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Should High Flow Nasal Cannula Be Used For Respiratory Support In Preterm Infants?

By Dominic JC Wilkinson, MD; Chad C. Andersen, MD; and Jim Holberton, MD

High flow nasal cannula (HFNC) is a novel means of respiratory support in infants that has been adopted by a large number of neonatal units in the US, UK and Australia in the last 5 years. HFNC refers to the delivery of heated, humidified and blended oxygen/air via small caliber nasal cannulae at flow rates of >1 l/min[1]. HFNC has been used post-extubation in extremely low birth weight infants[2,3] (when the use of conventional continuous positive airway pressure (CPAP) may be technically difficult, and lead to significant nasal trauma), as well as for the longer-term support of CPAP-dependent infants with evolving or manifest chronic lung disease. However, the popularity of this modality has caused some concern and controversy. To date, the evidence base for its use in preterm infants is thin, and it has been suggested that HFNC may subject infants to dangerously high and unmeasured pressures[4]. This paper will review the recent evidence for HFNC, and explore some of the specific reasons why HFNC may have become so popular so quickly. It will provide some practical guidelines for the use of HFNC while awaiting further trial evidence.

Why Use High Flow Nasal Cannulae?

Oxygen delivered by small calibre infra-nasal cannula at “low flow” is used commonly in growing convalescent preterm infants, often with chronic lung disease[5]. Traditionally this has not been thought to provide significant support to the infant’s breathing apart from the provision of oxygen. Two early studies suggested that flow rates of >1 l/min could deliver positive end-distending pressure in preterm infants[6,7]. However, the clinical use of flows as high as this was limited by the problem of gas drying and injuring the nasal mucosa[8,9]. The re-

> *“High flow nasal cannula (HFNC) is a novel means of respiratory support in infants that has been adopted by a large number of neonatal units in the US, UK and Australia in the last 5 years.”*


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cent advent of commercially available systems for heating, humidifying and blending gas for delivery by nasal cannulae (eg Vapotherm, Fisher and Paykel) has led to an increased interest in the use of HFNC.

What Is The Evidence For The Safety and Efficacy Of HFNC?

In the last 2 years, six small trials of HFNC have been published including a total of about 200 infants treated with HFNC (Table 1). Three of these were short-term crossover comparisons[10-12], and 2 were retrospective cohort studies[2,3]. There was one randomized controlled trial (RCT).[13] There were also two earlier crossover papers comparing HFNC with CPAP[7,14].

None of the crossover studies showed any clear benefit (or harm) from HFNC. In the study by Courtney et al, HFNC was associated with higher oxygen requirements and increased work of breathing than variable or fixed flow CPAP[14]. In that study the authors used nasal cannula connected directly to a CPAP circuit, and it is not clear how much flow was actually delivered. In a similar recent comparison by Boumecid et al, HFNC (flow of 2 l/min) was similar to constant flow CPAP, but was associated with lower tidal volumes and more thoraco-abdominal asynchrony than variable flow CPAP[10]. In another study humidified nasal cannula led to less local complications than non-humidified high flow nasal cannula[12].

The only published RCT to date used HFNC immediately post-extubation in intubated prem infants (<1250g), using flow rates of 1.4-1.7 l/min. There was a significantly higher rate of reintubation in the HFNC group. They used a formula derived from oesophageal pressures in an earlier study[7], to predict flow rates required to deliver equivalent CPAP. But the most likely explanation for the result is that the flow rates used were too low.

There are quite large differences in the flow rates used for HFNC in the published trials. This reflects uncertainty about

Table 1: Published Clinical Trials/Comparisons of High Flow Nasal Cannula

First Author, Year	Type of Study	Comparison	n	Flow (1/min)	Results
Sreenan 2001[7]	Crossover	Apnoea of prematurity, CPAP vs HFNC	40	1-2.5	No difference in frequency or duration of apnoea
Courtney 2001[14]	Crossover	CPAP (continuous/ variable flow), vs HFNC	32	(6)*	Increased FiO2 and resp effort with HFNC
Woodhead 2006[12]	Crossover	Post-extubation humidified vs non-humidified HFNC	30	~3	Non-humidified – higher 'failure' rate, less normal nasal mucosa
Campbell 2006[13]	RCT	Post-extubation CPAP (Infant Flow) vs HFNC	20 (20 CPAP)	1.4-1.7	Increased oxygen use, apnoeas and reintubation
Saslow 2006[11]	Crossover	CPAP/HFNC	18	3-5	No difference in work of breathing/oesophageal pressure
Shoemaker 2007[2]	Retrospective, descriptive	CPAP vs HFNC as early respiratory support (infants <30 weeks)	65 (36 CPAP)	2.5-8	'Well-tolerated; no apparent difference in adverse outcomes'
Holleman-Duray 2007[3]	Retrospective, descriptive	"Early Extubation protocol" and HFNC vs historical controls (infants 25-29 weeks)	58 (49 controls)	4-6	'Safe and well-tolerated,' less time on ventilator
Boumecid 2007[10]	Crossover	CPAP (continuous/ variable flow), vs HFNC	13	2	Variable flow CPAP, 'more effective respiratory support' than either constant flow CPAP or HFNC

Abbreviations: *HFNC High Flow Nasal Cannula; CPAP – Continuous positive airway pressure; FiO2 – fractional inspired oxygen concentration; RCT – Randomised Controlled Trial; n – total number of infants studied*

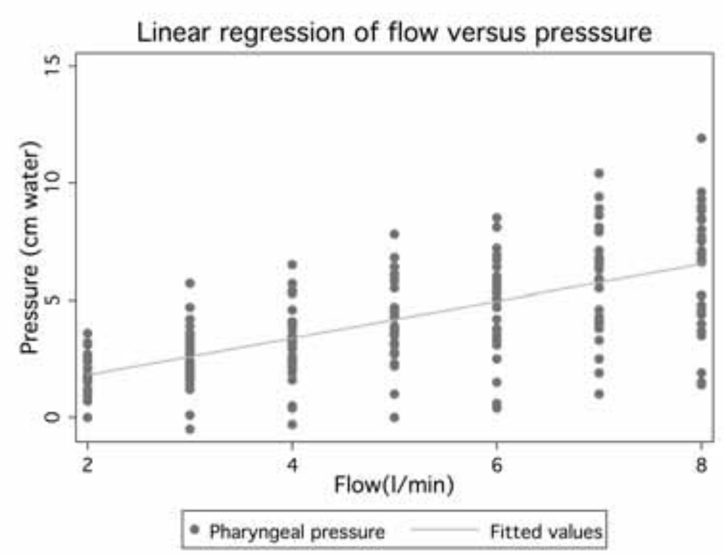

Figure 1. Pharyngeal pressures measured in preterm infants receiving high flow nasal cannula[15].

what flow rates are likely to be safe and effective in preterm infants, and what factors might determine pressure transmission to infants. We recently measured pharyngeal pressures in 18 preterm infants receiving HFNC using a solid-state pressure-tip catheter[15]. At flow rates of 2-8 l/min we measured clinically significant pressures similar to those observed in infants on nasal CPAP (Figure 1). Pharyngeal pressure was strongly associated with flow rate and infant weight, but not mouth position (open vs closed). We obtained a regression equation relating pharyngeal pressure to flow and infant weight:

*Pharyngeal Pressure (cm H_2O) = 0.7 + 1.1 * F*
F= Flow per kg (l/min/kg)

This model would predict a pharyngeal pressure of only 2.5cm water with the flows used in the randomized controlled trial mentioned above. This might explain why in that trial HFNC was less effective post extubation than nasal CPAP of 6cm H_2O.

Pharyngeal pressures very similar to those that we measured were recorded in another recently published study of HFNC in preterm infants[16], though a third study[17] recorded somehat lower pressures in the oral cavity.

Our study was not designed to answer the question of whether HFNC might lead to barotrauma. It is somewhat reassuring that transmitted pressures were similar to commonly used CPAP pressures, however two of the infants (weight 0.8kg and 1.6kg) had pressures of 12cm water at flow rates of 8l/min (the larger infant recorded this pressure only with his mouth actively closed).

Why Has HFNC Become Popular So Quickly?

The phenomenon of a form of respiratory support being enthusiastically adopted by many before there was much trial-based evidence for benefit is not new in newborn intensive care. Oxygen is a pertinent example, though more recently CPAP as a primary mode of respiratory support, was adopted by some centres (eg Jen-Tien Wung at Columbia), long before it was widely accepted in the neonatal community as being of benefit. Similarly, various modalities of mechanical ventilation might also fit into this category (eg pressure support, bi-level ventilation, airway pressure relief ventilation).

But specifically in terms of HFNC, there are a couple of reasons why it may have become popular so quickly. These relate to its relative simplicity and "everydayness" (we use nasal cannulae throughout the nursery everyday without second thought), and perhaps also to its appeal to a couple of philosophies of contemporary neonatal care. These are the idea that 'gentler' forms of support are likely to be better for infants, as well as the notion that we should amend our support wherever possible to provide developmentally appropriate care. Thus, the shift away from invasive to non-invasive means of respiratory support, may drive us to think that HFNC is a logical next step forward from CPAP. Anecdotally, HFNC allows infants to be handled less, makes it easier for them to receive kangaroo care, and breast-contact/feeding than CPAP. It may, therefore, be intuitively superior.

What Should We Do?

The paucity of evidence would support a cautious approach to the use of HFNC - particularly in those infants who are most at risk of harm (the smallest infants). HFNC may deliver high pharyngeal pressures in extremely low birth weight infants, and it would be prudent to limit flows used in such infants. We would not recommend flows of more than 6 l/min in infants <1kg. Although HFNC may be a less intensive intervention, infants receiving it should still be monitored (for example with capillary blood gases or chest x-rays) as they would on CPAP.

We have had more experience with the use of HFNC as support for premature infants who are slow to wean off CPAP, or where there has been significant nasal trauma and CPAP is otherwise difficult or impossible. We have used it infrequently as a primary mode of respiratory support, though others have described its use in this context[3]. Our experience (and affirmed by measurements of pharyngeal pressures) is that it is difficult to consistently deliver high pressures, particularly in larger infants. For term or near-term infants, or smaller infants who are dependent on high mean airway pressures (either from conventional CPAP or from mechanical ventilation), HFNC may not be an appropriate means of support.

The equation cited above may provide some guide to likely pharyngeal pressures in infants treated with HFNC. However, there was some variability between infants in pressures measured (Figure 1), and the results of our study cannot be necessarily extrapolated to flows >8l/min or infants <1kg or >4kg.

There is clearly a need for more research to guide decisions about HFNC. Where possible HFNC should be compared in a scientifically robust way with existing means of support (for example CPAP). Questions of efficacy and safety will only be answered by large randomized controlled trials. Where involvement in an RCT is not an option, there should at least be a means of auditing respiratory complications for infants who are treated with HFNC.

HFNC is an attractive means of respiratory support that may prove to be an effective alternative to nasal CPAP in some preterm infants. However where it is used we should be honest with parents that this is a novel, and largely untested means of treatment.

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Giving Birth to a Simulation Center

By Daniel J. Scherzer, MD

The decision to have a simulation center should be a conscious one. Predevelopment planning is a must. It is easy to envision high-tech mannequins, user-friendly software, touch screen waveform displays and presentation-ready video playback. These items characterize the readily visible technological trappings of the mature phenotype. Simulation, however, is not just about the technology; it is more than a technique. Simulation is an educational practice that reflects an acceptance of health care as a high risk industry and a commitment to become a highly reliable one.

Starting with Concepts

High risk industries (HRIs) are characterized by complexity that predisposes staff to making errors that can result in injury or death. Unlike the employees of other HRIs, health care personnel are not typically encompassed in that risk for injury and death. A flight crew's experience of a crashing plane is probably much different than a medical team's experience of a crashing patient. Nevertheless, our professionalism calls on us to accept the intensity of this risk on behalf of our patients.

Accepting our livelihood as high risk is the key to taking on the mission of creating a culture of safety. This is not to say, that as health care professionals, we are not already committed to safety. The safety culture concept refers to an understanding of safety that encompasses a systems approach to mitigating human factors. This is an idea that comes from the study of highly reliable organizations (HROs). HROs are organizations that demonstrate consistent, safe operation despite hazardous conditions and the performance of, what would otherwise be, inherently lethal activities. Examples are aircraft carriers and nuclear power plants.

A systems approach to safety considers human factors as part of the environment. 'Human factors' refers to the way we are designed to learn and work. Human factor considerations include:

- Ergonomics
- State of mind (fatigue, mood, distractibility)
- Common cognitive pitfalls (lacking insight into our biases and defending them)
- Imperfect intellect and memory
- Interactive variations, attitudes, morale
- The "social soup" – the way we affect each other

In a systems approach, human fallibility is a given. Over 25 years ago, NASA determined that more than 70% of commercial airline crashes were due to human errors, also called non-technical errors. These errors were described as failures of communication, leadership, decision-making and group awareness of the situation. We have similar findings in medicine. JCAHO has been collecting hospital-based sentinel event data since 1995. Communication errors are cited as the primary root cause in more than 60% of these events. The Institute of Medicine's (IOM) 2000 report To Err is Human stated that, out of 33.6 million annual admissions to U.S. hospitals, there were 44,000 to 98,000 preventable deaths yearly. It identified that 60-80% of adverse outcomes were due to human error, thus the title of the report[1].

So, health care is an HRI and not an HRO. To say it with more ownership, we are an HRI and not an HRO.

HROs rely on system barriers and teamwork principles to defend against human error. They create an environment where the reporting and discussion of errors and close calls is routine. They analyze near-misses closely with the understanding that contributory factors are always present. Those factors are called latent threats, and HROs seek them out. Every individual is part of the team and is a resource.

Making the Transformation

During the same time period as the IOM report, the United Kingdom's Maternal and Child Health Research Consortium reported that more than 75% of intrapartum-related stillbirths had evidence of suboptimal care. A 2000 study in the British Medical Journal stated that claims of negligence contributing to cerebral palsy comprised the majority of the National Health Services annual litigation bill. National experts and governing bodies recommended a multi-professional educational approach to address the problem[2].

Tim Draycott et al developed an educational program comprised of pre-reading a case-based workbook and attending a one day course. The one day course includes a lecture session, small group discussions and six "drill stations." The stations are case scenarios requiring the action of a multi-professional team. Since 2001, all obstetrical and midwifery staff at Southmead Hospital have been mandated to take the course annually. In a comparison of pre-training and post-training periods that included 19,460 infants, Draycott et al were able to demonstrate that their training program had been associated with a decrease in the number of neonates with:

- 5-minute Apgar scores of 6 or less from 86.6 to 44.6 per 10,000 births
- HIE from 27.3 to 13.6 per 10,000 births

This is the first time that an educational intervention has been associated with a significant change in clinical outcomes. Though one can argue that this is not 1A evidence for a correlation between simulation and better patient care, we certainly don't have anything like that for our traditional educational modalities.

The IOM report stated, "most care delivered today is done by teams of people, yet training remains focused on individual responsibilities, leaving practitioners inadequately prepared to enter complex settings….[this] can impede safety improvements."

The IOM went on to recommend that health care institutions:

- Provide strong, clear and visible attention to safety;
- Implement non-punitive systems for reporting and analyzing errors within their organizations;
- Incorporate well-understood safety principles, such as standardizing and simplifying equipment, supplies, and processes;
- Establish interdisciplinary team training programs for providers that incorporate proven methods of team training, such as simulation.

These sentiments have been echoed in recent literature by multidisciplinary authorship that addresses safety and education within the fields of Neonatology and Perinatology. Louis P. Halamek, et al described the development of a simulation-based training program designed "to bridge the gap between textbook and real life"[3]. The underlying theme is the integration of professional behavioral skills with the traditional emphasis on cognitive and procedural competency. These professional behavioral skills are also referred to as the components of "Crew Resource Management" (CRM). Halamek et al list them as:

- Know the environment
- Anticipate and plan
- Assume the leadership role
- Communicate effectively
- Distribute workload optimally
- Allocate attention wisely
- Utilize all available information
- Utilize all available resources
- Call for help early enough
- Maintain professional behavior

"Simulation is rapidly becoming one of the cornerstones of medical education. It has become the modality of choice in which to hone clinical skills and to develop teamwork, leadership and communication skills."

It may be tempting to dismiss such a list as "common sense." However, data reveals the difficulty of implementing such sense. The Joint Commission identified communication issues as the most frequently cited root causes of perinatal death or permanent disability not attributable to a congenital condition[4].

Simulation facilitates CRM practices and helps to probe the system. Essentially, CRM, when done well, enables optimal use of our cognitive and procedural "know-how." Simulation provides a dynamic real-time platform on which to assess and rehearse CRM principles in the context of the procedures and critical thinking that we want to optimize.

Simulation can help bridge the gaps between:

- Disciplines in silos vs disciplines collaborating
- Individual performance vs team performance
- Clinical emphasis vs clinical and human processes

In this regard, simulation expands the breadth of educational objectives to attitudinal, communication and teamwork skills. These objectives are easily integrated with the more traditional focus on knowledge, procedural skills, clinical assessment and clinical decision-making. The ability to integrate is important for two reasons. One, integration realistically prepares us for how we use our skills. Second, integration saves time. With decreased work hours, increased clinical demand and the ongoing information explosion, it is necessary to compress the acquisition of educational objectives.

It is also important to recognize that critical thinking involves more than clinical assessment and the ability to make decisions with incomplete or changing data. It also involves the ability to juggle competing demands, particularly in a time-constrained environment. Simulating complex or multiple scenarios is an ideal technique for challenging critical thinking.

Debriefing deserves special mention. In regards to educational objectives, debriefing is an opportunity to practice self and peer-to-peer assessment and feedback. The process of immediate assessment and feedback helps to coalesce other educational objectives. It is also a process that can be taken to the clinical arena. Perhaps more importantly, debriefing reinforces the other safety practices of team-building and the search for latent threats.

In Summary

Simulation is rapidly becoming one of the cornerstones of medical education. It has become the modality of choice in which to hone clinical skills and to develop teamwork, leadership and communication skills.

Simulation is immersive. Participants are engaged. Any and all of their skills may be called into play. The conditions are simulated, but the stress is real.

Simulation is dynamic. The simulator changes responsively, and a scenario can change directions. It isn't static like a lecture, a test or a simple mannequin. Numerous variations enable participants to experience a variety of unusual or difficult situations and helps them to develop the practice of anticipating contingencies.

Simulation is interactive. Not only do participants interact with the simulator, but they have to interact with each other to diagnose the problem and solve it. Simulation is the only venue where professionals from different disciplines can practice together before they work together. A wide range of conditions can be simulated to provide training to a diverse group of health care professionals.

Simulation emphasizes debriefing. Debriefing is what makes the learning sink in. Debriefing is itself a skill set that can be taken to the clinical arena and used for real life lessons. Debriefing is also another team-centered activity that emphasizes collaborative modes of thought and builds camaraderie.

Simulation facilitates the assessment of knowledge, procedural skills, clinical decision-making, communication effectiveness and teamwork skills.

Finally, simulation is safe. It is safe for both patients and practitioners. Simulation provides essential core aspects of training without putting real patients at risk. Simulation allows participants to fail, to experience how that happens and how to learn from that. This is a long way from, "see one, do one, teach one." More than anything, this is about implementing cultural change.

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Medical News, Products and Information

Water-Diffusion Technology Identifies Brain Regions Damaged by Prenatal Alcohol Exposure

Scientists know that children with Fetal Alcohol Spectrum Disorder (FASD) often have structural brain damage. Yet little is known about how white matter connections, and deep gray matter structures that act as relay stations, are affected in children with FASD. A new study has used diffusion tensor imaging (DTI) to identify several specific white matter regions as well as deep gray matter areas of the brain that appear sensitive to prenatal alcohol exposure. Results will be published in the October issue of *Alcoholism: Clinical & Experimental Research* and are currently available at Early View. http://www.blackwellpublishing.com/journal.asp?ref=0145-6008

"White matter tracts are bundles of axons that form connections between different parts of the brain," said Christian Beaulieu, Associate Professor in the Department of Biomedical Engineering at the University of Alberta and corresponding author for the study. "Highly interconnected deep gray matter structures, such as the basal ganglia and the thalamus, act as relay stations to integrate incoming sensory and motor input before it passes to the cortex; they also play a role in relaying cortical output. Both white matter tracts and deep gray matter structures are essential to the rapid communication and integration of information within the brain."

Carmen Rasmussen, Assistant Professor in the Department of Pediatrics at the University of Alberta added that researchers already knew that the corpus callosum, a major white matter tract connecting the left and right hemispheres of the brain, is affected in FASD.

"Abnormalities can vary from complete to more subtle malformations but, overall, brain white-matter volume is reduced in FASD, especially in the temporal and parietal lobes," she said. "Deep gray matter structures are also known to be smaller in individuals with FASD, and have decreased metabolic rates and abnormal metabolite ratios compared to those in children without FASD."

The researchers examined two groups: 24 children (13 boys, 11 girls), ages five to 13 years, previously diagnosed with FASD; and 95 healthy children (50 boys, 45 girls) from the same age range. Diffusion tractography was used to delineate 10 major white matter tracts in each individual, and region-of-interest analysis was used to assess four deep gray matter structures. Furthermore, an indicator of white matter integrity called "fractional anisotropy," and a measure of average water diffusion called "mean diffusivity," were assessed in all 14 brain structures.

"DTI is an advanced MRI technique that uses the properties of water diffusion within the brain to obtain information about fine brain structure," explained Catherine Lebel, a doctoral student in the Department of Biomedical Engineering working on the project. "If cell membranes and other tissue structures are degraded or malformed for some reason, then the water runs into less obstructions and the water travels further in the tissue, which can be measured with DTI. Tractography uses DTI data to virtually reconstruct white matter pathways through the brain, allowing for visualization and analysis of specific white matter tracts that are critical for various cognitive functions. Previous DTI did not use tractography to delineate individual white matter tracts, and none looked at deep gray matter structures."

Results showed that diffusion abnormalities in FASD go far beyond the corpus callosum region of the brain.

"Our results suggest that damage caused by prenatal alcohol exposure is very widespread and affects many regions of the brain," Lebel said. "Furthermore, the differences between children with FASD and controls were present across our age range, from 5 to 13 years of age. Finally, our findings on volume reductions and differences in the corpus callosum confirm previously reported differences, thereby supporting prior research on brain abnormalities amongst FASD populations."

Ideally, said Beaulieu, these findings will lead to a greater understanding of the relationship between the structural abnormalities and functional deficits that are associated with FASD, consequently helping to identify earlier and effectively treat and manage the condition.

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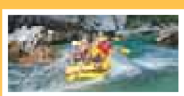

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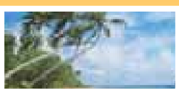

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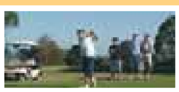
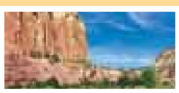
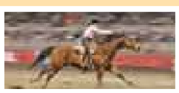


PANAMA CITY, FL



ALBUQUERQUE, NM



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What Is the First Step in the INOmax for Inhalation Reimbursement Process?

ICD-9 00.12

If your facility administers INOmax, reporting ICD-9 00.12 is important because...

- ICD-9 00.12 is the procedural code assigned to identify the administration of inhaled nitric oxide
- ICD-9 00.12 provides tracking data for payers that may affect current and future reimbursement levels
- ICD-9 00.12 may reduce claims-processing delays associated with miscellaneous HCPCS[a] or CPT[b] codes
- ICD-9 00.12 may trigger contractual payment mechanisms

[a] HCPCS, Healthcare Common Procedure Coding System.
[b] CPT, current procedural terminology.

 IMK111-00937

Next Steps...

Contact your hospital information management group to confirm that they are identifying and coding the administration of inhaled nitric oxide with ICD-9 00.12.

Reach out to your local sales representative for additional reimbursement services.

Call 1-877-KNOW-INO (1-877-566-9466) to learn more and be put in touch with a national account manager.

INOtherapy Reimbursement Service: 1-877-KNOW-INO (1-877-566-9466) or reimbursement@inotherapy.com.

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