and assayed with UV spectrophotometry (276 nm)., RESULTS: When nebulizer was placed close to patient, inhaled dose was higher with inspiration synchronized than continuous aerosol generation at all gas flows (p = 0.05) except at 5 L/min. When placed at the inlet of humidifier, compared to continuous, inspiration synchronized aerosol generated higher inhaled dose with gas flow set below 50% of patient inspiratory flow [23.9 (20.6, 28.3)% vs 18.1 (16.7, 19.6)%, p < 0.001], but lower inhaled dose with gas flow set above 50% of patient inspiratory flow [3.5 (2.2, 9.3)% vs 9.9 (8.2, 16.4)%, p = 0.001]. Regardless of breathing pattern, continuous aerosol delivered greater inhaled dose with nebulizer placed at humidifier than close to patient at all gas flows except at 5 L/min., CONCLUSION: When the HFNC gas flow was set higher than 50% of patient inspiratory flow, no significant advantage was found in inspiration synchronized over continuous aerosol. However, inspiration synchronized aerosol generated 30% more inhaled dose than continuous with gas flow set below 50% of patient inspiratory flow, regardless of nebulizer placement. Continuous nebulizer needs to be placed at the inlet of humidifier.

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1. **In vitro performance of an investigational vibrating-membrane nebulizer with surfactant under simulated, non-invasive neonatal ventilation conditions: Influence of continuous positive airway pressure interface and nebulizer positioning on the lung dose**  
   Bianco F. Pharmaceutics 2020;12:No page numbers.

Non-invasive delivery of nebulized surfactant has been a long-pursued goal in neonatology. Our aim was to evaluate the performance of an investigational vibrating-membrane nebulizer in a realistic non-invasive neonatal ventilation circuit with different configurations. Surfactant (aerosols were generated with a nebulizer in a set-up composed of a continuous positive airway pressure (CPAP) generator with a humidifier, a cast of the upper airway of a preterm infant (PrINT), and a breath simulator with a neonatal breathing pattern. The lung dose (LD), defined as the amount of surfactant collected in a filter placed at the distal end of the PrINT cast, was determined after placing the nebulizer at different locations of the circuit and using either infant nasal mask or nasal prongs as CPAP interfaces. The LD after delivering a range of nominal surfactant doses (100–600 mg/kg) was also investigated. Surfactant aerosol particle size distribution was determined by laser diffraction. Irrespective of the CPAP interface used, about 14% of the nominal dose (200 mg/kg) reached the LD filter. However, placing the nebulizer between the Y-piece and the CPAP interface significantly increased the LD compared with placing it 7 cm before the Y-piece, in the inspiratory limb. (14% ± 2.8 vs. 2.3% ± 0.8, nominal dose of 200 mg/kg). The customized eFlow Neos showed a constant aerosol generation rate and a mass median diameter of 2.7 µm after delivering high surfactant doses (600 mg/kg). The customized eFlow Neos nebulizer showed a constant performance even after nebulizing high doses of undiluted surfactant. Placing the nebulizer between the Y-piece and the CPAP interface achieves the highest LD under non-invasive ventilation conditions. © 2020 by the authors. Licensee MDPI, Basel, Switzerland.

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1. **Interventions for escalation of therapy for acute exacerbations of asthma in children: an overview of Cochrane Reviews**  
   Craig S. S. Cochrane Database Syst Rev 2020;8:Cd012977.

BACKGROUND: Asthma is an illness that commonly affects adults and children, and it serves as a common reason for children to attend emergency departments. An asthma exacerbation is characterised by acute or subacute worsening of shortness of breath, cough, wheezing, and chest tightness and may be triggered by viral respiratory infection, poor compliance with usual medication, a change in the weather, or exposure to allergens or irritants. Most children with asthma have mild or moderate exacerbations and respond well to first-line therapy (inhaled short-acting beta-agonists and systemic corticosteroids). However, the best treatment for the small proportion of seriously ill children who do not respond to first-line therapy is not well understood. Currently, a large number of treatment options are available and there is wide variation in management. OBJECTIVES: Main objective - To summarise Cochrane Reviews with or without meta-analyses of randomised controlled trials on the efficacy and safety of second-line treatment for children with acute exacerbations of asthma (i.e. after first-line treatments, titrated oxygen delivery, and administration of intermittent inhaled short-acting beta(2)-agonists and oral corticosteroids have been tried and have failed) Secondary objectives - To identify gaps in the current evidence base that will inform recommendations for future research and subsequent Cochrane Reviews - To categorise information on reported outcome measures used in trials of escalation of treatment for acute exacerbations of asthma in children, and to make recommendations for development and reporting of standard outcomes in future trials and reviews - To identify relevant randomised controlled trials that have been published since the date of publication of each included review METHODS: We included Cochrane Reviews assessing interventions for children with acute exacerbations of asthma. We searched the Cochrane Database of Systematic Reviews. The search is current to 28 December 2019. We also identified trials that were potentially eligible for, but were not currently included in, published reviews. We assessed the quality of included reviews using the ROBIS criteria (tool used to assess risk of bias in systematic reviews). We presented an evidence synthesis of data from reviews alongside an evidence map of clinical trials. Primary outcomes were length of stay, hospital admission, intensive care unit admission, and adverse effects. We summarised all findings in the text and reported data for each outcome in 'Additional tables'. MAIN RESULTS: We identified 17 potentially eligible Cochrane Reviews but extracted data from, and rated the quality of, 13 reviews that reported results for children alone. We excluded four reviews as one did not include any randomised controlled trials (RCTs), one did not provide subgroup data for children, and the last two had been updated and replaced by subsequent reviews. The 13 reviews included 67 trials; the number of trials in each review ranged from a single trial up to 27 trials. The vast majority of comparisons included between one and three trials, involving fewer than 100 participants. The total number of participants included in reviews ranged from 40 to 2630. All studies included children; 16 (24%) included children younger than two years of age. Most of the reviews reported search dates older than four years. We have summarised the published evidence as outlined in Cochrane Reviews. Key findings, in terms of our primary outcomes, are that (1) intravenous magnesium sulfate was the only intervention shown to reduce hospital length of stay (high-certainty evidence); (2) no evidence suggested that any intervention reduced the risk of intensive care admission (low- to very low-certainty evidence); (3) the risk of hospital admission was reduced by the addition of inhaled anticholinergic agents to inhaled beta(2)-agonists (moderate-certainty evidence), the use of intravenous magnesium sulfate (high-certainty evidence), and the use of inhaled heliox (low-certainty evidence); (4) the addition of inhaled magnesium sulfate to usual bronchodilator therapy appears to reduce serious adverse events during hospital admission (moderate-certainty evidence); (5) aminophylline increased vomiting compared to placebo (moderate-certainty evidence) and increased nausea and nausea/vomiting compared to intravenous beta(2)-agonists (low-certainty evidence); and (6) the addition of anticholinergic therapy to short-acting beta(2)-agonists appeared to reduce the risk of nausea (high-certainty evidence) and tremor (moderate-certainty evidence) but not vomiting (low-certainty evidence). We considered 4 of the 13 reviews to be at high risk of bias based on the ROBIS framework. In all cases, this was due to concerns regarding identification and selection of studies. The certainty of evidence varied widely (by review and also by outcome) and ranged from very low to high. AUTHORS' CONCLUSIONS: This overview provides the most up-to-date evidence on interventions for escalation of therapy for acute exacerbations of asthma in children from Cochrane Reviews of randomised controlled trials. A vast majority of comparisons involved between one and three trials and fewer than 100 participants, making it difficult to assess the balance between benefits and potential harms. Due to the lack of comparative studies between various treatment options, we are unable to make firm practice recommendations. Intravenous magnesium sulfate appears to reduce both hospital length of stay and the risk of hospital admission. Hospital admission is also reduced with the addition of inhaled anticholinergic agents to inhaled beta(2)-agonists. However, further research is required to determine which patients are most likely to benefit from these therapies. Due to the relatively rare incidence of acute severe paediatric asthma, multi-centre research will be required to generate high-quality evidence. A number of existing Cochrane Reviews should be updated, and we recommend that a new review be conducted on the use of high-flow nasal oxygen therapy. Important priorities include development of an internationally agreed core outcome set for future trials in acute severe asthma exacerbations and determination of clinically important differences in these outcomes, which can then inform adequately powered future trials.

1. **Management of diagnostic procedures and treatment of sleep related breathing disorders in the context of the coronavirus pandemic: German Respiratory Society (DGP), German Sleep Society (DGSM)**  
   Büchner N. Somnologie 2020;:No page numbers.

When providing sleep medical services special aspects must be taken into account in the context of the coronavirus pandemic. Despite all prevention, due to the high number of unrecognized cases, SARS-CoV2 contacts in the sleep laboratory must be expected and appropriate precautions are necessary. Nevertheless, the continuation or resumption of sleep medical services under the appropriate hygiene measures is strongly recommended to avoid medical and psychosocial complications. There is no evidence for a deterioration of COVID-19 through CPAP therapy. In principle, the application of positive pressure therapy via various mask systems can be accompanied by the formation of infectious aerosols. In the case of confirmed infection with SARS-CoV2, a pre-existing PAP therapy should be continued in an outpatient setting in accordance with the local guidelines for home isolation, since discontinuation of PAP therapy is associated with additional cardiopulmonary complications due to the untreated sleep-related breathing disorder. According to the current state of knowledge inhalation therapy, nasal high-flow (NHF), and PAP therapy can be carried out without increased risk of infection for health care workers (HCW) as long as appropriate personal protective equipment (eye protection, FFP2 or FFP-3 mask, gown) is being used. This position paper of the German Society for Pneumology and Respiratory Medicine (DGP) and the German Society for Sleep Medicine (DGSM) offers detailed recommendations for the implementation of sleep medicine diagnostics and therapy in the context of the coronavirus pandemic. © 2020, Springer Medizin Verlag GmbH, ein Teil von Springer Nature.

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1. **Nasal High Flow Use in COPD Patients with Hypercapnic Respiratory Failure: Treatment Algorithm & Review of the Literature**  
   Pantazopoulos I. COPD: Journal of Chronic Obstructive Pulmonary Disease 2020;17:101-111.

Nasal high flow (NHF) therapy has recently gained attention as a new respiratory support system and is increasingly being utilized in every day clinical practice. Recent studies suggest that it may also be effective in patients with hypercapnia and suggest NHF as a possible alternative for patients who cannot tolerate standard noninvasive ventilation. The present review discusses the mechanisms of action that make NHF potentially suitable for chronic obstructive pulmonary disease (COPD) patients and evaluates the current evidence of NHF use for treatment of stable hypercapnic COPD patients as well as acute hypercapnic exacerbation of COPD. An algorithm is also proposed for the clinical application of NHF in patients with acute hypercapnic exacerbation of COPD, based on current literature. © 2020, © 2020 Taylor & Francis Group, LLC.

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1. **Noninvasive respiratory support in acute hypoxemic respiratory failure associated with COVID-19 and other viral infections**  
   Crimi Claudia Minerva anestesiologica 2020;:No page numbers.

INTRODUCTION: Noninvasive respiratory support (NRS) such as noninvasive ventilation (NIV) and high flow nasal therapy (HFNT) have been used in the treatment of acute hypoxemic respiratory failure (AHRF) related to the coronavirus disease (COVID-19) and other viral infections. However, there is a lack of consensus in favor of or against NRS use due to the risks of worsening hypoxemia, intubation delay, and aerosols environmental contamination associated with the use of these tools. We aimed to summarize the evidence on the use of NRS in adult patients with COVID-19 and other viral pneumonia (i.e. H1N1, SARS, MERS) and AHRF. We also searched for studies evaluating the risk of aerosolization/contamination with these tools., EVIDENCE ACQUISITION: We searched MEDLINE, PubMed EMBASE and two major preprint servers (biorXiv and medRxiv) from inception to April 14, 2020, for studies on the use of respiratory support in AHRF and viral pneumonia., EVIDENCE SYNTHESIS: The search identified 4086 records and we found only one randomized controlled trial out of 58 studies included, with great variabilities in support utilization and failure rates. Fifteen studies explored the issue of aerosolization/contamination showing a high risk of airborne transmission via droplets generation during the use of these modalities., CONCLUSIONS: Use of NRS and treatment failure in the context of COVID-19 and viral infection associated-AHRF, varied widely. Dispersion of exhaled air is different depending on the type of respiratory therapies and interfaces. Data from randomized controlled trials are lacking.

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1. **Position Paper for the State of the Art Application of Respiratory Support in Patients with COVID-19: German Respiratory Society**  
   Pfeifer M. Pneumologie 2020;74:337-357.

Against the background of the pandemic caused by infection with the SARS-CoV-2, the German Society for Pneumology and Respiratory Medicine (DGP e.V.), in cooperation with other associations, has designated a team of experts in order to answer the currently pressing questions about therapy strategies in dealing with COVID-19 patients suffering from acute respiratory insufficiency (ARI). The position paper is based on the current knowledge that is evolving daily. Many of the published and cited studies require further review, also because many of them did not undergo standard review processes.Therefore, this position paper is also subject to a continuous review process and will be further developed in cooperation with the other professional societies. This position paper is structured into the following five topics: 1. Pathophysiology of acute respiratory insufficiency in patients without immunity infected with SARS-CoV-2 2. Temporal course and prognosis of acute respiratory insufficiency during the course of the disease 3. Oxygen insufflation, high-flow oxygen, non-invasive ventilation and invasive ventilation with special consideration of infectious aerosol formation 4. Non-invasive ventilation in ARI 5. Supply continuum for the treatment of ARI Key points have been highlighted as core statements and significant observations. Regarding the pathophysiological aspects of acute respiratory insufficiency (ARI), the pulmonary infection with SARS-CoV-2 COVID-19 runs through three phases: early infection, pulmonary manifestation and severe hyperinflammatory phase. There are differences between advanced COVID-19-induced lung damage and those changes seen in Acute Respiratory Distress Syndromes (ARDS) as defined by the Berlin criteria. In a pathophysiologically plausible - but currently not yet histopathologically substantiated - model, two types (L-type and H-type) are distinguished, which correspond to an early and late phase. This distinction can be taken into consideration in the differential instrumentation in the therapy of ARI. The assessment of the extent of ARI should be carried out by an arterial or capillary blood gas analysis under room air conditions and must include the calculation of the oxygen supply (measured from the variables of oxygen saturation, the Hb value, the corrected values of the Hüfner number and the cardiac output). In principle, aerosols can cause transmission of infectious viral particles. Open systems or leakage systems (so-called vented masks) can prevent the release of respirable particles. Procedures in which the invasive ventilation system must be opened, and endotracheal intubation must be carried out are associated with an increased risk of infection. The protection of personnel with personal protective equipment should have very high priority because fear of contagion must not be a primary reason for intubation. If the specifications for protective equipment (eye protection, FFP2 or FFP-3 mask, gown) are adhered to, inhalation therapy, nasal high-flow (NHF) therapy, CPAP therapy or NIV can be carried out according to the current state of knowledge without increased risk of infection to the staff. A significant proportion of patients with respiratory failure presents with relevant hypoxemia, often also caused by a high inspiratory oxygen fraction (FiO2) including NHF, and this hypoxemia cannot be not completely corrected. In this situation, CPAP/NIV therapy can be administered under use of a mouth and nose mask or a respiratory helmet as therapy escalation, as long as the criteria for endotracheal intubation are not fulfilled. In acute hypoxemic respiratory insufficiency, NIV should be performed in an intensive care unit or in a comparable unit by personnel with appropriate expertise. Under CPAP/NIV, a patient can deteriorate rapidly. For this reason, continuous monitoring with readiness to carry out intubation must be ensured at all times. If CPAP/NIV leads to further progression of ARI, intubation and subsequent invasive ventilation should be carried out without delay if no DNI orde is in place. In the case of patients in whom invasive ventilation, after exhausting all guideline-based measures, is not sufficient, extracorporeal membrane oxygenation procedure (ECMO) should be considered to ensure sufficient oxygen supply and to remove CO 2. © 2020 Georg Thieme Verlag. All rights reserved.

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1. **Position Paper for the State-of-the-Art Application of Respiratory Support in Patients with COVID-19**  
   Pfeifer M. Respiration 2020;:No page numbers.

Against the background of the pandemic caused by infection with the SARS-CoV-2 virus, the German Respiratory Society has appointed experts to develop therapy strategies for COVID-19 patients with acute respiratory failure (ARF). Here we present key position statements including observations about the pathophysiology of (ARF). In terms of the pathophysiology of pulmonary infection with SARS-CoV-2, COVID-19 can be divided into 3 phases. Pulmonary damage in advanced COVID-19 often differs from the known changes in acute respiratory distress syndrome (ARDS). Two types (type L and type H) are differentiated, corresponding to early- and late-stage lung damage. This differentiation should be taken into consideration in the respiratory support of ARF. The assessment of the extent of ARF should be based on arterial or capillary blood gas analysis under room air conditions, and it needs to include the calculation of oxygen supply (measured from the variables of oxygen saturation, hemoglobin level, the corrected values of Hüfner's factor, and cardiac output). Aerosols can cause transmission of infectious, virus-laden particles. Open systems or vented systems can increase the release of respirable particles. Procedures in which the invasive ventilation system must be opened and endotracheal intubation carried out are associated with an increased risk of infection. Personal protective equipment (PPE) should have top priority because fear of contagion should not be a primary reason for intubation. Based on the current knowledge, inhalation therapy, nasal high-flow therapy (NHF), continuous positive airway pressure (CPAP), or noninvasive ventilation (NIV) can be performed without an increased risk of infection to staff if PPE is provided. A significant proportion of patients with ARF present with relevant hypoxemia, which often cannot be fully corrected, even with a high inspired oxygen fraction (FiO2) under NHF. In this situation, the oxygen therapy can be escalated to CPAP or NIV when the criteria for endotracheal intubation are not met. In ARF, NIV should be carried out in an intensive care unit or a comparable setting by experienced staff. Under CPAP/NIV, a patient can deteriorate rapidly. For this reason, continuous monitoring and readiness for intubation are to be ensured at all times. If the ARF progresses under CPAP/NIV, intubation should be implemented without delay in patients who do not have a "do not intubate"order. © 2020 S. Karger AG, Basel. Copyright: All rights reserved.

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1. **Refractory Acute Respiratory Distress Syndrome Secondary to COVID-19 Successfully Extubated to Average Volume-assured Pressure Support Non-invasive Ventilator**  
   Mittal Abhinav Cureus 2020;12:e7849.

Coronavirus disease 2019 (COVID-19) is a respiratory illness caused by the highly infectious novel SARS-CoV-2 coronavirus spread by droplet transmission. Consequently, the use of respiratory devices that may potentially promote aerosolization like non-invasive positive pressure ventilation (NIPPV) for diseases such as obstructive sleep apnea (OSA), advanced chronic obstructive lung disease, pulmonary hypertension (PH), and neuromuscular respiratory disease has been called into question. We present a case of a patient with history of OSA and PH convalescing from refractory acute respiratory distress syndrome (ARDS) secondary to COVID-19 who was successfully extubated to average volume-assured pressure support (AVAPS). A 74-year-old male with medical history notable for OSA on NIPPV, PH, and hypertension presented with respiratory failure secondary to COVID-19 confirmed on polymerase chain reaction (PCR) test. His respiratory status worsened leading to ARDS requiring intubation. He was initially extubated to high flow nasal cannula (HFNC) due to hospital policy to avoid NIPPV due to concerns of viral dissemination. He did not tolerate HFNC and required re-intubation for prolonged period. He was then medically optimized for a second attempt and extubated two days later to AVAPS with an anti-viral filter and negative pressure room with a goal of optimizing his critical illness myopathy and pre-existing OSA and PH. He tolerated extubation well, and over the next five days was weaned from alternating AVAPS/HFNC to eventually requiring two liters nasal cannula in the day and AVAPS mode at night. This case highlights a potential therapeutic option for patients with severe respiratory failure secondary to COVID-19. This patient's pre-existing comorbidities of OSA and PH markedly increased his risk for extubation failure on HFNC. The use of AVAPS after his second extubation attempt helped ensure ventilation and oxygenation non-invasively. COVID-19 can lead to prolonged dependence on mechanical ventilation. This pandemic has the potential to create medical resource scarcities, especially in rural areas where ventilators and trained personnel are already in short supply. By using AVAPS mode, this patient was able to rehabilitate his myopathy and participate in intermittent weaning of HFNC to ultimately simple nasal cannula. AVAPS is useful tool to facilitate extubation, as it allows non-invasive support of respiratory dynamics, particularly in those with co-morbidities such as OSA and PH. Further, larger scale studies are needed to determine its exact role during the COVID-19 pandemic. Copyright © 2020, Mittal et al.

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1. **Respiratory support for adult patients with COVID-19**  
   Whittle Jessica S. Journal of the American College of Emergency Physicians open 2020;:No page numbers.

The COVID-19 pandemic is creating unique strains on the healthcare system. While only a small percentage of patients require mechanical ventilation and ICU care, the enormous size of the populations affected means that these critical resources may become limited. A number of non-invasive options exist to avert mechanical ventilation and ICU admission. This is a clinical review of these options and their applicability in adult COVID-19 patients. Summary recommendations include: (1) Avoid nebulized therapies. Consider metered dose inhaler alternatives. (2) Provide supplemental oxygen following usual treatment principles for hypoxic respiratory failure. Maintain awareness of the aerosol-generating potential of all devices, including nasal cannulas, simple face masks, and venturi masks. Use non-rebreather masks when possible. Be attentive to aerosol generation and the use of personal protective equipment. (3) High flow nasal oxygen is preferred for patients with higher oxygen support requirements. Non-invasive positive pressure ventilation may be associated with higher risk of nosocomial transmission. If used, measures special precautions should be used reduce aerosol formation. (4) Early intubation/mechanical ventilation may be prudent for patients deemed likely to progress to critical illness, multi-organ failure, or acute respiratory distress syndrome (ARDS). Copyright © 2020 The Authors. JACEP Open published by Wiley Periodicals LLC on behalf of the American College of Emergency Physicians.

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1. **Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China: Wu C, Chen X, Cai Y, et al. JAMA Intern Med. doi:10.1001/jamainternmed.2020.0994**  
   Eastin C. Journal of Emergency Medicine 2020;58:713-714.

Presenting symptoms of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) typically include fever, dyspnea, myalgia, and cough. Previous data suggest that older adults tend to have more severe illness. This study reports characteristics of and potential risk factors for patients who developed acute respiratory distress syndrome (ARDS) or who died as a result of SARS-CoV-2, the virus that causes COVID-19. Patients aged 21 to 83 who had confirmed COVID-19 and were admitted to Jinyintan Hospital in Wuhan, China between December 25, 2019 and January 26, 2020 were included in this retrospective study. Trained clinicians abstracted data through February 13, 2020 and included epidemiological data, clinical characteristics, laboratory and radiologic findings, treatments, and outcomes. All patients had confirmed SARS-CoV-2 by throat swab sampling. Older age was defined as over 65 years old and fever was defined as a temperature higher than 37.3 degrees Celsius. The primary outcomes were development of ARDS or death among patients with ARDS. A total of 201 patients met inclusion criteria. The median age was 51 (IQR 43-60), with 19.9% of patients aged 65 years or older. Major comorbidities included hypertension (19.4%), diabetes (10.9%), and cardiovascular disease (4.0%). The most common presenting symptoms were fever (93.5%), cough (81.1%), productive cough (41.3%), dyspnea (39.8%), or fatigue/myalgia (32.3%). Most (95%) had bilateral infiltrates on chest imaging. A separate respiratory viral panel was tested on 173 patients, but only 1 had a coinfection (Influenza A). Notable abnormal laboratory values included lymphocytopenia in 64%, elevated LDH (>150U/L) in 98%, elevated high sensitivity C-reactive protein (> 5mg/L) in 85.6%, elevated erythrocyte sedimentation rate (>15 mm/h) in 93.8%, and elevated d-dimer (>1.5ug/mL) in 23.3%, among others. Once admitted, 82% of patients required oxygen. The majority (48.8%) of patients were on nasal cannula, but many (30.3%) required noninvasive ventilation. Six patients were intubated and 1 of those was also treated with extracorporeal membrane oxygenation (ECMO). Most received antibiotics and antivirals (97.5% and 84.6%, respectively), half (52.7%) received antioxidant therapy, and systemic steroids were given to 30.8%. At the end of the study, 144 (71.6%) patients had been discharged and median length of stay was 13 days (IQR 10-16 days). A total of 44 patients (21.9%) died, all of whom had developed ARDS. The remainder of the patients remained hospitalized. In comparing patients with (84, 41.8%) or without ARDS, those with ARDS were older (mean difference 12 years, 95% CI [8-16]), more likely to have comorbidities like hypertension or diabetes (differences 13.7%, 95% CI [1.3%-26.1%] and 13.9%, 95% CI [3.6%-24.2%], respectively) and more likely to present with dyspnea (difference 33.9%, 95% CI [19.7%-48.1%]). Other findings more likely to occur in patients with ARDS included lymphocytopenia, neutrophilia, elevated liver or renal measurements, and elevated inflammatory markers. Of those with ARDS who subsequently died, these patients were older (difference 18 years, 95% CI [13-23]), had lower temperatures (difference in proportion of high fever -31.8%, 95% CI [-56.5% to -7.1%]), and received antivirals less often (difference -40.7%, 95% CI [-58.5% to -22.9%]). Additionally, they had even greater abnormalities of liver and renal function, inflammatory markers, or coagulation indices than those with ARDS who survived. High fever (>39oC) was found to be positively associated with developing ARDS (HR 1.77, 95% CI [1.11-2.84]) but was negatively associated with death (HR 0.41, 95% CI [0.21-0.82]) as was treatment with systemic steroids (HR 0.38, 95% CI [0.20-0.72]). The authors concluded that major risk factors for ARDS and subsequent death were older age, neutrophilia, and evidence of end-organ damage. Comorbidities and fever appeared to be associated with ARDS but not death. Limitations included selection bias, as only patients with severe COVID-19 were hospitalized therefore oor outcomes may appear inflated. Comment: This is a large dataset in the limited nascent SARS Co-V2/COVID-19 literature, and, though it should be interpreted with caution, it does provide some valuable guidance. This study is consistent with other data that those of increased age and with comorbid conditions have worse outcomes than younger, healthier patients. Interestingly, it appears some of those with ARDS did not receive mechanical ventilation, which brings the generalizability of these results into question. Antivirals and corticosteroids may have a role in treatment of patients with ARDS related to COVID-19, but this contradicts many other recommendations to avoid corticosteroids. More research is needed.Copyright © 2020

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1. **Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Contamination in Air and Environment in Temporary COVID-19 ICU Wards**  
   Cai Ying 2020;:No page numbers.

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1. **Short term effectiveness of structured exercise therapy protocol on cardio-respiratory parameters in subjects with covid**  
   Chintamani R. International Journal of Psychosocial Rehabilitation 2020;24:7693-7700.

Introduction: It is already proved that COVID subjects are known to have symptoms like breathless at rest, fever, sore throat and other pneumonia like symptoms. Few studies have demonstrated Physiotherapy intentionally enhances invulnerability towards infection by different exercises on the stipulated part, thus increasing the strength of that part. Cardio-Pulmonary Rehabilitation is known to be useful in treating subjects with cardio-respiratory symptoms. Few studies have already demonstrated exercises have strong significant effect for managing subjects with COVID on High flow nasal cannula as well as Mechanical ventilation. According to authors knowledge there are very less number of studies demonstrating the effectiveness of the Structured Exercise Therapy Protocol for COVID subjects in both types of Oxygen therapy, hence this study is been undertaken. Objective: To investigate the Short term Effectiveness of Structured Exercise Therapy Protocol in subjects diagnosed with COVID on High flow nasal cannula versus Structured Exercise Therapy Protocol on Mechanical ventilation. Methodology: This is a randomized clinical trial conducted on 124 subjects. Subjects were randomly divided into two groups, Group A: 62 subjects with High flow nasal cannula who were given Structured Exercise therapy protocol and Group B: 62 subjects with Mechanical ventilation who were given Structured Exercise Therapy Protocol. Results: Both the groups showed significant improvement with respect to Structured Exercise therapy protocol. On comparison Group A showed high significant results in improvement among modified Borg’s scale of dyspnea, SP02, Respiratory rate, X-ray changes, Heart rate and number of active cough extraction demonstrated significant changes with p value &lt;0.001, &lt;0.05, &lt;0.05 and &lt;0.001 respectively. Whereas Group B showed significant improvement with p value &lt;0.05 for all the parameters. Conclusion: The treatment showed significant improvement in all the outcome measures in group A that is subjects with High flow nasal cannula. Hence, the conclusion is that, Structured Exercise Physiotherapy protocol in subjects with High flow nasal cannula showed early and most significant improvement in subjects with COVID in all the respiratory parameters against subjects with Mechanical Ventilation. © 2020, Hampstead Psychological Associates. All rights reserved.

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1. **Subcutaneous tocilizumab treatment in patients with severe COVID-19-related cytokine release syndrome: An observational cohort study**  
   Mastroianni A. EClinicalMedicine 2020;24:100410.

BACKGROUND: Patients with severe coronavirus disease 2019 (COVID-19) have elevated levels of acute phase reactants and inflammatory cytokines, including interleukin-6, indicative of cytokine release syndrome (CRS). The interleukin-6 receptor inhibitor tocilizumab is used for the treatment of chimeric antigen receptor T-cell therapy-induced CRS. METHODS: Patients aged 18 years or older with laboratory-confirmed COVID-19 admitted to the Annunziata Hospital in Cosenza, Italy, through March 7, 2020, who received at least one dose of tocilizumab 162 mg subcutaneously for the treatment of COVID-19-related CRS in addition to standard care were included in this retrospective observational study. The primary observation was the incidence of grade 4 CRS after tocilizumab treatment. Chest computed tomography (CT) scans were evaluated to investigate lung manifestations. FINDINGS: Twelve patients were included; all had fever, cough, and fatigue at presentation, and all had at least one comorbidity (hypertension, six patients; diabetes, five patients; chronic obstructive lung disease, four patients). Seven patients received high-flow nasal cannula oxygen therapy and five received non-invasive mechanical ventilation for lung complications of COVID-19. No incidence of grade 4 CRS was observed within 1 week of tocilizumab administration in all 12 patients (100%) and within 2 days of tocilizumab administration in 5 patients (42%). The predominant pattern on chest CT scans at presentation was ground-glass opacity, air bronchograms, smooth or irregular interlobular or septal thickening, and thickening of the adjacent pleura. Follow-up CT scans 7 to 10 days after tocilizumab treatment showed improvement of lung manifestations in all patients. No adverse events or new safety concerns attributable to tocilizumab were reported. INTERPRETATION: Tocilizumab administered subcutaneously to patients with COVID-19 and CRS is a promising treatment for reduction in disease activity and improvement in lung function. The effect of tocilizumab should be confirmed in a randomised controlled trial.

1. **The influence of changing interfaces on aerosol delivery within high flow oxygen setting in adults: An in-vitro study: Impact of interface changing on aerosol in high flow oxygen setting**  
   Madney Y. M. Journal of Drug Delivery Science and Technology 2020;55:No page numbers.

Despite the fact that the nasal-cannula is more comfortable than facemask, using facemask with high flow oxygen therapy (HFOT) may be beneficial in mouth-breathers. The aim of the present work was to evaluate aerosol-delivery both between different interfaces and flows using HFOT setting. The experiment was conducted using an Aerogen-Solo vibrating mesh nebulizer connected proximally to the humidifier in HFOT circuit using three different interfaces (nasal-cannula, mouthpiece, and valved-facemask) at 10, 20 and 30 L/min oxygen-flows. The amount of drug deposited on each part was quantified using HPLC. Total inhalable dose using facemask and mouthpiece (15.3% and 13.7% of nominal-dose, respectively) was significantly higher (p < 0.001) than that delivered by nasal-cannula (6.5% of nominal-dose) at oxygen-flow 10 L/min. Aerosol-delivery was decreased with increasing oxygen-flow regardless of the interface used. Aerosol-deposition within the interface increased significantly with increasing gas flow in nasal-cannula only. The mean inhaled-dose delivered without oxygen was 11.1, 7.4 and 1.3% of nominal-dose by valved-facemask, mouthpiece and nasal-cannula, respectively. Aerosol-deposition in the tubing of nasal-cannula only was significantly (p < 0.001) increased when aerosol nebulization was not combined with oxygen-delivery (88.0% of nominal-dose). Valved-facemask or mouthpiece can serve as an acceptable option in mouth-breathers for HFOT combined with aerosol-delivery. Increasing gas-flow decreased dose-delivered. © 2019 Elsevier B.V.

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1. **The use of high-flow nasal oxygen in COVID-19**  
   Lyons C. Anaesthesia 2020;75:843-847.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=6f0814b31a93f4dc87db1a798f9e6b4b)

1. **The utility of high-flow nasal cannula oxygen therapy in the management of respiratory failure secondary to COVID-19 pneumonia**  
   Lalla U. South African Medical Journal 2020;110:432.

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1. **Universal mobile protection system for aerosol-generating medical interventions in COVID-19 patients**  
   Straube F. Critical Care 2020;24:264.

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1. **Update efficacy of aerosol therapy with noninvasive ventilator approach (non-invasive ventilation and nasal high flow): Aerosol delivery via noninvasive ventilation**  
   Harb H. S. Journal of Drug Delivery Science and Technology 2020;59:No page numbers.

Aerosol delivery by nebulizers and pressurized metered-dose inhalers (pMDIs) attached through an adapter or spacer into a ventilation circuit during noninvasive mechanical ventilation (NIV) and high flow nasal cannula (HFNC) add great benefits in the management of obstructive lung disease patients. The inhaled medication, given during NIV and HFNC, offers better and quicker clinical effects than with unassisted breathing. Unfortunately, there is no specific recommendation or guidelines to guide therapists/clinicians in their decisions while delivering aerosols to ventilated patients which puts the patients at risk of receiving either a sub-therapeutic or toxic dose of their inhaled medications. This increases the urgency for the development of recommendations/guidelines by a trusted board/society for aerosol delivery to such critically ill patients. This review article could serve as a good guide in this field especially the methods used to quantify aerosol delivery during NIV or HFNC. © 2020 Elsevier B.V.

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1. **Using HoloLens™ to reduce staff exposure to aerosol generating procedures during a global pandemic**  
   Cafferkey John 2020;:No page numbers.

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1. **Variations in Personal Protective Equipment Preparedness in Intensive Care Units during the COVID-19 Pandemic: A Survey of Asia-Pacific Countries**  
   Rajamani Arvind 2020;:No page numbers.

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1. **[Clinical experience of high-flow nasal cannula oxygen therapy in severe corona virus disease 2019 (COVID-19) patients]**  
   He G. Zhejiang Da Xue Xue Bao Yi Xue Ban 2020;49:0.

Acute respiratory failure due to acute hypoxemia is the major manifestation in severe coronavirus disease 2019 (COVID-19) induced by severe acute respiratory syndrome coronavirus 2 infection. Rational and effective respiratory support is crucial in the management of COVID-19 patients. High-flow nasal cannula (HFNC) has been utilized widely due to its superiority over other non-invasive respiratory support techniques. To avoid HFNC failure and intubation delay, the key issues are proper patients, timely application and improving compliance. It should be noted that elder patients are vulnerable for failed HFNC. We applied HFNC for oxygen therapy in severe and critical COVID-19 patients and summarized the following experiences. Firstly, to select the proper size of nasal catheter, to locate it at suitable place, and to confirm the nose and the upper respiratory airway unobstructed. Secondly, an initial flow of 60 L/min and 37℃ should be given immediately for patients with obvious respiratory distress or weak cough ability; otherwise, low-level support should be given first and the level gradually increased. Thirdly, to avoid hypoxia or hypoxemia, the treatment goal of HFNC should be maintained the oxygen saturation (SpO(2)) above 95% for patients without chronic pulmonary disease. Finally, patients should wear a surgical mask during HFNC treatment to reduce the risk of virus transmission through droplets or aerosols.

1. **[Expert consensus on preventing nosocomial transmission during respiratory care for critically ill patients infected by 2019 novel coronavirus pneumonia]**  
   Anon. Zhonghua Jie He He Hu Xi Za Zhi 2020;43:288-296.

Definite evidence has shown that the novel coronavirus (COVID-19) could be transmitted from person to person, so far more than 1 700 bedside clinicians have been infected. A lot of respiratory treatments for critically ill patients are deemed as high-risk factors for nosocomial transmission, such as intubation, manual ventilation by resuscitator, noninvasive ventilation, high-flow nasal cannula, bronchoscopy examination, suction and patient transportation, etc, due to its high possibility to cause or worsen the spread of the virus. As such, we developed this consensus recommendations on all those high-risk treatments, based on the current evidence as well as the resource limitation in some areas, with the aim to reduce the nosocomial transmission and optimize the treatment for the COVID-19 pneumonia patients. Those recommendations include: (1)Standard prevention and protection, and patient isolation; (2)Patient wearing mask during HFNC treatment; (3)Using dual limb ventilator with filters placed at the ventilator outlets, or using heat-moisture exchanger (HME) instead of heated humidification in single limb ventilator with HME placed between exhalation port and mask; avoid using mask with exhalation port on the mask; (4)Placing filter between resuscitator and mask or artificial airway; (5)For spontaneous breathing patients, placing mask for patients during bronchoscopy examination; for patients receiving noninvasive ventilation, using the special mask with bronchoscopy port to perform bronchoscopy; (6)Using sedation and paralytics during intubation, cuff pressure should be maintained between 25-30 cmH(2)O(1 cmH(2)O=0.098 kPa); (7)In-line suction catheter is recommended and it can be used for one week; (8)Dual-limb heated wire circuits are recommended and only changed with visible soiled; (9)For patients who need breathing support during transportation, placing an HME between ventilator and patient; (10)PSV is recommended for implementing spontaneous breathing trial (SBT), avoid using T-piece to do SBT. When tracheotomy patients are weaned from ventilator, HME should be used, avoid using T-piece or tracheostomy mask. (11)Avoid unnecessary bronchial hygiene therapy; (12) For patients who need aerosol therapy, dry powder inhaler metered dose inhaler with spacer is recommended for spontaneous breathing patients; while vibrating mesh nebulizer is recommended for ventilated patients and additional filter is recommended to be placed at the expiratory port of ventilation during nebulization.

1. **A comparative in vitro study of standard facemask jet nebulization and high-flow nebulization in bronchiolitis**  
   Valencia-Ramos J. Experimental Lung Research 2019;45:13-21.

Aim of Study: The use of a nebulizer paired with high-flow nasal cannulas (HFNC) has been proposed for drug delivery in bronchiolitis. Particle size nebulized is a relevant factor determining the efficacy of the nebulization. We replicated in vitro the theoretical parameters most widely used in bronchiolitis and we compared the size of the droplet nebulized with a standard nebulizer and a nebulizer integrated into HFNC. Materials and Methods: We used laser diffraction to analyze the particle size nebulized (volume median diameter Dv50). The standard system was a jet nebulizer connected to a facemask with a flow rate of 8 L/min (JN). Three designs were used as nebulizers integrated into HFNC: a vibrating mesh nebulizer set 1) before (HFNC-BH) and 2) after (HFNC-AH) the humidifier, and 3) a jet nebulizer connected before the nasal cannula (HFNC-BNC). HFNC was used with neonatal (3–8 L/min) and infant cannulas (8–15 L/min). Results: Droplet size was similar among the three drugs studied. A lower particle size was obtained when using the nebulization system integrated into HFNC compared to the standard nebulizer, regardless of the flow rate and the nasal cannula used when the position of the nebulizer was before the nasal cannula (p < 0.05): 6.89 µm (JN), 2.49 µm (HFNC-BNC 3 L/min), 2.59 µm (HFNC-BNC 5 L/min), 2.44 µm (HFNC-BNC 8 L/min), 3.22 µm (HFNC-BNC 10 L/min), 3.23 µm (HFNC-BNC 13 L/min), 3.16 µm (HFNC-BNC 15 L/min). The particle size was lower in HFNC-BF compared to the HFNC-AH using neonatal nasal cannula (3–8 L/min) (p < 0.05). Conclusion: The use of a nebulizer integrated with HFNC has shown promising results in an experimental scenario of bronchiolitis. The particle size achieved with the nebulizer placed before the humidifier is equivalent to the one obtained via conventional nebulization, and it is even smaller when the integrated nebulizer is placed before the nasal cannulas. © 2019, © 2019 Taylor & Francis Group, LLC.

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1. **Aerosol delivery through an adult high-flow nasal cannula circuit using low-flow oxygen**  
   Madney Y. M. Respiratory Care 2019;64:453-461.

BACKGROUND: There has been a growing trend toward delivering aerosolized medications using high-flow nasal cannula (HFNC). In some cases, patients who do not require high-flow oxygen to maintain adequate oxygenation may benefit from aerosol delivery while receiving low-flow oxygen via HFNC. The objective of this study was to quantify and compare the relative pulmonary and systemic delivery of salbutamol, with 2 different nebulizers, in patients with COPD receiving low-flow oxygen therapy through an HFNC. METHODS: Subjects were randomized to receive study doses of 5 mg salbutamol nebulized by either a jet nebulizer or a vibrating mesh nebulizer with a T-piece or spacer on days 1, 3, and 5 of admission. Subjects using the large spacer also received 2 puffs (100 μg each) of salbutamol via a pressurized metered-dose-inhaler prior to the nebulizer dose. Urinary salbutamol excretion 30 min post-inhalation and pooled samples of urinary salbutamol excretion up to 24 h post-inhalation were measured. On day 2, ex vivo studies were performed with salbutamol collected on filters placed between the HFNC and nebulizer, with drug eluted from filters and analyzed to determine inhaled dose. RESULTS: Twelve subjects (6 females), age 51.3 ± 11.2 y, were included. The vibrating mesh nebulizer demonstrated higher urinary salbutamol excretion at 30 min and 24 h post-inhalation compared to a jet nebulizer (P = .001 and P = .02, respectively). No significant difference was found between the T-piece and large-spacer configurations, even though the spacer provided a significantly larger emitted aerosol dose at the opening of the HFNC (P = .002). CONCLUSIONS: Aerosolized medication could be efficiently combined with low-flow oxygen, via HFNC, in COPD subjects without the need to interrupt the gas supply. The vibrating mesh nebulizer delivered larger doses to subjects compared to the jet nebulizer. However, there was no benefit of using the large spacer with HFNC in low-flow delivery, because the small inner diameter of the HFNC does not allow larger aerosol droplet sizes (preserved by the spacer) to reach the subject. © 2019 Daedalus Enterprises.

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1. **Aerosol Delivery Through an Adult High-Flow Nasal Cannula Circuit Using Low-Flow Oxygen.**  
   Yasmin M. Madney Respiratory care 2019;:No page numbers.

Aerosol Delivery Through an Adult High-Flow Nasal Cannula Circuit Using Low-Flow Oxygen. There has been a growing trend toward delivering aerosolized medications using high-flow nasal cannula (HFNC). In some cases, patients who do not require high-flow oxygen to maintain adequate oxygenation may benefit from aerosol delivery while receiving low-flow oxygen via HFNC. The objective of this study was to quantify and compare the relative pulmonary and systemic delivery of salbutamol, with 2 different nebulizers, in patients with COPD receiving low-flow oxygen therapy through an HFNC.Subjects were randomized to receive study doses of 5 mg salbutamol nebulized by either a jet nebulizer or a vibrating mesh nebulizer with a T-piece or spacer on days 1, 3, and 5 of admission. Subjects using the large spacer also received 2 puffs (100 μg each) of salbutamol via a pressurized metered-dose-inhaler prior to the nebulizer dose. Urinary salbutamol excretion 30 min post-inhalation and pooled samples of urinary salbutamol excretion up to 24 h post-inhalation were measured. On day 2, ex vivo studies were performed with salbutamol collected on filters placed between the HFNC and nebulizer, with drug eluted from filters and analyzed to determine inhaled dose.Twelve subjects (6 females), age 51.3 ± 11.2 y, were included. The vibrating mesh nebulizer demonstrated higher urinary salbutamol excretion at 30 min and 24 h post-inhalation compared to a jet nebulizer (P = .001 and P = .02, respectively). No significant difference was found between the T-piece and large-spacer configurations, even though the spacer provided a significantly larger emitted aerosol dose at the opening of the HFNC (P = .002).Aerosolized medication could be efficiently combined with low-flow oxygen, via HFNC, in COPD subjects without the need to interrupt the gas supply. The vibrating mesh nebulizer delivered larger doses to subjects compared to the jet nebulizer. However, there was no benefit of using the large spacer with HFNC in low-flow delivery, because the small inner diameter of the HFNC does not allow larger aerosol droplet sizes (preserved by the spacer) to reach the subject.Copyright © 2019 by Daedalus Enterprises.

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1. **Aerosol drug delivery to the lungs during nasal high flow therapy: an in vitro study**  
   Wallin Martin BMC pulmonary medicine 2019;19:42.

BACKGROUND: Aerosol delivery through a nasal high flow (NHF) system is attractive for clinicians as it allows for simultaneous administration of oxygen and inhalable drugs. However, delivering a fine particle fraction (FPF, particle wt. fraction < 5.0 mum) of drugs into the lungs has been very challenging, with highest value of only 8%. Here, we aim to develop an efficient nose-to-lung delivery system capable of delivering improved quantities (FPF > 16%) of dry powder aerosols to the lungs via an NHF system., METHODS: We evaluated the FPF of spray-dried mannitol with leucine with a next generation impactor connected to a nasopharyngeal outlet of an adult nasal airway replica. In addition, we investigated the influence of different dispersion (20-30 L/min) and inspiratory (20-40 L/min) flow rates, on FPF., RESULTS: We found an FPF of 32% with dispersion flow rate at 25 L/min and inspiratory flow rate at 40 L/min. The lowest FPF (21%) obtained was at the dispersion flow rate at 30 L/min and inspiratory flow rate at 30 L/min. A higher inspiratory flow rate was generally associated with a higher FPF. The nasal cannula accounted for most loss of aerosols., CONCLUSIONS: In conclusion, delivering a third of inhalable powder to the lungs is possible in vitro through an NHF system using a low dispersion airflow and a highly dispersible powder. Our results may lay the foundation for clinical evaluation of powder aerosol delivery to the lungs during NHF therapy in humans.

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1. **Assessment of aerosol delivery during simulated invasive ventilation, non-invasive ventilation and high flow nasal therapy**  
   Bennett G. Journal of Aerosol Medicine and Pulmonary Drug Delivery 2019;32:A5.

Patients receiving mechanical ventilation are often prescribed nebulised therapy. Non-invasive ventilation and high flow nasal therapy are increasingly used for ventilatory support in patients with acute respiratory failure. Some patients receiving these therapies may also benefit from inhaled drug delivery. The objective of this study was to evaluate aerosol delivery during simulated adult mechanical ventilation, non-invasive ventilation and high flow nasal therapy using a vibrating mesh nebuliser. Simulated adult mechanical ventilation assessed the filter dose beyond the endotracheal tube across four potential nebuliser placement positions within the circuit. Simulated non-invasive ventilation assessed the filter dose when the nebuliser (Aerogen Solo, Aerogen, Ireland) was positioned between the facemask (Pneumocare Health, India) and the patient circuit with continuous positive airway pressure (10cmH20 and 15cmH20). Simulated high flow nasal therapy assessed the filter dose downstream of the model oropharyngeal region at two clinically relevant gas flow rates, in line with the Fisher & Paykel Airvo 2. For each ventilation type, a 2mL dose of albuterol sulphate (2mg/mL) was nebulised using a vibratingmesh nebuliser (Aerogen Solo, Aerogen, Ireland) of similar droplet size (4.5lm). The drug captured on a filter was eluted using a 10mL buffer solution of 0.1M HCI. The mass of drug eluted was determined using UV spectroscopy at 276nm. The greatest aerosol delivery was observed during simulated noninvasive ventilation (26.79%), in comparison with invasive ventilation (22.81%) and high flow nasal therapy (21.00%). A one way analysis of variance resulted in a p-value of 0.0012, indicating that there was a statistically significance difference in aerosol delivery between each type of ventilatory support. This study suggests that continuity of high efficiency aerosol delivery is possible across both invasive and non-invasive patient interventions using a vibrating mesh nebuliser.

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1. **Comparison of high-flow nasal cannula versus oxygen face mask for environmental bacterial contamination in critically ill pneumonia patients: a randomized controlled crossover trial**  
   Leung C. C. H. Journal of Hospital Infection 2019;101:84-87.

Whereas high-flow nasal cannula use is gaining prevalence, its high gas flow raises concerns about aerosolization of infectious particles and spread of infection. This randomized controlled crossover non-inferiority trial (N = 20) evaluated the degree of environmental contamination by viable bacteria associated with the use of high-flow nasal cannula compared with conventional oxygen mask for critically ill patients with Gram-negative pneumonia. The results show that high-flow nasal cannula use was not associated with increased air or contact surface contamination by either Gram-negative bacteria or total bacteria, suggesting that additional infection control measures are not required. © 2018 The Author(s)

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1. **Decrease the flow setting to improve trans-nasal pulmonary aerosol delivery via “high-flow nasal cannula” to infants and toddlers**  
   Li J. Pediatric Pulmonology 2019;54:914-921.

Objectives: Trans-nasal pulmonary aerosol delivery for infants and toddlers has recently gained popularity, however, the reported lung deposition is low. We aimed to investigate the influential factors to improve the delivery. Methods: Anatomic airway manikins simulating infant (5 kg) and toddler (15 kg) with collecting filter connected the trachea and breath simulator, were set to represent quiet and distressed breathing. Nasal cannula flow was set at 0.125, 0.25, 0.5, 1, and 2 L/kg/min. A mesh nebulizer (Aerogen) was placed at the inlet of humidifier (Fisher & Paykel) and proximal to patient. Albuterol (5 mg in 1 mL) was nebulized for each condition (n = 3). Drug was eluted from the filter and assayed with UV spectrophotometry (276 nm). Results: Inhaled dose was higher with nebulizer placed at the inlet of humidifier than proximal to patient in all settings, except the infant model at low gas flow settings (0.125 and 0.25 L/kg/min). When nebulizer was placed at the inlet of humidifier, inhaled dose was higher when gas flow was below patient's inspiratory flow than when gas flow exceeded patient's inspiratory flow (8.77 ± 3.84 vs 2.16 ± 1.29%, P < 0.001); aerosol deposition increased as gas flow decreased, with greatest deposition at gas flow of 0.25 L/kg/min (11.29 ± 2.15%). A multiple linear regression identified gas flow as the primary predictor of aerosol delivery. Conclusions: Trans-nasal pulmonary aerosol delivery was significantly improved when gas flow was below patient's inspiratory flow, aerosol deposition increased with decreased nasal cannula flow, with greatest deposition at 0.25 L/kg/min. © 2019 Wiley Periodicals, Inc.

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1. **Development of a high-flow nasal cannula and pharmaceutical aerosol combination device**  
   Spence B. M. Journal of Aerosol Medicine and Pulmonary Drug Delivery 2019;32:224-241.

Background: Aerosol drug delivery to the lungs is known to be very inefficient during all forms of noninvasive ventilation, especially when the aerosol is administered simultaneously with high-flow nasal cannula (HFNC) therapy. The objective of this study was to develop a new combination device based on vibrating mesh nebulizers that can provide continuously heated and humidified HFNC therapy as well as on-demand pharmaceutical aerosols with high efficiency. Methods: The combination device implemented separate mesh nebulizers for generating humidity (humidity nebulizer) and delivering the medical aerosol (drug nebulizer). Nebulizers were actuated in an alternating manner with the drug nebulizer delivering the medication during a portion of an adult inhalation cycle. Aerosol entered a small-volume mixing region where it was combined with ventilation gas flow and then entered a heating channel to produce small particles that are desirable for nose-to-lung administration and potentially excipient enhanced growth delivery. Three assessment methods (analytical calculations, computational fluid dynamics [CFD] simulations, and in vitro experiments in three-dimensional [3D] printed devices) were used to improve the mixer-heater design to minimize depositional drug losses, maintain a small device volume, ensure sufficient droplet evaporation, and control the outlet thermodynamic conditions. Results: For an initial configuration (Design 1), good agreement in performance metrics was found using the three assessment methods. Based on insights gained from the CFD simulations of Design 1, two new designs were developed and produced with 3D printing. Experimental analysis indicated that the new designs both achieved <5% depositional loss in the mixer-heater even with cyclic operation and sufficiently dried the aerosol from an initial size of 5.3 μm to an outlet size of ∼1.0 μm. A combination of the applied methods indicated that the desired thermodynamic conditions of HFNC therapy were also met. Conclusions: Multiple methodological approaches were used concurrently to develop a new combination device for administering HFNC therapy and simultaneous on-demand pharmaceutical aerosols to the lungs with high efficiency. The use of a small-volume mixer-heater (<100 mL), synchronization of the drug nebulizer with inhalation, and small outlet particle size should enable high efficiency lung delivery of the aerosol. © Copyright 2019, Mary Ann Liebert, Inc., publishers 2019.

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1. **Effect of nebulizer type, delivery interface, and flow rate on aerosol drug delivery to spontaneously breathing pediatric and infant lung models**  
   Ari A. Pediatric Pulmonology 2019;54:1735-1741.

Background: Different types of nebulizers, interfaces, and flow rates are used to deliver aerosolized medications to children. The purpose of this study was to determine the effect of nebulizer type, delivery interface, and flow rate on aerosol drug delivery to spontaneously breathing pediatric and infant lung models. Methodology: A teaching mannequin was attached to a sinusoidal pump via a collecting filter at the bronchi to simulate a spontaneously breathing child (Vt: 250 mL, RR: 20 bpm and Ti: 1 second) and infant (Vt = 100 mL, RR = 30 bpm, Ti: 0.7 seconds). Albuterol sulfate was nebulized with jet (Misty Max 10; Cardinal Health) and mesh (Aerogen Solo; Aerogen) nebulizers using a low-flow nasal cannula (LFNC; Hudson), a high-flow nasal cannula (HFNC; Fisher & Paykel), face mask (FM; Hudson), and mouthpiece (MP; Cardinal Health). While all interfaces were used in the pediatric study, only LFNC, HFNC, and FM were tested in the infant study. The mesh nebulizer was tested at 2, 4, and 6 L/min with LFNC, 4 and 6 L/min with HFNC, and 6 L/min with FM and MP. The jet nebulizer was operated at 6 and 8 L/min with FM and 6 L/min with LFNC, HFNC, and MP (n = 5). The drug was eluted from the filter and analyzed by spectrophotometry. Factorial analysis of variance and post hoc comparisons were used for data analysis. P <.05 was considered statistically significant. Results: Delivery efficiency of mesh nebulizers is two to fourfold more than jet nebulizers used with HFNC, FM, and MP. No statistical difference was found between jet and mesh nebulizers used with LFNC in infants (P =.643) and pediatrics (P =.255). Aerosol delivery with MP was the best compared to other interfaces used in pediatrics (P <.05). As the second-best interface in aerosol drug delivery, the delivery efficiency of FM was greater than HFNC (P =.0001) and LFNC (P =.0001). Increasing flow rate with LFNC and HFNC decreased aerosol delivery with the mesh nebulizer in both infants and pediatrics. Conclusion: The type of nebulizer, delivery interface, and flow rate used in the treatment of children affect aerosol drug delivery. © 2019 Wiley Periodicals, Inc.

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1. **Evaluation of aerosol delivery across treatment modalities during simulated high flow nasal therapy**  
   Bennett G. Journal of Aerosol Medicine and Pulmonary Drug Delivery 2019;32:A20-A21.

Introduction: Current clinical practice for concurrent aerosol delivery during high flow nasal therapy (HFNT) can involve the use of a facemask placed over the nasal cannula. Here, we assess aerosol delivery across combinations of different drug delivery modalities, using two nebuliser types. Method(s): A vibrating mesh nebuliser (VMN) (Aerogen Solo, Aerogen, Ireland) was used with the Airvo 2 system (F&P, NZ), at a gas flow rate of 50LPM. A jet nebuliser ( JN) was used with a facemask (Cirrus2 at 8LPM driving gas flow rate, Intersurgical, UK). A facemask and/or nasal cannula were positioned on an adult nosethroat model that was connected to a breathing simulator (Ingmar Medical, US) via a filter (Baxter, Ireland) (Vt 500 ml, BPM 15, I:E 1:1). A 2mL dose of 2mg/mL albuterol sulphate (GSK, Ireland) was nebulised. The mass of drug captured on a filter placed distal to the trachea was quantified using UV spectroscopy at 276 nm. Result(s): Table 1. Tracheal dose (%) across modalities. Modality Tracheal dose (%) VMN + HFNT at 50LPM 2.88 +/- 0.15 Facemask + JN + HFNT at 50LPM 0.82 +/- 0.16 Facemask + JN 6.13 +/- 0.09 Conclusion(s): Greater aerosol delivery was observed when the VMN was integrated with HFNT (2.88 +/- 0.15), as opposed to standard practice JN and facemask, placed over the cannula (0.82 +/- 0.16). Increased aerosol delivery was observed when HFNT was discontinued, and a JN with facemask used (6.13 +/- 0.09). However in this scenario, the patient would not be receive supplemental oxygen.

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1. **Exhaled air dispersion during high-flow nasal cannula therapy versus CPAP via different masks - PubMed**  
   David S. Hui The European respiratory journal 2019;53(4):1802339 .

Exhaled air dispersion during HFNC and CPAP via different interfaces is limited provided there is good mask interface fitting.

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1. **HERPES SIMPLEX VIRUS-1 TRACHEITIS AND FAILURE TO WEAN FROM MECHANICAL VENTILATION IN AN IMMUNOCOMPETENT HOST**  
   Kohal T. Chest 2019;156:A794.

SESSION TITLE: Monday Medical Student/Resident Case Report Posters SESSION TYPE: Med Student/Res Case Rep Postr PRESENTED ON: 10/21/2019 02:30 PM - 03:15 PM INTRODUCTION: Herpes simplex virus-1 (HSV -1) is an ever-ubiquitous pathogen with the ability to infect multiple organ systems. In immunocompetent adult hosts, clinical infection with HSV-1 in the respiratory system is rare, though HSV-1 has been detected in respiratory secretions of mechanically ventilated, immunocompetent patients. It has also been implicated as a rare and reversible cause of tracheal stenosis in patients with failure to wean from mechanical ventilation. CASE PRESENTATION: We present a 42 year old woman with a past medical history of asthma, history of pulmonary embolism and prior history of tracheostomy, who presented to our intensive care unit (ICU) as a transfer from an outside hospital where she had been treated for non-productive cough, fever, chills and acute hypoxic respiratory failure. On admission to our facility, she had increased oxygen requirements which escalated from high flow nasal cannula to mechanical ventilation. A CT scan revealed diffuse bilateral airspace and interstitial disease as well as tracheal stenosis at the site of her prior tracheostomy. Though the patient had been treated appropriately with broad-spectrum antibiotics for an extensive period of time, she had worsening respiratory failure with persistent leukocytosis and fevers. A bronchoscopy with bronchoalveolar lavage was performed, revealing a negative microbial work up with exception of polymerase chain reaction (PCR) detection of HSV-1. She was started on acyclovir, and in under 48 hours, was subsequently weaned from the ventilator. DISCUSSION: Respiratory failure with tracheobronchial involvement secondary to HSV infection in immunocompetent hosts is likely under recognized and under-reported. Based on our case and limited literature, HSV-1 has the potential to cause tracheal stenosis with tracheitis and respiratory failure with failure to wean from ventilation. Current treatment with acyclovir is effective in resolving the infection, and may have the additional benefit of reversing tracheal stenosis. Post treatment bronchoscopy has even demonstrated resolution of the inflammation and narrowing in some reports. CONCLUSION(S): In immunocompetent hosts with respiratory failure with tracheal stenosis and failure to wean from ventilation, HSV infection of the trachea or bronchial tree should be considered. Testing of HSV via PCR is available, and further case series and reports can add to this growing body of literature. Reference #1: Luyt CE, Combes A, Nieszkowska A, Trouillet JL, Chastre J. Viral infections in the ICU. Curr Opin Crit Care. 2008;14(5):605-8. Reference #2: Roy C. St. john, M.D.; and Eric R. ltlcht, M.D., F.C.C.P. Tracheal Stenosis and Failure to Wean from Mechanical Ventilation due to Herpetic Tracheitis. CHEST. 1990. Reference #3: Hunt DP, Muse VV, Pitman MB. Case records of the Massachusetts General Hospital. Case 12-2013. An 18-year-old woman with pulmonary infiltrates and respiratory failure. N Engl J Med. 2013;368(16):1537-45. DISCLOSURES: No relevant relationships by David Henkin, source=Web Response No relevant relationships by Tania Kohal, source=Web ResponseCopyright © 2019 American College of Chest Physicians

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1. **High-Efficiency Nose-to-Lung Aerosol Delivery in an Infant: Development of a Validated Computational Fluid Dynamics Method**  
   Bass K. Journal of Aerosol Medicine and Pulmonary Drug Delivery 2019;32:132-148.

Background: Computational fluid dynamics (CFD) provides a powerful tool for developing new high-efficiency aerosol delivery strategies, such as nose-to-lung (N2L) aerosol administration to infants and children using correctly sized aerosols. The objective of this study was to establish numerically efficient CFD solution methods and guidelines for simulating N2L aerosol administration to an infant based on comparisons with concurrent in vitro experiments. Materials and Methods: N2L administration of a micrometer-sized aerosol (mass median aerodynamic diameter [MMAD] = 1.4 μm) was evaluated using concurrent CFD simulations and in vitro experiments. Aerosol transport and deposition was assessed in a new nasal airway geometry of a 6-month-old infant with a streamlined nasal cannula interface, which was constructed as a CFD mesh and three-dimensionally printed to form an identical physical prototype. CFD meshes explored were a conventional tetrahedral approach with near-wall (NW) prism elements and a new polyhedral mesh style with an equally refined NW layer. The presence of turbulence in the model was evaluated using a highly efficient low-Reynolds number (LRN) k-ω turbulence model, with previously established NW corrections that accounted for anisotropic wall-normal turbulence as well as improved NW velocity interpolations and hydrodynamic particle damping. Results: Use of the new polyhedral mesh was found to improve numerical efficiency by providing more rapid convergence and requiring fewer control volumes. Turbulent flow was found in the nasal geometry, generated by the inlet jets from the nasal cannula interface. However, due to the small particle size, turbulent dispersion was shown to have little effect on deposition. Good agreement was established between the CFD predictions using the numerically efficient LRN k-ω model with appropriate NW corrections and in vitro deposition data. Aerosol transmission efficiencies through the delivery tube, nasal cannula, and infant nasal model, based on experimental and CFD predictions, were 93.0% and 91.5%, respectively. Conclusions: A numerically efficient CFD approach was established to develop transnasal aerosol administration to infants and children. Small particle aerosols with aerodynamic diameters of ∼1.5 μm were confirmed to have low inertial depositional loss, and have low deposition from turbulent dispersion, making them ideal for high-efficiency lung delivery through an infant nasal cannula interface. © Copyright 2019 Mary Ann Liebert, Inc.

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1. **Impact of gas flow and humidity on trans-nasal aerosol deposition via nasal cannula in adults: A randomized cross-over study**  
   Alcoforado L. Pharmaceutics 2019;11:No page numbers.

Background: Trans-nasal pulmonary aerosol delivery using high flow nasal cannula (HFNC) devices is described with the administration of high gas flows exceeding patient inspiratory flow (HF) and with lower flows (LF). The aim of this pilot clinical trial was to compare deposition and distribution of radiolabeled aerosol via nasal cannula in healthy adults across three rates of gas flow delivered with active heated humidification, and to further identify the impact of aerosol administration without heated humidity. Methods: Twenty-three (23) healthy adults (16F) were randomized to receive aerosol with active heated humidification or unheated oxygen at gas flows of 10 L/min (n = 8), 30 L/min (n = 7), or 50 L/min (n = 8). Diethylenetriaminepentaacetic acid labeled with 1 millicurie (37 MBq) of Technetium-99m (DTPA-Tc99m) was mixed with NaCl to a fill volume of 1 mL, and administered via mesh nebulizer placed at the inlet of the humidifier. Radioactivity counts were performed using a gamma camera and the regions of interest (ROIs) were delimited with counts from the lungs, upper airways, stomach, nebulizer, circuit, and expiratory filter. A mass balance was calculated and each compartment was expressed as a percentage of the total. Results: Lung deposition (mean ± SD) with heated humidified gas was greater at 10 L/min than 30 L/min or 50 L/min (17.2 ± 6.8%, 5.71 ± 2.04%, and 3.46 ± 1.24%, respectively; p = 0.0001). Using unheated carrier gas, a lung dose of aerosol was similar to the active heated humidification condition at 10 L/min, but greater at 30 and 50 L/min (p = 0.011). Administered gas flow and lung deposition were negatively correlated (r = −0.880, p < 0.001). Conclusions: Both flow and active heated humidity inversely impact aerosol delivery through HFNC. Nevertheless, aerosol administration across the range of commonly used flows can provide measurable levels of lung deposition in healthy adult subjects (NCT 02519465). © 2019 by the author. Licensee MDPI, Basel, Switzerland.

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1. **Impact of Gas Flow and Humidity on Trans-Nasal Aerosol Deposition via Nasal Cannula in Adults: A Randomized Cross-Over Study.**  
   Luciana Alcoforado Pharmaceutics 2019;11:No page numbers.

Impact of Gas Flow and Humidity on Trans-Nasal Aerosol Deposition via Nasal Cannula in Adults: A Randomized Cross-Over Study. Trans-nasal pulmonary aerosol delivery using high flow nasal cannula (HFNC) devices is described with the administration of high gas flows exceeding patient inspiratory flow (HF) and with lower flows (LF). The aim of this pilot clinical trial was to compare deposition and distribution of radiolabeled aerosol via nasal cannula in healthy adults across three rates of gas flow delivered with active heated humidification, and to further identify the impact of aerosol administration without heated humidity.Twenty-three (23) healthy adults (16F) were randomized to receive aerosol with active heated humidification or unheated oxygen at gas flows of 10 L/min (n = 8), 30 L/min (n = 7), or 50 L/min (n = 8). Diethylenetriaminepentaacetic acid labeled with 1 millicurie (37 MBq) of Technetium-99m (DTPA-Tc99m) was mixed with NaCl to a fill volume of 1 mL, and administered via mesh nebulizer placed at the inlet of the humidifier. Radioactivity counts were performed using a gamma camera and the regions of interest (ROIs) were delimited with counts from the lungs, upper airways, stomach, nebulizer, circuit, and expiratory filter. A mass balance was calculated and each compartment was expressed as a percentage of the total.Lung deposition (mean ± SD) with heated humidified gas was greater at 10 L/min than 30 L/min or 50 L/min (17.2 ± 6.8%, 5.71 ± 2.04%, and 3.46 ± 1.24%, respectively; p = 0.0001). Using unheated carrier gas, a lung dose of aerosol was similar to the active heated humidification condition at 10 L/min, but greater at 30 and 50 L/min (p = 0.011). Administered gas flow and lung deposition were negatively correlated (r = -0.880, p < 0.001).Both flow and active heated humidity inversely impact aerosol delivery through HFNC. Nevertheless, aerosol administration across the range of commonly used flows can provide measurable levels of lung deposition in healthy adult subjects (NCT02519465).

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1. **In vitro comparison of breath synchronized and continuous aerosol via vibrating mesh nebulizer with different position and flows in adult trans-nasal aerosol delivery**  
   Li J. Journal of Aerosol Medicine and Pulmonary Drug Delivery 2019;32:A20.

Introduction: Breath synchronized (SYNC) aerosol is associated with higher inhaled dose than continuous (CONT) during mechanical ventilation, we aimed to compare SYNC and CONT aerosol by vibrating mesh nebulizer (VMN) via HFNC. Method(s): An adult manikin (Laerdal) with collecting filter distal to the trachea attached to pump simulating quiet and distressed breathing. Nasal cannula gas flows (GF) of 5, 10, 20, 40 and 60 L/min. VMN was placed at the inlet of humidifier and proximal to patient. SYNC aerosol was set 50% of the inspiratory time. Albuterol (2.5mg in 1mL) was nebulized for each condition (n=3). Drug was eluted from the filter and assayed with UV spectrophotometry (276 nm). Result(s): When GF < inspiratory flow (IF), SYNC inhaled dose was higher than that of GF < IF [20.5(12.9, 24.2) vs 4.0(2.2, 6.9) %, p < .001]. Moreover, SYNC inhaled dose was similar with both neb positions, but higher than CONT with neb placed at the inlet of humidifier [20.6(9.8, 27.2) vs 17.4(16.3, 19) %, p=.029]. When GF > IF, SYNC inhaled dose with neb placed proximal was greater than the inlet of humidifier [6.9(4.8, 7.5) vs 2.2(1.2, 3.5) %, p < .001], but similar with CONT at the inlet of humidifier. CONT inhaled dose was higher with VMN placed at the inlet of humidifier than proximal. Conclusion(s): When gas flow was lower than inspiratory flow, inhaled dose with VMN placed at the inlet of humidifier was higher than close to patient, and inhaled dose with SYNC VMN was higher than continuous aerosol.

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1. **Investigation of fugitive aerosols released into the environment during high-flow therapy**  
   McGrath J. A. Pharmaceutics 2019;11:No page numbers.

Background: Nebulised medical aerosols are designed to deliver drugs to the lungs to aid in the treatment of respiratory diseases. However, an unintended consequence is the potential for fugitive emissions during patient treatment, which may pose a risk factor in both clinical and homecare settings. Methods: The current study examined the potential for fugitive emissions, using albuterol sulphate as a tracer aerosol during high-flow therapy. A nasal cannula was connected to a head model or alternatively, a interface was connected to a tracheostomy tube in combination with a simulated adult and paediatric breathing profile. Two aerodynamic particle sizers (APS) recorded time-series aerosol concentrations and size distributions at two different distances relative to the simulated patient. Results: The results showed that the quantity and characteristics of the fugitive emissions were influenced by the interface type, patient type and supplemental gas-flow rate. There was a trend in the adult scenarios; as the flow rate increased, the fugitive emissions and the mass median aerodynamic diameter (MMAD) of the aerosol both decreased. The fugitive emissions were comparable when using the adult breathing profiles for the nasal cannula and tracheostomy interfaces; however, there was a noticeable distinction between the two interfaces when compared for the paediatric breathing profiles. The highest recorded aerosol concentration was 0.370 ± 0.046 mg m−3 from the tracheostomy interface during simulated paediatric breathing with a gas-flow rate of 20 L/min. The averaged MMAD across all combinations ranged from 1.248 to 1.793 µm by the APS at a distance of 0.8 m away from the patient interface. Conclusions: Overall, the results highlight the potential for secondary inhalation of fugitive emissions released during simulated aerosol treatment with concurrent high-flow therapy. The findings will help in developing policy and best practice for risk mitigation from fugitive emissions. © 2019 by the authors. Licensee MDPI, Basel, Switzerland

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1. **Is aerosol delivery by high-flow nasal cannula in children an effective alternative to face mask aerosol nebulization?**  
   Kesavan S. Pediatric Pulmonology 2019;54:1873-1874.

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1. **Klebsiella pneumoniae pneumonia complicated with an abscess and empyema in an alcoholic**  
   Fernandez-Caballero S. Intensive Care Medicine Experimental 2019;7:No page numbers.

Background Klebsiella pneumoniae is a common bacterial pathogen that can cause different diseases like pneumonia, bloodstream and urinary tract infections, liver abscess, necrotizing fasciitis, meningitis, sepsis. It is an unusual cause of community acquired pneumonia except in alcoholics. An important problem is the increasing number of strains resistant to antibiotics. Materials and Methods A 63-year-old male, with a history of alcohol abuse, presented to the Emergency Department with fever, dyspnea and productive cough with greenish sputum. He complained of nausea and vomiting for the last four days. Clinical examination revealed a conscious, oriented but distressed patient. He was clammy, sweaty, tachycardic (128 beats/min), hypotensive (85/50 mmHg), tachypneic (30 breaths/min), and his oxygen saturation was 88%. Lung auscultation showed crackles and his chest X-ray an extensive right upper lobe consolidation (Fig.1). Arterial blood gas displayed a mixed acidosis with pO2 56mmHg. Blood, urine, and sputum cultures were obtained and empiric antibiotics were initiated (piperacillin-tazobactam and azithromycin). He was immediately admitted to the High Dependency Unit (HDU) with the diagnosis of pneumonia and sepsis. High flow nasal cannula was started but the patient was using accessory muscles and showed a gradually worsening shortness of breath, requiring intubation and connection to mechanical ventilation. Blood test results revealed leucopenia, lactic acidosis, acute renal failure and high CReactive Protein (CRP). Results During his admission, the patient was hypoxic and in septic shock, requiring high FiO2 and fluid resuscitation plus vaso-active amine infusion, trying to achieve hemodynamic stabilization. Thoracic computed tomography (CT) scan exhibited the presence of extensive alveolar consolidation in right upper, middle and lower lobe. A Klebsiella pneumoniae was detected in sputum and blood cultures, and ceftazidimeavibactam was started. Even though the correct treatment was used, the patient was not improving. After 10 days, a second CT demonstrated worsening consolidation, abscess in right upper lobe and empyema (Fig.2). Progressive septic shock led to multiple organ failure not responding to the intensive management. Consent Written, informed consent for publication was obtained from the patient for publication of this case report. Conclusions Klebsiella pneumoniae is an opportunistic pathogen that can cause different nosocomial infections and must be considered in alcoholic patients with severe pneumonia. This pathogen always requires prior treatment due his virulence and multiple antimicrobial resistance. We have to be very cautious with invasive infections produced by this microorganism that are strongly associated with immunocompromised populations.

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1. **Nasal High-Flow Nebulization for Lung Drug Delivery: Theoretical, Experimental, and Clinical Application**  
   Dugernier J. Journal of Aerosol Medicine and Pulmonary Drug Delivery 2019;32:341-351.

The use of nasal high-flow (NHF) therapy is rapidly spreading across acute care facilities. This raises the question of optimal delivery of inhaled medication to patients undergoing this noninvasive ventilatory support consisting in delivering heated and humidified high gas flow rates through nasal cannulas. In this article, we review experimental and clinical work evaluating the delivery of inhaled medication within the NHF circuit to target the lung without interrupting the ventilatory support. Using vibrating mesh nebulizers placed immediately upstream or downstream of the humidification chamber, with flow rates of 30-45 L/min in adults and 2-6 L/min in children and infants, about 1%-10% of the drug charged in the nebulizer may be delivered to the lungs. Compared with conventional facemask aerosol interfaces, this amount is significantly lower than amounts delivered to adults (i.e., up to 25% of the nominal dose), but similar to amounts delivered to children and infants, the latter having a predominantly nasal breathing. However, significant clinical effects have been shown in both populations when delivering bronchodilators through NHF. This interface is particularly well tolerated and may be useful to improve aerosol therapy tolerance in the pediatric setting. Thus, among patients undergoing NHF therapy, bronchodilators may be delivered through this route. Whereas other drugs may be delivered this way or if there is a patient-centered benefit to specifically use NHF for aerosol therapy among patients without ongoing ventilatory support, requires further evaluation and technological development. © 2019, Mary Ann Liebert, Inc.

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1. **Preventing deoxygenation with high flow nasal cannula oxygen during induction of general anesthesia for rigid bronchoscopy: Two case reports**  
   Min J. Y. Medicine (Baltimore) 2019;98:e15998.

RATIONALE: Rigid bronchoscopy under general anesthesia enables performing diagnostic and/or therapeutic procedures in the tracheobronchial tree. As most patients undergoing rigid bronchoscopy have moderate to severe respiratory disease or central airway obstruction, the operators often face the risk of hypoxemia when inserting the rigid bronchoscope into the patients' airway. Applying high flow nasal cannula (HFNC) oxygen therapy before the insertion of the bronchoscope allows to maintain high fractional inspired oxygen (FiO2) and thus leading to maximizing apnea time before desaturation. PATIENT CONCERNS AND DIAGNOSIS: Case 1: A 70-year-old female patient was diagnosed with lung cancer in the left lower lobe and a tracheal mass of about 2.6 cm \* 0.8 cm in size.Case 2: A male patient, 77 years old, 55.7 kg and 157.3 cm in height, had been diagnosed with chronic obstructive pulmonary disease, and was scheduled for the bronchoscopic volume reduction surgery upon exacerbation of his symptoms of dyspnea and cough with sputum. INTERVENTIONS: Preoxygenation was performed with HFNC (Fisher&Paykel Optiflow Thrive, New Zealand) for 3 minutes before the administration of anesthetic medications. The oxygen flow was set at 50 L/min and the FiO2 at 1.0. SpO2 increased to 100%. OUTCOMES: The HFNC oxygen has shown its effectiveness in safely maintaining the patients' SpO2 during the prolonged apneic period of inserting bronchoscope. LESSONS: HFNC oxygen is an effective tool in oxygenating the patients during the induction of rigid bronchoscopy, and that it may be a superior alternative to the conventional method of preoxygenation.

1. **Rhinovirus-induced Rapidly Progressing Acute Respiratory Distress Syndrome in an Immunocompetent Host**  
   Ngu S. Cureus 2019;11:e3997.

A previously healthy, 59-year-old female presented with respiratory distress and dry cough for one week. Outpatient radiographic findings were suspicious for basilar pneumonia. Empiric broad-spectrum antibiotics were started; however, she continued to deteriorate rapidly over the next 48 hours, with chest X-ray showing diffuse bilateral multifocal airspace opacities consistent with acute respiratory distress syndrome. The ratio of partial pressure arterial oxygen to fraction of inspired oxygen was 225. She required a high-flow nasal cannula with a subsequent upgrade to the intensive care unit (ICU) for increasing respiratory compromise. Polymerase chain reaction (PCR) of the nasopharyngeal aspirate confirmed human rhinovirus (hRV). High-dose intravenous steroids were started as adjuvant therapy due to the rapid decline, presumably due to a dysregulated host immune response. After 10 days in the ICU, she was discharged with tiotropium and steroid taper. Historically thought to be limited to pandemic viruses, improved detection of hRV has led to its implication in serious respiratory disorders extending beyond the oropharynx in immunocompetent hosts. We report a rare case of hRV-induced severe acute respiratory distress syndrome (ARDS) in an immunocompetent host. This case highlights the need for the early identification of viral culprits, which can minimize the use of invasive diagnostic testing and antibiotic usage.

1. **SEVERE PNEUMONITIS AND PULMONARY FIBROSIS RELATED TO A COMMON CHEMOTHERAPY AGENT**  
   Raad S. Chest 2019;156:A1253-A1254.

SESSION TITLE: Tuesday Fellows Case Report Posters SESSION TYPE: Fellow Case Report Posters PRESENTED ON: 10/22/2019 01:00 PM - 02:00 PM INTRODUCTION: Oxaliplatin is used as a standard chemotherapy agent in a large number of patients with colorectal cancer. Data regarding its pulmonary toxicity is limited to few isolated case reports of respiratory insufficiency associated with pulmonary infiltrates evolving into pulmonary fibrosis. We present a case of severe form of pulmonary toxicity due to oxaliplatin use. CASE PRESENTATION: A 70-year-old female presented with rapidly progressive shortness of breath and hypoxemia. She had no cough, sputum production, hemoptysis, chest pain, fevers, chills or other systemic symptoms. She was recently diagnosed with metastatic sigmoid colorectal cancer and received FOLFOX chemotherapy (Folinic acid, 5-Fluorouracil and Oxaliplatin). Physical examination was significant for fine end-inspiratory crackles. Initial chest radiography showed bilateral interstitial infiltrates. A complete blood count showed normal white blood cell count with elevated neutrophils. A comprehensive metabolic panel was non-revealing. A thorough infectious work-up that included blood cultures, urinalysis, urine culture, urine legionella and streptococcal antigens, and respiratory viral panel was negative. She was initially treated with vancomycin, levofloxacin and doxycycline for presumed pneumonia. Nevertheless, she continued to have worsening hypoxemia requiring high flow nasal cannula. Computed tomography scan of the chest showed lower lobe predominant ground glass opacities with traction bronchiectasis concerning for drug induced pneumonitis. Hence, she was started on methylprednisolone. A broncholaleolar lavage (BAL) was performed and showed neutrophil predominance (92%) but was negative for any viral, bacterial, or fungal infection. Autoimmune work-up showed no evidence of connective tissue disease or vasculitis. Given worsening hypoxemia, steroid dose was increased to a pulse dose of one gram daily for three days. However, patient's hypoxemia continued to deteriorate requiring initiation of mechanical ventilation, paralytics, and inhaled epoprostenol. A repeat BAL was non-revealing. Patient was extubated, transitioned to comfort care per family wishes and eventually passed away. Microscopic examination of a limited autopsy of the lung showed significant fibrosis on the trichrome stain with no specific pattern and no evidence of granulomas, vasculitis or malignancy indicating that it was likely induced by oxaliplatin. DISCUSSION: This is a case of rapidly progressing drug induced pneumonitis that did not respond to conventional medical therapy. The extensive negative work-up for other causes and autopsy findings indicate that her respiratory failure can be attributed to oxaliplatin use. CONCLUSION(S): Most cases of oxaliplatin associated pulmonary fibrosis reported in literature have a rapid and fatal course similar to our patient. Reference #1: Arvalo Lobera S, Sagastibeltza Marielarena N, Elejoste Echeberra I, Mel Oliv M, Egaa Otao L, Basterretxea Badiola L, et al. Fatal pneumonitis induced by oxaliplatin. Clin Transl Oncol. 2008;10:7647. Reference #2: Ramanathan RK, Clark JW, Kemeny NE, Lenz HJ, Gococo KO, Haller DG, et al. Safety and toxicity analysis of oxaliplatin combined with fluorouracil or as a single agent in patients with previously treated advanced colorectal cancer. J Clin Oncol. 2003;21:290411. Reference #3: Yage XH, Soy E, Marino BQ, Puig J, Fabregat MB, Colomer R, et al. Interstitial pneumonitis after oxaliplatin treatment in colorectal cancer. Clin Transl Oncol. 2006;8:624. DISCLOSURES: No relevant relationships by Doaa Atwi, source=Web Response No relevant relationships by Salim Daouk, source=Web Response No relevant relationships by Samih Raad, source=Web ResponseCopyright © 2019 American College of Chest Physicians

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1. **The influence of changing interfaces on aerosol delivery within high flow oxygen setting in adults**  
   Madney Y. M. Journal of Aerosol Medicine and Pulmonary Drug Delivery 2019;32:A7.

Oral route has been considered superior for aerosol delivery in adults, including with both low and high flow oxygen therapy (HFT). The aim of the present work was to compare the efficiency of aerosol delivery using different interfaces at different gas flow rates using HFT device. Experiment was conducted using vibrating mesh nebulizer (Aerogen Solo) connected distal to heated humidifier attached with tubing to three interfaces: mouthpiece (MP); facemask (FM); and nasal cannula (NC) through an HFT circuit at 10, 20 and 30L/min flows of oxygen. Aerosol was collected with simulated quiet adult breathing (Vt 500 mL, 15 bpm). The amount of drug deposited on collecting filter was quantified through the application of High performance liquid chromatography. The total inhalable dose (TID) decreased with increasing oxygen flow rate with each tested interface (nasal cannula, mouthpiece and face mask). At oxygen flow rate 10L/min TID with FM (15.34% of nominal dose) was higher MP (13.7%) or NC (6.5%). The difference in delivery decreased by increasing flow to 20 L/min and 30 L/min (FM (3.1%, 3.0%), MP (7.2%, 1.3%) or NC (3.9%, 2.1%, respectively). Aerosol delivery decreased with increasing oxygen flow rate regardless of the interface used within HFT setting. Facemask interface delivered more aerosol at low flow only.

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1. **The ratio of nasal cannula gas flow to patient inspiratory flow on trans-nasal pulmonary aerosol delivery for adults: An in vitro study**  
   Li J. Pharmaceutics 2019;11:No page numbers.

Trans-nasal aerosol deposition during distressed breathing is higher than quiet breathing, and decreases as administered gas flow increases. We hypothesize that inhaled dose is related to the ratio of gas flow to patient inspiratory flow (GF:IF). An adult manikin (Laerdal) with a collecting filter placed at trachea was connected to a dual-chamber model lung, which was driven by a ventilator to simulate quiet and distressed breathing with different inspiratory flows. Gas flow was set at 5, 10, 20, 40 and 60 L/min. Albuterol (2.5mg in 1 mL) was nebulized by vibrating mesh nebulizer at the inlet of humidifier at 37◦C for each condition (n = 3). Drug was eluted from the filter and assayed with UV spectrophotometry (276 nm). GF:IF was the primary predictor of inhaled dose (p &lt; 0.001). When the ratio was &lt; 1.0, the inhaled dose was higher than ratio &gt; 1.0 (21.8 ± 3.8% vs. 9.0 ± 3.7%, p &lt; 0.001), and the inhaled dose was similar between quiet and distressed breathing (22.3 ± 5.0% vs. 21.3 ± 2.7%, p = 0.379). During trans-nasal aerosol delivery, GF:IF primarily affected the inhaled dose. Compared to the ratio above 1.0, the ratio below 1.0 produced a higher and more-consistent inhaled dose. © 2019 by the authors. Licensee MDPI, Basel, Switzerland.

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1. **The use of heliox and high heated humidity nasal cannula to treat a copd patient with a bronchiectasis exacerbation**  
   Morgan S. E. American Journal of Respiratory and Critical Care Medicine 2019;199:No page numbers.

Introduction: Chronic Obstructive Pulmonary Disease (COPD) is characterized by persistent irreversible air-flow limitations associated with chronic inflammatory response and is often associated with bronchiectasis infections. Bronchiectasis is a clinical and radiological diagnosis associated with sputum production and recurrent respiratory infections that are bacterial and/or viral in origin. The diagnosis of COPD and bronchiectasis often overlap. Patients with COPD and pre-morbid bronchiectasis often have difficulty mobilizing secretion (MS) for airway clearance (AWC). Associated inter-current respiratory infections often result in increased hospitalizations from deterioration in lung function that affects gas exchange related to refractory AWC. Case Review: An 80 year old female diagnosed with COPD - chronic bronchiectasis along with other co-morbidities is on home oxygen was hospitalized for worsening dyspnea and cough. The respiratory viral panel revealed human metapneumovirus, high resolution CT-Scan showed bronchiectasis and bronchial wall thickening. Despite aggressive aerosolized beta-agonist, AWC and oxygen therapy she became more tachypnea with increased dyspnea and hypoxemia necessitating transfer to medical intensive care unit (MICU). She had mild relief from noninvasive ventilation (NIV), continuous beta-agonist therapy and alternative AWC therapies. Her clinical outlook did not improve. She opted not to be intubated, and elected "Do Not Intubated" (DNI), and placed in comfort care. While on comfort therapy, a trial of heliox with high heated humidity nasal cannula (HHHNC) (Fisher & Paykel); heated (37C) with 100% humidity was administered. She was started on heliox 70/30 at 20 L/min heliox via heliox blender (Precision Medical). Fifteen minutes into therapy, she stated that she could breathe easier. An in-line duo beta-agonist nebulizer treatment with HHHNC via Aerogen Nebulizer (Galway, Ireland) with heliox was delivered. For the first time in weeks; she had a productive cough with decreased work of breathing. The heliox was discontinued after 5h; she stayed on HHHNC overnight FIO2 40% at 10 L/min. The next day she was discharged from MICU in stable condition, 2d later discharged home. Conclusion(s): Exacerbations caused by lung infections in patients with COPD and bronchiectasis can be life threatening events. The use of heliox may have reduced turbulent obstructive gas flow dynamics and facilitated laminar gas flow, thus, improving gas exchange while HHHNC may have helped with MS and AWC resulting in remarkable improvement. Better understanding of pathogenesis of worsening pulmonary status is important for appropriate therapy selection for better outcomes in these vulnerable patients. These adjunctive modalities warrant prospective investigation for treatment of bronchiectasis related airflow limitations.

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1. **Treat the underlying cause**  
   O'Hannigan F. Irish Journal of Medical Science 2019;188:S91-S92.

Background: This case is of a 77 year old gentleman who presented with 6/52 history of shortness of breath, a cough productive of clear sputum and fevers. He had 2 recent admissions for treatment of lower respiratory tract infection, with symptoms becoming progressively worse at each presentation. His medical history was significant for ischaemic heart disease and hypertension. He is an ex-smoker of 45 years with a 15 pack-year history. The patient was in Type 1 respiratory failure and became increasingly oxygen dependant in ED. Despite best efforts with non-invasive ventilation, oxygen saturations were not maintained and he was transferred to ICU for ventilation. High resolution CT was performed which showed ground-glass changes consistent with a likely new diagnosis of interstitial lung disease. He was treated with IV Methylprednisolone and Tazobactam/piperacillin to great improvement and was extubated after 5/7. After extubation, methylprednisolone was switched to Prednisolone. Unfortunately any attempts to wean the steroid was unsuccessful and he remained on Airvo with an Fi02 of 45%. An antibody screen returned positive for anti-Ro(SSA-A), anti PL-12, and anti RO-52. ANA test was also positive for connective tissue disease, as was RA factor. These antibodies were consistent with anti-synthetase syndrome and he was worked up for Rituximab therapy. Interestingly an immunomodulator screen was positive for Hepatitis B core antibody (HBSAg negative). This was not a previously known diagnosis, nor had he any history of jaundice or liver disease. Due to this complication, our patient was commenced on Tenofovir prior to receiving Rituximab. Conclusion(s): Since commencement on rituximab this gentleman has weaned prednisolone to 10mg and is now on 6L oxygen through nasal cannula. He is currently being worked-up with physiotherapy for discharge with portable oxygen. This is a rare case of anti-synthetase syndrome presenting with pulmonary symptoms in the absence of myositis.

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1. **An unusual presentation of CMV pneumonitis**  
   Mehta G. American Journal of Respiratory and Critical Care Medicine 2018;197:No page numbers.

Pneumomediastinum with subcutaneous emphysema, also known as Hamman's syndrome, is a syndrome most commonly associated with bronchial asthma, severe cough, and even childbirth. We present to you a rare case of cytomegalovirus (CMV) pneumonitis presenting with Hamman's syndrome. A 74-year-old man presented initially to the emergency department with symptoms of cough, and malaise for five days which had progressively worsened prompting his hospital visit. His cough was productive with minimal amounts yellow tinged sputum. The patient has a medical history significant for biopsy proven AL-amyloidosis with gastrointestinal and renal involvement. He had recently completed a course of bortezomib therapy with a prolonged steroid taper. On examination, he was noted to be tachypneic with a respiratory rate of 32 and oxygen saturation of 90% on 4 liters of oxygen via nasal cannula. Chest auscultation revealed diffuse coarse breath sounds bilaterally with poor inspiratory effort. His work of breathing continued to worsen and the patient developed acute hypoxic and hypercapnic respiratory failure. Decision was made to proceed with endotracheal intubation at that time. A moderate amount of secretions were noted with suctioning of the endotracheal tube, therefore bronchoscopy was performed with bronchoalveolar lavage (BAL) and community acquired pneumonia treatment was initiated. Bronchoscopy revealed a patent airway and thick white secretions in the lower lobes. The patient continued to deteriorate clinically manifesting as increasing peak airway and plateau pressures despite a lung protective ventilator strategy. A computed tomography scan of the chest (figure 1) was obtained which revealed extensive soft tissue emphysema in the chest along with pneumomediastinum, no pneumothorax, and diffuse ground glass opacities in both lungs. High oxygen therapy was administered, and paralytics were employed. Subsequently, BAL viral cultures returned positive for CMV as did CMV DNA quantitative testing in serum to a level of 1920 IU/ml. The patient was started on prolonged intravenous ganciclovir therapy. Gradually, oxygenation and ventilation improved with corresponding improvement in chest imaging and resolution of subcutaneous emphysema and pneumomediastinum. This case illustrates a rare association between CMV pneumonitis and Hamman's syndrome in a critically ill patient. Recognition of this syndrome and its precipitant factors is critical to the institution of appropriate therapy and prevention of complications. (Figure presented) .

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1. **Application of an inline dry powder inhaler to deliver high dose pharmaceutical aerosols during low flow nasal cannula therapy**  
   Farkas D. International Journal of Pharmaceutics 2018;546:1-9.

Inline dry powder inhalers (DPIs) offer a potentially effective option to deliver high dose inhaled medications simultaneously with mechanical ventilation. The objective of this study was to develop an inline DPI that is actuated using a low volume of air (LV-DPI) to efficiently deliver pharmaceutical aerosols during low flow nasal cannula (LFNC) therapy. A characteristic feature of the new inline LV-DPIs was the use of hollow capillary tubes that both pierced the capsule and provided a pathway for inlet air and exiting aerosol. Aerosolization characteristics, LFNC depositional losses and emitted dose (ED) were determined using 10 mg powder masses of a small-particle excipient enhanced growth (EEG) formulation. While increasing the number of inlet capillaries from one to three did not improve performance, retracting the inlet and outlet capillaries did improve ED by over 30%. It was theorized that high quality performance requires both high turbulent energy to deaggregate the powder and high wall shear stresses to minimize capsule retention. Best case performance included a device ED of approximately 85% (of loaded dose) and device emitted mass median aerodynamic diameter of 1.77 µm. Maximum ED through the LFNC system and small diameter (4 mm) nasal cannula was approximately 65% of the loaded dose. Potential applications of this device include the delivery of high dose inhaled medications such as surfactants, antibiotics, mucolytics, and anti-inflammatories. © 2018 Elsevier B.V.

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1. **Benzocaine spray-induced methemoglobinemia**  
   Jiwa N. American Journal of Respiratory and Critical Care Medicine 2018;197:No page numbers.

Introduction: Severe cases of acquired methemoglobinemia are caused by the use of topical anesthetic agents, however have been noted to be uncommon. This case highlights the importance of recognizing methemoglobinemia as a cause of the saturation gap, and implementing urgent intervention of acquired methemoglobinemia Case:A 78-year-old lady status post craniotomy for a tumor resection developed post-operative atelectasis and acute hypoxic respiratory failure with mucous plugging noted on her chest X-ray. Due to her increasing oxygen requirements on 3 liters nasal cannula (NC), a bronchoscopy was performed for airway clearance and sputum analysis. Prior to the procedure, she received 3 sprays of 20% benzocaine. Post bronchoscopy, she was saturating 91% on 50% venti-mask. She subsequently desaturated to 85% requiring oxygen via non-rebreather mask. She was tachycardic and tachypneic with a cyanotic appearance. An arterial blood gas (ABG) was drawn with arterial blood noted to be a dark brown color, significant for a MetHb of 33.2%. Intravenous methylene blue was then administered and within 10 minutes, her oxygen requirements decreased to 3 liters NC. A repeat ABG 1 hour later revealed a reduced MethHb of 2.2% with clinical improvement in her oxygenation. Blood tests were repeated after 24 hours to rule out rebound methemoglobinemia, and work up was negative for glucose-6-phosphate dehydrogenase deficiency. Discussion(s): Methemoglobinemia is a rare but pathologic condition and occurs when iron in the deoxygenated heme molecule is oxidized from the ferrous to ferric state, which oxygen is unable to bind to. This reduces the ability of heme to unload oxygen to the tissues. Topical anesthetics such as benzocaine increase the oxidation of hemoglobin, whereby the internal pathways that usually convert small amounts of methemoglobin back to hemoglobin are exceeded. Symptoms of methemoglobinemia at 30-40%, include dyspnea, weakness, and headache. Severe methemoglobinemia (MetHb> 40%) leads to respiratory depression, seizures and death. Cyanosis is apparent usually 30 minutes after the administration of the inciting agent. It is critical to recognize a saturation gap, defined as a difference of >5% between the calculated oxygen saturation from an ABG and the reading from a pulse oximeter, which indicates an abnormal oxygen carrying capacity. In methemoglobinemia, the hypoxemia is refractory to oxygen therapy for this reason. Treatment for drug induced methemoglobinemia is methylene blue with continuous respiratory support and monitoring in the intensive care unit. Given this complication, judicious use of benzocaine spray should be practiced and alternative anesthetics should be considered.

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1. **Case report-child with severe pards secundary to adenovirus**  
   Rezende Caino De Oliveira F. Pediatric Critical Care Medicine 2018;19:115.

Aims & Objectives: Adenovirus infections occur primarily in infants and children<5 years of age and account for 2% to 5% of respiratory illnesses among pediatric. Although most children with an adenovirus infection develop mild upper respiratory tract disease, more severe cases may occur with lower respiratory tract involvement. Methods Case report of a child with ARDS treated in the PICU Results L A P, 2 years, 10,295 Kg, entered with a history of 5 days of fever and productive cough and vomiting. Introduced antibiotics on diagnosis of Pneumonia. She presented worsening of the respiratory effort, transferred to PICU, initially receiving support of High Flow Nasal Canula. Positive for Adenovirus and Echocardiogram with discrete alteration. Mechanical Ventilation with protective strategy and sedoanalgesia without satisfactory response observed. Increased ventilatory parameters, maintaining hypercapnia and severe hypoxemia, hemodynamic instability in the use of Amines in high doses.Adjuvant therapies such as prone position and Nitric Oxide were done. It continued with respiratory acidosis and hypoxemia, opting for High Frequency Oscillatory Ventilation associated with the adjuvant therapies. After this therapy, progressive improvement and in five days progressed weaning to conventional ventilation for another 6 days being extubated successfully receiving discharge to ward without sequelae Conclusions Adenovirus pneumonia in children can manifest with severe pulmonary morbidity and life-threatening respiratory failure, which results in the need for prolonged mechanical support; unique lung recruitment by HFOV can be a useful therapeutic option for severe ARDS patients as ours in the report and make the difference in the outcome.

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1. **Diffuse alveolar hemorrhage mimicking pneumonia secondary to apixaban administration**  
   Katta S. T. American Journal of Respiratory and Critical Care Medicine 2018;197:No page numbers.

Novel oral anticoagulants (NOACs) are a common group of medications used for anticoagulation in the present era secondary to their safety profile and lack of need for daily monitoring; however, bleeding complications are always a concern. An 83-year-old male presenting with progressive shortness of breath associated with a cough productive of whitish sputum for past three weeks. patient denied chest pain, hemoptysis, orthopnea, peripheral edema, fever, nausea or vomiting. He had received treatment for community acquired pneumonia (CAP) in the outpatient setting without significant improvement. His past medical history includes atrial fibrillation, chronic obstructive pulmonary disease, and hypothyroidism. The patient had recently been started on apixaban for permanent atrial fibrillation. On examination, the patient was normotensive and hypoxic saturating at 90% on the 8L of oxygen via nasal cannula. The exam was negative for jugular venous distension, pedal edema, and has diffuse lung crackles. Chest X-ray (CXR) revealed diffuse bilateral infiltrates and complete blood count showed mild leukocytosis and drop in hemoglobin form 10g/dl to 7.9g/dl when compared to labs from two weeks prior. The patient was treated for CAP and was diuresed with minimal improvement of symptoms. The patient was admitted and started on noninvasive mechanical ventilation. Emergent bronchoscopy was performed with findings of diffuse clotted blood involving the airways including the trachea. The airways were then lavaged and suctioned until clear. Eighty milliliters of broncho-alveolar lavage obtained with bloody mucus material. Cytological examination revealed multiple hemosiderin-laden macrophages. Subsequent workup was unremarkable including ANA, CANCA, PANCA, glomerular basement membrane antibody and microbiologic studies. Echocardiogram showed Left ventricular ejection fraction of 55-60% with mild pulmonary hypertension and no valvular abnormalities. Based on the clinical findings with chest imaging and cytological analysis, a case of diffuse alveolar hemorrhage secondary to apixaban use was established. After bronchoscopy, patient was weaned off oxygen and CXR improved slowly. He was discharged home on oxygen and was started on low dose aspirin. The patient was seen in the outpatient pulmonology clinic and repeat CXR revealed clearance of lung parenchyma and patient was weaned off oxygen completely. Diffuse alveolar hemorrhage is one of the rare diseases of exclusion in the patient with hypoxemia and lung infiltrates, mainly associated with other autoimmune and connective tissue disease. It is important to keep high suspicion of DAH in patients on novel oral anticoagulants mainly apixaban as reports of DAH associated with apixaban are very much limited and maybe under-reported.

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1. **Does aspiration worsen enterovirus infection and lead to type 1 respiratory failure in non-immunocompromised adults? A case series**  
   Macauley P. American Journal of Respiratory and Critical Care Medicine 2018;197:No page numbers.

Introduction Enterovirus infection usually presents as mild upper respiratory tract infection in adults but can cause severe illness in children and immunocompromised adults. We present four cases of acute respiratory failure with suspected aspiration pneumonia and enterovirus detection on respiratory swab during the month of October. Case presentation Patient 1: 64 year old male with a history of coronary artery disease presents with cough, pleuritic chest pain cough, fever, shortness of breath and confusion for two days. At presentation he was hypoxic with chest radiograph finding of right middle and lower lobe infiltrate. Course and Outcome: mechanical ventilation and tracheostomy. Patient 2: 32 year old female with history of mood and seizure disorder presents after being found unresponsive on the floor incontinent of urine with vomitus in the vicinity and had a prodrome of cough productive of yellow sputum. At presentation she was hypoxic and febrile. CT chest: near complete atelectasis of right middle, right lower and left lower lobe with heterogeneity likely superimposed infectious process. Course and outcome: high flow oxygen therapy and complete recovery. Patient 3: 93 year old male with a history of treated colon cancer presents with fevers, malaise and chills. On presentation patient was febrile and hypoxic. Chest radiography: bilateral pleural effusions, left lower lung filed opacification. Course and outcome: failed dysphagia evaluation. Initiation of high flow oxygen therapy followed by intubation, mechanical ventilation and successful liberation. Patient 4: 82 year old male with a history of early Parkinson's disease and dysphagia due to a cricopharyngeal bar presents with cough and vomiting. At presentation patient was hypotensive and hypoxic. Course and outcome: non-invasive positive pressure ventilation followed by oxygen therapy via nasal cannula and full recovery. Conclusion Enteroviruses belong to the picornaviridae family and are single stranded RNA viruses that mostly cause self-limiting illnesses with prominent summer-fall seasonality in temperate climates. All our patients had negative bacterial respiratory cultures and had risk factors that predispose to aspiration such as a change in mental status, vomiting or dysphagia. We suspect that colonisation of the upper respiratory tract with enterovirus and subsequent aspiration can lead to a more severe presentation of respiratory failure in an otherwise healthy host.

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1. **Efficient Nose-to-Lung Aerosol Delivery with an Inline DPI Requiring Low Actuation Air Volume**  
   Farkas D. Pharmaceutical Research 2018;35:No page numbers.

Purpose: To demonstrate efficient aerosol delivery through an in vitro nasal model using a dry powder inhaler (DPI) requiring low actuation air volumes (LV) applied during low-flow nasal cannula (LFNC) therapy. Methods: A previously developed LV-DPI was connected to a LFNC system with 4 mm diameter tubing. System connections and the nasal cannula interface were replaced with streamlined components. To simulate nasal respiration, an in vitro nasal model was connected to a downstream lung simulator that produced either passive or deep nasal respiration. Performance of a commercial mesh nebulizer system was also considered. Results: For the optimized system, steady state cannula emitted dose was 75% of the capsule loaded dose. With cyclic nasal breathing, delivery efficiency to the tracheal filter was 53–55% of the loaded dose, which was just under the design target of 60%. Compared with a commercially available mesh nebulizer, the optimal LV-DPI was 40-fold more efficient and 150 times faster in terms of delivering aerosol to the lungs. Conclusions: The optimized LV-DPI system is capable of high efficiency lung delivery of powder aerosols through a challenging nasal cannula interface. © 2018, Springer Science+Business Media, LLC, part of Springer Nature.

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1. **High-flow nasal cannula in pediatric patients: A survey of clinical practice**  
   Miller A. G. Respiratory Care 2018;63:894-899.

BACKGROUND: High-flow nasal cannula (HFNC) use has greatly increased in recent years. In non-neonatal pediatric patients, there are limited data available to guide HFNC use, and clinical practice may vary significantly. The goal of this study was to evaluate current HFNC practice by surveying practicing pediatric respiratory therapists. METHODS: A survey instrument was posted on the American Association for Respiratory Care’s AARConnect online social media platform in March 2017. Paper versions of the survey were also distributed at the annual Children Hospitals Association meeting. RESULTS: There were 63 responses, of which 98% used HFNC. HFNC was defined as any heated gas delivered by nasal cannula by 49% of respondents, whereas 21% defined HFNC as heated gas delivered via nasal cannula at flow greater than or equal to the patient’s inspiratory demand, and 16% defined HFNC as any gas delivered via nasal cannula above predefined thresholds. Initial flow was set per provider orders by 34% of respondents, per respiratory therapist-driven protocol by 28%, per patient weight by 15%, per patient age by 15%; 5% of respondents used other methods. Noninvasive ventilation or CPAP was used by 88% of respondents as the next step for patients who failed HFNC, with 7% opting for intubation and 5% using other interventions. Aerosol therapy was delivered by 75% of respondents during HFNC, with 77% of these respondents delivering aerosol via vibrating mesh nebulizer. During aerosol therapy, 13% of respondents decreased HFNC flow, while 23% removed patients from HFNC. CONCLUSION: There was no consensus on the definition of HFNC, how to set initial flow, or how to make adjustments. Aerosols were delivered by 75% of respondents, predominantly via a vibrating mesh nebulizer placed on the dry side of the humidifier. The definition of HFNC, how to set flow, and aerosolized medication delivery are areas in which more research is needed. © 2018 Daedalus Enterprises.

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1. **High-flow nasal cannula oxygen in immunocompromised patient with acute hypoxic respiratory failure**  
   Rajdev K. American Journal of Respiratory and Critical Care Medicine 2018;197:No page numbers.

Introduction: Acute hypoxic respiratory failure (AHRF) is a known complication of lung transplant recipients. Recurrent and polymicrobial infections are among the most common etiologies. There is no consensus on how to treat hypoxia in these patients, invasive mechanical ventilation (IMV) is often required but it increases the morbidity and mortality significantly. Noninvasive positive pressure ventilation (NPPV) has shown some promise but overall carries high failure rate. High flow nasal cannula (HFNC) has emerged as an alternative to IMV and NPPV. We present a case of a bilateral lung transplant recipient with severe neutropenic sepsis presented with AHRF, and HFNC was successfully used to avoid IMV. Case Description: A 77 y/o male with chronic respiratory failure on home O2, bilateral lung transplant due to pulmonary fibrosis, hypertension and diabetes presented with productive cough, fever and dyspnea of 1 week duration. He was discharged 4 weeks prior to presentation from his transplant hospital after being treated for CMV pneumonitis. His home medications included tacrolimus, prednisone, posaconazole and gancyclovir. He was tachypnic and in respiratory distress with O2 saturation of 84% on 5L O2. He was started on nonrebreather mask with 100% O2. Blood gas showed PaO2 60 and mild hypercapnia of 45 with a normal pH. Chest Xray revealed right lower lobe opacity. Meanwhile, he remained hypoxic to 89% on pulse oximetry. He didn't want to be intubated, therefore, was started on HFNC with flow of 60 L and 100% oxygen. His dyspnea and O2 saturation improved and he appeared comfortable. He was started on broad spectrum antibiotics. He responded well to HFNC and over the course of next 48hrs, his FiO2 was reduced to 0.6 with 50L gas flow. His blood, sputum and urine cultures came back negative, urine legionella and streptococcus antigen, CMV IgM antibody were also negative. On day 6 of his admission, he was switched to nasal cannula with 5 L oxygen and eventually transferred to the medicine floor. Discussion(s): Growing body of evidence suggests that the use of HFNC is associated with lower mortality and intubation rates as compared to standard O2 or NIV, in immunocompromised patients admitted to ICU for AHRF. However, these studies excluded the patients with chronic respiratory failure, underlying chronic lung disease and profound neutropenia. We report this case because our patient had severe neutropenia, chronic lung disease and chronic respiratory failure and benefitted with the use of HFNC for AHRF.

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1. **Incorporating a Nebulizer System Into High-Flow Nasal Cannula Improves Comfort in Infants With Bronchiolitis.**  
   Juan Valencia-Ramos Respiratory care 2018;63:886-893.

Incorporating a Nebulizer System Into High-Flow Nasal Cannula Improves Comfort in Infants With Bronchiolitis. High-flow nasal cannula (HFNC) is increasingly used to provide respiratory support in infants with bronchiolitis. The delivery of aerosol therapy through a jet nebulizer is widely indicated despite its controversial efficacy and poor tolerability.This randomized cross-over study aimed to evaluate the comfort and satisfaction of the delivery of aerosol therapy using a nebulization system integrated into HFNC compared with the standard practice of using a jet nebulizer with a face mask. The COMFORT-Behavior (COMFORT-B) scale, a visual analog scale, and a numeric rating scale were used by health professionals and caregivers to assess subjects' levels of comfort and satisfaction.A total of 113 nebulizations (64 via nebulizer with HFNC; 49 via jet nebulizer) were delivered to the 6 subjects included in the study. Use of the nebulizer with HFNC showed increased comfort and satisfaction during nebulization compared to use of the jet nebulizer, as measured by the COMFORT-B scale, the visual analog scale, and the numeric rating scale, with the following median (interquartile range) scores: 10.7 (7-16) versus 14.5 (10-20) (P = .006), 8.5 (6-10) versus 7 (4-9) (P = .02), and 3.84 (3.61-4.07) versus 1.83 (1.58-2.08) (P < .001), respectively. Correlation between the COMFORT-B scale and the visual analog scale using Spearman's rho was -0.757 (P < .001). The intraclass correlation coefficient for the COMFORT-B scale, visual analog scale, and numeric rating scale, as measured by 2 different nurses, was between 0.75 and 0.87.The use of a nebulizer incorporated into HFNC therapy results in an increased level of comfort and satisfaction compared to the use of a conventional jet nebulizer in subjects with bronchiolitis who required HFNC therapy. Further studies are needed to determine whether aerosol therapy delivered through HFNC improves the clinical course of this pathology.Copyright © 2018 by Daedalus Enterprises.

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1. **Not your typical pneumonia: A case of acute eosino-philic pneumonia**  
   Saxena A. Journal of General Internal Medicine 2018;33:579.

Learning Objective #1: Distinguish eosinophilic pneumonia from other pneumonias. Learning Objective #2: Treat acute eosinophilic pneumonia. CASE: A 59-year-old woman with allergic rhinitis presented with 1 month of cough with blood-streaked sputum and progressive dyspnea. She denied fevers, weight loss, or sick contacts. She was diagnosed with pneumonia at an outside clinic 2 weeks prior to presentation and treated with levofloxacin with no change in her symptoms. Physical exam was significant for low-grade fever, tachypnea, accessory muscle use on high flow nasal cannula, and crackles throughout the bilateral lung fields. Laboratory work was notable for a WBC of 8.7 (82% neutrophils, 3% eosinophils). An infectious work-up, including blood and respiratory cultures, extended viral panel, AFB, HIV, and parasitic panel was unremarkable. IgE level was > 1000, CRP 272, and ESR 70. Vasculitis and connective tissue disease markers were negative. Chest CT demonstrated mul-tifocal consolidation. She developed hypoxemic respiratory failure soon after admission requiring intubation and worsening bilateral opacities on imaging concerning for ARDS. Bronchoalveolar lavage (BAL) demonstrated 40% eo-sinophils and trans-bronchial biopsy results were consistent with eosinophilic pneumonia. She was started on high dose steroids with gradual improvement in her respiratory function and discharged home 2 weeks later. IMPACT: This case has changed my thinking in regards to diagnosing pneumonia. It highlights the importance of a broad differential for pneumonia, especially in patients not improving with antibiotics and/or presenting with severe hypoxemic respiratory failure. DISCUSSION: Idiopathic acute eosinophilic pneumonia (AEP) is a rare condition with an unknown cause, though a hypersensitivity reaction to an inhaled antigen has been postulated as a trigger. Symptoms are usually present for less than 4 weeks and include non-productive cough, dyspnea, and fever. Patients can be quite ill on initial presentation; approximately two-thirds of patients with AEP required intubation for hypoxemic respiratory failure in one case series. Labs are notable for a neutrophilic leukocytosis (peripheral eosin-ophilia develops later in the illness course) and elevated ESR, CRP, and IgE levels. Diagnostic criteria include febrile illness less than 1 month duration, hypoxemia, diffuse pulmonary opacities on imaging, BAL with greater than 25% eosinophils, and absence of identifiable causes of eosinophilic pneumonias. The latter include drug reaction, fungal or parasitic infections, asthma/atopic disease, and eosinophilic granulomatosis with polyangiitis. Patients improve within 12-48 hours after initiation of high-dose steroids with the ideal dose and duration dependent upon the clinical situation. Early diagnosis and treatment can potentially decrease the frequency/duration of mechanical ventilation in addition to improving symptom burden.

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1. **The Role of Gas Flow in Transnasal Pulmonary Aerosol Delivery: A Double-blinded, Randomized Controlled Trial**  
   Anon. Clinical Trials 2018;:No page numbers.

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1. **Aerosol delivery through adult high flow nasal cannula with heliox and oxygen**  
   Dailey P. A. Respiratory Care 2017;62:1186-1192.

BACKGROUND: Heliox (helium-oxygen mixture) has been shown to reduce turbulence and improve aerosol delivery in a range of clinical settings. We questioned whether heliox as compared with oxygen via high-flow nasal cannula (HFNC) would affect aerosol delivery. We hypothesized that heliox would have a significant effect on aerosol delivery as compared with oxygen with both quiet and distressed breathing patterns. METHODS: A vibrating mesh nebulizer was placed at the inlet of a humidifier via HFNC with small adult cannula distal to the heated-wire circuit with prongs placed into simulated nares with a T-shaped trap and absolute filter connected to a breath simulator set to adult quiet and distressed breathing parameters. Albuterol sulfate (0.083% 2.5 mg/3 mL) was aerosolized with heliox (80:20) and oxygen (100%) at 10, 30, and 50 L/min. Drug eluted from the filter was assayed with UV spectrophotometry (276 nm). Descriptive statistics, Kruskal-Wallis test, and Mann-Whitney U test were used for data analysis. P &lt;.05 was considered statistically significant. RESULTS: Increasing flows with heliox and oxygen significantly decreased percentage inhaled dose (inhaled dose) of aerosol with a quiet breathing pattern (P =.02 and P =.030, respectively). In contrast, with a distressed breathing pattern, inhaled dose at 10 L/min was lower than at 30 and 50 L/min (P =.009 and P =.01, respectively) with both oxygen and heliox (P =.009 and P =.009, respectively). Despite a trend to higher aerosol deposition with heliox versus oxygen, the differences were not significant. CONCLUSIONS: With a distressed breathing pattern, aerosol delivery was greater at 30 and 50 L/min than with a quiet breathing pattern. Trends toward higher inhaled dose with heliox during HFNC were not significant. © 2017 Daedalus Enterprises.

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1. **Aerosol Delivery with Two Nebulizers Through High-Flow Nasal Cannula: A Randomized Cross-Over Single-Photon Emission Computed Tomography-Computed Tomography Study**  
   Dugernier J. Journal of Aerosol Medicine and Pulmonary Drug Delivery 2017;30:349-358.

Background: High-flow nasal cannula use is developing in ICUs. The aim of this study was to compare aerosol efficiency by using two nebulizers through a high-flow nasal cannula: the most commonly used jet nebulizer (JN) and a more efficient vibrating-mesh nebulizer (VN). Methods: Aerosol delivery of diethylenetriaminepentaacetic acid labeled with technetium-99m (4 mCi/4 mL) to the lungs by using a VN (Aerogen Solo®; Aerogen Ltd., Galway, Ireland) and a constant-output JN (Opti-Mist Plus Nebulizer®; ConvaTec, Bridgewater, NJ) through a high-flow nasal cannula (Optiflow®; Fisher &amp; Paykel, New Zealand) was compared in six healthy subjects. Flow rate was set at 30 L/min through the heated humidified circuit. Pulmonary and extrapulmonary deposition was measured by single-photon emission computed tomography combined with a low-dose computed tomographic scan and by planar scintigraphy. Results: Lung deposition was only 3.6 (2.1-4.4) and 1 (0.7-2)% of the nominal dose with the VN and the JN, respectively (p &lt; 0.05). The JN showed higher retained doses than the VN. However, both nebulizers were associated with substantial deposition in the single limb circuit, the humidification chamber, and the nasal cannula [58.2 (51.6-61.6)% of the nominal dose with the VN versus 19.2 (15.8-22.9)% of the nominal dose with the JN, p &lt; 0.05] and in the upper respiratory tract [17.6 (13.4-27.9)% of the nominal dose with the VN and 8.6 (6.0-11.0)% of the nominal dose with the JN, p &lt; 0.05], especially in the nasal cavity. Conclusions: In the specific conditions of the study, pulmonary drug delivery through the high-flow nasal cannula is about 1%-4% of the initial amount of drugs placed in the nebulizer, despite the higher efficiency of the VN as compared with the JN. © 2017, Mary Ann Liebert, Inc. 2017.

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1. **Aerosol drug delivery through high flow nasal cannula**  
   Ari A. Current Pharmaceutical Biotechnology 2017;18:877-882.

Background: High flow nasal cannula (HFNC) is widely utilized to support critically ill adults, pediatrics and neonates. Through the continuous delivery of oxygen at high flow rates that meet or exceed patients’ inspiratory flow, HFNC improves oxygenation, respiratory rates, patient comfort, and tolerance during therapy. As HFNC becomes more widely employed, clinicians have started to consider aerosol drug delivery through HFNC. Conclusion: Using HFNC along with nebulizers as a potential therapy in aerosol medicine is a new and innovative approach for aerosol drug delivery to patients with pulmonary diseases. The purpose of this paper is to review current in vitro and in vivo studies on aerosol drug delivery through HFNC in adults and children. © 2017 Bentham Science Publishers.

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1. **Aerosol therapy through high flow nasal cannula in pediatric patients**  
   Al-Subu A. M. Expert Review of Respiratory Medicine 2017;11:945-953.

Introduction: High flow nasal cannula (HFNC) is increasingly used in pediatric patients suffering from respiratory failure. In some disease processes, patients may also benefit from aerosol therapy. Therefore, the use of HFNC to deliver aerosolized medications is a convenient and attractive option. Areas covered: This review aims to appraise available evidence concerning the efficiency of aerosol nebulized therapy delivery using HFNC in pediatric patients. Expert commentary: Delivery of aerosol particles is a very complex process and depends on the use of oxygen vs. heliox, nebulizer type and position within the HFNC circuit, patient’s breathing effort and pattern, and more importantly cannula size and flow rates. Current in vitro evidence suggests the amount of aerosol delivery is likely to be very low at high flows. Clinical studies are limited in pediatric patients and given the limited clinical data, it is not possible to make recommendations for or against aerosol delivery through HFNC for pediatric patients. © 2017 Informa UK Limited, trading as Taylor & Francis Group.

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1. **Can aerosol therapy keep pace with innovations in patient care? A review**  
   Mac Loughlin R. Journal of Aerosol Medicine and Pulmonary Drug Delivery 2017;30:A3-A4.

Summary The opportunity for aerosol mediated therapy exists across all patient types and all patient settings. Patients ranging from very low birth weight premature infants to the elderly and obese may benefit from aerosol therapy, and whilst it is well understood that the associated range of breathing patterns has a significant bearing on the ultimate efficiency of delivery of aerosol to the lung, so too does the interface that facilitates connection between the aerosol generator and the patient airway. The aim of this review was to assess the effect of selected interfaces on the quantity of aerosol being delivered to the lung. For the purposes of this review, patient interventions were broadly divided between those for use with spontaneously breathing patients and those for use with patients requiring ventilatory support. The aerosol generators included in the review were Vibrating Mesh Nebulisers (VMN), Jet Nebulisers ( JN) and pressurised Metered Dose Inhalers (pMDI). The patient interventions and associated interfaces assessed included facemasks, mouthpieces, tracheostomy tubes, high flow nasal therapy, endotracheal tubes and mask-mediated non-invasive ventilation. Following a review of the literature it is clear that the different aerosol generators can be significantly affected by choice of interface and published data is provided to support the contention that each interface introduces the risk of altered aerosol therapy. This work should allow end users and drug developers make more informed decisions around interface and paired device selection early in their respective decision making and development processes.

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1. **Evaluation on the Efficacy of Bronchodilator Nebulization Via High Flow Nasal Cannula**  
   Anon. Clinical Trials 2017;:No page numbers.

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1. **High Flow Nasal Cannula in Children With Status Asthmaticus**  
   Anon. Clinical Trials 2017;:No page numbers.

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1. **Nasal high flow nebulization in infants and toddlers: An in vitro and in vivo scintigraphic study**  
   Réminiac F. Pediatric Pulmonology 2017;52:337-344.

Aerosol therapy in infants and toddlers is challenging. Nebulization within a nasal high flow (NHF) circuit is attractive. The aim of this study was to quantify aerosol lung deposition when combined with NHF as compared with standard practice. Lung doses were measured scintigraphically after nebulization with jet and mesh nebulizer placed within a NHF circuit in a spontaneously breathing non-human primate model (macaque) and in the anatomical bench SAINT model, respectively representing a full-term newborn and a 9-month-old toddler. In the SAINT model, lung depositions observed with the mesh nebulizer placed in the NHF circuit set at 2 and 4 L/min were 3.3% and 4.2% of the nebulizer charge, respectively, and similar to the 1.70% observed with the control standard facemask jet nebulization (6 L/min flow). In the macaque model, the depositions observed with the mesh nebulizer in the NHF circuit set at 2 and 4 L/min were 0.49% and 0.85%, respectively, also similar to the control measurement (0.71%). Mesh nebulization within a NHF circuit set at 8 L/min and jet nebulization either within a NHF circuit or placed on top of the cannula (NHF set at 2 L/min; total flow of 8 L/min), resulted in a significantly lower lung depositions. Mesh nebulization within a NHF circuit delivering up to 4 L/min gas is likely to be at least as effective than jet nebulization with a facemask in infants and toddlers. Aerosol facemask placement on top of cannulas or jet nebulization within the NHF circuit may be less effective. Pediatr Pulmonol. 2017;52:337–344. © 2016 Wiley Periodicals, Inc. © 2016 Wiley Periodicals, Inc.

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1. **Nebulizers and spacers for aerosol delivery through adult nasal cannula at low oxygen flow rate: An in-vitro study**  
   Madney Y. M. Journal of Drug Delivery Science and Technology 2017;39:260-265.

Combining oxygen therapy with aerosol delivery within High flow nasal cannula oxygen therapy (HFNC) is an attractive practice. Delivered dose (DD) was found to decrease with increasing gas flow rates and with smaller sized cannulas. The aim of this study was to quantify amount of aerosol emitted at the cannula outlet using different aerosol generators at low oxygen flow. Aerogen Solo vibrating mesh (SOLO), jet nebulizers, Combihaler connected to metered dose inhaler (MDI) and SOLO, MDI connected AeroChamber Vent and MDI connected AeroChamber Mini were used to deliver aerosol in HFNC in-vitro setting. SOLO with its T-piece delivers DD∼35% of nebulizer charge with high fine-particle-dose (FPD). Both Combihaler and jet-nebulizer delivered∼18% with lower FPD. MDI with both spacers delivers only 2.1 and 1.3% of nominal dose, respectively. Mass median aerodynamic diameters were small for the SOLO, Combihaler and jet nebulizers and high for the two spacers. Inhaled aerosols can be delivered efficiently at low oxygen flow using SOLO, with both T-piece and Combihaler, and jet nebulizer in HFNC system. While MDIs with spacers delivers negligible amounts of drug below that expected for clinical response at this flow. © 2017

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1. **Pediatric aerosol therapy**  
   Berlinski A. Respiratory Care 2017;62:662-677.

Inhaled medications are the mainstay of therapy for many pediatric pulmonary diseases. Device and delivery technique selection is key to improving lung deposition of inhaled drugs. This paper will review the subject in relationship to several pediatric clinical situations: acute pediatric asthma, transnasal aerosol delivery, delivery through tracheostomies, and delivery during noninvasive and invasive mechanical ventilation. This review will focus on the pediatric age group and will not include neonates. © 2017 Daedalus Enterprises.

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1. **Pharmacokinetics and safety of fentanyl sublingual spray and fentanyl citrate intravenous: a multiple ascending dose study in opioid-naïve healthy volunteers**  
   Rauck R. L. Current Medical Research and Opinion 2017;33:1921-1933.

Objective: Fentanyl sublingual spray, with its rapid onset for pain relief, may be efficacious in the management of acute or post-operative pain. Because patients in these settings may be opioid-naïve, the study was conducted to determine the safety, tolerability, and pharmacokinetics of multiple dose administration of fentanyl sublingual spray in an opioid-naïve population. Methods: Fentanyl sublingual spray (100 mcg, 200 mcg, and 400 mcg) and fentanyl citrate intravenous (IV; 50 mcg) were administered every 0.5, 1.0, 2.0, and 4.0 h for up to three doses per cohort in opioid-naïve subjects (ClinicalTrials.gov identifier: NCT02641340). Eight subjects in each cohort were randomly assigned (six subjects received fentanyl sublingual spray; two subjects received fentanyl citrate IV). Pharmacokinetic and safety-related pharmacodynamic assessments were performed through 24 h post-first dose. Safety assessments were collected through Day 7. Results: Ninety-six opioid-naïve subjects, aged 20–55 years, with a body mass index of 18.7–31.5 kg/m2, participated in the study. Multiple doses of fentanyl sublingual spray (100, 200, and 400 mcg) were generally well tolerated. Hypoxia, observed in the 200-mcg and 400-mcg dose groups, increased with increasing doses and higher dosing frequency, but was readily managed by nasal cannula oxygenation. Overall, nausea increased with increasing doses, and ∼52.6% (10 out of 19) cases of nausea that occurred at the highest dose of 400 mcg were treated with concomitant medication. Overall, the reported adverse events were consistent with the known safety profile of fentanyl. Conclusion: Fentanyl sublingual spray (100 mcg, 200 mg, and 400 mcg) administered every 0.5, 1, 2, and 4 h was generally well tolerated in an opioid-naïve population. The results suggest that doses of 200 mcg or lower may be safe for use in an opioid-naïve population. © 2017 Informa UK Limited, trading as Taylor & Francis Group.

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1. **When watchful waiting fails in bronchopulmonary fistula**  
   Tornatore M. American Journal of Respiratory and Critical Care Medicine 2017;195:No page numbers.

A 46 year old man with a 30 pack-year smoking history and no medical follow up for >10 years presented with several weeks of worsening shortness of breath, productive cough, malaise, nasal congestion and night sweats. He was found to be hypoxic, febrile, hypotensive, and with leukocytosis. A CTA chest showed a large left sided hydropneumothorax, a cavitary lesion in the left lung apex communicating with the left pleural space, ground-glass opacification throughout the lungs bilaterally, a dense consolidation at the lung bases, small fluid collection in the left lung, suggestive of multifocal pneumonia with abscess and empyema. He was admitted to the ICU for ventilator and pressor support. Left chest tube was placed and patient was started on broad spectrum antibiotics. Pleural fluid cultures grew Peptostreptococcus. Extubation to nasal cannula was accomplished after treatment with Unasyn, however he had persistent air leak and evidence of pneumothorax on chest Xrays. Cardiothoracic surgery was consulted who performed flexible bronchoscopy with lavage, video-assisted thorascopic surgery for decortication as well as suture repair of necrotic lung tissue with a pleural patch. Under direct visualization the left lower lobe did not fully expand due to a bronchopleural fistula, so two chest tubes were inserted. Chest tubes remained to suction with small but persistent left pneumothorax. One chest remained in place and a Heimlich valve was applied. Patient improved and was discharged with the Heimlich valve. On outpatient follow up his pneumothorax remained stable, and the chest tube was removed. Alveolar air leak (AAL) from either bronchopulmonary fistula or alveolopleural fistula is a common complication of thoracic surgery, bronchiectasis, structural lung disease, and cavitary lung disorders that remains a problem both for clinicians and patients leading to significantly increased morbidity and mortality. There have been many modalities described for both preventing and treating these air leaks. Intraoperative preventative measures include buttressing staple lines, topical sealants, creation of apical pleural tent, and using pneumoperitoneum. Post operative treatments remain limited and include chest tube suction with or without one-way Heimlich valves, tissue flap, or pleurodesis with blood patch or sclerosing materials. There have been 6 observational studies reported with a combined 148 patients reporting results for one-way valves in the outpatient setting. There has not, however, been enough evidence to recommend one treatment or preventative modality over another and this remains a large area for further research.

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1. **[Pneumonia and Streptococcal Toxic Shock Syndrome Due to Group A Streptococci: A Case Report]**  
   Makino Hideki Kansenshogaku zasshi. The Journal of the Japanese Association for Infectious Diseases 2017;91:155-8.

A 71-year-old woman who was undergoing immunosuppressive therapy presented with a 7-day history of productive cough and 2-day history of fever. She was diagnosed with severe pneumonia and septic shock. Meropenem, azithromycin, large amounts of fluids, and noradrenaline were administered, and high-flow nasal cannula oxygen therapy was provided. The gross appearance of the aspirated sputum was ginger-like, and the gram-positive cocci in chains were identified as group A beta-hemolytic streptococci (GAS), Streptococcus pyogenes. The blood sample culture test revealed negative results. Based on Stevens' criteria, the patient was finally diagnosed as having streptococcal toxic shock syndrome (STSS). Antibiotics were switched to ampicillin/sulbactam and clindamycin as an antitoxin treatment, and the patient was discharged on day 33. Serotypes of GAS were T1, M1, and emm1. Superantigens spe A, spe B, and spe F were present, and spe C was absent. These observations were compatible with the clinical features of hypotension. GAS is an uncommon cause of community-acquired pneumonia, which when potentially complicated with STSS can lead to a high mortality rate, and the rapid progression is particularly a striking feature. We should be aware that GAS can cause pneumonia, and antitoxin treatment can play a key role in STSS management.

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1. **36th International Symposium on Intensive Care and Emergency Medicine : Brussels, Belgium. 15-18 March 2016**  
   Bateman R. M. Crit Care 2016;20:94.

P001 - Sepsis impairs the capillary response within hypoxic capillaries and decreases erythrocyte oxygen-dependent ATP efflux R. M. Bateman, M. D. Sharpe, J. E. Jagger, C. G. Ellis P002 - Lower serum immunoglobulin G2 level does not predispose to severe flu. J. Solé-Violán, M. López-Rodríguez, E. Herrera-Ramos, J. Ruíz-Hernández, L. Borderías, J. Horcajada, N. González-Quevedo, O. Rajas, M. Briones, F. Rodríguez de Castro, C. Rodríguez Gallego P003 - Brain protective effects of intravenous immunoglobulin through inhibition of complement activation and apoptosis in a rat model of sepsis F. Esen, G. Orhun, P. Ergin Ozcan, E. Senturk, C. Ugur Yilmaz, N. Orhan, N. Arican, M. Kaya, M. Kucukerden, M. Giris, U. Akcan, S. Bilgic Gazioglu, E. Tuzun P004 - Adenosine a1 receptor dysfunction is associated with leukopenia: A possible mechanism for sepsis-induced leukopenia R. Riff, O. Naamani, A. Douvdevani P005 - Analysis of neutrophil by hyper spectral imaging - A preliminary report R. Takegawa, H. Yoshida, T. Hirose, N. Yamamoto, H. Hagiya, M. Ojima, Y. Akeda, O. Tasaki, K. Tomono, T. Shimazu P006 - Chemiluminescent intensity assessed by eaa predicts the incidence of postoperative infectious complications following gastrointestinal surgery S. Ono, T. Kubo, S. Suda, T. Ueno, T. Ikeda P007 - Serial change of c1 inhibitor in patients with sepsis – A prospective observational study T. Hirose, H. Ogura, H. Takahashi, M. Ojima, J. Kang, Y. Nakamura, T. Kojima, T. Shimazu P008 - Comparison of bacteremia and sepsis on sepsis related biomarkers T. Ikeda, S. Suda, Y. Izutani, T. Ueno, S. Ono P009 - The changes of procalcitonin levels in critical patients with abdominal septic shock during blood purification T. Taniguchi, M. O P010 - Validation of a new sensitive point of care device for rapid measurement of procalcitonin C. Dinter, J. Lotz, B. Eilers, C. Wissmann, R. Lott P011 - Infection biomarkers in primary care patients with acute respiratory tract infections – Comparison of procalcitonin and C-reactive protein M. M. Meili, P. S. Schuetz P012 - Do we need a lower procalcitonin cut off? H. Hawa, M. Sharshir, M. Aburageila, N. Salahuddin P013 - The predictive role of C-reactive protein and procalcitonin biomarkers in central nervous system infections with extensively drug resistant bacteria V. Chantziara, S. Georgiou, A. Tsimogianni, P. Alexandropoulos, A. Vassi, F. Lagiou, M. Valta, G. Micha, E. Chinou, G. Michaloudis P014 - Changes in endotoxin activity assay and procalcitonin levels after direct hemoperfusion with polymyxin-b immobilized fiber A. Kodaira, T. Ikeda, S. Ono, T. Ueno, S. Suda, Y. Izutani, H. Imaizumi P015 - Diagnostic usefullness of combination biomarkers on ICU admission M. V. De la Torre-Prados, A. Garcia-De la Torre, A. Enguix-Armada, A. Puerto-Morlan, V. Perez-Valero, A. Garcia-Alcantara P016 - Platelet function analysis utilising the PFA-100 does not predict infection, bacteraemia, sepsis or outcome in critically ill patients N. Bolton, J. Dudziak, S. Bonney, A. Tridente, P. Nee P017 - Extracellular histone H3 levels are inversely correlated with antithrombin levels and platelet counts and are associated with mortality in sepsis patients G. Nicolaes, M. Wiewel, M. Schultz, K. Wildhagen, J. Horn, R. Schrijver, T. Van der Poll, C. Reutelingsperger P018 - Il-8: is this a more reliable biomarker for sepsis severity than CRP, Procalcitonin, E-selectin, IL-6 and TNF-[alpha] S. Pillai, G. Davies, G. Mills, R. Aubrey, K. Morris, P. Williams, P. Evans P019 - Relation between adrenomedullin and short-term outcome in ICU patients: Results from the frog ICU study E. G. Gayat, J. Struck, A. Cariou, N. Deye, B. Guidet, S. Jabert, J. Launay, M. Legrand, M. Léone, M. Resche-Rigon, E. Vicaut, A. Vieillard-Baron, A. 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Leclerc P364 - A comparison of mortality scores in burns patients on the intensive care unit. O. Howarth, K. Davenport, P.

1. **Acute hypersensitivity pneumonia in the disguise of community acquired pneumonia in a young adult working as exterminator**  
   Konda M. K. Journal of General Internal Medicine 2016;31:S538.

LEARNING OBJECTIVE #1: Acute hypersensitivity pneumonia can mimic community acquired pneumonia in clinical presentation. A detailed occupational history and history of exposure to various inhaled chemicals can give important clues to the diagnosis. LEARNING OBJECTIVE #2: Removal of offending agent is all that is needed in treatment of most cases. CASE: 39-year-old male with no past medical illnesses presented to emergency department with 4-day history of worsening shortness of breath and productive cough with black colored sputum. He had associated features of subjective fevers, chills and decreased oral intake for past 3 days. Occupational history was significant for extermination with exposure to multiple chemicals and was working without mask recently. Physical examination was positive for fever of 102.8 F, 87 % oxygen saturation on 5-l nasal cannula, diffuse crackles and diminished breath sounds over right lower lobe. Laboratory work including CBC, CMP, lactic acid and procalcitonin were unremarkable. A chest x-ray showed bilateral peri-hilar streaky multinodular opacities. He was admitted to general medical floor with a presumable diagnosis of community acquired pneumonia and initially treated with ceftriaxone and azithromycin. The patient clinically deteriorated in 24 h requiring endotracheal intubation and mechanical ventilation. A high resolution CT chest showed nonspecific multifocal groundglass pulmonary opacities suggestive of hypersensitivity pneumonitis. A bronchoscopy showed normal appearing bronchial mucosa and testing of bronchoalveolar lavage (BAL) suggested the diagnosis of acute hypersensitivity pneumonitis (HP) most likely related to his occupation as exterminator (exposed to Maxxthor/Suspend SC/Tempo dust/Termidor/Gentrol and other chemicals). There were 5596/cmm nucleated cells with 87 % polymorphonuclear cells and 13 % mononuclear cells and 3954/cmm RBCs. Blood cultures and cultures of BAL were negative. Mycoplasma, streptococcus pneumoniae and legionella testing were also negative. Patient improved clinically with elimination of offending agent and ventilator support and was extubated in 72 h. The combination of negative cultures and other infectious markers, clinical improvement with removal of offending agent and absence of other explanatory findings made acute HP most likely diagnosis and a lung biopsy was not performed. DISCUSSION: Epidemiology of acute HP is mostly unknown and varies considerably depending on case definitions, inciting agents, geographical distribution. Farmers lung is most commonly studied form of HP and prevalence per 100,000 varies from 420 to 3000. It is commonly mistaken for viral or bacterial infection as occurred in our patient. Most classic form occurs after heavy exposure to inciting agent. Removal from exposure to the inciting agent results in resolution of symptoms within 12 h to several days and radiologic recovery takes several weeks. Scattered multinodular, interstitial opacities in lower and middle lung zones on chest x ray and presence of ground glass opacities on high resolution CT confirms the presence of pneumonitis in the right clinical scenario. The cell counts and differential on BAL is helpful in suggesting the diagnosis. Histopathology confirms the diagnosis and can differentiate between acute versus subacute or intermittent HP. Systemic glucocorticoids are only occasionally required as all categories of HP improve with removal from exposure to inciting agent. Repeated exposures can result in chronic fibrosing lung disease. Our patient was discharged with close pulmonology follow up and advised to avoid future occupational exposure or use effective protection equipment.

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1. **Acute respiratory failure caused by hepatopulmonary fistula in a patient with hepatocellular carcinoma**  
   Lee J. Tuberculosis and Respiratory Diseases 2016;79:179-183.

A 59-year-old man presented with acute dyspnea following sudden productive cough and expectoration of a full cup of "blood-tinged" sputum. He had been diagnosed with hepatitis B virus-related hepatocellular carcinoma and had received transarterial chemoembolization 5 years ago for a 20-cm hepatic mass; he denied any history of hematemesis and the last esophagogastroduodenoscopy from a year ago showed absence of varix. Chest computed tomography (CT) with angiography showed new appearance of right basal lung consolidation but no bleeding focus. Despite the use of systemic antibiotics, the patient developed respiratory failure on day 7 of hospitalization. After intubation, a massive amount of brown sputum with anchovy-paste-like consistency was suctioned via the endotracheal tube. Bronchoscopic toileting was performed and the patient was extubated. In the ward, he continued to expectorate the brown sputum. On day 25 of hospitalization, a repeat CT scan showed simultaneous disappearance of the pneumonic consolidation and the necrotic fluid within the hepatic mass, suggesting the presence of a fistula. He has continued to receive systemic antibiotics, sorafenib, and entecavir, and follow up by respiratory and hepato-oncology specialists. © Copyright 2016 The Korean Academy of Tuberculosis and Respiratory Diseases. All rights reserved.

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1. **Aerosol therapy during noninvasive ventilatory support**  
   Reminiac F. Reanimation 2016;25:11-20.

Noninvasive ventilation (NIV) and high flow nasal therapy (HFT) are increasingly used in intensive care units. Patients undergoing these respiratory supports often require inhaled therapies, mainly bronchodilators. The principles of aerosol practice in intubated patients in part apply to NIV. Aerosol therapy may nevertheless be challenging because of spontaneous non-controlled breathing and the noninvasive interfaces used. Bench studies evaluating aerosol therapy during NIV show that, with single limb circuits, a greater amount of aerosol is delivered when the aerosol generator is placed between the leak port and the patient. Bench studies of HFT, mainly in pediatric models, show encouraging results, provided that the aerosol generator is positioned closed to the humidification chamber. Clinical studies, only available for NIV, show that significant drug amounts are delivered to the lungs of healthy subject. In patients with obstructive lung disease, significant bronchodilation has been observed after bronchodilator nebulization in the NIV circuit. It is therefore feasible to practice aerosol therapy during NIV in the clinical setting. Some studies even suggested an additive or even synergistic effect of both therapies. If confirmed, those results may trigger specific NIV delivery in order to improve therapeutic efficacy of inhaled drugs. Bench results of aerosol therapy during HFT need to be confirmed in the clinical setting.Copyright © 2015, Societe de reanimation de langue francaise (SRLF) and Springer-Verlag France.

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1. **Aerosol Therapy in Adults Receiving High Flow Nasal Cannula Oxygen Therapy**  
   Reminiac F. Journal of Aerosol Medicine and Pulmonary Drug Delivery 2016;29:134-141.

Background: High flow nasal cannula oxygen therapy (HFT) is increasingly used in intensive and emergency care departments. Patients suffering from respiratory failure, who are likely to benefit from HFT, may require aerosolized bronchodilators; therefore, combining nebulization with HFT may be relevant. This study aimed to identify the optimal settings for the implementation of nebulization within an adult HFT circuit. Method(s): We assessed the mass and the particle size distribution of the aerosol emitted from the nasal cannula (inhalable mass) using mesh- and jet-nebulizers placed at various positions in the HFT circuit. Thereafter, the most relevant combination was used to evaluate the mass of salbutamol delivered downstream of an anatomical model reproducing aerosol deposition and leakage at the nasal and pharyngeal levels (respirable mass). The influence of HFT flow rate (30, 45, and 60 L/min), of breathing pattern (quiet and respiratory distress pattern) as well as of opened and closed mouth breathing was assessed. Result(s): The most efficient position was that of a nebulizer placed upstream from the humidification chamber (inhalable mass ranging from 26% to 32% of the nebulizer charge). Using a mesh nebulizer, we observed a respirable mass ranging from 2% to 10% of the nebulizer charge. Higher HFT flow rates and open mouth breathing were associated with a lower efficiency. Simulating respiratory distress (i.e., increasing the simulated patient inspiratory flow) did not hamper drug delivery as compared to a quiet breathing pattern. Conclusion(s): Placing nebulizers within a HFT circuit upstream from the humidification chamber may enable to deliver clinically relevant masses of aerosol at the cannula outlet, but more importantly downstream of the nose and pharynx, even in case of high patients' inspiratory flow. This method of aerosol therapy is expected to produce a bronchodilatatory effect to be evaluated in the clinical settings.Copyright © 2016 Mary Ann Liebert, Inc.

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1. **Aerosol Therapy in Obese COPD Patients.**  
   Anon. Clinical Trials 2016;:No page numbers.

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1. **Current evidence for the effectiveness of heated and humidified high flow nasal cannula supportive therapy in adult patients with respiratory failure**  
   Roca O. Critical Care 2016;20:No page numbers.

High flow nasal cannula (HFNC) supportive therapy has emerged as a safe, useful therapy in patients with respiratory failure, improving oxygenation and comfort. Recently several clinical trials have analyzed the effectiveness of HFNC therapy in different clinical situations and have reported promising results. Here we review the current knowledge about HFNC therapy, from its mechanisms of action to its effects on outcomes in different clinical situations. © 2016 Roca et al.

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1. **Fundamentals of aerosol therapy in critical care**  
   Dhanani J. Critical Care 2016;20:No page numbers.

Drug dosing in critically ill patients is challenging due to the altered drug pharmacokinetics-pharmacodynamics associated with systemic therapies. For many drug therapies, there is potential to use the respiratory system as an alternative route for drug delivery. Aerosol drug delivery can provide many advantages over conventional therapy. Given that respiratory diseases are the commonest causes of critical illness, use of aerosol therapy to provide high local drug concentrations with minimal systemic side effects makes this route an attractive option. To date, limited evidence has restricted its wider application. The efficacy of aerosol drug therapy depends on drug-related factors (particle size, molecular weight), device factors, patient-related factors (airway anatomy, inhalation patterns) and mechanical ventilation-related factors (humidification, airway). This review identifies the relevant factors which require attention for optimization of aerosol drug delivery that can achieve better drug concentrations at the target sites and potentially improve clinical outcomes. © 2016 The Author(s).

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1. **High-flow nasal cannula oxygen supply as treatment in hypercapnic respiratory failure**  
   Lepere V. American Journal of Emergency Medicine 2016;34:1914.e1-1914.e2.

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1. **High-flow oxygen therapy and other inhaled therapies in intensive care units**  
   Levy S. D. The Lancet 2016;387:1867-1878.

In this Series paper, we review the current evidence for the use of high-flow oxygen therapy, inhaled gases, and aerosols in the care of critically ill patients. The available evidence supports the use of high-flow nasal cannulae for selected patients with acute hypoxaemic respiratory failure. Heliox might prevent intubation or improve gas flow in mechanically ventilated patients with severe asthma. Additionally, it might improve the delivery of aerosolised bronchodilators in obstructive lung disease in general. Inhaled nitric oxide might improve outcomes in a subset of patients with postoperative pulmonary hypertension who had cardiac surgery; however, it has not been shown to provide long-term benefit in patients with acute respiratory distress syndrome (ARDS). Inhaled prostacyclins, similar to inhaled nitric oxide, are not recommended for routine use in patients with ARDS, but can be used to improve oxygenation in patients who are not adequately stabilised with traditional therapies. Aerosolised bronchodilators are useful in mechanically ventilated patients with asthma and chronic obstructive pulmonary disease, but are not recommended for those with ARDS. Use of aerosolised antibiotics for ventilator-associated pneumonia and ventilator-associated tracheobronchitis shows promise, but the delivered dose can be highly variable if proper attention is not paid to the delivery method. © 2016 Elsevier Ltd.

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1. **Pulmonary tuberculosis-associated ARDS has a significantly high mortality: ECMO offers hope**  
   Bhardwaj A. Critical Care Medicine 2016;44:559.

Learning Objectives: Tuberculosis (TB) associated Acute Respiratory Distress Syndrome (ARDS) is a rare clinical condition in the United States. We present a case of a 24 year old patient who developed ARDS due to pulmonary TB. Prompt initiation of anti-TB therapy along with VV-ECMO support was a lifesaving intervention. Method(s): A 24-year-old female with no known past medical history presented to an outside hospital with a 2-week history of shortness of breath, productive cough and fever. Chest x-ray showed right upper lobe consolidation with middle and lower lobe alveolar infiltrates. She was admitted and started on broad spectrum antibiotics for pneumonia. On day 3, she developed severe hypoxemia requiring mechanical ventilation (MV). CT chest revealed no pulmonary embolism, a right upper lobe cavitary lesion and dense multifocal consolidations. Echo showed an EF of 57%. On day 7, she was transferred to our hospital for ARDS care. After elicitation of further history from family, patient was found to have emigrated from Ghana 8 years ago. Her sputum was found to be positive for TB and she was started on anti-TB regimen. She was deeply sedated, paralyzed, started on inhaled epoprostenol and continued on lung protective MV with low tidal volume (5ml/kg) and high PEEP. Despite these interventions, she remained severely hypoxemic with an ABG: 7.46/40/69/28/85% on AC/26/330/100/20. She was started on VV-ECMO on day 8. Her post ECMO ABG was 7.54/30/376/25/98% on AC/26/330/100/20. FiO2 was dropped to 40%. She was supported on VV-ECMO for a total of 8 days and underwent tracheostomy due to a prolonged wean secondary to delirium. After 45 days, she was discharged home on nasal cannula and on anti-TB regimen. Result(s): In low endemic areas, a detailed history and high clinical suspicion helps in prompt diagnosis and early treatment of TB. As a reversible condition, VV-ECMO should be considered in patients with persistent hypoxemic respiratory failure despite lung protective MV. To our knowledge, this is the first reported case of successful VVECMO use in an adult with TB associated ARDS in the United States.

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1. **Use of high-flow nasal cannula oxygenation in ICU adults: a narrative review**  
   Papazian L. Intensive Care Medicine 2016;42:1336-1349.

Oxygen therapy can be delivered using low-flow, intermediate-flow (air entrainment mask), or high-flow devices. Low/intermediate-flow oxygen devices have several drawbacks that cause critically ill patients discomfort and translate into suboptimal clinical results. These include limitation of the FiO2 (due to the high inspiratory flow often observed in patients with respiratory failure), and insufficient humidification and warming of the inspired gas. High-flow nasal cannula oxygenation (HFNCO) delivers oxygen flow rates of up to 60 L/min and over the last decade its effect on clinical outcomes has widely been evaluated, such as in the improvement of respiratory distress, the need for intubation, and mortality. Mechanisms of action of HFNCO are complex and not limited to the increased oxygen flow rate. The main aim of this review is to guide clinicians towards evidence-based clinical practice guidelines. It summarizes current knowledge about HFNCO use in ICU patients and the potential areas of uncertainties. For instance, it has been recently suggested that HFNCO could improve the outcome of patients with hypoxemic acute respiratory failure. In other settings, research is ongoing and additional evidence is needed. For instance, if intubation is required, studies suggest that HFNCO may help to improve preoxygenation and can be used after extubation. Likewise, HFNCO might be used in obese patients, or to prevent respiratory deterioration in hypoxemic patients requiring bronchoscopy, or for the delivery of aerosol therapy. However, areas for which conclusive data exist are limited and interventions using standardized HFNCO protocols, comparators, and relevant clinical outcomes are warranted. © 2016, Springer-Verlag Berlin Heidelberg and ESICM.

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1. **Aerosol therapy during noninvasive ventilation or high-flow nasal cannula**  
   Hess D. R. Respiratory Care 2015;60:880-891.

Noninvasive ventilation (NIV) and high-flow nasal cannula (HFNC) are increasingly used for patients with acute respiratory failure. Some patients receiving these therapies might also benefit from inhaled drug delivery. Thus, it is attractive to combine aerosol therapy with NIV or HFNC. The purpose of this paper is to review the available evidence related to the use of inhaled aerosols with NIV or HFNC. Available evidence supports the delivery of aerosols during NIV. Inhaled bronchodilator response might be improved with the use of NIV in acute asthma, but the evidence is not sufficiently mature to recommend this as standard therapy. Evidence does support aerosol delivery without discontinuation of NIV. Clinical studies on aerosol delivery during HFNC are needed, and based on the available in vitro evidence, it is not possible to make a recommendation for or against aerosol delivery during HFNC. © 2015 Daedalus Enterprises.

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1. **Clinical controversies in aerosol therapy for infants and children**  
   DiBlasi R. M. Respiratory Care 2015;60:894-914.

Pediatric patients are different from adult patients with respect to airway anatomy and breathing patterns. They are also incapable of following commands and often reject breathing treatments. For these reasons, aerosol drug delivery is one of the most technically challenging aspects for clinicians providing respiratory care to young children. Improvements in nebulizer technology have provided better delivery options for pediatric patients. This review highlights research related to pediatric nebulizer and interface devices and how they can be used to provide the safest and most efficient treatments with the array of treatment delivery options. Also addressed are clinical controversies and debates in pediatric aerosol science, including drug delivery in crying versus resting infants, pressurized metered-dose inhalers and small-volume nebulizers for bronchodilator administration, continuous nebulization, noninvasive drug delivery options, and optimization of nebulizer performance during infant and large pediatric conventional and high-frequency ventilation. © 2015 Daedalus Enterprises.

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1. **Comparison of HFNC, bubble CPAP and SiPAP on aerosol delivery in neonates: An in-vitro study**  
   Sunbul F. S. Pediatric Pulmonology 2015;50:1099-1106.

Aerosol drug delivery via high flow nasal cannula (HFNC), bubble continuous positive airway pressure (CPAP), and synchronized inspiratory positive airway pressure (SiPAP) has not been quantified in spontaneously breathing premature infants. Objectives: The purpose of this study was to compare aerosol delivery via HFNC, bubble CPAP, and SiPAP in a model of a simulated spontaneously breathing preterm infant. Working hypothesis: The types of CPAP systems and nebulizer positions used during aerosol therapy will impact aerosol deposition in simulated spontaneously breathing infants. Study design: Quantitative, comparative, in-vitro study. Methodology: A breath simulator was set to preterm infant settings (VT: 9 ml, RR: 50 bpm and Ti: 0.5 sec) and connected to the trachea of an anatomical upper airway model of a preterm infant via collecting filter distal to the trachea. The HFNC (Optiflow; Fisher &amp; Paykel), Bubble CPAP (Fisher &amp; Paykel), and SiPAP (Carefusion) were attached to the nares of the model via each device's proprietary nasal cannula and set to deliver a baseline of 5 cm H2O pressure. Albuterol sulfate (2.5 mg/0.5 ml) was aerosolized with a mesh nebulizer (Aeroneb Solo) positioned1 proximal to the patient and2 prior to the humidifier (n = 5). The drug was eluted from the filter with 0.1 N HCl and analyzed via spectrophotometry (276 nm). Data were analyzed using descriptive statistics, t-tests, and one-way analysis of variance (ANOVA), with P &lt; 0.05 significant. Results: At position 1, the trend of lower deposition (mean ± SD%) across devices was not significant (0.90 ± 0.26, 0.70 ± 0.16 and 0.59 ± 0.19, respectively; P = 0.098); however, in position 2, drug delivery with SiPAP (0.79 ± 0.11) was lower compared to both HFNC (1.30 ± 0.17; P = 0.003) and bubble CPAP (1.24 ± 0.24; p = 0.008). Placement of the nebulizer prior to the humidifier increased deposition with all devices (P &lt; 0.05). Conclusions: Aerosol can be delivered via all three devices used in this study. Device selection and nebulizer position impacted aerosol delivery in this simulated model of a spontaneously breathing preterm infant. Pediatr Pulmonol. 2015; 50:1099-1106. © 2014 Wiley Periodicals, Inc.

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1. **Efficient nose-to-lung (N2L) aerosol delivery with a dry powder inhaler**  
   Longest P. W. Journal of Aerosol Medicine and Pulmonary Drug Delivery 2015;28:189-201.

Purpose: Delivering aerosols to the lungs through the nasal route has a number of advantages, but its use has been limited by high depositional loss in the extrathoracic airways. The objective of this study was to evaluate the nose-to-lung (N2L) delivery of excipient enhanced growth (EEG) formulation aerosols generated with a new inline dry powder inhaler (DPI). The device was also adapted to enable aerosol delivery to a patient simultaneously receiving respiratory support from high flow nasal cannula (HFNC) therapy. Methods: The inhaler delivered the antibiotic ciprofloxacin, which was formulated as submicrometer combination particles containing a hygroscopic excipient prepared by spray-drying. Nose-to-lung delivery was assessed using in vitro and computational fluid dynamics (CFD) methods in an airway model that continued through the upper tracheobronchial region. Results: The best performing device contained a 2.3 mm flow control orifice and a 3D rod array with a 3-4-3 rod pattern. Based on in vitro experiments, the emitted dose from the streamlined nasal cannula had a fine particle fraction <5 μm of 95.9% and mass median aerodynamic diameter of 1.4 μm, which was considered ideal for nose-to-lung EEG delivery. With the 2.3-343 device, condensational growth in the airways increased the aerosol size to 2.5-2.7 μm and extrathoracic deposition was <10%. CFD results closely matched the in vitro experiments and predicted that nasal deposition was <2%. Conclusions: The developed DPI produced high efficiency aerosolization with significant size increase of the aerosol within the airways that can be used to enable nose-to-lung delivery and aerosol administration during HFNC therapy. © Copyright 2015, Mary Ann Liebert, Inc. 2015.

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1. **Evaluation of Lung Deposition of Aerosol Via HFNC in Healthy Adults**  
   Anon. Clinical Trials 2015;:No page numbers.

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1. **High-Flow Nasal Cannula and Aerosolized β Agonists for Rescue Therapy in Children With Bronchiolitis: A Case Series**  
   Morgan S. E. Respir Care 2015;60:e161-5.

Asthma and bronchiolitis are episodic obstructive pulmonary diseases characterized by bronchoconstriction, airway wall inflammation, increased mucus production, and air-flow obstruction. We present the cases of 5 infants treated for acute bronchiolitis with respiratory distress using a combination of high-flow nasal cannula oxygen (HFNC) and an Aerogen nebulizer to deliver aerosolized β-agonist therapy. In all infants, we found that HFNC resulted in a greater heart rate increase than delivery via a facemask. We also found that patients tolerated inhaled therapy better with HFNC than a facemask.

1. **Simultaneous administration of low flow nasal cannula oxygen support and pharmaceutical aerosols**  
   Longest P. W. American Journal of Respiratory and Critical Care Medicine 2015;191:No page numbers.

Rationale. The delivery of aerosols to the lungs through the nose can be convenient for medications that need continuous delivery, require frequent administration, have high doses, or need to be delivered during non-invasive ventilation. However, aerosols are typically not administered through low flow nasal cannula (LFNC) oxygen delivery systems due to expected poor lung delivery efficiency. A combination of spray dried excipient enhanced growth (EEG) particles together with a new inline dry powder inhaler DPI (figure below) and redesigned nasal cannula interfaces can potentially allow for concurrent LFNC oxygen therapy and efficient aerosol delivery to the lungs. Methods. Two submicrometer EEG dry powder formulations were produced using a spray drying technique containing albuterol sulfate or ciprofloxacin as the drug and a hygroscopic excipient (mannitol). A new inline DPI device was connected with 4 mm tubing to a new streamlined nasal cannula interface. The in vitro test system employed an adult nose-mouth-throat (NMT) geometry and either steady inhalation at 45 L/min or a transient sinusoidal breathing profile with an inhalation period of 2 s and a tidal volume of 750 ml. Drug aerosol characteristics, deposition, and lung delivery were assessed in vitro and optimized using computational fluid dynamics (CFD). Results. Optimization of the inline DPI with the albuterol formulation using a constant ventilatory gas flow of 5 L/min produced an emitted dose out of the cannula of 61.4% with a fine particle fraction (FPF) < 5 mum of 85.3%, indicating a very high quality aerosol. The corresponding deposition in the nasal cavity geometry at a constant inhalation of 45 L/min was 1.1%, which was desirable for high efficiency lung delivery of the aerosol. Using a cyclic respiratory profile and pulsing the ventilatory gas flow to actuate the inhaler for 2 s to coincide with inhalation maintained low NMT depositional loss (4.1%) but increased respiratory losses to the environment (19.8%) resulting in a lung delivery efficiency of 34.8% for the ciprofloxacin formulation. Subsequent CFD simulations indicated that limiting the DPI activation period to 1 s increased lung delivery to approximately 70%. Conclusions. Through a combination of particle engineering leading to EEG powder formulations, a new inline DPI, and redesigned low flow nasal cannula interface, aerosols can be effectively delivered to the lungs during the administration of LFNC oxygen therapy. The developed DPI can be simply connected inline while the patient receives LFNC oxygen support or operated intermittently to coincide with patient inhalation. (Figure Presented).

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1. **Tomographic Comparison of Aerosol Lung Distribution With Two Nebulizers Through a High Flow Nasal Cannula**  
   Anon. Clinical Trials 2015;:No page numbers.

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1. **Year in review 2014: Aerosol delivery devices**  
   Myers T. R. Respiratory Care 2015;60:1190-1196.

After centuries of discoveries and technological growth, aerosol therapy remains a cornerstone of care in the management of both acute and chronic respiratory conditions. Aerosol therapy embraces the concept that medicine is both an art and a science, where an explicit understanding of the science of aerosol therapy, the nuances of the different delivery devices, and the ability to provide accurate and reliable education to patients become increasingly important. The purpose of this article is to review recent literature regarding aerosol delivery devices in a style that readers of RESPIRATORY CARE may use as a key topic resource. © 2015 Daedalus Enterprises.

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1. **[The therapeutic effect of high flow nasal cannula oxygen therapy for the first imported case of Middle East respiratory syndrome to China]**  
   Luo Y. Zhonghua Wei Zhong Bing Ji Jiu Yi Xue 2015;27:841-4.

OBJECTIVE: To investigate the value of high flow nasal cannula (HFNC) in treating a patient with Middle East respiratory syndrome (MERS). METHODS: The effect of HFNC applied in the first imported MERS patient with complication of acute respiratory distress syndrome (ARDS) to China was observed. The patient was admitted to Department of Critical Care Medicine of Huizhou Municipal Central Hospital on May 28th, 2015, and the changes in various clinical parameters and their significance were analyzed. RESULTS: A 43-year old male was admitted to negative pressure isolation intensive care unit with the complaint of back ache for 7 days and fever for 2 days. Vital signs and saturation of pulse oximetry (SpO2) were monitored continuously. After admission, ribavirin was given orally for 12 days and α-interferon was administered once on the first day. However, after 2-week anti-virus therapy, the virus test was positive. Ceftriaxone was given on the 4th day, and it was changed to meropenem on the 3rd day for 2 weeks. Immune globulin was given on the 4th day and continued for 1 week. Thymosin-α1 was given on the 8th day and continued for 2 weeks. According to his past history, methimazole had been given continuously for hyperthyroidism and other symptomatic treatment. Oxygen inhalation (6 L/min) was given immediately after admission, but the condition of patient worsened with the following symptoms: frequent cough and obvious shortness of breath. Moreover pleural effusion gradually increased as shown by X-ray. SPO2 was maintained only at about 0.91. Oxygenation index (PaO2/FiO2) decreased to 144 mmHg (1 mmHg = 0.133 kPa). So oxygen inhalation via nasal cannula was changed to HFNC after 2 days. The parameters were set as follows: temperature 34 degrees C, flow rate 20 L/min, fraction of inspired oxygen (FiO2) 0.50. The flow was raised 5 L/min every 10 minutes, and was continued till the target value reached 60 L/min. FiO2 was modified according to SpO2 and PaO2/FiO2. FiO2 was set to 0.80 on the 5th day of admission. Shortness of breath of the patient was improved on the 7th day of admission after the application of HFNC. FiO2 was then decreased to 0.58 as PaO2/FiO2 rose. Then the flow was gradually decreased to 30 L/min. HFNC was reduced with continuous improvement in PaO2/FiO2. HFNC was changed to low flow oxygen inhalation nasal cannula (2-3 L/min) on the 20th day. Oxygen treatment was stopped on the 23rd day, and SpO2 was maintained at 0.98-1.00. Activities on bed were gradually increased. The patient was cured and discharged from hospital on June 26th. The patient showed good tolerance and high compliance during the treatment with HFNC. No nosocomial spread occurred during the treatment. CONCLUSIONS: HFNC could improve respiratory function of the patient with MERS obviously, and complication ARDS was prevented. HFNC might reduce nosocomial spread.

1. **Aerosol dispersion during various respiratory therapies: A risk assessment model of nosocomial infection to health care workers**  
   Hui D. S. C. Hong Kong Medical Journal 2014;20:9-13.

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1. **Development of a transient flow aerosol mixer-heater system for lung delivery of nasally administered aerosols using a nasal cannula**  
   Golshahi L. Aerosol Science and Technology 2014;48:1009-1021.

Previous studies have demonstrated improved nose-to-lung aerosol drug delivery with controlled condensational growth methods using a mixer-heater developed to synchronize aerosol delivery with patient inhalation. The goal of this study was to develop a new mixer-heater that delivers aerosols with a transient flow profile similar to a sinusoidal breathing waveform. The mixer-heater consisted of a chamber with two blowers delivering aerosol during the inhalation cycle of three sinusoidal breathing profiles. The effects of breathing profiles and mode of condensational growth delivery were studied using two in vitro extrathoracic airway models (closed- and open-mouth options). In excipient enhanced growth (EEG) delivery mode, increasing peak exhalation breathing flow rate decreased the emitted dose from the mixer-heater using the closed-mouth model. The mean (SD) emitted doses were 92 (2)%, 77 (2)%, and 70 (2)%, with 23, 35, and 44 L/min peak exhalation breathing flow rates, respectively. Using the in vitro open-mouth model mitigated the effect of breathing and the emitted doses were 93 (0.5)%, 83 (3)%, and 90 (4)% using the breathing profiles. The emitted doses in enhanced condensational growth (ECG) delivery mode using the breathing profiles with peak flow rates of 23, 35, and 44 L/min were 63 (4)%, 58 (2)%, and 58 (1)%, which were consistently lower than with EEG. Similarly, using the open-mouth model in ECG mode increased emitted doses to 77 (3)%, 73 (2)%, and 77 (8)%, respectively. The developed aerosol mixer-heater delivered greater than 50% of the nominal dose using a flow profile of sinusoidal inhalation, which represents a significant improvement compared to the current methods.Copyright 2014 American Association for Aerosol Research © 2014 American Association for Aerosol Research.

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1. **Development of high efficiency ventilation bag actuated dry powder inhalers**  
   Behara S. R. B. International Journal of Pharmaceutics 2014;465:52-62.

New active dry powder inhaler systems were developed and tested to efficiently aerosolize a carrier-free formulation. To assess inhaler performance, a challenging case study of aerosol lung delivery during high-flow nasal cannula (HFNC) therapy was selected. The active delivery system consisted of a ventilation bag for actuating the device, the DPI containing a flow control orifice and 3D rod array, and streamlined nasal cannula with separate inlets for the aerosol and HFNC therapy gas. In vitro experiments were conducted to assess deposition in the device, emitted dose (ED) from the nasal cannula, and powder deaggregation. The best performing systems achieved EDs of 70-80% with fine particle fractions <5 μm of 65-85% and mass median aerodynamic diameters of 1.5 μm, which were target conditions for controlled condensational growth aerosol delivery. Decreasing the size of the flow control orifice from 3.6 to 2.3 mm reduced the flow rate through the system with manual bag actuations from an average of 35 to 15 LPM, while improving ED and aerosolization performance. The new devices can be applied to improve aerosol delivery during mechanical ventilation, nose-to-lung aerosol administration, and to assist patients that cannot reproducibly use passive DPIs. © 2014 Elsevier B.V.

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1. **Editor's commentary**  
   Anon. Respiratory Care 2014;59:473.

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1. **Emerging aerosol drug delivery strategies: From bench to clinic**  
   Rubin B. K. Advanced Drug Delivery Reviews 2014;75:141-148.

Patients with tracheostomies, those requiring mechanical ventilation, and those too small or compromised for conventional devices, are realizing the benefits of increasingly sophisticated aerosol delivery systems. New medicines and novel aerosol formulations, have enhanced our ability to treat lung disease, and are opening the doors for therapy to treat diseases like diabetes, pulmonary hypertension, and cancer. Progress in the aerosol delivery of drugs has been spurred by the significant benefits, including ease of use, patient comfort, greater selectivity of effect, and the potential to decrease side effects. © 2014 Elsevier B.V.

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1. **Engineered aerosol medicine and drug delivery methods for optimal respiratory therapy**  
   Ali M. Respiratory Care 2014;59:1608-1610.

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1. **How to avoid interface problems in acute noninvasive ventilation**  
   Brill A. K. Breathe 2014;10:231-242.

Noninvasive ventilation (NIV) applied via different interfaces is increasingly used in the treatment of acute respiratory failure. One of the key factors determining the success of NIV is the choice of interface. Interface selection, fitting and handling can be challenging as NIV application can be complicated by discomfort, air leaks, skin damage or conjunctivitis. The aim of this article is to provide practical information on interface choice, technical aspects of mask fitting and prevention of mask-related problems during the acute delivery of NIV. © 2015, European Respiratory Society. All rights reserved.

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1. **In vitro evaluation of radio-labeled aerosol delivery via a variable-flow infant CPAP system**  
   Farney K. D. Respiratory Care 2014;59:340-344.

Background: Nasal CPAP is widely used in neonatal ICUs. Aerosolized medications such as inhaled steroids and β agonists are commonly administered in-line through nasal CPAP, especially to infants with bronchopulmonary dysplasia. We hypothesized that aerosol delivery to the lungs via variable-flow nasal CPAP in an in vitro model would be unreliable, and that the delivery would depend on the position of the aerosol generator within the nasal CPAP circuit. Methods: We used a system that employed a test lung placed in a plastic jar and subjected to negative pressure. Simulated inspiration effort was measured with a heated-wire anemometer. We used technetium-99m-labeled diethylene triamine penta-acetic acid as our aerosol. The nebulizer was placed either close to the humidifier or close to the nasal prongs in the circuit, and patient effort was simulated with a minute ventilation of 0.4 L/min. Results: Relative aerosol delivery to the infant test lung with the nebulizer close to the humidifier was extremely low (0.3 ± 0.4%), whereas placing the nebulizer close to the nasal prongs resulted in significantly (P <.001) improved delivery (21 ± 11%). Major areas of aerosol deposition with the nebulizer close to the humidifier versus close to the nasal prongs were: nebulizer (10 ± 4% vs 33 ± 13%, P <.001), exhalation limb (9 ± 17% vs 26 ± 30%, P =.23), and generator tubing (21 ± 11% vs 19 ± 20%, P =.86). Placing the nebulizer close to the humidifier resulted in 59 ± 8% of the aerosol being deposited in the inhalation tubing along the heater wire. Conclusions: Isotope delivery from an aerosol generator placed near the humidifier on variable-flow nasal CPAP was negligible in this in vitro setup; however, such delivery was significantly improved by locating the aerosol generator closer to the nasal CPAP interface. © 2014 Daedalus Enterprises.

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1. **Intermittent aerosol delivery to the lungs during high-flow nasal cannula therapy**  
   Golshahi L. Respiratory Care 2014;59:1476-1486.

INTRODUCTION: Use of submicrometer particles combined with condensational growth techniques has been proposed to reduce drug losses within components of high-flow nasal cannula therapy systems and to enhance the dose reaching the lower respiratory tract. These methods have been evaluated using continuous inhalation flow rather than realistic inhalation/exhalation breathing cycles. The goal of this study was to evaluate in vitro aerosol drug delivery using condensational growth techniques during high-flow nasal cannula therapy using realistic breathing profiles and incorporating intermittent aerosol delivery techniques. METHODS: A mixer-heater combined with a vibrating mesh nebulizer was used to generate a submicrometer aerosol using a formulation of 0.2% albuterol sulfate and 0.2% sodium chloride in water. Delivery efficiency of the aerosol for 1 min through a nasal cannula was considered using an intermittent delivery regime with aerosol being emitted for either the entire inhalation time (2 s) or half of the inhalation period (1 s) and compared with continuous delivery. The deposition of the aerosol was evaluated in the nasal delivery components (ventilator tubing and cannula) and an in vitro adult nose-mouth-throat (NMT) model using 3 realistic breathing profiles. RESULTS: Significant improvements in dose delivered to the exit of the NMT model (ex-NMT) were observed for both condensational growth methods using intermittent aerosol delivery compared with continuous delivery, and increasing the tidal volume was found useful. The combination of the largest tidal volume with the shortest intermittent delivery time resulted in the lowest respiration losses and the highest ex-NMT delivered dose. CONCLUSIONS: Intermittent aerosol delivery using realistic breathing profiles of submicrometer condensational growth aerosols was found to be efficient in delivering nasally administered drugs in an in vitro airway model. © 2014 Daedalus Enterprises.

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1. **Targeted lung delivery of nasally administered aerosols**  
   Tian G. Aerosol Science and Technology 2014;48:434-449.

Using the nasal route to deliver pharmaceutical aerosols to the lungs has a number of advantages, including coadministration during noninvasive ventilation. The objective of this study was to evaluate the growth and deposition characteristics of nasally administered aerosol throughout the conducting airways based on delivery with streamlined interfaces implementing two forms of controlled condensational growth technology. Characteristic conducting airways were considered including a nose-mouth-throat (NMT) geometry, complete upper tracheobronchial (TB) model through the third bifurcation (B3), and stochastic individual path (SIP) model to the terminal bronchioles (B15). Previously developed streamlined nasal cannula interfaces were used for the delivery of submicrometer particles using either enhanced condensational growth (ECG) or excipient enhanced growth (EEG) techniques. Computational fluid dynamics (CFD) simulations predicted aerosol transport, growth, and deposition for a control (4.7 μm) and three submicrometer condensational aerosols with budesonide as a model insoluble drug. Depositional losses with condensational aerosols in the cannula and NMT were less than 5% of the initial dose, which represents an order-of-magnitude reduction compared to the control. The condensational growth techniques increased the TB dose by a factor of 1.1-2.6×, delivered at least 70% of the dose to the alveolar region, and produced final aerosol sizes ≥2.5 μm. Compared to multiple commercial orally inhaled products, the nose-to-lung delivery approach increased dose to the biologically important lower TB region by factors as large as 35×. In conclusion, nose-to-lung delivery with streamlined nasal cannulas and condensational aerosols was highly efficient and targeted deposition to the lower TB and alveolar regions. © 2014 Copyright Taylor and Francis Group, LLC.

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1. **A case of hypoxia in a teenager**  
   Dangayach P. Journal of General Internal Medicine 2013;28:S254.

LEARNING OBJECTIVE 1: Recognize the association between cigarette smoking and acute eosinophilic pneumonia. LEARNING OBJECTIVE 2: Recognize the clinical features of AEP, a potentially life threatening yet fully reversible disease CASE: An 18-year-old Caucasian female presented to the emergency room with nausea, vomiting, and non-bloody diarrhea associated with fevers, chills, and epigastric pain. She noted an outbreak of food poisoning at the shelter where she lives. Her medical history included depression and anxiety. On review of systems, she noted a mild cough minimally productive of yellow sputum for the past month after initiating smoking several cigarettes daily. She denied shortness of breath, hemoptysis, and chest pain. She had no known allergies and denied use of alcohol, drugs, or new medications. On examination, her temperature was 103 F, heart rate 130-140 beats/minute, normotensive, with a respiratory rate of 35 with an oxygen saturation of 85 % on room air. Her oxygen saturation improved to 95 % with 3 L of supplemental oxygen by nasal cannula. She had course breath sounds with diminished air movement in bilateral lung fields. ABG showed pH 7.43, PCO2 24.3, P02 149 on 3 L O2. Her WBC count was 26,200 uL with a differential of 90 % neutrophils, 5 % lymphocytes, 4 % monocytes, and 1 % eosinophils. A chest x-ray showed moderate bibasilar reticulonodular opacities. An abdominal CT scan was performed for her abdominal symptoms, which incidentally noted diffuse groundglass opacities in the right middle lobe and lingula with bilateral intralobular septal thickening. To further investigate the findings, bronchoscopy with bronchoalveolar lavage (BAL) was performed. The cell count differential revealed marked eosinophilia (34 % eosinophils). Routine cultures, cytology, AFB stain and culture, ova and parasite exam, and hypersensitivity panel were negative. The diagnosis of acute eosinophilic pneumonia (AEP) was made with cigarette smoking as the etiology. She was initiated on 60 mg of oral prednisone daily and was educated on her "allergy" to cigarettes. Her chest x-ray, oxygen saturation, and tachypnea remarkably improved, and she was discharged from the hospital on room air with a three-week prednisone taper. After discharge, she resumed smoking. Within a week of doing so, she returned to the ED with symptoms of subcostal pain and cough. Her symptoms again improved with steroids. DISCUSSION: Although this patient's presenting gastrointestinal symptoms are not classic for AEP, the findings of fever, hypoxemic respiratory failure, and BAL with greater than 25 % eosinophilia with significant response to corticosteroids are diagnostic of AEP. Literature suggests recent onset cigarette smoking is a trigger for this acute hypersensitivity reaction. Re-exposure to cigarette smoke helped confirm that this was the inciting agent for the patient's AEP. Without prompt treatment, this disease can progress to respiratory failure, necessitating mechanical ventilation. This case highlights the importance for physicians to recognize cigarette smoking as an inciting agent for acute eosinophilic pneumonia in order to recognize this potentially life threatening yet fully reversible disease.

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1. **Aerosol delivery through high flow nasal cannulae**  
   Navratil T. Journal of Aerosol Medicine and Pulmonary Drug Delivery 2013;26:A4.

Trans-nasal pulmonary aerosol delivery via nasal cannula offers benefits over the oral administration for a range of patients and healthcare care settings. Trans-nasal delivery originated during non-invasive ventilation with high flow therapy, utilizing high flow nasal cannulae. However, the clinical utility of trans-nasal aerosol delivery has been historically limited by low pulmonary deposition (1-4% in Chua et al. 1994), significant rainout in the nasal cannula, and the absence of available delivery systems capable of efficiently delivering aerosols though ergonomic, comfortable cannulae. Over the last decade, novel approaches and evaluation of novel delivery systems identified critical factors for improving trans-nasal delivery. First, the potential for efficient aerosol delivery via nasal cannula and loss of efficiency due in part to large particles was described by Corcoran et al. Second, Ari and Fink demonstrated the dilutive effects of increasing gas flow and the benefits of improved laminar flow with heliox at higher flow. Third, Bennett and Zeman, while exploring the nasal deposition of fine particles, described the potential for decreased nasal deposition and improved overall pulmonary deposition with 1mum and 2mum monodisperse carnauba wax particles. Lastly, the in-silico and in-vitro work of Longest and Hindle demonstrated the potential of enhanced condensational growth and excipient enhanced hygroscopic growth to improve trans-nasal pulmonary deposition efficiency. Building on these concepts and integrating them with additional innovative technologies, a novel transnasal pulmonary aerosol delivery (tPAD) platform with nasal cannulae optimized for aerosol conductance was developed by Parion Sciences. The tPAD platform achieved ~ten-fold higher pulmonary deposition efficiency (~38% of the emitted dose) compared to the established trans-nasal pulmonary deposition efficiency values, with minimal deposition in the nose in healthy adult subjects. These advances support the future clinical use of the trans-nasal aerosol delivery to the lung with a variety of therapeutic agents to treat a broad range of pulmonary disorders.

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1. **Aerosol therapy in children: Challenges and solutions**  
   Ari A. Expert Review of Respiratory Medicine 2013;7:665-672.

Using aerosolized medications for the treatment of children has gained importance over the years. However, aerosol drug delivery to infants and pediatrics is not an easy task as it has been influenced by many challenges. Most aerosol devices have been designed for use in adults not for children. Therefore, they require some critical assessment in device selection and often a level of adaptation for use with smaller children. It is well documented that each aerosol device and interface that have been used for the treatment of children has its own advantages and challenges in drug delivery. This paper provides a comprehensive review of dosing, drug-device combination, aerosol devices and interfaces used for drug delivery to children with pulmonary diseases. Solutions to the challenges with the aim of optimizing aerosol therapy in this patient population are also discussed. © 2013 Informa UK Ltd.

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1. **Bypassing upper airway aerosol deposition with enhanced condensational growth**  
   Hindle M. Journal of Aerosol Medicine and Pulmonary Drug Delivery 2013;26:A4.

Aerosol delivery to the lungs during non-invasive ventilation (NIV) is characterized by poor delivery efficiency (< 1-10%) due to high depositional losses in the delivery tubing, cannula and nasal airways. In part, this is due to the particle size of the aerosols generated by commercial nebulizers. Enhanced condensation growth (ECG) is a technique that employs submicrometer drug aerosols to minimize depositional losses within the delivery setup and nasal airways. Condensational growth of these aerosols in the presence of co-administered heated and humidified air produces micrometer-sized droplets in the lungs allowing airway deposition to occur. In this study, in vitro experiments and computational fluid dynamic (CFD) simulations were used to compare the delivery of conventional nebulized aerosols with ECG aerosols generated from the Aeroneb Lab nebulizer and dried in a prototype dryer system to produce submicrometer particles. In vitro lung delivery efficiency of these aerosols was assessed and deposition in the delivery setup and nasal model determined with steady state and transient inhalation profiles. For both steady state and transient inhalation, deposition in the delivery tubing and cannula was low (~10%) for the submicrometer ECG aerosols. Delivery through the nose to the airways during steady state flow using ECG was about 90% of the recovered dose. A series of strategies including streamlining the cannula geometry and inhalation synchronized aerosol administration were combined with the ECG approach to improve lung delivery of the drug during transient inhalation. The use of the ECG approach may allow efficient pharmaceutical aerosol delivery to patients receiving NIV.

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1. **Delivery of aerosols from nasal high flow cannula to the respiratory tract using condensational growth techniques**  
   Tian G. Journal of Aerosol Medicine and Pulmonary Drug Delivery 2013;26:A43-A44.

Aerosol drug delivery during non-invasive ventilation (NIV) including high flow therapy (HFT) through a nasal cannula interface is known to be inefficient due to high depositional losses. To improve respiratory drug delivery during NIV, the concept of enhanced condensational growth (ECG) was recently proposed in which submicrometer aerosols are delivered to one nostril and warm air saturated with water vapor is delivered to the other nostril. Using a similar excipient enhanced growth (EEG) approach, submicrometer particles composed of a drug and hygroscopic excipient are delivered to both nostrils through a nasal cannula interface. The submicrometer particles are inhaled through the cannula interface and nasal passages resulting in low depositional losses. Subsequent aerosol growth in the tracheobronchial (TB) airways occurs for ECG and EEG, due to mixing with the inhaled saturated air or the natural relative humidity of the airways, respectively. The objective of this study is to evaluate the growth and deposition characteristics of nasally administered submicrometer aerosols throughout the conducting airways for ECG and EEG delivery methods. Computational fluid dynamics simulations were validated based on in vitro experiments in a characteristic nasal airway model extending through the trachea. Results indicate that the ECG and EEG approaches both produce very low nasal depositional losses and increased the aerosol size to 2 mum and above within the conducting airways. Ultimately, the proposed technology will provide a highly effective method for delivering pharmaceutical aerosols to patients for local or systemic therapy during NIV.

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1. **Evaluation of vibrating mesh nebulizer performance during nasal high flow therapy**  
   MacLoughlin R. Journal of Aerosol Medicine and Pulmonary Drug Delivery 2013;26:A51-A52.

The aerosol performance of a vibrating mesh nebulizer (Aeroneb Solo, Aerogen) was evaluated during simulated adult nasal high flow therapy across a range of humidified gas flow rates. Adult high flow nasal cannula were used (Optiflow, Fisher & Paykel). Albuterol (2mg/mL) was nebulized as a marker aerosol. Emitted dose at each flow rate under test (15, 30, 45LPM) was recorded on an absolute filter placed at the exit of the cannula (n = 3). A breathing simulator was used to generate the breath (BPM15 Tv 500mL, I:E 1:1) and respirable dose was recorded distal to the LUCY adult airway model (n = 3). Drug eluted from the filters was analysed using spectrophotometry (at 276nm) and expressed as a percentage of the nominal dose placed in the nebulizer's medication cup. Time to delivery of a full 3mL dose was recorded at approximately 7 minutes for each run. As expected, higher gas flow rates were associated with reduced efficiency of delivery of drug through this model of an adult nasal high flow system. This is likely due to impactional losses within the circuit tubing and upper airways of the LUCY model. Respirable dose efficiencies are comparable to those reported in the literature with the Aeroneb Solo nebulizer during both invasive and non-invasive mechanical ventilation. These results provide further proof of concept for concurrent and, for the first time, highly efficient aerosol delivery in nasal high flow setting. Further studies are currently underway on the evaluation of aerosol delivery in both paediatric and neonate nasal high flow systems. Finally, investigation of continuous aerosol therapy over extended periods is warranted.

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1. **Generation and effective delivery of submicrometer aerosols through high flow nasal cannula during noninvasive ventilation**  
   Walenga R. Journal of Aerosol Medicine and Pulmonary Drug Delivery 2013;26:A43.

Enhanced condensational growth (ECG) has been shown to improve pulmonary aerosol delivery through a nasal cannula interface by introducing submicrometer particles that combine with heated and humidified air in the nasopharynx to cause aerosol size increase. An aerosol delivery system capable of producing submicrometer aerosol particles with minimal system losses is required for the successful implementation of ECG. Computational fluid dynamics (CFD)was used with in vitro experimental results to evaluate aerosols generated using an existing radial aerosol mixer design and an improved aerosol mixer with a compact heattransfer region. Aerosol delivery through the commercially available Optiflow nasal cannula, a divided (D) nasal cannula, and a divided and streamlined (DS) nasal cannula was also considered. The improved mixer was shown to reliably produce submicrometer aerosols (900nm) with device depositional losses that were 3 times lower than the radial design at flowrates of 10 and 15 LPM. The DS cannula was demonstrated to reduce depositional losses by a factor of 2-3 in comparison to the Optiflow and D cannulas at flow rates of 10 and 15 LPM. The DS cannula was also shown to be capable of delivering 80%ormore of conventional size particles to the nose at flow rates up to 15 LPM. The optimized system has an overall high delivery efficiency of about 90% and it effectively produced submicrometer particles. The system may be combined with the ECG concept to improve drug delivery when used with non-invasive ventilation and high flow therapy.

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1. **High-efficiency generation and delivery of aerosols through nasal cannula during noninvasive ventilation**  
   Longest P. Worth Journal of aerosol medicine and pulmonary drug delivery 2013;26:266-79.

BACKGROUND: Previous studies have demonstrated the delivery of pharmaceutical aerosols through nasal cannula and the feasibility of enhanced condensational growth (ECG) with a nasal interface. The objectives of this study were to develop a device for generating submicrometer aerosols with minimal depositional loss in the formation process and to improve aerosol delivery efficiencies through nasal cannulas., METHODS: A combination of in vitro experiments and computational fluid dynamics (CFD) simulations that used the strengths of each method was applied. Aerosols were formed using a conventional mesh nebulizer, mixed with ventilation gas, and heated to produce submicrometer sizes. An improved version of the mixer and heater unit was developed based on CFD simulations, and performance was verified with experiments. Aerosol delivery was considered through a commercial large-bore adult cannula, a divided (D) design for use with ECG, and a divided and streamlined (DS) design., RESULTS: The improved mixer design reduced the total deposition fraction (DF) of drug within the mixer by a factor of 3 compared with an initial version, had a total DF of approximately 10%, and produced submicrometer aerosols at flow rates of 10 and 15 L/min. Compared with the commercial and D designs for submicrometer aerosols, the DS cannula reduced depositional losses by a factor of 2-3 and retained only approximately 5% or less of the nebulized dose at all flow rates considered. For conventional-sized aerosols (3.9 and 4.7 mum), the DS device provided delivery efficiencies of approximately 80% and above at flow rates of 2-15 L/min., CONCLUSIONS: Submicrometer aerosols can be formed using a conventional mesh nebulizer and delivered through a nasal cannula with total delivery efficiencies of 80-90%. Streamlining the nasal cannula significantly improved the delivery efficiency of both submicrometer and micrometer aerosols; however, use of submicrometer particles with ECG delivery resulted in overall lower depositional losses.

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1. **Improving pharmaceutical aerosol delivery during noninvasive ventilation: effects of streamlined components**  
   Longest P. W. Ann Biomed Eng 2013;41:1217-32.

Aerosol delivery efficiency during noninvasive ventilation (NIV) is known to be low (~10%) and is associated with poor outcomes of aerosol therapy. The objective of this study was to demonstrate the benefit of redesigning ventilation circuit components using a streamlining approach to improve aerosol delivery during nasal high flow therapy in adults with a conventional-sized aerosol from a mesh nebulizer. The ventilation circuit consisted of a humidifier, mesh nebulizer, mixing T-connector (with 90° angle), 10 mm tubing, and nasal cannula interface. In vitro experiments and computational fluid dynamics analyses were used to evaluate depositional losses in a system of existing components and a newly proposed streamlined T-connector and cannula at flow rates of 30 and 45 LPM. Streamlined designs reduced deposition in the T-connector by a factor of 4. In the nasal cannula, the streamlined designs reduced depositional losses by factors of 1.25-2.0. With the streamlined designs, the highest emitted dose achieved was >40% for a conventional-sized aerosol at 30 LPM. Streamlined geometries offer an effective method to significantly improve the delivery of aerosols through components of NIV systems. This increase in delivery efficiency is important for new inhaled medications with narrow therapeutic windows, increased costs, or long delivery times.

1. **NIV applications for acute respiratory care: NIV for acute hypercapnic patients**  
   Riera J. Minerva Pneumologica 2013;52:1-14.

There's high quality evidence about the benefits of using noninvasive ventilation (NIV) in patients suffering acute hypercapnic respiratory failure (AHRF). The acute exacerbation of chronic obstructive pulmonary disease (AECOPD) is the most common cause of AHRF. A very important point is the early and precise identification of those patients with AHRF who could clearly benefit from the application of NIV and those ventilated subjects in whom the technique is failing. This accurate selection could significantly improve NIV success. Another imperative condition to achieve NIV success is the patient's tolerance to the technique. Choosing an appropriate interface, a suitable and effective mode of ventilation and a correct air humidification could contribute to a better adherence to NIV by the patient. The remarkable good tolerance of the high-flow nasal cannula system and its effects on the respiratory function makes it an optional mode to ventilate hypercapnic patients. Moreover, the recently simplified extracorporeal systems may be associated with NIV in order to avoid invasive ventilation. In this paper, the abovementioned issues are reviewed on the bases of the available scientific evidence. The review is firstly focused on evidence-based indications and contraindications of NIV for patients with AHRF, continues with an overview of important points associated to NIV application and ends with new therapies linked to it.

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1. **Severe acute respiratory syndrome (SARS): Lessons learnt in Hong Kong**  
   Hui D. S. Journal of Thoracic Disease 2013;5:S122-S126.

Many healthcare workers were infected while looking after the SARS patients on the medical wards in 2003. The high infectivity of the SARS coronavirus with peak viral load on day 10 of illness when patients were ill, overcrowding of the old medical wards with low air changes/hr (ACH), and aerosol-generating procedures while resuscitating the patients were the major factors. Procedures reported to present an increased risk of SARS transmission include tracheal intubation, noninvasive ventilation, tracheotomy and manual ventilation before intubation whereas oxygen therapy and bed distance <1 m were also implicated. Studies based on laser visualization technique with smoke particles as smokers in the human patient simulator has shown that oxygen therapy via Hudson mask and nasal cannula could disperse exhaled air of patients to 0.4 and 1 m respectively whereas jet nebulizer could disperse exhaled air >0.8 m from the patient. Bigger isolation rooms with 16 ACH are more effective than smaller isolation rooms with 12 ACH in removing exhaled air and preventing room contamination but at the expense of more noise and electricity consumption. Non-invasive ventilation via face masks and single circuit can disperse exhaled air from 0.4 to 1 m. Both higher inspiratory pressures and use of whisper swivel device (to facilitate carbon dioxide removal) could increase the exhaled air leakage and isolation room contamination during on-invasive ventilation. Addition of a viral-bacterial filter during manual ventilation by bagging may reduce the exhaled air leakage forward and yet increase the sideway leakage. N95 mask was more effective than surgical mask in preventing expelled air leakage during patient's coughing but there was still significant sideway leakage to 15 cm. Clinicians should be aware of air leakage from the various face masks and adopt strict infection control measures during resuscitation of patients with severe respiratory infections. Carefully designed clinical trials are required to determine the optimal timing and dosage of any antiviral agents, convalescent plasma, and immuno-modulating agents in the treatment of the possibly immunemediated lung injury in SARS and newly emerged infection such as the Middle East Respiratory Syndrome. © Pioneer Bioscience Publishing Company.

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1. **Streamlined designs to reduce aerosol deposition losses in circuits used for invasive and non-invasive ventilation**  
   Golshahi L. Journal of Aerosol Medicine and Pulmonary Drug Delivery 2013;26:A18.

Pharmaceutical aerosol delivery to the lungs during invasive and non-invasive ventilation is associated with dose variability and drug depositional losses. In part, these losses are due to regions of sudden flow contraction and expansion, and angle changes within the circuit. To address this issue, key components of two delivery circuits were produced using streamlined designs that originated from computational fluid dynamics simulations. Aerosol drug deposition was determined in a model invasive delivery circuit consisting of an Aeroneb adult Tadapter connected to a wye connector and then an endotracheal tube (7-9mm diameter). Similarly, deposition was determined in a model non-invasive delivery circuit consisting of an Aeroneb neonate T-adapter and an Optiflow nasal cannula connected using 20 cm of tubing (10mm diameter). Albuterol sulfate aerosols were generated using the Aeroneb Lab Nebulizer and delivered to the circuits with humidified air (> 90%RH, 25degreeC) at 30LPM. Commercial and custom-made streamlined T-adapters, wye connectors and cannula designs were tested in each system. For the invasive ventilation circuit, deposition in the commercial wye connector was high (33.8 +/- 1.2%). The streamlined wye connector reduced deposition to 5.1 +/- 0.8%. As the endotracheal tube size was increased, this 6 fold reduction in depositional losses resulted in higher delivery fractions of the drug to the patient. For the non-invasive ventilation circuit, there was significant deposition in the neonate T-adapter (30.6 +/- 1.9%). A streamlined design T-adapter resulted in deposition losses of 5.7 +/- 0.4%. The combination of streamlined T-adapter and cannula improved total delivery fraction through the non-invasive circuit by a factor of approximately 2x.

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1. **The use of condensational growth methods for efficient drug delivery to the lungs during noninvasive ventilation high flow therapy**  
   Golshahi L. Pharmaceutical Research 2013;30:2917-2930.

Purpose: The objective of this study was to evaluate the delivery of nasally administered aerosols to the lungs during noninvasive ventilation using controlled condensational growth techniques. Methods: An optimized mixer, combined with a mesh nebulizer, was used to generate submicrometer aerosol particles using drug alone (albuterol sulfate) and with mannitol or sodium chloride added as hygroscopic excipients. The deposition and growth of these particles were evaluated in an adult nose-mouth-throat (NMT) model using in vitro experimental methods and computational fluid dynamics simulations. Results: Significant improvement in the lung dose (3-4× increase) was observed using excipient enhanced growth (EEG) and enhanced condensational growth (ECG) delivery modes compared to control studies performed with a conventional size aerosol (~5 μm). This was due to reduced device retention and minimal deposition in the NMT airways. Increased condensational growth of the initially submicrometer particles was observed using the ECG mode and in the presence of hygroscopic excipients. CFD predictions for regional drug deposition and aerosol size increase were in good agreement with the observed experimental results. Conclusions: These controlled condensational growth techniques for the delivery of submicrometer aerosols were found to be highly efficient methods for delivering nasally-administered drugs to the lungs. © 2013 Springer Science+Business Media New York.

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1. **Aerosol therapy in patients receiving noninvasive positive pressure ventilation**  
   Dhand R. Journal of Aerosol Medicine and Pulmonary Drug Delivery 2012;25:63-78.

In selected patients, noninvasive positive pressure ventilation (NIPPV) with a facemask is now commonly employed as the first choice for providing mechanical ventilation in the intensive care unit (ICU). Aerosol therapy for treatment of acute or acute-on-chronic respiratory failure in this setting may be delivered by pressurized metered-dose inhaler (pMDI) with a chamber spacer and facemask or nebulizer and facemask. This article reviews the host of factors influencing aerosol delivery with these devices during NIPPV. These factors include (1) the type of ventilator, (2) mode of ventilation, (3) circuit conditions, (4) type of interface, (5) type of aerosol generator, (6) drug-related factors, (7) breathing parameters, and (8) patient-related factors. Despite the impediments to efficient aerosol delivery because of continuous gas flow, high inspiratory flow rates, air leaks, circuit humidity, and patient-ventilator asynchrony, significant therapeutic effects are achieved after inhaled bronchodilator administration to patients with asthma and chronic obstructive pulmonary disease. Similarly to invasive mechanical ventilation, careful attention to the technique of drug administration is required to optimize therapeutic effects of inhaled therapies during NIPPV. Assessment of the patient's ability to tolerate a facemask, the level of respiratory distress, hemodynamic status, and synchronization of aerosol generation with inspiratory airflow are important factors contributing to the success of aerosol delivery during NIPPV. Further research into novel delivery methods, such as the use of NIPPV with nasal cannulae, could enhance the efficiency, ease of use, and reproducibility of inhalation therapy during noninvasive ventilation. © 2012 Mary Ann Liebert, Inc.

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1. **The non-intubated, spontaneously breathing, continuous positive airway pressure (CPAP) ventilated pre-term lamb: A unique animal model**  
   Rahmel D. K. Reproductive Toxicology 2012;34:204-215.

Neonatologists prefer non-invasive ventilation methods for pre-term neonates, who often require surfactant treatment. Therefore, a technology for non-invasive surfactant administration would be highly appreciated. We have developed a Continuous Powder Aerosolization (CPA) system for the generation of a humidified recombinant surfactant protein-C (rSP-C) surfactant aerosol for non-invasive administration to pre-term neonates via bi-nasal prongs. Before conducting clinical trials, safety testing in an adequate pre-clinical animal model is necessary. In contrast to existing pre-term lamb models, this model should use non-intubated animals to include upper airways for safety testing. Pre-term animals should have already a sufficient respiratory drive to breathe spontaneously on non-invasive continuous positive airway pressure (CPAP) support, but their lungs should still be pre-mature to be comparable with the clinical situation for the treatment of pre-term infants. The aim of this feasibility study was therefore to establish a CPAP-stable, non-intubated pre-term lamb model for the investigation of safety, efficacy, and pulmonary deposition of a humidified rSP-C surfactant aerosol. For this purpose, 19 pre-term lambs with a gestational age of 135-137 days (term: about 144 days) were delivered via Caesarean section. Four animals died before start of treatment, while the remaining animals were treated via customized bi-nasal prongs with rSP-C surfactant aerosol or humidified air as vehicle control. To determine pulmonary deposition, selected animals received rSP-C surfactant labelled with samarium oxide as non-radioactive tracer. Treatment was started at 30. min of age and was continued for 1 or 2.5. h. Investigations during the in-life phase included observation of clinical signs, haematology, blood gas analysis, and determination of minute volume. At 3. h of age, animals were euthanized and organs removed for histopathology investigation or for determination of pulmonary deposition. Administration of humidified, aerosolized rSP-C surfactant was well tolerated, and histopathology investigation of upper airways and lungs revealed no aerosol-related changes. Mean body weight-corrected pulmonary deposition of rSP-C surfactant ranged from 1.7 to 7.7. mg/kg depending on the duration of treatment and aerosolization parameters used. A trend towards reduced spontaneous minute volumes indicating reduced breathing efforts and towards reduced lung weights indicating less fluid in the lungs of surfactant-treated animals compared to animals of the vehicle control group could be seen. Taken together, a CPAP-stable, non-intubated pre-term lamb model was successfully established and the parameters for the investigation of safety, efficacy, and pulmonary deposition of aerosolized rSP-C surfactant for the subsequent main study were identified. © 2012 Elsevier Inc.

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1. **A dramatic presentation with a happy ending-a story of silo filler's disease**  
   Duran-Castillo M. Journal of Hospital Medicine 2011;6:S174.

Case Presentation: This is a 39-year-old farmer admitted with dyspnea and productive cough with dark sputum. The patient stepped into a closed silo 3 days prior to admission. Approximately 8 hours later, he developed significant dyspnea, productive cough with dark sputum, fever, and malaise. The cough became dry subsequently. In the emergency department he was found to have a temperature of 39degreeC, tachycardia, and a white blood cell count of 20,000; the chest roentgenogram was normal. He received a dose of ceftriaxone and azithromycin and was transferred to our hospital. History was significant for well-controlled gout on allopurinol, morbid obesity, and impaired fasting glucose; the patient recalled that along with his father, he experienced a brief episode of shortness of breath the first time he went into the silo a year before. An arterial blood gas showed methemoglobin of 2.1%. A computed tomography of the chest was normal. He was started on intravenous methylprednisolone 0.5 mg/kg intravenously every 6 hours; oxygen was administered via nasal cannula at 2 L/min, resulting in an oxygen saturation of 98%-100% with no distress. He was able to be weaned to room air within 24 hours. A formal prophylactic recommendation was given to the patient for the next silo filling: to start daily prednisone 40 mg by mouth 2 days before silo filling, on the day of silo filling, and 2 days after. Discussion(s): Silo filler's disease is a preventable occupational disease that causes acute lung injury secondary to inhalation of nitrogen dioxide gases in an agricultural silo. These gases form rapidly in farm silos that are filled with fresh organic material (e.g., grains, hay). Toxic and lethal levels of nitrogen dioxide accumulate on top of the silage; the clinical presentation is related to the duration of exposure and the concentration of this gas. The exposure period starts from the day of silo filling and up to 10 days. As in our case, most symptomatic exposures are mild and self-limited; however, the clinical presentation can be dramatic, causing acute respiratory distress syndrome, bronchiolitis obliterans, and even death from asphyxiation. The new generation of farmers may be unaware of the potential risks involved with this preventable but potentially fatal disorder. In the lung, nitrogen dioxide hydrolyzes to nitrous and nitric acid, causing profound chemical pneumonitis, pulmonary edema, and methemoglobinemia. This results in a leftward shift of the hemoglobin dissociation curve with impaired oxygen delivery and compounds the already-present hypoxia. This is prevented by venting the silos, avoiding immediate exposure when opening the hatches, using special respirators, and taking prophylactic steroids prior to exposure. The treatment is supportive, including oxygen supplementation, mechanical ventilation, and steroids. Conclusion(s): The hospitalist, especially in rural areas, shall be aware of silo filler's disease, its broad clinical spectrum, and its prophylaxis and treatment.

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1. **Exhaled air dispersion and removal is influenced by isolation room size and ventilation settings during oxygen delivery via nasal cannula**  
   Hui D. S. Respirology 2011;16:1005-1013.

Background and objective: We compared the exhaled air dispersion distances during oxygen delivery via nasal cannula to a human-patient simulator (HPS) in two different isolation rooms. Methods: Airflow was marked with intrapulmonary smoke for visualization. Oxygen flow was gradually increased from 1 to 5 L/min, with the HPS sitting at 45°. The leakage jet plume was revealed by laser light-sheet and images captured by high-definition video. Smoke concentration in the plume was estimated from the light scattered by smoke particles. The experiments were conducted at a double-door, negative pressure isolation room with a dimension of 4.1×5.1×2.6 m, pressure of -7.4 Pa and 16 air exchanges/h (ACH) (room A). Results were compared with experiments repeated in a smaller isolation room with a dimension of 2.7×4.2×2.4 m, pressure of -5 Pa and 12 ACH (room B). Results: Room A: an exhalation jet spread almost horizontally outward from the nostrils of the HPS to 0.66 m and 1 m towards the end of bed when oxygen flow was increased from 1 to 5 L/min respectively. Room B: there was interaction between the downward ceiling ventilation current and the exhaled air from the HPS, leading to deflection of exhaled smoke towards the head of the HPS at an oxygen flow rate of 1 L/min. As oxygen flow was increased gradually to 5 L/min, more room contamination with smoke was noted. Conclusions: Substantial exposure to exhaled air occurs within 1 m towards the end of the bed from patients receiving oxygen via nasal cannula. Room dimension and air exchange rate are important factors in preventing contamination in isolation rooms. This study demonstrates that larger isolation rooms with 16 air exchanges/h (ACH) are relatively better than the smaller isolation room with 12 ACH in air mixing and dilution ventilation for removing exhaled air from the patient and preventing room contamination during administration of oxygen therapy. © 2011 Asian Pacific Society of Respirology.

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1. **In vitro comparison of heliox and oxygen in aerosol delivery using pediatric high flow nasal cannula**  
   Ari A. Pediatric Pulmonology 2011;46:795-801.

Drug administration via high flow nasal cannula (HFNC) has been described in pediatrics but the amount of albuterol delivery with an HFNC is not known. The purpose of this study is to quantify aerosol delivery with heliox and oxygen (O 2) in a model of pediatric ventilation. A vibrating mesh nebulizer (Aeroneb Solo, Aerogen) was placed on the inspiratory inlet of a heated humidifier and heated wire circuit attached to a pediatric nasal cannula (Optiflow, Fisher &amp; Paykel). Breathing parameters were tidal volume (V t) 100 ml, respiratory rate (RR) 20/min, and I-time of 1 sec. Albuterol sulfate (2.5 mg/3 ml) was administered through a pediatric HFNC with O 2 (100%) and heliox (80/20% mixture). A total of 12 runs, using O 2 and heliox were conducted at 3 and 6 L/min (n = 3). Drug was collected on an absolute filter, eluted and measured using spectrophotometry. The percent inhaled dose (mean ± SD) was similar with heliox and O 2 at 3 L/min (11.41 ± 1.54 and 10.65 ± 0.51, respectively; P = 0.465). However at 6 L/min drug deposition was ≥2-fold greater with heliox (5.42 ± 0.54) than O 2 (1.95 ± 0.50; P = 0.01). Using a pediatric model of HFNC, reducing delivered flow from 6 to 3 L/min increased inhaled albuterol delivery ≥2-fold but eliminated the increase in inhaled drug efficiency associated with heliox. © 2011 Wiley-Liss, Inc.

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1. **Aerosol delivery through nasal cannulas: An in vitro study**  
   Bhashyam A. R. Journal of Aerosol Medicine and Pulmonary Drug Delivery 2008;21:181-188.

In most circumstances, a nasal route for the delivery of pulmonary aerosol medications is rarely considered; however, in specific instances, this route may be quite useful. Consider, for example, the delivery of aerosol treatments during humidified high-flow nasal cannula use in pediatric critical care, or continuous aerosol delivery via cannula for medications with short durations of action. The goal of this study was to evaluate the potential for delivering aerosols via nasal cannula through in vitro studies of aerosol output and size. The system utilized for testing included an Aerogen Solo nebulizer downstream of a heater/humidifier system, followed by a nasal cannula and an aerosol collection apparatus. Adult, pediatric, and infant cannulas were tested with and without an inhalation-only breathing simulator. The cannulas were driven by 3 lpm (50 psig) oxygen flows. Dose quantification was performed using radioisotope techniques. Total cannula output and system losses were measured. Aerosol size measurements were made from the nebulizer, from the heating tube, and from the prongs of the adult and pediatric cannulas, using laser-diffraction techniques. Total cannula output ranged from 8.4-25.1% and 18.6-26.9% of loaded dose, without and with the addition of inhalation flows. Volume median diameters were 2.2 ± 0.2 μm from the adult cannula and 1.9 ± 0.3 μm from the pediatric cannula. Ninety percent of the aerosol volume was in sizes smaller than 4.2 ± 0.4 μm (adult) and 3.8 ± 0.5 μm (pediatric). System losses were highest in the nebulizer-humidifier connectors, heated tube, and humidifier. Losses in the nebulizer were very low (2.2-3.5%). This study demonstrates that aerosols can be efficiently delivered through a humidified high-flow nasal cannula system. Further study is required to determine if this route is viable for pulmonary delivery. © 2008 Mary Ann Liebert, Inc.

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1. **Nebulization of drugs in a nasal CPAP system**  
   Smedsaas-Löfvenberg A. Acta Paediatrica, International Journal of Paediatrics 1999;88:89-92.

Aerosolized drugs have been used in infants for the treatment of respiratory distress syndrome and bronchopulmonary dysplasia (β-agonists, steroids and surfactant) and bronchiolitis due to respiratory syncytial virus (epinephrine and ribavirin). Controlled clinical trials have, however, produced conflicting results, probably due in part to problems with the transportation of the aerosol from the nebulizer to the bronchioli. We have modified a nasal continuous positive airway pressure (CPAP) system permitting an aerosol to flow through a canal to the nasal prongs and into the airways of the infant. It has been used successfully for the administration of epinephrine, salbutamol, budesonide, acetylcysteine, natural surfactant and ribavirin to sick infants. The modified nasal CPAP system is a simple, safe, cost-efficient and baby-friendly system for respiratory support and drug treatment, which can be used in future trials of aerosolized drugs.

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1. **Metastatic carcinoma of the breast: An unusual presentation mimicking Wegener granulomatosis**  
   Bakst A. E. Chest 1998;114:413S-414S.

Introduction: Vasculitis can be idiopathic or associated with a variety of underlying conditions, including autoimmune syndromes, infections, allergic disorders, or malignant neoplasms. Cutaneous paraneoplastic syndromes are the non-contiguous skin and mucous membrane changes that are caused by cancer. Since they may be the first indication of a new or recurrent tumor, failure to recognize their importance may have significant consequences. Herein, we report a case of metastatic breast cancer in a patient with cutaneous vasculitis, respiratory failure, microhematuria and a reactive c-ANCA (antineutrophil cytoplasmic antibody). Case Presentation: A 50 year old woman was in her usual state of good health until one month prior to presentation when she developed episcleritis in her left eye. One week prior to admission she developed a low grade fever, myalgias, progressive dyspnea, a cough productive of blood-tinged sputum and pleuritic chest pain. She had been diagnosed three years earlier with infiltrating ductal carcinoma of the breast treated with a modified radical mastectomy and adjuvant cyclophosphamide, doxorubicin and radiation. She remained in remission until this illness. On physical examination, she had a temperature of 100°F, a respiratory rate of 24 per minute and was hemodynamically stable. There was mild conjunctival injection. Examination of her heart was normal. Chest auscultation revealed crackles in all lung zones. There was no lymphadenopathy. A petechial rash was noted on her thighs, legs and arms. Laboratory data included a normal complete blood count, blood urea nitrogen and creatinine. Urinalysis revealed 10-15 RBC/hpf and few red cell casts. Oxygen saturation by pulse oximetry was 93% on nasal cannula at 3 liters/minute. All cultures were negative. Urine legionella antigen was negative as was mycoplasma serology. ANA titer was 1:40. Chest roentgenogram revealed bilateral, alveolar infiltrates and a cat scan of her chest demonstrated diffuse bilateral air space disease with ground glass opacity. She was initially treated for a community acquired pneumonia but had progressive respiratory distress necessitating intubation and mechanical ventilation. Her hematocrit declined from 35 g/dl to 22 g/dl. Fiberoptic bronchoscopy with bronchoalveolar lavage showed many pigment laden macrophages with few inflammatory cells. A transbronchial biopsy demonstrated non-specific inflammation but the pathologic features of the vessels were not representative to comment if vasculitis was present. Severe leukocytoclastic vasculitis was noted on a biopsy of the skin rash. Further workup included a negative anti-GBM assay, mildly elevated complement levels, and a c-ANCA titer of 1:72. While awaiting the c-ANCA result, a thoracoscopic wedge biopsy of the lung was performed which showed no evidence of capillaritis, vasculitis or granulomas. The interlobular septae were widened by the presence of metastatic, well differentiated adenocarcinoma with features of ductal carcinoma. Tumor was also present in the adjacent alveolar spaces and in the lymphatic channels. Immunoperoxidase stains for estrogen and progesterone receptors were positive in the nuclei of 90% and 40% of the tumor cells respectively. She was treated with taxotere and extubated 10 days later with resolution of the airspace disease and skin rash. Discussion: In general, the signs and symptoms of vasculitis in patients with and without cancer are similar.1,2 Leukocytoclastic vasculitis of small dermal vessels is characteristic of cutaneous necrotizing vasculitis,3 the most frequently encountered type of cutaneous vasculitis, especially with malignancy. Because of the morbidity and expense associated with biopsy, c-ANCA has attracted interest as a rapid and non-invasive way to diagnose Wegener granulomatosis. In fact, some investigators advocate immunosuppressive therapy for patients with positive c-ANCA results and symptoms compatible with Wegener granulomatosis, even in the absence of biopsy results.4 However, a meta-analysis of the clinical utility of c-A

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1. **Oxygen delivery for ambulatory patients. How the Micro-Trach increases mobility**  
   Heimlich H. J. Postgraduate Medicine 1988;84:68-79.

Transtracheal oxygen delivery with the Micro-Trach is state-of-the-art treatment for patients requiring long-term oxygen therapy. The Micro-Trach diminishes dyspnea because it bypasses the anatomic dead space in the respiratory tract. It eliminates the waste of oxygen that escapes from the nose and mouth when a nasal cannula is used. Therefore, a small oxygen container lasts longer, increasing the patient's mobility. The patient's appetite improves because oxygen is not diverted during deglutition, and the senses of smell and taste are restored. Rehabilitation is enchanced through increased mobility and improved nutrition. Transtracheal instillation of saline solution cleanses the respiratory tract and stimulates coughing, opening occluded air passages. There are fewer lung infections and hospitalizations for infective exacerbations of disease. Prescribed saline solution, mucolytics, and antibiotics can also be instilled through the Micro-Trach to treat cystic fibrosis. This use and others are still being explored.

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1. **Continuous positive-pressure breathing with nasal tube after cardiac surgery in infancy**  
   Bernardi M. Acta Anaesthesiologica Italica 1979;30:849-855.

Infants subjected to cardiac operations frequently develop respiratory complications of various degrees. In the severe cases it is necessary to proceed to mechanical ventilation, whereas in the other cases it is useful to employ continuous positive-pressure breathing. The latter, generally applied with a naso-tracheal tube, can also be used with an appropriate nasal tube. It can be connected to a ventilator which allows spontaneous breathing with a continuous positive pressure rather than to a traditional Gregory system. A positive pressure of 5 to 10 cm H2O with an initial FiO2 of 70% are adopted at the beginning of the procedure. According to the improvement in the systemic arterial pO2, the FiO2 first, and then the continuous positive pressure, when the respiratory function is optimal, are progressively reduced. The clinical indications are represented by dyspnoea and polypnoea with 100% O2 and actelectasis on the chest roentgenogram. Arterial pO2 ≤ 80 mmHg in acyanotic heart disease, and lower than 30 mmHg in the cyanotic forms and arterial pCO2 higher than 60 mmHg represent the blood gas values that indicate the use of this technique. Contraindications are cardiac tamponade, reduced pulmonary blood flow, residual right ventricular failure and tricuspid atresia corrected with the Fontan technique. The nasal tube avoids the possible complications of the naso-tracheal tube and stimulates the patients to cough. The use of the ventilator allows a rapid switch from a continuous positive-pressure breathing to a controlled or assisted ventilation with naso-tracheal tube and vice versa. The results obtained with this method are encouraging. In our experience we have observed the resolution of pulmonary actelectasis with improvement in blood gas values without any instance of abdominal distension.

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