NON-INVASIVE VENTILATION IN PEDIATRIC PATIENTS

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SUMMARY:
1. INTRODUCTION:

The first massive use of non-invasive ventilation (NIV) occurred during the 1952 Copenhagen poliomyelitis epidemic with the so-called iron lung. These devices applied negative pressures on the thorax, creating a differential pressure and facilitating the patient’s spontaneous breathing. However, nowadays, NIV usually employs intermittent positive pressure or “Non-invasive intermittent positive pressure ventilation” (NIPPV), to create positive pressure through ventilators that are directly applied to the airway through an interface, usually a mask, thereby avoiding endotracheal intubation. Although there are other types of NIV that do not employ positive pressure in the airway, for example, a cuirass (tortoise shell), a poncho wrap ventilator, a pneumatic abdominal belt or an oscillating bed, all of these are much less effective and much less frequently used than NIPPV. Therefore, this chapter on non-invasive ventilation in pediatric patients will always refer to NIPPV.

There are several physiological and physiopathologic respiratory differences between children and adults, that make children totally different from adults in the way they sicken and therefore in their respiratory management. Since research and development are always done with adults, pediatric clinicians must make themselves familiar with the latest breakthroughs, which are almost always focused on adults, and then adjust and adapt them to children. Clinicians who have only treated adults should be aware of the main respiratory differences between adults and children because, in an emergency situation they might be involved in the treatment of an infant until they can be transferred to a Pediatric Hospital, in even worse conditions and with fewer materials than pediatricians usually have. Therefore we would recommend that, just as pediatricians should be familiar with publications on adult respiratory care, the adult
clinicians should know the basic differences that apply to pediatric patients because this knowledge might even help them with their adult patients.

The ventilatory differences between a pediatric and an adult patient are inversely proportional to the child’s development. There are four levels: premature and neonates (< 4 kg), infants up to 10 kilos (under 2 years old); children up to 20 kilos (about 6 years old) and older children. As the organs and body continue to mature, the physiological and physiopathologic differences in behavior and responses become closer to those of an adult.

This chapter will not exhaustively comment on all the physiological and physiopathologic differences between respiration in children and adults, but it will discuss the most important and specific aspects of pediatric patients that differ from adults, with particular attention to aspects of non-invasive ventilation in children.

Managing NIV in children is different from in an adult and we must be aware of these differences because they can cause this technique to fail in children. The differences are due as much as to technical and material peculiarities (interfaces, ventilators and ventilatory modes) as to the different medical and surgical indications as to the differences in respiratory physiology between pediatric patients and adults.²-⁷

2. THE MOST IMPORTANT RESPIRATORY DIFFERENCES BETWEEN CHILDREN & ADULTS:

At birth the neonate must generate an extremely negative pressure (up to - 80 cm H₂O) in order to expand his/her lungs for the first time. This means it is extremely important to avoid pulmonary collapse or atelectases in the newborn lung since recruiting the alveoli once they close requires an even higher pressure than the one required to avoid collapse.⁸⁻¹⁰
The main characteristic of the neonate lung is its low functional residual capacity (FRC), and this affects different aspects – a stronger tendency toward pulmonary collapse and the formation of atelectases on one hand and, on the other, a lower apneic oxygenation time. This decrease in FRC is the result of the elastic pulmonary forces (elastic recoil) that make the newborn lung prone to collapse since these factors are not yet countered by the effects of the cartilaginous thoracic box. In physiological conditions, healthy neonates avoid this dangerous situation by keeping a larger air volume inside their lung at the end of expiration than their FRC, which is called the end-expiratory lung volume (EELV), and it coincides with FRC in adults. Another factor aggravating the situation is that a newborn is always decubitus, since they cannot sit or stand so the abdomen is continuously pushing against the diaphragm, reducing the FRC \(^9,11\). Thus, the neonate’s FRC is quite close to the critical alveolar closing volume, and therefore any situation that increases the closure volume and/or decreases EELV, with the least degree of apnea, for example, during anesthetic or the administration of respiratory depressing drugs, will cause the lung of a neonate to collapse more quickly than would that of an adult. Under physiological conditions, a neonate has a glottic closure reflex and the Hering-Breuer expiratory reflex which close the vocal cords before the end of the expiration and arrest lung emptying, thereby avoiding pulmonary collapse. These reflexes allow the neonate to maintain a pulmonary volume at the end of the expiration (EELV) that is greater than his/her FRC and to prevent atelectases under physiological conditions \(^9,10,12-21\).

Another important physiological characteristic in neonates is the fact that their oxygen consumption is 2.5 times higher than an adult’s (5-6 ml/kg/min. Vs 2-3 ml/kg/min.). This increase in oxygen consumption contributes to the much shorter apneic oxygenation time in neonates than adults. Apneic oxygenation time, defined as
the time a person can maintain an oxygen saturation of at least 91% without ventilation, is an important clinical consideration because it controls the time available for intubation when we are inducing anesthesia. Thus, while the apneic oxygenation time in a healthy adult can last minutes, it is always less than 30 seconds in a healthy neonate 8-10,12-15,21-24.

Another important clinical difference is the relative immaturity of the neonate respiratory center; as a result of this immaturity some children can present apneas and can even develop a congenital central hypoventilation syndrome (CCHS) 25-29. Another result of respiratory immaturity is that the response to opiate respiratory depression is extremely labile and a low therapeutic dose (even a little as 1 mcgr/kg fentanyl) may result in delayed post-anesthetic apnea that can appear as a respiratory arrest even hours after anesthesia, so at least 24 hours’ monitoring after general anesthesia of a neonate or premature baby aged up to 50 weeks post-conception is strongly recommended 8,9,14,16-20,22,23,30.

Basic physiology differences also mean that the complications derived from invasive mechanical ventilation are more frequent and more severe in children than adults. First, neonates’ lung compliance ($C_L$) is quite low (< 5 ml/cm H$_2$O) while compared to their thoracic wall compliance ($C_W$) is quite high (100 ml/cm H$_2$O). The difference in compliance leaves the neonate at risk of barotrauma secondary to positive pressure invasive ventilation, since the thoracic wall cannot contain or control a pulmonary over-inflation 9,10,14,16-21,23,24,31.

Small children generate strong resistance to respiratory flow, since the diameters of the smallest endotracheal tubes (2.5-4 mm) convert a laminar air flow into a turbulent flow and therefore resistance is not lineal to the flow and becomes proportional to the square of the flow 32. The most important factor for determining resistance to the
inspiratory and expiratory flows is tube radius, thus, a simple post-intubation edema in a 1-2 year old can reduce the tracheal lumen by half and generate such a respiratory effort that it induces respiratory arrest within a few minutes 8,9,14,19,20,32.

Also, children tend to be much more prone than adults to suffer alterations and lesions from intubation and in a shorter time. Children who are intubated for more than four days can already develop granulomas on their vocal chords or present ischemic lesions in their tracheal mucosas that produce clinically relevant tracheal stenosis in fewer days of mechanical ventilation than in adult patients. In addition, the tracheotomies used in prolonged intubations more frequently present long-term complications than in adults 8,9,14,24,33,34.

The weaning from invasive ventilation in children is also quite different from in adults 35. Randolph et al studied this process and concluded that in contrast with adult patients, the majority of children are weaned from mechanical ventilator support in two days or less and weaning protocols do not significantly shorten this brief duration of weaning. Another important difference is that neonates and infants under 10 kilos usually need NIV in the immediate post-extubated period to avoid atelectases 13,14,36,37.

For these reasons, achieving effective ventilatory support without intubation and its complications acquires special relevance in the pediatric patient. Children’s lungs are much more prone to barotrauma, volutrauma, biotrauma and atelectrauma than those of adults. The child’s lungs also require earlier ventilatory support to avoid the pulmonary collapse that threatens as soon as the child goes into hypoventilation. In light of all the above, it could be said that non-invasive mechanical ventilation seems to have been especially developed for children, or perhaps, that the child’s lung has been especially designed for non-invasive mechanical ventilation 8,9,13,14,23.
3. INDICATIONS OF NIV IN PEDIATRIC PATIENTS:

NIV is a mechanical ventilation technique that is indicated as support for respiratory system function when, due to various causes, the respiratory system fails and cannot produce sufficient gaseous exchange to cover the patient’s metabolic necessities. This situation of respiratory insufficiency has been defined as gasometry measures of PaO₂ < 60 mmHg (hypoxemic respiratory insufficiency) and/or PCO₂ > 45 mmHg (ventilatory insufficiency or hypercapnic respiratory insufficiency) in a patient who is conscious, resting and breathing room air. If this insufficiency has established itself in a short time (hours or days), it is called acute respiratory insufficiency, and if it has been going on for weeks or months, it is called chronic respiratory insufficiency.\(^3,12,38\)

The principal causes for respiratory insufficiency can be classified as: decreased air oxygen (altitude); alveolar hypoventilation (respiratory center alterations); alterations in the ventilation/perfusion ration (pneumonia); arterial-venous shunts (congenital cardiopathies); altered pulmonary diffusion (edema); and increased CO₂ production (sepsis). All of them provoke respiratory failure through three basic mechanisms. Respiratory center failure provokes apnea or hypoventilation and is much more frequent in one year old children than in adults. Musculoskeletal alterations of the thorax are also more frequent in children than in adults and increase the work of breathing, eventually producing respiratory muscle fatigue. Fatigue is more common in one-year-old children than in adults. Children’s respiratory muscles are less resistant to muscular fatigue because they have a larger proportion of Type IIA glucolytic fast muscle fibers, which are quite prone to fatigue and a low proportion of type I slow oxidative fibers, which are more resistant to muscle fatiguex.\(^{12,39}\)
3.1. Indications in chronic respiratory insufficiency (CRI):

The benefits of NIV are summarized in Table I, they all improve respiratory system function, acting like a ventilatory pump\(^{40,41}\). A pure hypoxemia with normal or low CO\(_2\) levels is characteristic of a chronic intrinsic pulmonary pathology (emphysema, pulmonary fibrosis, etc) and in these situations of simple chronic hypoxemic respiratory insufficiency, the primary measure is oxygen therapy, not NIV\(^{2,3,6,7,12,42-47}\).

Nevertheless chronic hypercapnic respiratory insufficiency is a classic indication for NIV and has had good results. Its principal causes in children are listed in table II\(^{40-42,48-50}\). Usually, pneumologists have already been applying NIV to these patients regularly at their homes, either intermittently or continuously so as to improve their quality of life, functional status, sleep quality and duration, avoid exacerbations and increase their survival\(^{40-42,48-50}\). The best time for initiating NIV in these patients is decided by evaluating the existence of signs of chronic hypercapnia (morning headache, hyper-somnolence and tiredness), and requires a nocturnal sleep study, without waiting for the appearance of diurnal gasometric alterations\(^{3,4,6,38-43,47-52}\). In cystic fibrosis patients with end-stage lung disease Fauroux et al and Efrati et al. demonstrated that long-term NIV can stabilize and improve such physiological parameters as ventilation, arterial blood gases and body mass index as well as subjective parameters like sleep pattern, diurnal activity level and morning headache in cystic fibrosis patients with end-stage lung disease\(^{12,38,44-46,53-56}\).

Patients already receiving regular NIV are obligatory candidates, with better results than other patients, both when their respiratory insufficiency worsens as well as during the per-operative period. NIV is applied in order to: optimize the patient in the pre-operative period, and, in selected cases, for intra-operative ventilatory management.
(associated with a regional anesthetic technique), and during weaning from invasive ventilation during the post-operative period (Application algorithm for NIV in CRF see Figure 1).

3.2. Indications in acute respiratory insufficiency (ARF):

Acute respiratory failure (ARF) has become the NIV battlefield over the last few years and is a main topic in this section. Possible uses of NIV in ARF children are listed in table III. The ARF patients who are chosen as NIV candidates must be very carefully selected because contradictory results have been published in the literature, although gradually the results reported for NIV in children with ARF have been improving. The first major difference that must be mentioned is the difference between hypercapnic respiratory failure and hypoxemic respiratory failure with or without associated hypercapnic failure.

Ventilatory failure, or acute hypercapnic respiratory failure (AHRF), has two major groups, mild or moderate hypercapnic failure, in which excellent results have begun to be obtained from NIV, with a pH > 7.2 and a PCO₂ between 45-90 mmHg and severe hypercapnic failure with pH < 7.2 and PCO₂ > 90 mmHg. NIV is beginning to give quite good results in mild or moderate acute hypercapnic respiratory failure and there are multiple prognostic factors that influence the final result which will be discussed in this chapter. The two most important factors are the NIV experience and training of the care unit and the rapidity in the diagnosis and initiation of NIV. NIV in patients with severe acute hypercapnic failure should be restricted to units with a long experience in NIV and that are already regularly obtaining good results in less severe hypercapnic failure. If this is not the case, invasive ventilation is the best option for these patients.
The published results in acute hypoxemic respiratory failure vary markedly between authors, indicating that patient selection is a key to good results with NIV \(^ {58,63-66,72,73}\). The first factor to take into account is the rapidity in initiating NIV and the patient’s response in correcting the hypoxemia. Those patients in whom hypoxemia is corrected quickly, within one hour of applying NIV, will respond better to NIV in general than those who take longer or who do not show a correction within that time. However, there does not appear to be any connection between the severity of the respiratory failure as measured by the \(\text{PO}_2/\text{FiO}_2\) ratio and the success or failure of NIV. The other major factor in prescribing NIV for a child with acute hypoxemic respiratory failure is the etiology of the respiratory failure. Etiologies with short courses, like acute pulmonary edema, usually respond well to NIV, while pulmonary pathologies with a slow evolution, like severe pneumonia, acute lung injury (ALI), acute respiratory distress syndrome (ARDS), etc., usually do not respond well to NIV therapy. Another factor to take into account before indicating NIV for a child with a hypoxemic respiratory failure is whether hypercapnia is or is not also present. Children with hypercapnia in addition to hypoxemia respond better to NIV than children with normal or low \(\text{CO}_2\) levels, since, as we stated at the beginning of the chapter, the principal benefit from NIV is its effect as a supplemental ventilatory pump \(^ {4,6,12,38,44,45,58,59,67-69,73-79}\) (Algorithm for applying NIV in ARF see Figure 2).

### 4. VENTILATORS AND NIV MODES IN PEDIATRICS:

Until relatively recently, NIV has been administrated with very elemental circuits and interfaces. The origin of NIV lies in Mapleson circuits, which used a continuous flow and a valve that resisted expiration, managed to control CPAP level. The next step was the first NIV machines that generated a continuous flow from the room air creating a CPAP for nocturnal treatment of sleep apnea. This was followed by
the basic step of maintaining continuous positive pressure in the airway using two pressure levels (BIPAP; Bi-level positive airway pressure) in the NIV ventilators whose original main limitation was that they could not synchronize themselves with the patient’s spontaneous breaths and could not monitor either the expiratory volume or the FiO₂. Meanwhile, attempts to employ conventional invasive ventilation ventilators in non-invasive ventilation began, despite limitations particularly for the smallest pediatric patients (see section 4.2). At the present time, NIV is undergoing many technological advances. Interface models are ever-easier to adapt to patients’ faces, and this creates less problems for the patients. The NIV ventilators are undergoing enormous changes, and offer an even larger variety of ventilatory modes, capacity to synchronize with the patient’s breathing, to measure expiratory volume and leaks and to regulate FiO₂. The latest generation of NIV ventilators are now equipped to supply NIV modes that can effectively compensate for leakage ⁶,¹²,¹⁴,³⁸,⁶⁸.

Nevertheless, the main problem with NIV that is still to be commercially solved is the lack of a wide range of interfaces designed for pediatric patients. In the best situations, the manufacturers with the largest supply can only offer one or two pediatric sizes, and this size range is clearly insufficient to cover the anatomical variations that occur in a growing child in the first years of life ⁶,¹²,¹⁴,³⁸,⁶⁸.

4.1. Continuous positive airway pressure (CPAP)

Nowadays, CPAP is not itself considered to be a non-invasive ventilation mode, although no one can doubt that it was the great precursor of INV. The reason some authors do not consider CPAP to be non-invasive mechanical ventilation is that CPAP can be generated without any machine or respirator, simply with a Mapleson circuit, a continuous flow and an expiratory resistance valve. CPAP can also be produced with conventional intermittent flow invasive ventilation ventilators using an expiratory
resistance valve. However, this method is not recommended in small children because it increases the imposed respiratory work since, for each breath, the child will have to activate the inspiratory sensitivity valve to obtain a fresh gas flow. Last come neonatal continuous flow ventilators and NIV ventilators that supply gas flow in inspiratory and expiratory phases so a child can always freely get air at any point of the respiratory cycle. The ideal CPAP system would be a method that administered a continuous flow but allowed the child to get air when he/she wanted and also monitored volume, respiratory frequency, FiO2 and pressure \(^{12,80-83}\).

The fundamental actions of CPAP are: increase FRC, increase the apneic oxygenation time, decrease the tendency to atelectases formation and finally, facilitate permeability in the upper airways. These actions are especially important in neonates, since, as was explained in the section on pulmonary physiology, they have substantially less FRC than adults. This is why any indication whatsoever of respiratory insufficiency in a neonate must be treated as soon as possible with CPAP. Also, when weaning a neonate with a pulmonary pathology, a CPAP of 4-6 cm H\(_2\)O as a routine protocol in the first hours after extubation is recommended and will deter the formation of atelectases because it will raise the FRC above the closing volume \(^{12,80-85}\).

The fundamental indications for CPAP in pediatric patients are: obstructive sleep apnea syndromes, neonate ventilatory weaning, cardiac pulmonary edema, pulmonary edema due to negative pressure, any tendency toward upper airway obstruction (laryngospasm, laryngeal or tracheal malacia, macroglossia, etc.) \(^{12,80-82,84-86}\).

The main drawbacks are that CPAP cannot support the patient’s breathing, so it cannot substantially improve tidal volume. In addition, if the patient hypoventilates or goes into apnea, it will not give them respiratory support, and using pressures above 8-
10 cm H₂O creates a risk of dynamic pulmonary hyperinflation, which is even more deleterious in children than adults. ¹⁵,³¹,⁸⁰-⁸²,⁸⁷-⁸⁹.

4.2. NIV with conventional invasive ventilation intermittent flow ventilators:

Invasive ventilation ventilators were initially used in NIV in order to optimize the material resources in critical care units since these machines offer a large variety of ventilatory modes: controlled, assisted, assisted/controlled, SIMV, pressure support, etc. Nevertheless, one must also remember the limitations of these machines especially in pediatrics. The first and fundamental drawback is that their inspiratory flow peak is usually not high enough to compensate for the leaks that so easily occur in NIV, particularly in pediatric patients ⁹₀. Other important limitations are the pressure trigger systems of conventional ventilators, which, since they are designed for invasive ventilation and are technologically older, make it very difficult for the machine to synchronize correctly with pediatric patients. Pressure triggers create a greater imposed respiratory work in children since to be activated, the child must generate negative pressure during the inspiratory phase (the so called inspiratory trigger pressure). Therefore pressure triggers also create a greater trigger delay time, or time taken for the ventilator to increase airway pressure above baseline from the onset of inspiration, than the flow triggers that require a lower inspiratory trigger pressure and thus shorter trigger delay time (please see section 4.4.1.) ⁹¹-⁹⁷. The third and most important problem with using conventional ventilators for non invasive ventilation in pediatric patients is that these ventilators are designed for intermittent flow and that means that the gas flow through the circuit stops during expiration. This situation increases the respiratory effort for the child who will in each breath have to activate the inspiratory trigger if air
flow is to be established. If the child cannot do this it will be impossible to breathe, and in addition, the lack of gas flow during the expiratory phase will not improve the child’s FRC nor help keep the airway open, something that is obtained with CPAP 91-97.

Another problem associated with the use of these ventilators in NIV was that volume programmed modalities were used in the beginning and this had various drawbacks that are especially important in pediatric patients. The main advantage of pressure programmed modes versus those that use a volume programmed mode in NIV is that pressure ventilation makes it possible for leak compensation to occur while a volume mode does not. Air leaks are very common during NIV, particularly in children and this may lead to under treatment. Beside a pressure preset ventilation should respond to increased flow and a greater tidal volume (Vt), in contrast to volume preset ventilation where Vt is fixed 83,90,91. Another added problem is that the only way that volume modalities have to compensate for the mask dead space is to increase tidal volume in order to be sure there is no alveolar hypoventilation, and that could be dangerous for children (volutrauma). However, as will be explained in greater detail in the section on interfaces, if one uses a pressure ventilatory mode and allows a certain level of controlled leaks in the interface , the dead space in the mask is cleaned and the child will not re-inhale CO2. 92-97.

Due to these dangers, we summarize by saying that the use of conventional intermittent flow invasive ventilation ventilators is not advisable in pediatric patients. However, the newest invasive ventilation respirator models can be used because they have been especially designed for use in both invasive and non-invasive ventilation 83,91.
4.3. NIV with NIV ventilators:

4.3.1. Bi-level pressure preset ventilators:

Ventilators with a BIPAP (Bi-level positive airway pressure) have revolutionized NIV. It is still the most frequently used NIV modality in most patients and in most situations. 12,83,91,98-104.

NIV respirators consist of a flow generator, usually a turbine with variable rpm, so that variations in spin speed produce a larger or smaller flow. The turbine generates a continuous flow in both the inspiratory phase and the expiratory phase, but of different magnitudes, thereby generating two pressure levels. The inspiratory phase generates a higher flow up to a programmed IPAP and, during expiration, the flow magnitude decreases until it can sustain the expiratory programmed pressure (EPAP) 12,25,83,86,91,98-105.

The programmable parameters are:

- **IPAP (Inspiratory Positive Airway Pressure):** This must be programmed. It controls tidal volume (Vt). The greater the IPAP, the greater the Vt 98,106.

- **EPAP (Expiratory Positive Airway Pressure):** This must be programmed. It improves FRC, avoids atelectases, facilitates airway permeability and facilitates mask interface dead space washing 31,98-100,106.

- **Respiratory Frequency and I:E ratio or inspiratory time percentage:** This is a parameter used in the time-programmed mode that assigns IPAP cycle rate and duration 98,106.

- **Ramp slope, flow magnitude or inspiratory delay:** These parameters regulate the same thing, the magnitude of maximum inspiratory flow to reach IPAP. The larger the magnitude of the inspiratory flow the sooner IPAP will be reached, but the patient’s adaptation to NIV will be worse. This parameter is very important and difficult to
regulate in pediatric patients. On one hand, smaller children adapt worse to very large inspiratory flows, so one should use small inspiratory flows or high respiratory delays times. But on the other hand, the physiological respiratory frequency is much higher in children than in adults, so that an inspiratory time (Ti) for a given I:E ratio, is much shorter than in adults (neonate Ti of 0.6 sec. vs. adult Ti of 1.2 sec), so a neonate lung must be filled in half the time it takes to fill an adult lung. If we decrease the maximum inspiratory flow by a great deal in order to achieve better NIV adaptation in the child, we must be careful to not reduce the tidal volume and hypoventilate him/her because we have allowed enough time to fill his/her lungs during inspiration\textsuperscript{12,98,106}.

- **Inspiratory trigger sensitivity**: This is the most critical and important point in adapting ventilators to pediatric use. The objective of the trigger is to activate inspiration provoking the least possible imposed respiratory work on the patient, and once the trigger is activated, the machine should begin to deliver the gas inspiratory flow as soon as possible while avoiding any auto-triggering or trigger activations that are not provoked by the patient’s respiratory effort at all times. The first triggers used in invasive ventilation were pressure triggers that as we mentioned above, have been replaced by flow triggers, particularly for pediatric patients. Flow triggering has been shown to reduce pediatric patient effort compared to pressure triggering while maintaining equivalent ventilation levels \textsuperscript{91,106}. The flow triggers cause the respirator to supply a continuous flow both during the inspiratory phase (very high) and during the expiratory phase (low magnitude), so that the air is available to the child has at all times. The second advantage is that the imposed respiratory work is less with a flow trigger than with the classic pressure triggers, since they require less negative pressure to be activated. Finally, since there is a basic constant flow during the expiratory phase, the time or delay in receiving the inspiratory flow once the trigger is activated is shorter
with the flow triggers than with the pressure triggers \cite{91,95,97,106,107}. Nevertheless, the problem with flow triggering is that any leak will produce auto-triggering, and while leaks are not a problem in invasive ventilation, they are quite frequent in NIV. To avoid this problem, the NIV ventilators with flow triggering have developed systems that regulate trigger sensitivity and that differentiate unintentional leaks from the patient’s own respiratory effort.

Another trigger used specifically in neonates is the impedance inspiratory trigger, which is based on detecting abdominal muscle motion. It employs the same system as the apnea monitors for neonates and infants at risk of sudden infant death syndrome (SIDS) \cite{108}. Studies comparing the impedance trigger with the flow trigger in preterm neonates have found that the flow trigger mechanism produces fewer auto-triggering events and less trigger delay than the impedance trigger system, which is more susceptible to artifacts and chest wall distortion \cite{82,91,97,102,106}.

- **Expiratory trigger**: The machine’s mechanism to end IPAP during a patient’s spontaneous breathing. It controls the duration of the patient-initiated IPAP cycle allowing it to continue until a certain level of reduction in the maximum inspiratory flow, which can be pre-established by either the machine, or by the operator, is reached. The IPAP expiratory trigger is normally programmed to end the IPAP period when the inspiratory flow drops to 25% of the maximum flow reached at the beginning of the inspiratory period \cite{98-100,106}.

- **FiO₂**: The original NIV models did not have FiO₂ regulators because they only used room air. The only way to increase FiO₂ in those ventilators is by enriching room air with an external oxygen source that is connected to the circuit before the heater-humidifier. To know exactly how much FiO₂ is administered, an oxygen analyzer must be attached to the mask, although ventilators now come with some tables that will give
an estimate of FiO₂ based on the number of liters of oxygen that have been externally administered. 98-100,106.

- **Alarms**: Depending on the ventilator and the degree of monitoring that is possible, there will be more or fewer alarms (apnea, respiratory frequency, tidal volume, minute volume, pressure, etc…). This is an important point since NIV always requires greater vigilance for patients with acute respiratory insufficiency. 98,106

To summarize, the specific respirators for NIV are preset pressure ventilators with the capacity to generate two different inspiratory pressure levels: one inspiratory (IPAP) and the other expiratory (EPAP). These ventilators can be programmed with four fundamental ventilatory modes: CPAP, Time programmed Mode (T); Spontaneous Mode (S); and Timed spontaneous/programmed mode (S/T). 12,79,82,86,98-101,104-106.

The **CPAP mode** consists of programming the same value for the IPAP and the EPAP, and that value is the CPAP value we want to use. Most of the time this mode is not really useful with an NIV ventilator because BIPAP usually has more clinical advantages. The only exceptions are in pulmonary edema (cardiogenic or due to negative pressure), and to prevent post-extubation respiratory insufficiency in neonates. In these circumstances CPAP appears to achieve better results than BIPAP. 12,98,106.

**Timed programmed mode (T)** was the first mode to appear in the earliest units. It requires the operator to program the number of breaths with a given IPAP pressure to be administered to the patient, and the rest of the time the patient has a minimum pressure or EPAP, independent of the patient’s respiratory efforts. Thus the operator programs the respiratory frequency and inspiratory and expiratory times. This mode is not presently recommended because it does not synchronize itself with the child’s spontaneous breathing, resulting in machine-patient asynchronisms. 12,98-100,106.
**Spontaneous mode (S)** is similar to a continuous flow support pressure, that is to say, the patient does the breathing and the respirator supports each breath with the programmed IPAP while maintaining the minimum continuous pressure (EPAP) the rest of the time. Respiratory frequency and inspiratory time are patient controlled. This mode requires a good system for synchronizing the patient and the machine and the highest possible trigger sensitivity\textsuperscript{12,105,106}.

**Spontaneous or programmed time (S/T) mode** is presently the most commonly used because it offers the advantages of both of the earlier described modes. The operator programs a minimum respiratory frequency, and if the patient is breathing faster than that frequency, the ventilator acts as if it were in spontaneous mode, so that each time the patient initiates a respiration, the machine supports it with the programmed IPAP pressure. But, if the patient’s respiratory frequency drops below the programmed minimum frequency, the ventilator cycles into an IPAP, the inspiratory time, and EPAP at the already programmed minimum frequency. This is usually the initial mode to be selected in most indications for NIV\textsuperscript{12,99,100,104-106,109}.

There is not much existing bibliography on BIPAP in pediatric patients with acute respiratory insufficiency. However, authors that have used it in infants with bronchiolitis and asthmatic children report that it offers many advantages over invasive ventilation.\textsuperscript{12,15,25,34,63,79,86,99,100,103-106,109}

**4.3.2. Proportional assist ventilation (PAV)**

Proportional assist ventilation (PAV) is a ventilatory mode that is available for both invasive and non-invasive ventilation. It supplies partial ventilatory assistance or support that is synchronized with the patients’ spontaneous breaths. For each breath, the respirator supplies a support pressure and inspiratory flow that is variable and
modified by the patient in a manner that is directly proportional to the patient’s inspiratory effort\textsuperscript{110-117}.

Using a pneumotachograph, the respirator measures the volume and flow generated in each breath by the patient and with these data it calculates the corresponding flow resistances and elastic recoil. The respirator administers a greater or lesser inspiratory pressure as a function of the calculated elastic recoil and the programmed assisted volume. At the same time, the respirator administers a greater or lesser inspiratory flow depending on the calculated resistances and the programmed assisted flow. Last, the operator programs the percentage of assistance that the respirator should provide 20-100\%, which is to say that the percentage of the work of breathing (WOB) that the ventilator will do and the amount that the patient will do.\textsuperscript{110-119}

The main drawback with PAV is the initial programming, since, theoretically, one should first calculate the patient’s respiratory system elastic recoil and resistance\textsuperscript{113,115,118-123}. However, analysis of respiratory mechanics in a non-intubated, critical patient who may have a decreased level of conscience is quite difficult. This difficulty is even more marked in pediatric patients, given their classic lack of collaboration, and even more difficult the younger the patient. In adults, these problems are avoided by suitting the initial settings to the clinical evaluation of the patient. One begins with a small ventilatory assistance that is increased until there is good adaptation and the symptoms of respiratory insufficiency disappear\textsuperscript{113,115,116,118-125}.

Asynchronic phenomena have been reported due to a lack of expiratory sensitivity when support is above 80\% in adults, in situations in which the ventilator continues to administer flow although the patient has finished inhaling\textsuperscript{126}. This phenomenon is more important and dangerous in children, since their respiratory time constant (pulmonary compliance x pulmonary resistance) is smaller than in adults. In
fact, it is approximately half the adult level, so the child’s lungs fill and empty in about half the time required for an adult. This respiratory asynchrony generates dynamic hyperinsufflation phenomena that are much more severe and have more repercussions in small children than in adults.

Another danger with this respiratory mode is the risk of hypoventilation. The VAP Vt directly depends on the patient’s respiratory effort. If the child decreases his/her effort by taking superficial breaths, the ventilator can give him little help. If the patient does not breathe, the ventilator cannot supply any support.

At this time, there are hardly any reports of non invasive PAV in pediatric patients. Thus, we would advise that it be used in patients over six years of age, who show few respiratory differences with adult patients and for whom the data obtained in adult studies will be more applicable.

4.4. NIV with NIV-ADAPTED Invasive Ventilation Ventilators:

The latest invasive ventilation ventilators allow NIV since they are supplied with more sensitive inspiratory flow trigger systems than the classic pressure trigger systems. Flow triggers are even more useful in children than in adults, as we mentioned above.

Another advantage of most of the new invasive ventilators is that they are equipped with mixed inspiratory triggers, or flow and pressure triggers, that allow greater synchronization between the patient and the machine throughout the entire respiratory cycle. The flow trigger is activated during the expiratory phase of the respiratory cycle, and the pressure trigger is activated during the inspiratory phase; thus, if there is a drop in pressure (-2 cm H2O) during inspiration, the machine considers the patient to be requesting more ventilatory assistance and it increases the inspiratory flow and support pressure during the rest of the inspiratory phase. This inspiratory trigger
system is much better than a simple pressure trigger not only because it allows inspiration activation during the expiratory phase, but also because it allows any inspiratory demand to be satisfied during any part of the respiratory cycle, whether inspiratory or expiratory\textsuperscript{97,127,128}.

As well as the possibility of employing a two-limb breathing circuit (inspiratory and expiratory), invasive ventilators make it possible to quantify volumes and avoid CO\textsubscript{2} reinhalation, particularly in small infants, in whom the mask dead spaces and resistances generated by the single limb breathing circuit with an exhalation valve of NIV ventilators can produce problems with CO\textsubscript{2} reinhalation and hypercapnia\textsuperscript{97,127-129}.

The new invasive ventilation ventilators that are adaptable for NIV can increase peak inspiratory flow, and therefore are more effective in compensating for leaks than the old invasive ventilators\textsuperscript{90,97,127-129}. Another advantage of the new invasive ventilators is that they present a large number of NIV ventilatory modes, although the two most frequently used modes are pressure support and pressure control. Respiratory frequency and inspiratory time are determined by the patient in the pressure support mode, while a minimum frequency and inspiratory time are programmed into the machine in the pressure controlled mode, although the patient can take more spontaneous breaths than programmed\textsuperscript{89}. It should always be possible to program a maximum limit on inspiratory time in pediatric patients because if there are leaks, which are quite frequent with NIV, the inspiratory flow may take a while to fall below the programmed expiratory trigger, thus excessively prolonging the duration of the inspiration and producing asynchronisms between the child and the ventilator\textsuperscript{89,97,127-129}.
5. PERI-OPERATIVE NIV-USES IN PEDIATRICS:

Here we present some indications for NIV in the peri-operative period in pediatrics focusing on the surgery patient and indications in the pre, intra, and post-operative period while providing the key-points of NIV uses.

5.1. Neurosurgery:

Numerous and diverse neurological pathologies may require surgery in a child. We shall focus our attention on those pathologies with the highest incidence of ventilatory complications in the immediate post-operative period such as myelomeningocele reparation and posterior fossa tumoral resections.

The prevalence of moderate to severe sleep-disordered breathing (SDB) in patients with myelomeningocele may be as high as 20%, but little information is available regarding treatment of these patients. Kirk et al recommend the use of non-invasive ventilation for good post-operative ventilatory management to avoid the respiratory complications that these patients may present.

The pathology most frequently associated with problems in mechanical ventilation weaning is posterior fossa tumoral resection, which not infrequently affects the respiratory center and may produce respiratory dysfunctions that are more or less serious. It is absolutely necessary to employ non-invasive mechanical ventilation using BIPAP and an EPAP of about 4-6 cm H$_2$O with this type of pathology. At the same time, plateau expiratory valves should be used, or even one of the orifices in the mask should be opened so as to avoid any CO$_2$ re-inhalation at all, since this is particularly noxious in these patients. IPAP should be adjusted to the degree of respiratory failure in each individual patient, and should usually be set at between 13 and 18 cm H$_2$O.
Recuperation of respiratory center regulation can take a while, even weeks in patients with a brain stem lesion, and the necessary non-invasive ventilatory support will need to be slowly reduced. The child’s characteristic neuronal plasticity can mean that important defects in respiratory regulation will resolve themselves spontaneously, given enough time. The important therapeutic extra supplied by non-invasive ventilation in this type of patient is that the technique allows us to gradually decrease the respiratory support supply without producing a permanent tracheal lesion as would occur with a tracheotomy.\textsuperscript{5,58,59,130,132,133}

5.2. Complex congenital heart defects:

The child with a congenital heart defect is more prone to hemodynamic imbalances induced by invasive mechanical ventilation in the change-over from spontaneous ventilation with negative pressures to ventilation with intermittent positive pressures. These imbalances are due to the decrease in the venous return and pulmonary blood flows.\textsuperscript{134-141}

The most effective advanced vital support measures in other children, such as expansion of the intravascular space via aggressive fluid therapy, or pulmonary recruitment maneuvers, do present the problem that any one of them can precipitate a critical imbalance in children with complex congenital heart defects. Frequently these patients can be stabilized with spontaneous ventilation, but then become imbalanced and go into an irreversible cyanosis once they are intubated with an elevated positive pressure in the course of an anesthetic induction (Fallot’s crisis).\textsuperscript{134-141}

This is why the patient who most benefits from very early extubation in the postoperative is a child with congenital cyanotic cardiopathy in whom pulmonary flow depends exclusively on pulmonary resistance. Excessively delaying extubation in these
patients can set off a hypoxemic crisis that is very difficult to manage because the hypoxia and hypercapnia are supported by the patient’s own elevated pulmonary resistance. That is why a fast weaning and extubation in these patients is vital and NIV is a helpful tool to achieve that end 134-142.

Among patients with congenital heart defects, the worst vital prognosis is the child with the worst prior ventricular function, the most cyanosis and the lowest pulmonary flow and, a determining factor in the poor prognosis is right ventricular failure 134-143. We recommend using BIPAP with an elevated EPAP (4-7 cm H2O) in these patients to clear the CO2 and the lowest possible IPAP in order to attain adequate ventilation at 10-14 cm H2O and to avoid any hemodynamic repercussions on the right ventricle.

Another clear indication for NIV in patients with pulmonary hyper-flow is in processes of acute respiratory insufficiency. These patients commonly present a large number of acute respiratory insufficiencies that are secondary to an edema generated by their increased pulmonary blood flow. In these processes, CPAP is a good alternative to BIPAP, because keeping a continuous constant positive pressure helps to reduce the pulmonary blood flow, which is necessary in these patients 5,134-143.

5.3. Severe Burn Patients:

Patients with severe burns are at the highest risk of developing infections during their postoperative period. Among the multiple reasons for infection are the lost continuity of their skin barrier against infection, which exposes patients to nosocomial infections, their frequent need for prolonged mechanical ventilation, an easily broken intestinal barrier, the severe depression of the immune system in the acute inflammatory phase and the multiple surgeries and polytransfusions they receive 144,145.
The keys to acute treatment of the severely burned patient include restoration of the hydroelectrolyte balance, scar desbridement and enteral nutrition with antibiotic prophylaxis. Scar desbridement should be done as soon as possible. Enteral nutrition must begin within the first hours after admission, but prolonging parenteral nutrition or wide-spectrum antibiotic prophylaxis should be avoided\(^{144-146}\).

In these patients, NIV has two objectives: first, to support gaseous exchange in situations in which intubation is not necessary and second, as support during weaning from invasive mechanical ventilation in very difficult-to-treat inhalation syndromes that may have destroyed pulmonary parenchyma\(^{5,58,144-146}\).

One of the major drawbacks in burn patients is that on many occasions the burns involve their face and airways, making it impossible to use an interface. The use of non-invasive ventilation in the first twenty-four hours post burn, can, if the burnt airway develops inflammation and edema, result in a physical situation that makes intubation much more difficult and may convert what would otherwise have been a relatively normal patient into one who is difficult to intubate and ventilate\(^{5,58,144-146}\).(See Figure 3)

5.4. Patients with upper air obstruction:

The most frequent upper airway obstruction patients in pediatric surgery are children with adenotonsillar hypertrophy and those with face and neck polymalformation syndromes\(^{82,147,148}\).

These children frequently present episodes of complete or partial obstruction of the upper airways that is generally accompanied by snoring and respiratory effort, which alter the child’s normal ventilation and sleep patterns. In their study, Katz et al has concluded that, in children, pulse transit time as a measure of arousal and respiratory effort is a more sensitive measure of obstructive events than visible EEG
arousals. Obstructive episodes are most frequent between the ages of two and six in children with adenotonsillar hypertrophies and they are an indication for adenotonsillectomy if there is nocturnal desaturation. These children frequently present an obstructive sleep apnea syndrome (OSAS) in the immediate postoperative period and particular care should be taken in children with intermediate OSAS scores who only undergo adenoidectomy because they may present acute episodes of airway obstruction. A nasal CPAP of 5-10 cm H20 with anti-inflammatories (dexametaxon 0.15 mg/Kg) for the first 24-48 hours post-surgery can be very useful in these patients and reverse all of their symptoms.

Polymalformation syndromes like Pierre Robin, Down, or Plader-Willi, Morquio, among others, can present different degrees of obstruction and may begin producing respiratory symptoms from birth. The possibility of maxillofacial correction can be considered in the most severe cases and apart from their tendency toward airway obstruction, the main surgical and post-surgical management problem is that the syndrome makes them very difficult to intubate. Thus it is very important that extubation is done when they are quite awake and that the initiation of extubation be supported with a nasal CPAP. It is also advisable that when working with these patients one always has a laryngeal mask of their size to hand in case the ventilatory situation suddenly becomes complicated.

5.5. Patients with restrictive pathology: Scoliosis and neuromuscular pathologies:

One of the NIV indications in pediatrics with the best results is neuromuscular pathologies with respiratory muscle affection. This group of patients is formed by many different pathologies (see table II), but they all have in common the possibility of suffering a chronic respiratory insufficiency and a good response to NIV.
Patients with severe scoliosis present, together with a notable pulmonary restriction, another series of factors that negatively affect pulmonary function: First, most severe scoliosis cases have a neuromuscular origin, so the patient also has a more-or-less severe associated respiratory muscle weakness. \(^{42,47,56,58,59,152,154}\) Second, the surgery itself will markedly alter pulmonary function because it will directly destroy some muscles probably most particularly affecting the anterior pathways due to the open thoracotomy. Third, the anesthetic agents may also worsen the already poor respiratory function. \(^{5,46,52,153,155}\)

The two greatest advances in this type of surgery have been changing the surgical approach from the classic open thoracotomy to video-assisted thoracoscopic surgery (VATS), and second, the use of non-invasive ventilation employing BIPAP in the immediate postoperative period. In so far as anesthetic technique, it is advisable to employ a minimum dose of neuromuscular relaxants and, if it is technically possible, an epidural catheter with local anesthetic that can avoid the deleterious effects of opiates on this type of pathology. \(^{155,156}\) A good alternative to intra-operative muscle relaxants could be the use of an above Minimum Alveolar Concentration (MAC) dose of inhalational agents, since as Garcia-Fernandez et al recently reported, a MAC sevoflurane dose produces analgesia and muscle relaxation at the spinal level and these effects completely disappear once this anesthetic is eliminated from the system without leaving any secondary effect or requiring any other antagonist agent. \(^{157,158}\)

The recommended type of non-invasive ventilation in this situation is a BIPAP with nasal mask, which is the best tolerated by pediatric patients, at an EPAP of 4-5 cmH\(_2\)O, and IPAP of 14-20 cmH\(_2\)O, at a respiratory frequency corresponding to the child’s weigh (neonate 35 rpm, under 10 kilos 25 rpm, between 10 and 20 kilos 20 rpm and above 20 kilos 15 rpm) \(^{52,56,155}\). (See Figure 4)
5.6. *Newborns with surgical thoracic pathology*:

In some newborns with congenital diaphragmatic hernia, esophageal atresia, vascular rings, congenital lobar emphysema or other processes that restrict pulmonary parenchyma and/or alter the intrathoracic airways, CPAP alone or combined with other cycles like nasal SIMV after extubation can help shorten intubation time, stabilize the airway and decrease respiratory effort and oxygen consumption \(^{31,36,73,80,84,88,89,102,159}\).

5.7. *NIV for anesthetic procedures*:

Although reports are still infrequent, NIV is beginning to be used for ventilatory control during sedations and anesthetic procedures. The most common application is to sedate patients during fiberoptic bronchoscopy, and in fact, NIV provides better gas exchange and airway permeability than a nasal oxygen cannula in this procedure \(^{160-167}\). NIV is also being used inside the operating room for ventilatory control in patients with an existing respiratory pathology who will be undergoing surgery with a regional anesthetic technique and sedation \(^{168}\). However this is more difficult in children, who do not tolerate being conscious during surgery, although it could be helpful in older children or to wean children with severe chronic pulmonary pathology weaning in the operating room \(^{37,57,163,166,167}\). (See Figure 5)

6. **KEYPOINTS FOR USE OF NIV IN PEDIATRIC PATIENTS:**

NIV cannot be considered a panacea for all respiratory problems, but as a ventilatory support technique it is not ineffective. There is serious error at both extremes of the value scale and one must be clear that in pediatrics, NIV cannot and should not completely replace intubated endotracheal mechanical ventilation, while, on the other hand pediatric critical care units that do not have protocols for NIV are also
robbing their patients of the undoubted benefits of NIV. Keypoints are summarized in table IV

Key points for NIV in children are:

6.1. **Ventilators:**

   It is very important to know how to evaluate whether the machine actually fulfills minimum prerequisites for safe NIV, since this lack is often the primary cause of technique failure. The first fundamental prerequisite is that the peak flow produced by the ventilator’s flow generator be elevated (>100-150 l/min). The flow generator must be potent because the greater the peak flow, the better it will be able to compensate for the inevitable leaks of NIV, and this is particularly important in pediatric patients, who are never still and thus have more leaks than adults. The most wide-spread flow generators are turbines that can rapidly increase or decrease their rpm to compensate for leaks and quickly recuperate the programmed pressure. This does not mean that other types of flow generators like injectors are useless, but they should always be able to supply a comparatively elevated peak flow, and this can be a problem with anesthesia work stations that in normal conditions do not have to face large leaks and employ quite low peak flows (< 100 l/min). The second important point when evaluating the appropriateness of a machine for pediatric NIV is the availability of ventilatory pressure modes. NIV ventilatory modes need to be pressure-regulated because that is the best way to compensate for leaks. However, the availability of more or fewer ventilatory modes will also condition the success of the technique. A machine with only continuous air way positive pressure (CPAP) is not as good as one with CPAP and two positive pressure levels in the air way (BIPAP) but, if it does not have any kind of synchronization with the patient’s spontaneous breathing, it will not be as good as a BIPAP with a very sensitive, quickly-responding trigger that can supply greater
volumes at lower pressures to avoid gastric insufflation and machine-patient asynchronisms.\cite{6,12,14,44,83,91-93,95-97,106}. Therefore, we must never forget that one of the main causes of NIV failure in children is the inadequacy of a ventilator that was not designed for NIV or that does not have synchronized pressure ventilatory modes\cite{83,92}.

Another necessary requirement is the possibility to program inspiratory oxygen fraction of the gas flow (FiO$_2$), and this is now available in most NIV ventilators, but it was not possible in the earliest models. Not being able to control FiO$_2$ in the NIV ventilators employing room air means that the flow must be enriched with extra oxygen. This situation makes it impossible to know exactly what FiO$_2$ is actually received by the patient at any time. Since the inspiratory gas flow can vary markedly with any leak, FiO$_2$ will be constantly changing despite receiving a controlled, constant external oxygen flow, so a gas analyzer must be continuously used at the facemask to confirm the actual FiO$_2$\cite{12,83,91,92}.

### 6.2 Interfaces:

This is one of the most important sources of NIV failure in children. There is a great scarcity of interfaces designed specifically for pediatric patients. The human face shape changes enormously between birth and six-years of age hoping to cover these differences with only one or two mask sizes is completely impossible. Most interface manufacturers design many more styles for adults than for very small children, complicating NIV in children enormously. A clear example is the total-face masks that give such good results in adults, but none are yet available for children. The worst situation is in infants and children under two years old since although some are interfaces designed specifically for neonates (binasal cannula, nasal masks, nasal adaptors), there are no other size variations in the pediatric interfaces that are available
on the market, making it quite difficult to find the most appropriate interface for infants and small children. (See figure 6 and 7) The three most important aspects in selecting the most appropriate interface are:

1. **Adaptability:** This means choosing the interface that can make the best seal with the least pressure on the facial surface, to avoid leaks. This parameter is basic because it will determine the possibility of cutaneous pressure lesions or ocular lesions from possible leaks or simply that the child tolerates the interface. Silicone masks that can be adapted to the patient’s face by heating the mask in warm water before fitting, and masks with a wide contact surface and low pressure air cushion are much more useful than the classic plastic masks without special padding. This is a crucial point in pediatric patients, in that one must have available the largest possible number of interface designs in different sizes so as to choose the best interface for each child.

2. **Interface Dead Space:** This is much more important in pediatric patients than in adults. Although anatomic dead space per kilo of body weight is more or less the same in adults as in children (2-3 ml/kg), the total value is logically, much higher in adults than children. For example, for an average 75 kg adult, the dead space is about 185 ml while a 3 kilo neonate has a dead space of about 7.5 ml. So, if we suppose that the interface adds a dead space of as little as 10 ml, it will increase dead space by 6% in an adult, an amount without any significant clinical repercussions. However those 10 ml will double the neonate’s dead space, reducing the effective alveolar Vt (by as many additional ml as added dead space), and favor reinhalation and hypercapnia phenomena. Moreover, the expiratory resistances to expiratory flow in the expiratory valves are proportionately greater in children than adults since the expiratory force generated by pulmonary elastic recoil in a child is less than in adults. The elevated gas flow
employed in inspiratory and expiratory NIV, together with the inevitable leaks, usually wash the interface dead spaces and preclude significant reinhalation effects. It is so important to avoid increasing dead space in neonates that interfaces with silicone nasal cannulas or nasal minimasks with extremely little dead space are used (see figures 6 and 7). In older infants and children, dead space is still an important factor. The first choice for NIV is a nasal mask, or the smallest possible oronasal mask. The other important variable for solving the problems of dead space and reinhalation in the pediatric patient is to program an elevated expiratory positive airway pressure (EPAP) (4-5 cm H2O), and intentionally provoke controlled leaks in the mask, by, for example, opening one of the lateral orifices that are usually found on the mask to provoke a greater fresh gas flow during the expiratory phase and so perfectly clear out the dead space and avoid CO₂ reinhalation (see figures 8 and 9). The dead space problem conditions the use of a helmet or a total-face mask in neonates and the smallest children; these must be designed and adapted to have the least possible dead space while still allowing adequate clearance of the gas expired by the patient during the expiratory phase with an elevated fresh gas flow. Piastra et al have reported that non-invasive ventilation via a helmet can offer effective ventilatory support and improve gas exchange in the treatment of acute respiratory failure (ARF) in four over 9-year-old hematology pediatric patients.

3. **Type of respiratory pathology to be treated**: If the patient presents a primarily hypoxemic respiratory insufficiency, the interface should be able to transmit the programmed pressures as exactly as possible to the lower airway. Therefore, a nasal mask that will allow oral leaks will be less effective than an oronasal mask or a total-face mask. However, if the respiratory problem is basically hypercapnic respiratory insufficiency, a nasal mask will be more effective than an oronasal mask. The nasal
mask gives a better washing of the anatomic and interface dead spaces since it achieves
a better clearance in the nasal and oropharyngeal dead spaces during the expiratory
phase, depending on the degree of EPAP that we program, and higher EPAP-s will give
better clearance. In general, nasal mask are better tolerated by children than oronasal
mask that would other wise control the respiratory insufficiency better than the former
2,70,169,170,173,176,181. (See Figures 8 and 9)

6.3. Staff training:

The first recommendation is that this technique be applied by units that are
familiar with pediatric patients. There are so many respiratory differences between
children and adults, even in physiological situations, that if a child is very ill it is better
that he/she be treated by specialist 2,70,83,90,174,182,183.

Training and experience on the part of the medical and paramedical personnel of
the unit applying NIV is so important that it will decisively influence the results of the
technique. Various studies have reported very negative results with NIV in certain
conditions although several years later these same teams have published very positive
results with NIV in the same clinical situations 184,185. The minimum learning curve for
a NIV unit is about five years and only after this time will the results not be influenced
by inexperience 2,55,174,176,186.

Before establishing protocol for NIV in a pediatric critical care unit, all of the
personnel should be familiar with the ventilators, ventilatory modes, interfaces,
expiratory valves, gas humidification systems, straps, etc. One of the main differences
between NIV and conventional ventilation is that the former requires a greater level of
effort and work, for both nurses and doctors. The first hours after putting a child on
NIV are a time of great vigilance and observation. Both the doctor and the nurse must
pay close attention because this is when most technique failures occur and also when
intervention must be the speediest. The way in which NIV is initiated can also strongly affect technique success. The result of NIV being initiated by the anesthetist gently applying the interface by hand or with the help of the parents and allowing a certain level of leakage is quite different to what occurs if mask is strapped down as tight as possible using all possible straps so as to avoid the smallest possible leak – the latter will provoke the child’s rejection of the technique and early cutaneous lesions

After the first hours, and if the child has adapted to NIV, it is unlikely that any failure will be due to technical problems and the only late failures in NIV are due to poor clinical evolution of the pathology originating the respiratory insufficiency. As soon as the child realizes that NIV is solving their respiratory problem and that they can breathe with less dysnea and difficulties, they will relax and synchronize perfectly with the NIV. However a patient on NIV will always require adequate vigilance on the part of staff even though they have gotten through the initial adaptation phase, since there are many other factors that can cause the technique to fail interface maladjustment, leaks, disconnection, secretion plugs, vomiting, agitation, etc.

6.4. NIV Patient selection:

Different aspects need to be simultaneous evaluated to identify the patients that will benefits from NIV. The first factor is to ensure any formal counter-indication for the technique: cardio-respiratory arrest, multiorganic failure, facial lesions that are incompatible with the interfaces, etc. (See the section on contraindications). Since the learning curve for successful NIV application is so long, one of the first considerations in patients selection is the capacity of the staff to successfully manage the patients clinical condition with NIV, and last, one must carefully evaluate the clinical co-
existing factors that can predict the success or failure of NIV in each patient\textsuperscript{2,55,75-78,169,174,176,186-188}.

NIV is recommended in patients with the best indication and best probable results, such as those with a mild or moderate hypercapnic respiratory failure (pH > 7.25 and PCO\textsubscript{2} < 80 mmHg). Once good clinical results are obtained in these situations, one can expand the indications for NIV in the unit to more severe hypercapnic or hypoxemic respiratory failures\textsuperscript{67-69,71,174,183,187,188}.

The success predictors for NIV in hypercapnic failure are basically two: basal pH and PCO\textsubscript{2} levels before initiating NIV and the evolution in these parameters once NIV is begun. The lowest basal pH’s (< 7.2) and highest PCO\textsubscript{2}’s (> 90 mmHg) are indicative of the greatest risk of NIV failure, while success is found in the opposite situation. The other important factor is that if pH continues to fall and PCO\textsubscript{2} continues to rise after one hour on NIV, the probabilities are that NIV will fail\textsuperscript{71,174,187,188}.

There are three prognostic factors to be considered when evaluating possible NIV success in hypoxemic respiratory failure. The first is whether hypoxemic failure is associated with a hypercapnic failure or not. If hypercapnic failure is associated there is a better possibility of a favorable response to NIV than when alveolar hypoventilation is no associated. The second factor to be evaluated is the rapidity in response to NIV in correcting the hypoxemia. NIV is more likely to succeed in those patients who respond to NIV quickly, within the first hours, than in those who take longer. The third and perhaps most important factor to evaluate is the type of pathology that has produced the respiratory failure and its evolution in time. A cardiogenic pulmonary edema or edema due to negative pressure usually responds well to NIV because these pathologies have a short evolution. On the other hand, respiratory distress and severe pneumonia do not usually respond well to NIV since their course is longer. However no good correlation
has yet been found between the basal severity of the hypoxemic failure (PO2/FiO2 ratio) and the success or failure of NIV67,68,71,75-78,174,187,188.

Another important prognostic factor for NIV in children that is independent of the type of respiratory failure is the severity of the patient’s disease. The more serious the pathology, the greater the possibility of NIV failure. Children with failure of two or more organs, apart from pulmonary failure, are probably best intubated since NIV fails most often in these patients67,68,71,75,76,78,169,174.

Finally, it is important to keep the patient’s degree of cooperation and level of consciousness in mind when considering NIV. This is particularly important in children who are generally less cooperative than adults. Also, one must be very careful about the possibility of administering an excessive amount of sedatives, since it is as important to maintain a good level of consciousness as it is to obtain good cooperation from the child. The child must be conscious to assure effective spontaneous ventilation and a good control of the air way and to be able to detect complications like hypercapnia as soon as they occurs. The best way to achieve cooperation is to adapt the interface carefully, perhaps even with the parents’ assistance, so that the patient can experience how the NIV relieves his muscular fatigue and sensation of dysnea if this happens he will tolerate and accept the interface. If the patient is agitated and still does not tolerate the apparatus after an hour, NIV is probably failing and sedation will not resolve the situation67,68,71,174,189 (Figures 1 and 2).

**6.5. Choosing the right time to introduce NIV:**

Once the patient has been adequately selected according to the above criteria, the moment of initiating NIV is also equally important. A child in post-surgery after scoliosis surgery who has hypercapnic respiratory insufficiency is a good candidate for NIV, but, if NIV is delayed and the hypercapnia provokes decreased consciousness or
even a respiratory arrest, the child will require intubation and then is not such a good NIV candidate. Once the patient has been correctly selected, clinical and gasometric analysis should be done as soon as possible so that NIV can be applied, “the sooner the better”, as the saying goes 12,174,190,191.

6.6. Humidification and gas heating:

The temperature and moisture of the gases are vitally important in pediatric patients. Even with conventional ventilation using much lower inspiratory gas flows than in NIV, it is very important to condition inspiratory gases for pediatric patients. Just a few hours of a cold, dry gas can generate lesions and even tracheal mucosal necrosis in neonates. The inspiratory gases used in pediatric patients must necessarily be warmed and humidified. There are different systems to achieve this: The gas can be passed through coils with room temperature water, it can be bubbled under water, or heat and moisture exchangers can be used 107,192-197. However, the only truly effective systems for NIV are heated humidifiers that consist of a heater with a thermostat to heat a metal-bottomed recipient that holds the water in a closed system. By passing it through this device, the gas is simultaneously heated and humidified. The thermostat temperature controls the level of humidification, since the higher the temperature, the greater the humidification 107,192-197. When drops of water start to condense inside the tubes near the mask or interface, but not on the patient’s face, the gas is warm and moist enough and this is usually achieved at a temperature of between 35-38 °C. The larger the leaks in the NIV interface, the higher the inspiratory gas flow that the machine must generate to compensate for the leaks so, the higher the temperature needed to humidify the gases adequately 55,107,192-198. (See Figure 10)

Curiously, the question of gas humidification is receiving more attention in adults as a way to avoid the secretion plugs that are a frequent and important
complication in adults NIV. Interestingly, the solution that many manufacturers are offering is to adapt the classic heated humidifiers for neonates for their use in adults, demonstrating that understanding pediatric patients ventilatory peculiarities can even help professionals that only treat adults with ventilatory problems.

6.7. Selecting Hospital environment for NIV:

Complete coordination is necessary among the different areas through which a respiratory insufficiency patient on NIV will pass. Many enter the hospital in the Emergency area, and many can be attended and even treated with NIV and the released without requiring admission to the pediatric critical care unit. Of course, in cases of extremely severe acute respiratory insufficiency, NIV will be applied in the pediatric critical care units and post-surgical reanimation units who are familiar with intubation and cardiopulmonary reanimation and who can apply these techniques immediately if there is needed. But it is also necessary to know how to practice NIV in the units of intermediate care and even in the regular hospital ward. Patients who are recovering from extreme situations, once they recuperate from the acute phase and leave critical care, sometimes need NIV for their definitive recuperation. They might also require sporadic NIV if they have chronic hypercapnic respiratory insufficiency due to a neuromuscular pathology or obstructive sleep apnea syndrome (OSAS). It is important that patients who have received NIV receive good follow-up and a continuous ventilatory therapy, regardless of the different hospital units through which they may pass. This can be achieved by clearly specifying the doctors and nurses who will be responsible for NIV in each hospital unit and making sure that their training, practice, criteria and protocols are uniform and coordinated.

One must always remember that delaying endotracheal intubation in a patient who needs it can cause iatrogenic damage. That is why NIV is not appropriate for
managing acute hypoxemic respiratory failure in units that are unfamiliar with tracheal intubation and cardiopulmonary reanimation. The technique is not recommendable either in severe hypercapnic respiratory failure (pH < 7.2, PCO₂ > 90 mmHg) or in patients with associated failure of other organs in addition to the lungs on the hospital floors.\textsuperscript{55,83,160,190}

7. THE MOST FREQUENT PITFALLS IN NIV IN PEDIATRIC PATIENTS:

The failures that occur when NIV is applied in pediatric patients in a unit without prior experience with this technique are usually due to common beginner’s mistakes that result in failures that are not due to the technique itself. It is very important to be aware of these common mistakes so that the only possible cause for NIV failure will be the patients’ pathology and not lack of staff training. These beginner’s errors are motivated by approaching NIV as if it were like conventional invasive ventilation and also by a lack of familiarity with the specific respiratory characteristics of children versus those of adults.\textsuperscript{9,12,38}

The first mistake is to attempt to block any possible leak between patient and interface. It is a conceptual error that leads one to adjust the interface as tight possible, even producing extremely elevated pressure on the child’s face. Children tolerate foreign bodies on their face much worse than adults and if something bothers or pokes them, they will not be still. For example, plain nasal oxygen cannula - it is quite easy to convince an adult that he must have them in his nose, but a child will not stop trying to get them out. Also, pressure sores develop much more easily and sooner on a child’s face than on an adult’s. That is why the golden rule is that the interface must be placed by hand without straps (the parents can help with this), and a certain amount of leakage should be tolerated, as long as it is within the compensation capabilities of the ventilator.
being used. Once the interface has been adjusted and the child accepts it, and only then, can the interface be strapped in place\textsuperscript{12,171,177,179,180,198-201}.

Another frequent beginner’s error in NIV is to let what some authors have called the therapeutic “window of opportunity” go by and initiate NIV too late\textsuperscript{202,203}. A clear example is in neonate weaning. Neonates are the patients that can most benefit from NIV, both to avoid intubation entirely, or during weaning from endotracheal intubation. NIV has become an almost necessary technique for weaning any neonate who has had any acute pulmonary pathology from conventional ventilation. If, instead of applying a 5-8 cm H\textsubscript{2}O CPAP to a neonate as soon as he is extubated, which is what should be done, we placed a simple nasal cannula with an elevated FiO\textsubscript{2}, the neonate will initially maintain his oxygen saturation above normal. However, a few hours later he will begin to be desaturate, even though the FiO\textsubscript{2} has been progressively incremented by increasing the flow in the nasal cannula, and it will probably even become necessary to reintubate the patient. If NIV is attempted at this point it will be much more difficult to avoid endotracheal reintubation, while, if as soon as the patient was extubated, NIV with a simple CPAP or BIPAP or support pressure had been initiated, the possible need for reintubation would be significantly decreased. Another example would be the case of a child with acute hypercapnic respiratory insufficiency; if once the child had begun showing signs of increased respiratory effort (tachypnea, nasal fluttering, sternum retraction, …) and the gasometry readings showed increased PCO\textsubscript{2} without significant acidosis or hypoxemia, we apply nasal cannula, the oxygen saturation will improve. However if the respiratory pump is the cause of the failure, the child will tire himself until he produces a significant respiratory acidosis with clear hypoxemia. At this point it is probably too late for NIV, because the patient not requires endotracheal intubation and invasive ventilation. However, if we had diagnosed the respiratory insufficiency
early enough, we would have originally applied NIV instead of the oxygen nasal cannula. It is probable that NIV would have been successful and invasive ventilation would have been completely avoided since, NIV would have assisted the patient’s respiratory muscles from the beginning, something that enriching the oxygen level in the nasal cannula would never have achieved\textsuperscript{199,202,203}.

Another frequent mistake is to begin using NIV in a unit with insufficient prior experience and no specific NIV training, applying unclear or dubious NIV indications\textsuperscript{74}. This is dangerous and should be avoided because delaying necessary intubation can result in iatrogenic damage. When NIV is begun in a unit, it should be applied in the most obvious, simple and clear indications. An example would be patients with musculoskeletal diseases, who in many cases are receiving NIV at home and can benefit from NIV in their post surgical period\textsuperscript{47,154}. In these patients, using NIV for post surgical weaning is beneficial because they are accustomed to this type of ventilation and to the interfaces, so that the only thing they need during the post-surgical period is a little more pressure support for a little longer than usual\textsuperscript{50}. Thus the unit’s personnel will become familiar with the ventilators and the different interfaces. The next step is to use the technique in patients with acute hypercapnic respiratory failure, since this condition usually responds quite well to NIV as long as it is not very severe or NIV is not too long delayed. Therefore, the unit should begin by treating mild and moderate hypercapnic respiratory failures (pH > 7.25 and PCO\textsubscript{2} < 80mmHg), leaving the more severe cases (pH < 7.25 and PCO\textsubscript{2} > 90 mmHg) for units with more experience in NIV and with good clinical results in less severe situations. The last step in NIV indications is acute hypoxemic respiratory failure; this should be treated in units with long experience in NIV and who already regularly obtain good results in patients with acute hypercapnic respiratory failure (figures 1 and 2)\textsuperscript{169,171,190,200}. 
Another frequent beginner’s mistake is to apply NIV using a respirator that is not prepared for NIV or use an inappropriate interface for that particular patient. Both problems are quite common, since in the beginning, the unit may not have specific pediatric NIV materials. This will result in certain failure because a conventional ventilation respirator is not designed for NIV and does not have a flow peak high enough to compensate for leaks or to generate the pressures that are programmed in NIV. The same thing happens with the interfaces. If pediatric interfaces are not available in the unit, the technique will likely fail because the dead space in the adult interfaces is too big for children. The adult expiratory valves are usually inoperable in children because they require a expiratory flow that is much greater than what a child can produce and this will produce progressive hypercapnia as a result, not of NIV failure per se, but of not having chosen the appropriate interface for that child 169,171,172,178,190,200.

The use of NIV for pediatric patients in non-pediatric units is fraught with difficulties. If, in an emergency, a unit that does not usually treat children is involved in treating a child with an acute respiratory insufficiency, NIV can be quite complicated. On one hand, they will have to deal with the requirements of a pediatric patient in a non pediatric medium, and this makes things more difficult. And, on the other hand, they will also have to deal with the differences in managing NIV in a child vs. in an adult9,169.

The most important recommendation is that, before beginning NIV in a child, the medical and paramedical staff of the unit have proper training and adequate experience, the appropriate pediatric material and they must begin by applying NIV in the simplest and most specific cases before widening their applications of NIV as they become familiar with the procedure 169.
8. CONTRAINDICATIONS FOR NIV IN PEDIATRICS:

The main absolute contraindications for non-invasive mechanical ventilation are: respiratory or cardiac arrest, acute airway obstruction, danger of aspiration, and active acute digestive hemorrhage, severe hemodynamic instability and coma (see table V). In groups with the most experience with NIV, what were absolute contraindications for NIV are becoming relative contraindications and they can obtain good results with NIV in situations in which these techniques have not been effective in the past. For example, in coma, which until now has been considered an absolute contraindication, some authors, like Diaz et al, have reported that selected patients with hypercapnic coma secondary to acute respiratory failure (ARF) can be treated as successfully with NPPV as awake patients. So the main issue with the indications for non-invasive ventilation is the experience that the group has had, and thus unsurprisingly, what is a contraindication for some groups is an indication with good results for more experienced groups.

In post-surgical reanimation units, the most common indication for NIV is to support early weaning from invasive mechanical ventilation. In this situation BIPAP and synchronized support pressure are obtaining good results, although, as we said earlier, a great deal depends on the unit’s experience with this type of ventilation. The results reported in the literature until now are still contradictory and there has been little published on NIV in pediatric patients.

9. SUMMARY:

The technique of non-invasive ventilation cannot be considered as opposite to conventional ventilation. There are clear indications for endotracheal intubation and it makes no sense to question this technique when it is necessary. Likewise, it also makes no sense to baldly reject non-invasive ventilation simply because it is a new ventilatory
technique that requires specific training and greater vigilance and effort on our part. The secret lies in recognizing that non-invasive ventilation is complementary to the conventional technique, both when considering intubation, as a possible alternative, or after intubation, in order to facilitate a complicated weaning process. Another added problem is the lack of material specifically designed for the smallest patients. It is to be hoped that the manufacturers will make an effort to make this pediatric material available in the future. What is important is that anesthetists, reanimators, neonatologists, pediatricians and intensivists, who all ventilate the same patients, remember is that the life of our most critical patients depends on our careful ventilatory management, whether in the surgical theater or in the intensive care unit. All of these considerations become even more important when ventilating pediatric patients, and particularly neonates and premature babies who have extremely delicate lungs.

Non-invasive positive pressure ventilation (NIPPV) is a ventilatory support technique that gives general support to the patient’s respiration or treats different types of respiratory failure without tracheal intubation. Many people support this ventilatory mode while others are convinced that it is not as good as reported. This controversy probably means that the indications for NIV need to be better defined and that the professionals applying this ventilatory mode require more stringent training. All of these questions are even more important in pediatric patients because there is a lack of specific devices for babies, making it even more complicated to apply this ventilatory technique in small children. However, sanitary professionals have the responsibility of mastering this new technique so that any patient who might benefit does not lose the opportunity due to the professional’s lack of adequate training.
**Common Abbreviations:**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tbody>
<tr>
<td>ALI</td>
<td>Acute lung injury.</td>
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<tr>
<td>ARDS</td>
<td>Acute respiratory distress syndrome.</td>
</tr>
<tr>
<td>ARF</td>
<td>Acute respiratory failure.</td>
</tr>
<tr>
<td>ARI</td>
<td>Acute respiratory insufficiency.</td>
</tr>
<tr>
<td>AHRF</td>
<td>Acute hypercapnic respiratory failure.</td>
</tr>
<tr>
<td>BIPAP</td>
<td>Bi-level positive airways pressure.</td>
</tr>
<tr>
<td>CRF</td>
<td>Chronic respiratory failure.</td>
</tr>
<tr>
<td>CRI</td>
<td>Chronic respiratory insufficiency.</td>
</tr>
<tr>
<td>CPAP</td>
<td>Continuous positive airways pressure.</td>
</tr>
<tr>
<td>CCHS</td>
<td>Congenital central hypoventilation syndrome.</td>
</tr>
<tr>
<td>CL</td>
<td>Compliance of the lung.</td>
</tr>
<tr>
<td>CW</td>
<td>Compliance of the chest wall.</td>
</tr>
<tr>
<td>EELV</td>
<td>End-expiratory lung volume.</td>
</tr>
<tr>
<td>EPAP</td>
<td>Expiratory positive airways pressure.</td>
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<tr>
<td>FRC</td>
<td>Functional residual capacity.</td>
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<tr>
<td>IPAP</td>
<td>Inspiratory positive airways pressure.</td>
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<tr>
<td>NIPPV</td>
<td>Non-invasive positive pressure ventilation.</td>
</tr>
<tr>
<td>NIV</td>
<td>Non-invasive ventilation.</td>
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<tr>
<td>OSAS</td>
<td>Obstructive sleep apnea syndrome.</td>
</tr>
<tr>
<td>PEEP</td>
<td>Positive end-expiratory pressure.</td>
</tr>
<tr>
<td>PAV</td>
<td>Proportional assist ventilation.</td>
</tr>
<tr>
<td>PIP</td>
<td>Positive inspiratory pressure.</td>
</tr>
<tr>
<td>PSV</td>
<td>Pressure support ventilation.</td>
</tr>
<tr>
<td>SDB</td>
<td>Sleep-disordered breathing.</td>
</tr>
<tr>
<td>SIDS</td>
<td>Sudden infant death syndrome.</td>
</tr>
<tr>
<td>SIMV</td>
<td>Synchronized intermittent mandatory ventilation.</td>
</tr>
<tr>
<td>Ti</td>
<td>Inspiratory time.</td>
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<tr>
<td>Te</td>
<td>Expiratory time.</td>
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<tr>
<td>VILI</td>
<td>Ventilator-induced lung injury.</td>
</tr>
<tr>
<td>VATS</td>
<td>Video-assisted thorascopy surgery.</td>
</tr>
<tr>
<td>VT</td>
<td>Tidal volume.</td>
</tr>
<tr>
<td>WOB</td>
<td>Work of breathing.</td>
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</tbody>
</table>
NIV BENEFITS IN PEDIATRIC PATIENTS:

1. By improving respiratory mechanic and assisting in work of breathing, allows the respiratory muscles to rest.

2. By decreasing work of breathing, decreases total oxygen consumption.

3. Decreases hypercapnia and increases the Vt through the IPAP.

4. Increases functional residual capacity (FRC) and end-expiratory lung volume (EELV) through both EPAP and CPAP.

5. Prevents atelectases formation by increasing the difference between FRC and closure volume.

6. Helps maintain upper airway permeability.

7. Decreases the symptoms of respiratory insufficiency, by normalizing respiratory frequency and decreasing dysnea.

8. Improve the patient’s comfort (subjective sensation of respiratory insufficiency)

9. The patient can stay awake and sedation is not necessary.

10. Avoids the complications associated with endotracheal intubation and endotracheal tubes.

Table I. BENEFITS OF NIV FOR CHILDREN
### POSSIBLE ETIOLOGIES FOR NIV-TREATABLE CHRONIC HYPERCAPNIC RESPIRATORY INSUFFICIENCIES:

1. **Central Nervous System Diseases:**
   a. Arnold-Chiari malformation
   b. Central Hypoventilation syndromes
   c. Myelomeningocele
   d. Spinal Cord traumas
   e. Cranioencephalic trauma
   f. Fossa Posterior tumors

2. **Neuromuscular Diseases:**
   a. Spinal Amyotrophia
   b. Myopathies (congenital, mitochondrial, metabolic, inflammatory)
   c. Muscular Dystrophy (Duchenne’s Disease, etc.)
   d. Guillain-Barré syndrome.
   e. Myasthenia gravis and congenital myasthenic syndromes
   f. Phrenic nerve palsy
   g. Myotonic Dystrophy
   h. Poliomyelitis and its sequelae
   i. Botulism

3. **Upper airway Alterations:**
   a. Pierre-Robin Syndrome
   b. Tracheomalacia
   c. Obstructive sleep apnea syndrome

4. **Pulmonary Diseases:**
   a. Bronchopulmonary Dysplasia
   b. Cystic Fibrosis
   c. Pulmonary fibrosing diseases
   d. Bronchiectasis

5. **Respiratory Sleep Alterations:**
   a. Obesity-Hypoventilation syndrome
   b. Prader-Willi syndrome.
   c. Williams syndrome.

### Table II. CAUSES OF NIV-TREATABLE HYPERCAPNIC RESPIRATORY INSUFFICIENCIES IN CHILDREN:
POSSIBLE ETIOLOGIES FOR NIV-TREATABLE ACUTE HYPOXEMIC RESPIRATORY INSUFFICIENCIES:

1. Primarily obstructive pulmonary diseases:
   - Bronchiolitis
   - Asthmatic Crises
   - Upper airway obstructions (epiglottitis, laryngitis, etc.)
   - Cystic Fibrosis

2. Primarily restrictive pulmonary diseases:
   - Neuromuscular disease relapses
   - Obesity-Hypoventilation syndrome
   - Worsening of scoliosis
   - Thoracic trauma

3. Pulmonary Parenchyma Diseases:
   - Mild or moderate pneumonia
   - Acute lung injury.
   - Lung acute edema (cardiogenic or by negative pressure).
   - Acute exacerbations of chronic pulmonary pathologies (pulmonary fibrosis, bronchopulmonary dysplasia, etc.)

4. Perioperative respiratory insufficiency:
   - d. Complications in adenotonsillectomy
   - e. Post-operative weaning for severe scoliosis
   - f. Endotracheal weaning for Home-NIV patients
   - g. Endotracheal weaning in patients with chronic pulmonary pathology

Table III. ETIOLOGY OF NIV-TREATABLE ACUTE RESPIRATORY INSUFFICIENCIES:
KEYPOINTS FOR USE OF NIV IN PEDIATRIC PATIENTS

1. **Ventilators:***
   - Minimum peak inspiratory flow of at least 100 liters/min (better if > 150 liters/min).
   - Pressure modes (support and control).
   - Good synchronization with patient breathing: high inspiratory and expiratory trigger sensitivity.
   - FiO₂ programmer

2. **Interfaces:**
   - High adaptability: Appropriate pediatric sizes.
   - Low interface dead space.
   - Choose the correct interface according to the type of respiratory pathology to be treated.

3. **Good Staff Training:**

4. **NIV Patient selection:**
   - First step indication: Chronic hypercapnic insufficiency.
   - Second step indication: Acute hypercapnic failure.
   - Third step indication: Acute hypoxemic failure.

5. **Choose the correct moment for using NIV:**
   - After correct indication the rule is “the sooner the better”.

6. **Always humidify and heat the gas flow:**

7. **Choose the correct environment:**
   - Intensive care unit for: Hypoxemic respiratory failure and severe hypercapnic respiratory failure.
   - Medical ward: Chronic hypercapnic failure and acute mild-moderate hypercapnic respiratory failure.

Table IV. KEYS TO NIV IN PEDIATRIC PATIENTS
CONTRAINDICATIONS FOR NIV IN CHILDREN

1. Cardiac and/or respiratory arrest
2. Acute complete airway obstruction
3. Risk of pulmonary aspiration
4. Active acute digestive hemorrhage
5. Severe hemodynamic instability
6. Coma (Glasgow score below 10)
7. Patients in whom two or more organs other than the lungs are failing
8. Patients who are unable to protect their airway (swallowing alterations, poor airway pulmonary secretion clearance, inability to cough, etc.)
10. Trauma, facial malformation or surgery that impede placement and fixing of any interface model.

Table V. NIV CONTRAINDICATIONS IN CHILDREN
Figure 1. Application algorithm for NIV in chronic respiratory failure in children:
Acute Respiratory Failure (ARF)

Only hypercapnic ARF
- Mild or moderate ARF:
  - pH < 7.35 and > 7.2
  - PCO₂ > 45 and < 90 mmHg
- Severe ARF:
  - pH < 7.2
  - PCO₂ > 90 mmHg
  - Good Training and equipment.
  - No other organ failures.
  - Patient cooperation.
  - After first hour of NIV: arterial blood gas improvement.

Hypoxemic ARF with or without hypercapnia
- Adequate training and equipment.
- No other organ failures.
- Patient cooperation.
- Hypercapnia associated.
- Quick resolution of lung pathology expected

First option NIV
- Success of NIV
- Intubation & Invasive Ventilation

Success of NIV
- Yes
  - NIV
  - After first hour of NIV: arterial blood gas improvement.
  - Yes
    - NIV
    - Success of NIV
  - No
    - Failure
    - NIV
    - Failure

Intubation & Invasive Ventilation
- No

Figure 2. Application algorithm for NIV in acute respiratory failure in children:
21 month old child without other pathologies who presents 2\textsuperscript{nd} and 3\textsuperscript{rd} degree burns on 65% of his body surface. BIPAP with nasal mask was necessary for his definitive weaning from conventional ventilation. Hypercapnia was eventually resolved starting with a high EPAP (4-6 cm H\textsubscript{2}O), placement of an expiratory valve and, last, leaving the mask openings open to allow controlled leakage and avoid any CO\textsubscript{2} re-inhalation.
A nine year old girl with severe scoliosis whose preoperative respiratory function tests show a forced vital capacity (FVC) of 45 % and a normal forced expiratory volume FEV1/FVC ratio (pure severe restrictive pattern). Scoliosis was corrected by an anterior approach thoracotomy. Weaning from invasive ventilation required a continuous BIPAP with an EPAP of 4 cm H₂O and an IPAP of 14 cm H₂O for four days in the intensive care unit and an EPAP of 4 cm H₂O with an IPAP of 9 cm H₂O for two weeks followed by nocturnal NIV at home during three months after discharge.
Figure 5  Intraoperative NIV uses:

This eight-year-old girl’s preoperative respiratory function tests show a forced vital capacity (FVC) of 29%. Her severe bronchiectasis mainly affected the left lung so she was programmed for a left pneumonectomy. In order to extubate the patient in the operating room at the end of the surgery and avoid ventilator-associated pneumonia, we applied a thoracic epidural to reduce the opiate dose and then a continuous BIPAP to maintain her oxygen saturation above 90% in the operating room just after extubation with an EPAP of 4 cm H₂O and an IPAP of 13 cm H₂O. She used the BIPAP for one week in the post-surgical intensive care unit at an EPAP of 4 cm H₂O with an IPAP of 9 cm H₂O for 10 days followed by nocturnal NIV at home after discharge.
Figure 6 Neonate’s interfaces:

Neonates are the most susceptible to the increases in dead space created by interfaces. A bi-nasal cannula will not increase dead space because its tubes fill the anatomical dead space in the rhino-pharynx. Other option is nasal minimasks that make it possible to exhale through the mouth and some even incorporate continuous gas flow systems to clear the mask dead space.
Figure 7  Bi-nasal Cannulas in Neonates:

The drawback with bi-nasal cannulas is that their openings are quite small and they are made of very soft pliable materials like silicone, so they can bend and twist quite easily inside the rhino-pharynx. Another drawback is that they are impossible to use in neonates with a nasogastric tube, something that is quite common in the postoperative period. An effective and simple alternative is to use a normal endotracheal tube, sized age appropriately, as a nasopharyngeal cannula through the free nostril. The endotracheal tube should be cut at its proximal end at the height of the nostril to avoid dead space. Endotracheal tubes are much less prone to obstructions and twisting than silicone bi-nasal cannula.
**Inspiratory phase:** Blue arrows represent the fresh gas flow. There are some leaks through the mouth in IPAP period what make this interface a little less effective than the oronasal mask.

**Expiratory phase:** Blue arrows represent fresh gas flow and red ones represent exhaled CO₂. See how the expiratory fresh gas flow (EPAP) helps to clearance CO₂ avoiding re-inhalation.

**Figure 8. Nasal mask:**
The nasal mask has two advantages over an oronasal mask. First, it is better accepted by children, and secondly, it allows better mask and rhino and oropharyngeal dead space clearance in children, making CO₂ re-inhalation less frequent. CO₂ re-inhalation is very difficult to encounter in adults with NIV although it is a phenomenon to watch out for and avoid in children less than two years of age.
Inspiratory phase: Blue arrows represent the fresh gas flow.

Expiratory phase: Blue arrows represent fresh gas flow and red ones represent exhaled CO₂.

Figure 9. Oronasal mask:
The oronasal mask is the interface design that best pressurizes the airways during inspiration, and, therefore, it is the design that best transmits the programmed pressure into the lungs, and this is very beneficial in hypoxemic respiratory insufficiency. The problem is that children usually reject this interface design which also has more dead space than the nasal mask and does not provide clearance for the rhino- and oropharyngeal dead spaces. The way to improve dead space clearance is to allow small controlled leaks by opening one of the two openings that are usually on the back of the mask thus allowing good CO₂ clearance during expiration and avoiding CO₂ reinhalation.
Figure 10. Heated humidifiers:

Heated humidifiers are indispensable for NIV in children. The old ones (left side picture) was dangerous because they had a large compressive volume, a high tendency to significant leakage, and it was not possible to control temperature exactly. The new ones (right side picture) have a very low compressive volume, are airtight and the temperature to heat the patient’s gas flow can be exactly programmed.