



**Success with Failure** 



**Treatment of Acute  
Cardiogenic  
Pulmonary Edema:  
Integrating with  
Chronic Heart  
Failure  
Management**

John Bosomworth, MD, CCFP, FCFP  
Web page: [www.palmedpage.com](http://www.palmedpage.com)

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**Objectives** 



- Pragmatic objectives – avoidance of intubation, transport, ICU admission and death.
- Based on evidence rather than guidelines or “standard therapy”.
- Appropriate to a rural setting.

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**Objectives** 



- Treatment must avoid harm in patients with an incorrect diagnosis.
- Integrated with chronic disease status of patient prior to and after the acute event.

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**Patient Subset** 



- **Sickest of the acute decompensated heart failure patients.**
- **Respiratory failure secondary to pulmonary edema.**

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**Patient Subset** 



- **Increased LV filling pressures secondary to increased afterload (hypertensive, vascular) or myocardial dysfunction (infarction, ischemia).**
- **Those presenting in cardiogenic shock and hypotension (<10%) have poor prognosis and are best managed using ACLS protocols.**

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**Patient Subset** 



- **15-20% in-hospital mortality.**
- **40% mortality if associated with MI.**
- **80% mortality if associated with hypotension.**

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# Patient Subset



- Lowest mortality associated with hypertension, highest with hypotension.
- 30% will die within a year.
- If advanced directives not established on admission, should be in place by discharge.

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# Pathophysiology



## Goals of treatment



- Decrease preload
- Decrease afterload
- Improve LV contractility
- If first 2 goals are met, contractility usually improves.

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# Causes



Remember to consider the cause

MADHATTER mnemonic:

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**Rural  
Critical  
Care**

## Causes



- Myocardial infarction 25%
- Angina, unstable (16%)
- Anemia
- Drugs, Diet (salt)
- Hypertension 29%
- Arrhythmia (Atrial fib. 4%)
- Thyroid disease
- Toxic (Resp infection 8%)
- Embolism (pulmonary) Endocarditis, valvular disease (9%)
- Renal failure

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**Rural  
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## Clinical Scenario

- 76 year old woman, COPD, inferior MI 10 yr ago, no chest pain.
- Chronic CHF, EF 40%, slight cardiac enlargement, BP 130/70
- Meds ECASA, Atorvastatin 40 mg., Hct. 12.5 mg., Ramipril 2.5 mg bid, Metoprolol 12.5 mg. bid., Salbutamol, Atrovent.
- Postural hypotension on furosemide and larger ACE dose
- Fatigue on beta blocker

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**Rural  
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## Clinical Scenario

- Gradual increase in dyspnoea, wt gain and orthopnoea.
- Sudden onset acute dyspnoea, rales, rhonchi, diaphoresis, anxiety.
- P 110 regular, BP 140/100, O2 sat 89% on non-rebreather.
- No acute CXR or ECG changes.
- BNP and ECHO not available. Troponin neg, other labs normal
- Meds checked – possibly not taking metoprolol regularly.

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## Clinical Scenario



What is your initial treatment?

1. Morphine
2. Lasix
3. Morphine + Lasix
4. NTG + 1 of above
5. Nesiritide (recombinant BNP) + 1 of above
6. None of the above

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## Preload & Afterload Reduction



- Morphine
- Furosemide
- Nitroglycerin
- Sublingual Captopril
- Noninvasive Positive Pressure Ventilation

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## Morphine



- No studies have ever shown benefit
- Reduced symptoms due to sedation and respiratory depression.
- Not demonstrated to produce venodilation or reduce preload in Swan studies\*.

\* Lappas DG et al. Filling pressures of the heart and pulmonary circulation of the patient with coronary artery disease after large intravenous doses of morphine. *Anesthesiology* 1975; 42(2): 153-159.

\* Timmis AD et al. Haemodynamic effects of intravenous morphine in patients with acute myocardial infarction complicated by severe left ventricular failure. *BMJ* 1980; 280(6219): 980-982.

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## Morphine



- Increased intubation and death in large retrospective studies.
- Poorer outcomes for pre-hospital patients, especially those with a missed respiratory diagnosis.
- Benzodiazepines safer for sedation
- Should probably not be used unless for pain or palliation.

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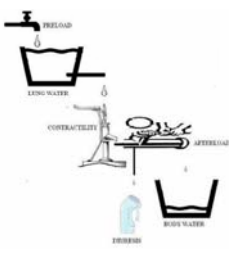
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## Furosemide



- Swan studies show increased preload and afterload prior to diuresis\*.
- Preload reduction does not occur until diuresis.

\* Kraus PA, Lipman J, Becker PJ. Acute preload effects of furosemide. Chest 1990; 98: 124-128.

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## Furosemide



- Diuresis safely delayed for 30-120 minutes and may be preceded by clinical improvement.
- Typical renal blood flow is 20% of normal in pulmonary edema. Prior treatment with vasodilators (NTG and captopril) produces immediate diuresis.

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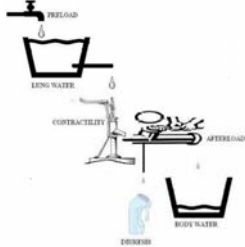
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# Furosemide



- 40-50% of patients are not volume overloaded\*.
- Vigorous use of diuretics in volume depletion results in hypotension when vasodilators are used as first line agents.

\* Figueras J, Weil MH. Blood volume prior to and following treatment of acute cardiogenic pulmonary edema. Circulation 1978; 57(2): 349-355.

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# Furosemide



- Vigorous use of diuresis often results in hypotension the following day.
- Patients with a missed respiratory diagnosis are often volume depleted and will be made worse.

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# Furosemide Summary



- Renal blood flow in pulmonary edema is 20% of normal. Use vasodilators for at least 30 min. prior to furosemide.
- Early administration of furosemide increases afterload and reduces cardiac output. Preload not reduced until diuresis. Timely afterload reduction cannot occur without vasodilators.

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# Furosemide Summary



- 40-50% of patients with dyspnoea are volume depleted. Some have a primary respiratory diagnosis. They will get worse with furosemide.
- Effect accelerated by vasodilator pretreatment. Diuresis may occur with vasodilators alone.
- Third line after vasodilators. Use the minimum dose.

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# Nitroglycerin



- First line intervention along with CPAP
- Preload reduction with low doses
- Afterload reduction with high doses
- High-dose therapy superior to morphine and furosemide, high-dose furosemide and CPAP alone.

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# Nitroglycerin



- Standard dose
- Up to 60ug/min
- Preload reduction only
- Venodilation peaks in 2 hr at low doses

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## Nitroglycerin



- Doses 60-100ug/min and higher required for afterload reduction.
- Progressive arteriolar dilation with increasing dose.
- This improves cardiac output and stroke volume when L ventricular function is impaired

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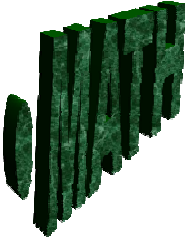
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**Rural  
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## Nitroglycerin



- 0.4 mg. SL nitroglycerine q 5 min. x 3 = 1200 ug.
- In 15 min @ 75% absorption = 900 ug. over 15 min. = 60 ug./min
- Most patients present with hypertension and tolerate this well.
- Used in management of acute coronary syndrome.

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## Nitroglycerin

**Prehospital: Safety in misdiagnosis:**

- Retrospective study of acute dyspnoea with prehospital treatment of 493 patients
- 18% rate of misdiagnosis (asthma, COPD, pneumonia)
- Those given only NTG had 2% mortality
- Those given morphine and/or furosemide had 22% mortality
- CHF patients misdiagnosed and given bronchodilators had no increase in mortality

Wuerz RC, et al. Effects of prehospital medications on mortality and length of stay in congestive heart failure. Ann Emerg Med 1992; 669-674.

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## Nitroglycerin and Mortality



- No prospective trials sufficiently powered to demonstrate mortality reduction.
- Patients with MI and hypertension with or without pulmonary edema have a relative risk of death of 0.81 at 2 days.\*

\*Perez MI, et al. Effect of early treatment with anti-hypertensive drugs on short and long-term mortality in patients with an acute cardiovascular event. Cochrane Database of Systematic Reviews 2006, Issue 4. Art. No.: CD006743.

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## NTG IV Protocol



- SL NTG 0.4 mg. every 5 min. x 4.
- Equivalent to 60ug/min for 20 min.
- Check BP before each dose
- Treat any hypotension with 500 cc. bolus normal saline.
- This frees up 20 min. for application of CPAP and preparation of the NTG drip.
- Many patients will improve with only SL dosing and CPAP.

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## NTG IV Protocol



- Prepare 400ug/ml NTG solution
- This is 100 mg. NTG in 250 ml. G5W in a glass bottle (preferred for solution stability, but not suitable for air transfer).
- Premixed preparations are available.
- 1.5 ml./hr infusion administers 10 ug/min

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## NTG IV Protocol

IV Rate	Dosage Given	Minutes after First SL Dose
7.5 ml/hr	50 ug/min	25
9 ml/hr	60 ug/min	30
10.5 ml/hr	70 ug/min	35
12 ml/hr	80 ug/min	40
13.5 ml/hr	90 ug/min	45
15 ml/hr	100 ug/min	50
16.5 ml/hr	110 ug/min	55
18 ml/hr	120 ug/min	60

- **Infusion**
  - Begin IV NTG infusion at 7.5 ml/hr = 50 ug/min (lower than SL rate).
  - Increase infusion by 1.5 ml/hr = 10 ug/min every 5 min (Table).
  - Check BP prior to each increase
  - Treat hypotension with bolus 500 ml. normal saline.

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## NTG IV Protocol



- **Treat to Target**
  - Most studies aim for O2 sat of 96% with oxygen or CPAP.
  - Dyspnoea, resp rate, pulse rate, BP and mental status should improve.
  - A drop in BP of 30% is a reasonable target for the majority of patients presenting with hypertension.
  - A low BP limit should prompt slowing or discontinuation of infusion.

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## NTG IV Protocol



- **Tailored Therapy**
- **Systolic pressure >140 (50% of patients). Best prognosis.**
  - Often older, female, hypertensive with good systolic function.
  - Not often fluid overloaded. Furosemide should be delayed 30-120 min. if given.
  - Aggressive high-dose NTG can be used.

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## NTG IV Protocol



- Tailored Therapy
- Systolic pressure 100-140 (>40% of patients)
- Likely some impairment of systolic function
- Some are fluid overloaded. Delay furosemide at least 30 minutes.
- High-dose NTG can be used, but some increased risk of hypotension.

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## NTG IV Protocol



- Tailored Therapy
- Systolic pressure <100 (<10% of patients). Poor prognosis
- Volume depletion or cardiogenic shock if hypoperfused.
- Bolus 500 cc. normal saline.
- If no response go to ACLS protocols including inotropes.

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## NTG IV Protocol



- Contraindications
- Phosphodiesterase inhibitors
- Severe volume depletion
- Hypotension
- Preload dependent states:
  - Right ventricular infarction
  - Aortic stenosis
  - Mitral regurgitation
  - Pulmonary hypertension

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## NTG IV Protocol



- **Adverse Outcomes:**
  - Tachyphylaxis after 2-12 hr.
  - Reflex tachycardia unusual.
  - Bradycardia rare. Use ACLS protocols.
  - Hypotension usually responds to fluid bolus or discontinuation of drip within 2-3 min.
  - Headache or nausea in up to 11%

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## NTG Summary



- A first-line intervention shown to be superior to CPAP and diuretics.
- Safe in pre-hospital use and when diagnosis is in doubt.
- Must be given early and titrated to high dose for optimal outcomes.

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## NTG Summary



- Treatment to target symptoms and clinical parameters determines optimal therapy
- Tailored therapy to presenting systolic BP determines minimum BP tolerated and whether use of diuretics may be beneficial.

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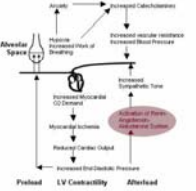
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## ACE Inhibitors





- Specific inhibition of maladaptive feedback loop
- Evidence exists for IV Enalapril and SL Captopril
- Captopril readily available and easily used as single dose.

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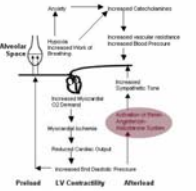
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## ACE Inhibitors





- Modest preload and potent afterload reduction. Can be used as single agent if NTG not tolerated.
- Good hemodynamic stability and few adverse effects\*.
- Fewer ICU days and fewer intubations with no increased hypotension.†

\*Hamilton RJ, et al. Rapid improvement of acute pulmonary edema with sublingual captopril. Acad. Emerg Med 1996; 3: 205-12.  
 †Southall, JC, et al. ACE inhibitors in acutely decompensated congestive heart failure. Acad. Emerg Med 2004; 11(5): 503

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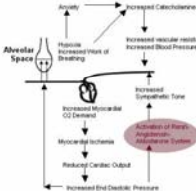
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## ACE Inhibitors





- Can be used with NTG with additive effect.
- Early use may avoid need for diuretics.
- Delay diuretic administration 30 minutes after vasodilators.

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## Captopril



- Oral tab dipped in water and given SL for more rapid absorption.
- Systolic BP > 110 dosage 25 mg.
- Systolic BP < 110 dosage 12.5 mg.
- Onset of action within 5 minutes\*.
- Given as single dose.

\*Ceyhan B, et al. Comparison of sublingual captopril and sublingual nifedipine in hypertensive emergencies. Jpn J Pharmacol 1990; 52: 189-193.

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**Rural  
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## Captopril Summary



- Can be used in place of NTG
- Good hemodynamic stability with few side effects.
- Easily administered in single dose.

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**Rural  
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## Captopril Summary



- Additive effects when used with NTG.
- Reduces ICU use and need for intubation.
- Good second line intervention

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**Rural  
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## CPAP



- Non-invasive ventilation includes CPAP and BiPAP
- CPAP much simpler to administer and equally effective
- CPAP of 10 cm. water used in most studies.
- Preload and afterload reduction.
- Early implementation gives the best results.

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**Rural  
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## CPAP

- **3 meta-analyses show reduced mortality and intubation rates.**

"it does not seem advisable, from an **ethical** point of view, to pursue further research comparing non-invasive ventilation methods with SMT in ACPE patients."

Winck JC, et al. Efficacy and safety of non-invasive ventilation in the treatment of acute cardiogenic pulmonary edema - a systematic review and meta-analysis. *Critical Care* 2006; 10:R69

"... it was not deemed **ethical** to include a group with oxygen alone because CPAP and bilevel PAP had already been shown to improve respiratory distress and to reduce the intubation rate"

Moritz F, et al. Continuous positive airway pressure versus bilevel noninvasive ventilation in acute cardiogenic pulmonary edema: a randomized multicenter trial. *Ann Emerg Med* 2007; 50:666-675.

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**Rural  
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## CPAP

- **A dissenting opinion: *N Engl J Med* 2008; 59: 142-51.**

THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

### Noninvasive Ventilation in Acute Cardiogenic Pulmonary Edema

Alasdair Gray, M.D., Steve Goodacre, Ph.D., David E. Newby, M.D.,  
Moyra Masson, M.Sc., Fiona Sampson, M.Sc., and Jon Nicholl, M.Sc.,  
for the 3CPO Trialists\*

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**Rural  
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## CPAP Summary

- CPAP equally effective to BiPAP and easier to use.
- **Must be applied early.** Few contraindications. Very safe.
- Strong evidence for early improvement in symptoms and physiologic parameters.

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**Rural  
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## CPAP Summary

- Patients treated initially with NIV do better than those with standard therapy even if intubation eventually needed.\*
- Still uncertain whether intubation or death are reduced.
- Any further large prospective studies need to avoid crossover of treatments. Doubtful if this will clear ethics.

\*Tallman TA, Peacock FW, Emerman CL, Lopatin M, Blicher JZ, et al. Noninvasive Ventilation Outcomes in 2,430 Acute Decompensated Heart Failure Patients: An ADHERE Registry Analysis. Acad Emerg Med 2008; 15(4): 355-362.

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**Rural  
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## CPAP Application

Criteria for respiratory failure usually present:

- Respiratory distress, use of accessory muscles
- Tachypnoea (RR 24-30)
- pH <7.35
- pCO2 >45
- pO2 <90 on maximal FIO2

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**Rural  
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## CPAP Application

- Chest X-ray may be useful in diagnosis, but is not sensitive enough for decision making. Changes due to acute pulmonary edema may take many hours to appear.
- No evidence for harm if applied in absence of resp failure.
- Outstanding evidence for use in COPD exacerbation if diagnosis uncertain. Early application is the issue.

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**Rural  
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## CPAP Application

- Indications with decreasing level of evidence
- COPD with exacerbation
- Acute cardiogenic pulmonary edema
- Pneumonia with immunocompromised patient.
- Do Not Intubate status
- Extubation failure
- Asthma
- Other causes of respiratory failure (ARDS, Trauma)

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## CPAP Application



- Complications
- Pain or ulcer over bridge of nose
- Mucosal dryness
- Fear that device is limiting ability to breathe
- Eye irritation if mask seal is suboptimal
- Aspiration or gastric insufflation (rare)
- Pneumothorax (very rare)

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## Rural Critical Care

# CPAP Application



**Contraindications:**

- Need for intubation
- Pneumothorax: always exclude.
- Reduced LOC with airway at risk
- Vomiting
- Agitation or poor mask seal
- Hypotension with SBP <90
- Any preload dependent condition.
- High intracranial pressure

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## Rural Critical Care

# CPAP Application

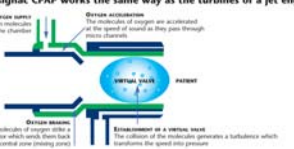
**The Boussignac CPAP System: An easily applied method for non-invasive ventilation.**

**Boussignac CPAP works the same way as the turbines of a jet engine.**

**Oxygen source**  
Oxygen molecules enter the chamber.

**Oxygen acceleration**  
The molecules of oxygen are accelerated as the speed of sound is then passed through micro-ducts.


**Oxygen deceleration**  
The molecules of oxygen strike a diaphragm which sends them back to the central zone (static zone).



**Oxygen acceleration**  
The molecules of oxygen are accelerated as the speed of sound is then passed through micro-ducts.

**Oxygen deceleration**  
The molecules of oxygen strike a diaphragm which sends them back to the central zone (static zone).

**Treatment at a vertical neck**  
The collision of the molecules generates a turbulence which transforms the speed into pressure.



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## Rural Critical Care

# CPAP Application

**System components:**

- Sized mask, valve, tubing for oxygen connection
- Oxygen port capable of 25 L/min. with flow regulator.
- Optional pressure manometer
- Optional nebulizer.
- Port for optional (recommended) ET<sub>CO</sub><sub>2</sub> monitor.




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## CPAP Application

Rural Critical Care



- Select mask size.  
child - #3  
adult female - #4-5  
adult male #5-6
- Inflate the air cuff around the mask using 20-40 cc. air. Have a 20 cc syringe available to create an air-tight seal.

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## CPAP Application

Rural Critical Care



- Connect green tubing to oxygen source
- Connect white end of the valve to the face mask
- Connect the end tidal CO2 sensor, if used, to the clear port. A cannula can also be slipped under the mask.

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## CPAP Application

Rural Critical Care



- In the sitting position, hold the mask to the patient's face, begin oxygen at 15 L/min (CPAP of 5 cm. H<sub>2</sub>O), and take time to explain.
- Secure the harness around the head with straps above and below the ears. Check for leaks and adjust the air seal as necessary.

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## Rural Critical Care

# CPAP Application



- Gradually increase oxygen flow to 25 L/min (CPAP of 10 cm. H<sub>2</sub>O) as tolerated .
- Suction through the large end port of the mask as necessary .

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## Rural Critical Care

# CPAP Application



- If the manometer is used, place it in line between the valve and the mask.
- If a nebulizer is used, place it in line between the valve and the mask . Set the valve oxygen source at 15 L/min. and the nebulizer source at 6 L/min.

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## Rural Critical Care

# CPAP Application

**Subsequent actions:**

- Do not remove CPAP without a backup plan—continue CPAP or intubation
- Assure that intervention is working:
  1. Reduced respiratory rate
  2. Reduced heart rate
  3. Reduced dyspnoea
  4. Normalization of BP
  5. Increasing oxygen saturation
  6. Normalizing end tidal CO<sub>2</sub>
  7. Improving mental status

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**Rural  
Critical  
Care**

## CPAP Application



- If not improving:
- Troubleshoot the equipment
- Check for pneumothorax
- Consider conditions which might reduce preload (hypovolemia, dehydration)
- Consider pulmonary embolism. 1 in 4 admitted COPD exacerbation patients may have PE.
- Consider proceeding to intubation

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**Rural  
Critical  
Care**

## Goals of Treatment



- Decrease preload
- Decrease afterload
- Improve LV contractility

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**Rural  
Critical  
Care**

## Goals of Treatment



- Improve LV contractility
- Always consider a fluid bolus.

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Rural  
Critical  
Care

## Tailored Therapy Algorithm

<b>If SBP&gt;140</b> CPAP+Nitrates Avoid diuretics unless volume overload	<b>If SBP 100-140</b> CPAP+Nitrates Volume overload is possible	<b>If SBP&lt;100</b> Fluid challenge +Inotropes +Vasopressors Referral
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• Systolic BP - a reliable guide for choice of therapy within minutes of admission.

Chatt R, et al. Algorithm for therapeutic management of acute heart failure syndromes. Heart Fail Rev 2007; 12: 113-117

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Rural  
Critical  
Care

## Harm Reduction



- Early CPAP helpful or not harmful in misdiagnosis of COPD, pneumonia, asthma, pulmonary fibrosis.
- Early NTG causes no harm in misdiagnosis
- Beta agonists do not worsen pulmonary edema if diagnosis is in doubt.
- Use morphine only for pain or palliation.
- Use furosemide only in volume overload and in lowest doses. Delay at least 30 minutes. Avoid if diagnosis is in doubt.

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Rural  
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## Clinical Scenario

- Immediate 10 cm CPAP and SL NTG X4.
- Comfortable by the time IV nitro was started at 50 ug/min. BP110/70, O<sub>2</sub> sat 95%
- Rales starting to clear, but many rhonchi. Salbutamol by nebulizer via CPAP.
- Chest clearing by 45 min. IV NTG at 90 ug/min. Comfortable, O<sub>2</sub> sat 96%, BP110/70, Pulse 70 reg. No diuresis. No further NTG increase.
- Large diuresis at 60 min. Reducing levels of NTG and CPAP

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**Rural  
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## Clinical Scenario

- Metoprolol continued in hospital
- Locum sent her home on Ramipril 5 mg. bid
- Phone call in a week. "Weak and dizzy". Seen at home. BP 110/70 > 90/50 standing. No CHF.
- No new lab or ECG abnormalities. Ramipril reduced to 2.5 mg. bid. Urged to continue metoprolol.
- Discussed her prognosis and advanced directives. She is willing to tolerate metoprolol symptoms to avoid hospital. No decision on CPR and intubation.

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**Rural  
Critical  
Care**

## Rural Management

- Use of treatment algorithm based on BP and exam.
- Early administration of 10 mm Hg. CPAP. First line
- Early high dose sublingual and IV nitroglycerin. First line
- Early consideration of SL captopril in specific settings. Second line.
- Delayed administration of furosemide in volume overload. Third line.

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**Rural  
Critical  
Care**

## Rural Management

- Avoidance of morphine
- Consider trial of volume replacement for hypotension
- Consider early referral if inotropes or vasoconstrictors are needed
- When diagnosis is in doubt, use of CPAP, nitroglycerin and salbutamol do not seem to impart increased risk
- Establish advanced directives to cover the next event.

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# Cardiogenic Pulmonary Edema

Rural  
Critical  
Care



END

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