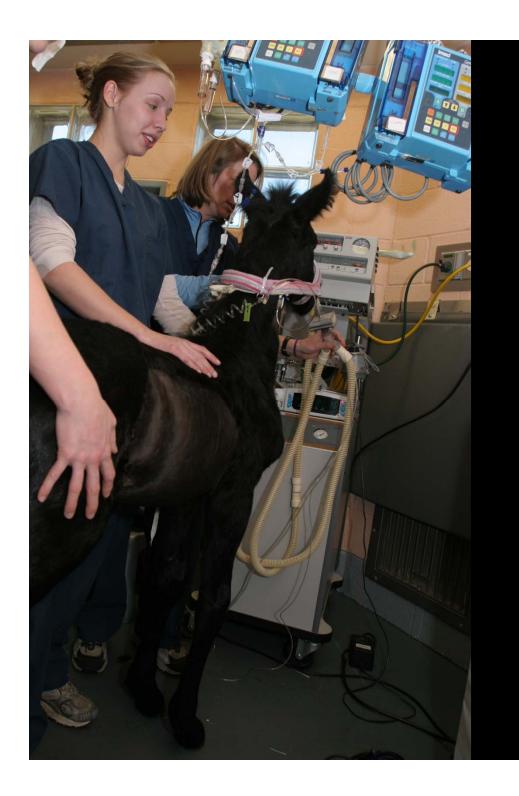
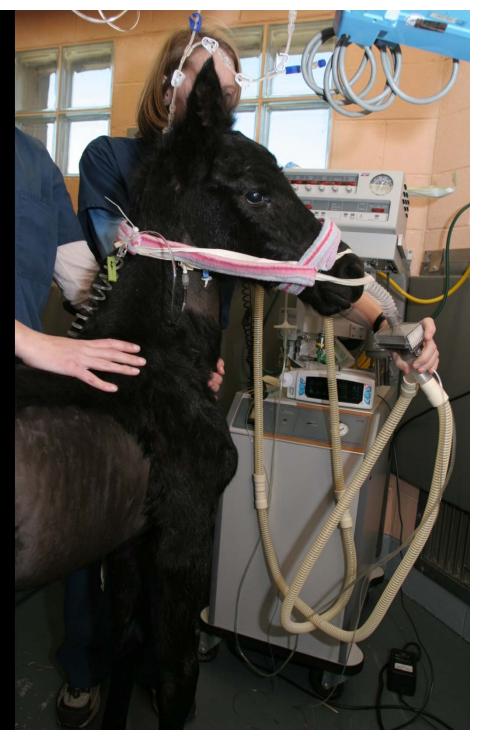
Mechanical Ventilation of the Neonatal Foal



Jon Palmer, VMD, DACVIM
New Bolton Center







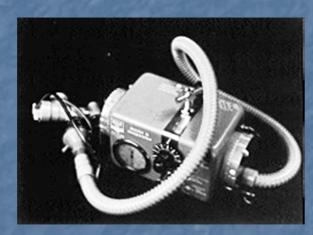
History of Pediatric Ventilation

- 10th Century BC Hebrew doctors
- 4th Century BC Hippocrates
- 1667 Hooke bellows inflate dog's lungs
- 1806 Chaussier
 - O₂ Rx, Intubation/ventilation premature/newborns
- 1845 1st ventilator manufacture
- 1887 Case series 50 children ventilated
- 1904 Negative pressure ventilator
- 1905 CPAP
- 1907 Positive pressure mechanical ventilator
- 1960-1970 Birth of neonatology
- 1963 First baby successfully ventilated



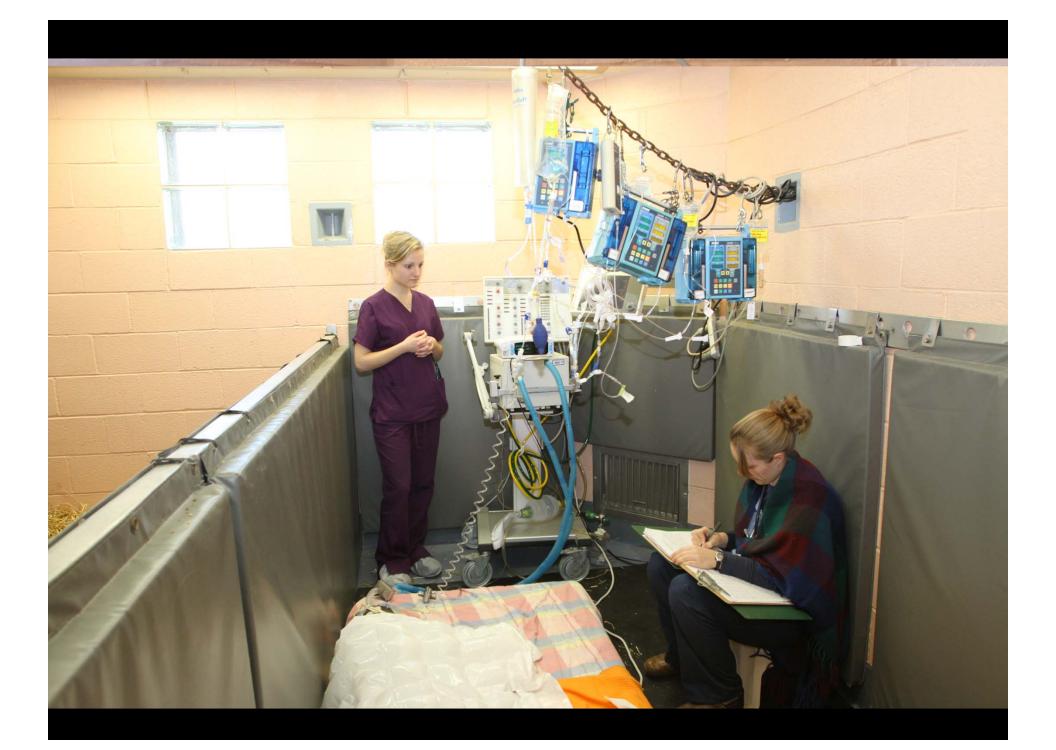
First Successfully Ventilated Infant 1963











Ventilation of NICU Patients

- Equine Neonatal Intensive Care Unit
 - First foals ventilated 35 years
 - Ventilating foals with secondary respiratory failure
 - Botulism or neonatal encephalopathy
 - 80% of such patients survive to discharged
 - Many become productive athletes
 - Most challenging cases
 - Viral pneumonia
 - ARDS
 - Sepsis MODS



Positive Pressure Ventilation Goals

- Pulmonary gas exchange
 - Support exchange
 - Allow manipulation V/Q matching
- Manipulate lung volume
 - Returning normal FRC
- Decrease work of breathing
 - Allow fatigued muscles to rest
 - Decrease O₂ and energy utilization
 - Redirect perfusion



Positive Pressure Ventilation Clinical Indications

- Neonatal Encephalopathy
- Weakness
- Persistent pulmonary hypertension
- Acute respiratory failure
 - ARDS
 - Infectious pneumonia
 - Non-infectious pneumonia
- Upper airway obstruction
- Septic shock
- Neuromuscular disorders



Goal of Ventilation

Provide respiratory support while therapies for underlying cause of the acute event are initiated and allow time for recovery



Case 1

- 50-day-old Morgan colt
- June 13
 - Normal in the morning
 - Evening found down in the field
 - Weak
- Rx
 - Intravenous fluids
 - Antibiotics
 - Tube fed milk
- June 14 6:00 a.m.
 - Respiratory distress
 - Cyanotic

Ventilation Case 1

- Admission Physical Exam
 - Weak, no eyelid tone
 - No tongue tone, weak tail tone
 - Shallow, rapid respiratory pattern
 - Mark nostril flare
- Therapy
 - Botulism antitoxin
 - Intravenous fluids
 - Intravenous ceftiofur sodium
 - Indwelling nasogastric tube
 - Ventilation



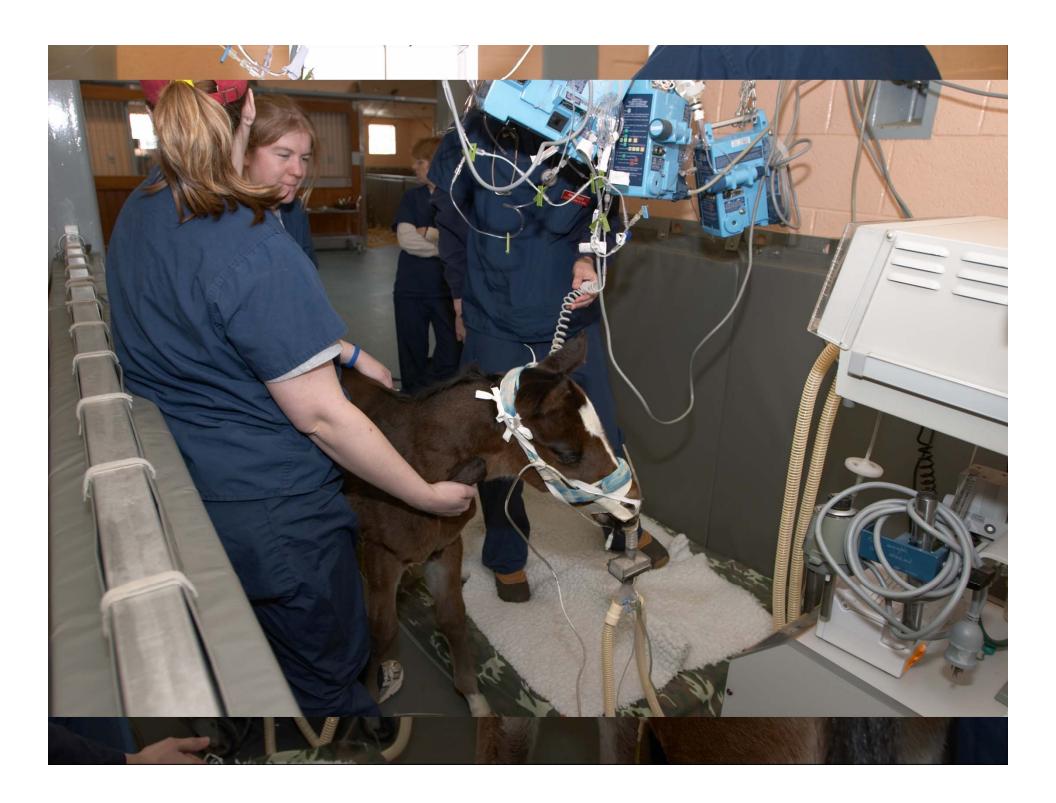
Case 1

	Adm	40 min	2 hr
рН	7.325	7.265	7.289
Pco ₂	56	68	70
Po ₂	40	229	243
SAT	64.5	99.7	99.7
HCO ₃	29.6	31.1	33.5
BE	+2.7	+2.6	+5.5
	RA	10 lpm	10 lpm



Ventilator Modes

- Continuous mandatory ventilation (CMV)
 - Volume controlled (VC-CMV)
 - Pressure controlled (PC-CMV)
- Intermittent mandatory ventilation (IMV)
 - Volume controlled (VC-IMV)
 - Pressure controlled (PC-IMV)
- Continuous Spontaneous Ventilation (CSV)
 - Pressure support ventilation (PSV)
 - Continuous positive airway pressure (CPAP)
- Proprietary modes



Intermittent Mandatory Ventilation (IMV)

- Combination of spontaneous and CMV
- Mechanical breath is synchronized with spontaneous breaths
- Mandatory set rate
- Spontaneous efforts
 - Can trip mandatory breaths

Intermittent Mandatory Ventilation (IMV)

- If spontaneous breathing occurs faster
 - Extra breaths
 - Warmed, Humidified, Oxygen-enriched gas
 - No preset volume or pressure
- IMV is better tolerated than CMV
 - Extra breaths completely patient controlled
 - Timing, depth, duration
 - Pressure Support Ventilation (PSV)
 - Preset breaths
 - Unforgiving



Pressure Support Ventilation (PSV)

- Partial ventilatory support
 - Assist flow-cycled mode
 - Support spontaneous breathing effort
 - Providing satisfactory oxygenation
 - Decreased the work of breathing
- Breathing controlled by foal
 - Inspiratory time
 - Inspiratory flow rate
 - Tidal volume
- Reduced work of breathing
- "Off-switch" value
 - 25% of the peak flow
 - Fixed low inspiratory flow rate



Pressure Support Ventilation Detrimental

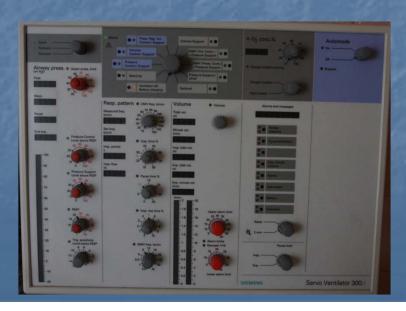
- Dyspneic despite ventilation
 - Risk of alveolar collapse
- High initial flow rate
 - Early termination of PS
 - Not provide sufficient minute ventilation
- Low initial flow rate
 - Late termination
 - Deliver large TV
- Ventilator-patient dyssynchrony

Pressure Support Ventilation New Ventilators

- Pressure targeted, time-cycled breath
 - Control inspiratory time
- Control of the pressure slope
 - Rapid peak resulting in a higher peak flow and thus a shorter inspiratory time
 - Slow peak initial flow resulting in a longer inspiratory time
- Allow adjustment of the "off-switch"
 - Flow criteria

Pressure Support Ventilation New Ventilators

- Volume Support Ventilation
 - Pressure support
 - Target volume
 - Breath to breath changes in parameters
 - Adjust Pressure Support to a volume goal





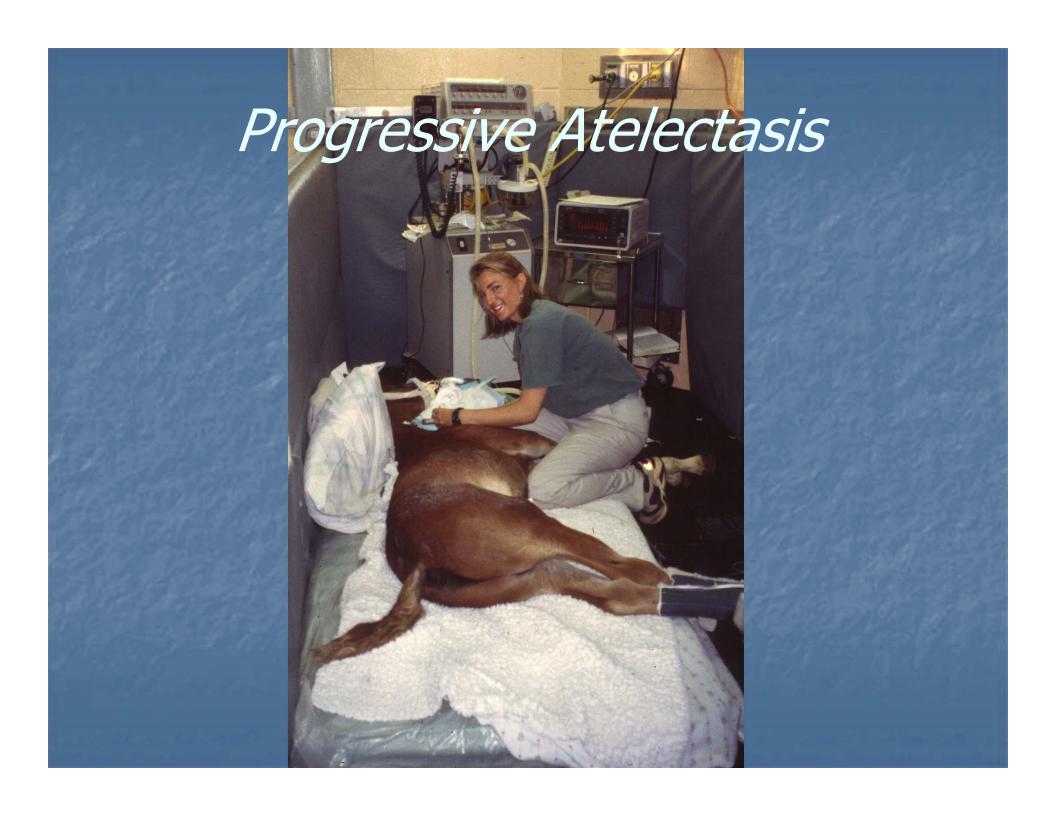
Positive End-Expiratory Pressure (PEEP) Continuous Positive Airway Pressure (CPAP)

PEEP

- Positive pressure between ventilator breaths
- CPAP
 - Positive pressure throughout spontaneous respiration
- Physiologic effect
 - Increase functional residual capacity (FRC)
 - Decreases intrapulmonary shunting
 - Increase V/Q mismatch

PEEP/CPAP

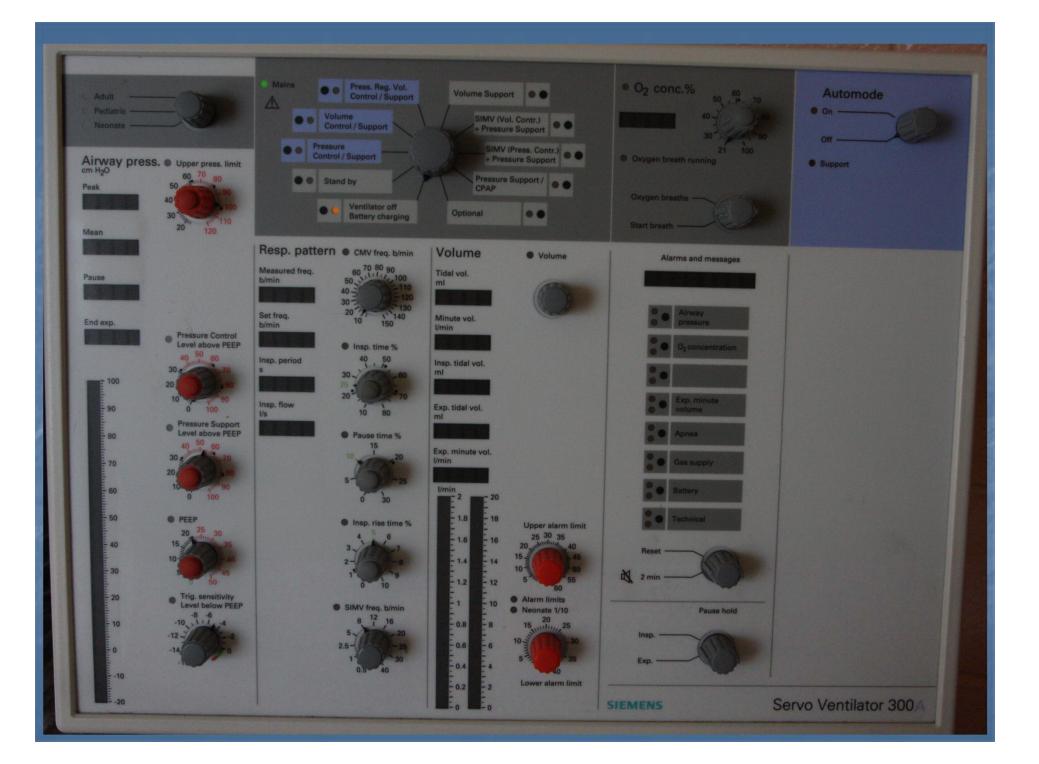
- Ideal FRC best compliance
- Ideal FRC least airway resistance
 - Less atelectasis
- Cardiovascular effects
 - Excessive PEEP
 - Decrease cardiac return
 - Increase pulmonary Resistance
 - Depends on the lung compliance
 - Low compliance less transmitted to vessels
 - Hypovolemia increase negative effect
- V/Q matching



PEEP

- Full recruitment
 - Requires 15 to 20 minutes
 - PEEP does not recruit but stabilizes lung
 - Break in circuit begin again
- Optimal PEEP
 - Maximum improvement pulmonary function
 - Minimal hemodynamic compromise
 - Inflection points on PV curves
 - PEEP/CPAP grid
 - Pao₂
 - Static Compliance
- Optimal PEEP is a balance
 - Holding open recruitable alveoli diseased regions
 - Not overdistending alveoli healthier lung





Fio₂

- Dictate by
 - Pre-ventilation Pao₂
 - Response to INO₂
- Usually 0.3-0.5

TV

- Depends on lung pathology
- Goal maintain low airway pressures
- Usually 6 10 ml/kg
- Species differences stacking breaths

Respiratory rate

- Often set by patient
- Machine rate minimal rate
- Set with TV to achieve a minute volume (Paco2)
- Usually 20 30 and adjusted with ETCO2
- Target pH not Paco2
 - Permissive hypercapnia vs appropriate hypercapnia



- Peak Flow (insp time; insp rise time)
 - Determines inspiratory time of machine breath
 - Setting depends on
 - Pulmonary mechanics
 - Airway resistance
 - Time constants
 - Airway pressure gradients
 - No clear formula
 - Initially set
 - Inspiratory time is similar to unventilated patient
 - I/E ratio of approximately 1:2 (1/3 resp cycle)
 - Dynamically adjusted
 - Prevent negative airway pressures
 - Improperly set peak flow
 - Source of patient-ventilator dyssynchrony

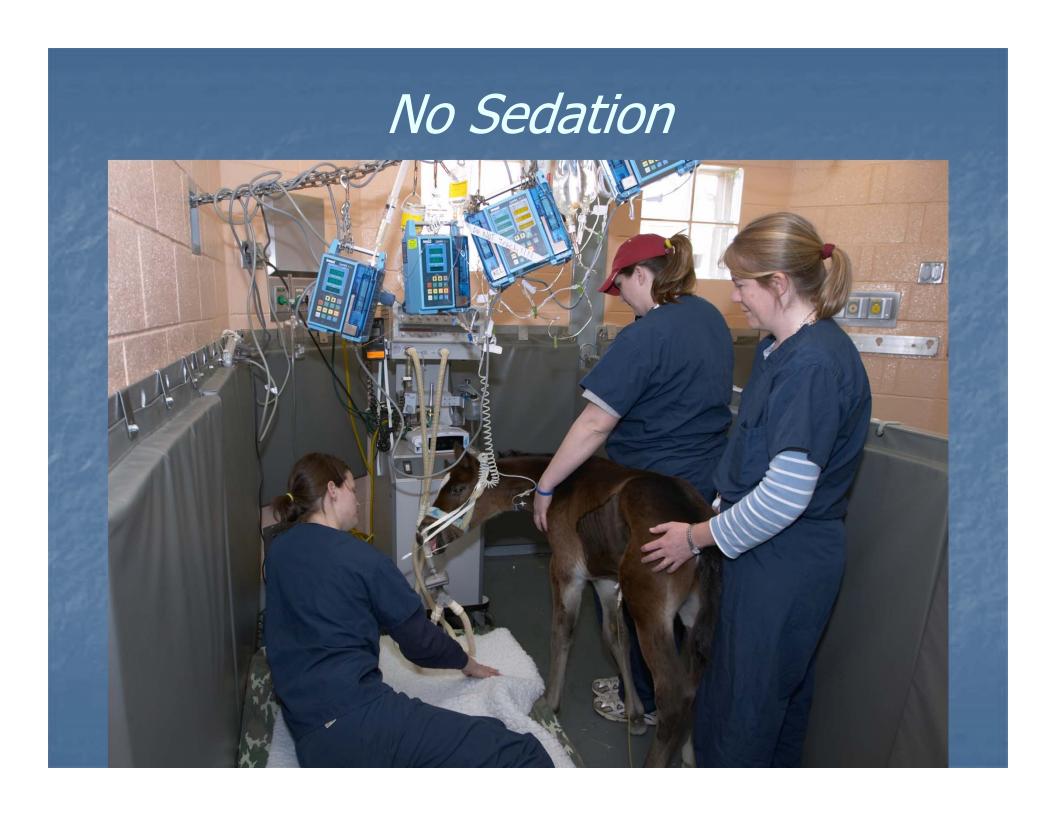
- Inspiratory pause
 - Depends on airway resistance
- Trigger sensitivity
 - Pressure based or flow based
 - Flow based smoother transition
 - Pressure 2-3 cm H₂O
 - Non-respiratory triggering
 - High pressure used in weaning

PEEP/CPAP

- Usually $4 9 \text{ cm H}_2\text{O}$
- Initially 4 − 5 cm H₂O
- Once the foal is stable adjust by aid of
 - Flow loops
 - Compliance grid
 - Pao₂ grid



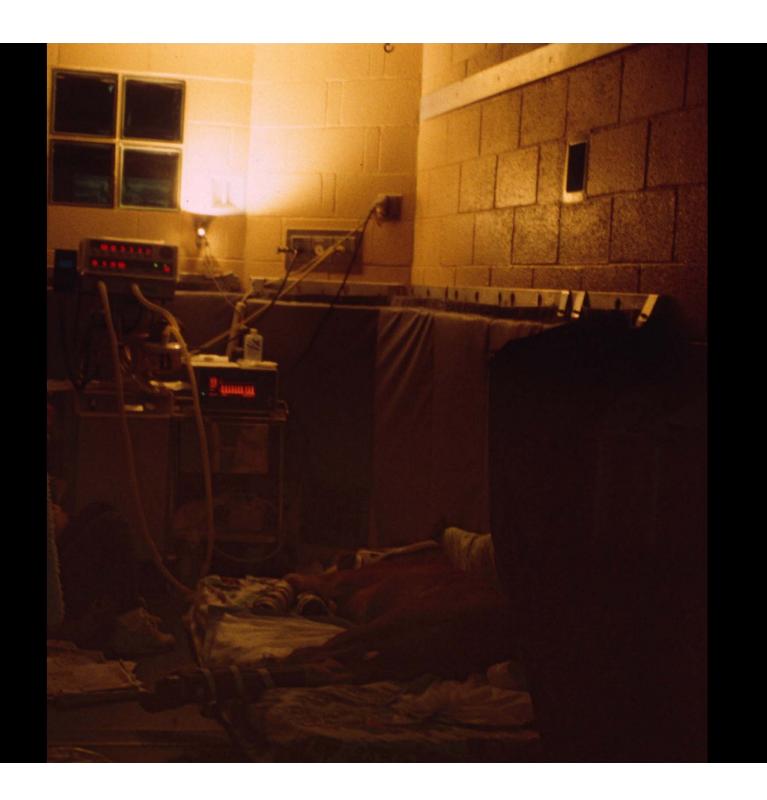
- Pressure Support
 - Level dependent on
 - Resistance and compliance of ventilator
 - Airway resistance
 - Lung compliance
 - Inspiratory effort
 - Absence of lung disease 8 − 12 cmH₂O
 - Low compliance as high as 20 25 cm H2O
 - Higher PS helpful in patient-ventilator dyssynchrony
 - When inspiratory effort exceeds rate of gas delivery



Case 1 Ventilator Set Up

- Goals
 - Decrease work of breathing
 - Maintain FRC
- Mode: Pressure Support with CPAP
 - PS initially set at 9
 - Normal lungs
 - CPAP initially set at 4
 - Normal lungs
- Parameters set by foal
 - Tidal Volume = 5.6 6.2 ml/kg (7 ml/kg)
 - RR 32
 - \blacksquare PIP = 18-20 mmH₂O

рН	7 hr 7.393	HD 2 7.385	HD 2 7.396	HD 7 7.414	Cas	se 1
Pco ₂	53	51	51	48	mode	PS
Po ₂	97	74	127	114	mode	
SAT	96.7	92.8	98.4	98.4	TV	550-680
Cont		17	17.4	17.1	RR	32 – 26
HCO ₃	32	31	31	31	PIP	20 – 18
BE	+6.5	+5.2	+6.0	+6.0		
FIO ₂	0.3	0.3	0.4	0.3	P _{Plat}	24 – 18
PEEP	4	4	5	5		
ETCO ₂	53	48	49	48		
PS	9	11	11	11		



Ventilator Settings

- All ventilator settings
 - Adjusted dynamically
 - Success dependent on tailoring to the individual
 - Monitor
 - Pulmonary mechanics
 - ETCO₂
 - Airway pressures
 - Clinical status
 - ABG determinations





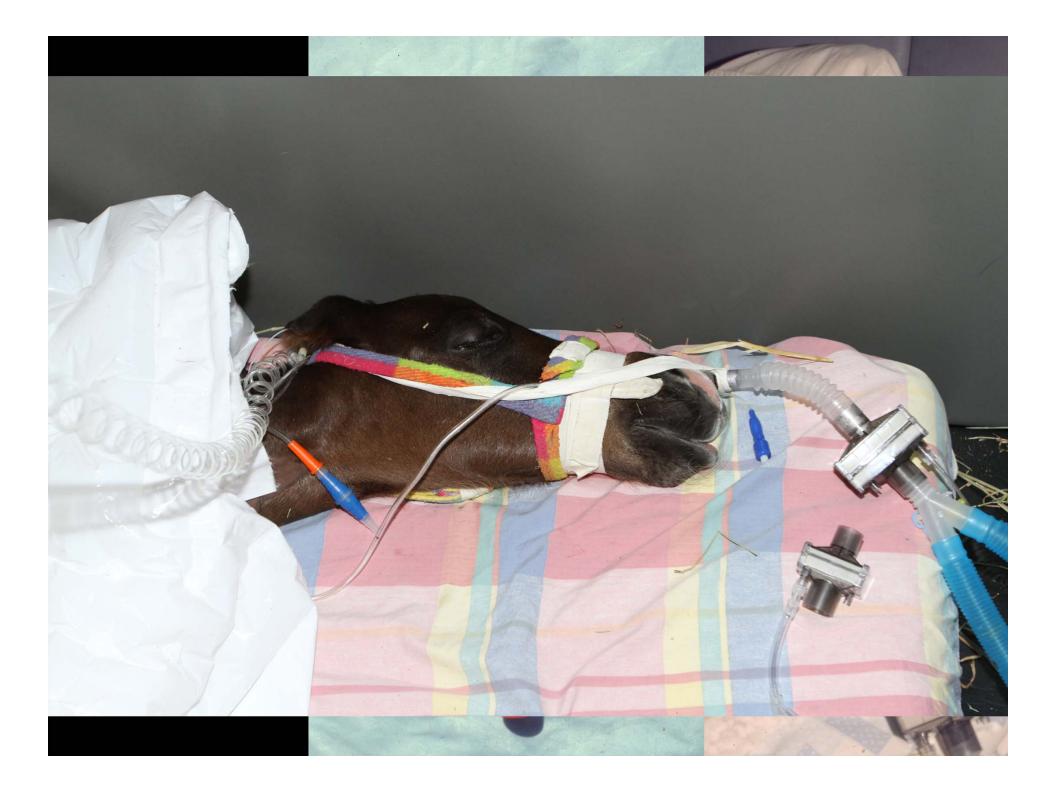
Preconditioning Ventilator Gases

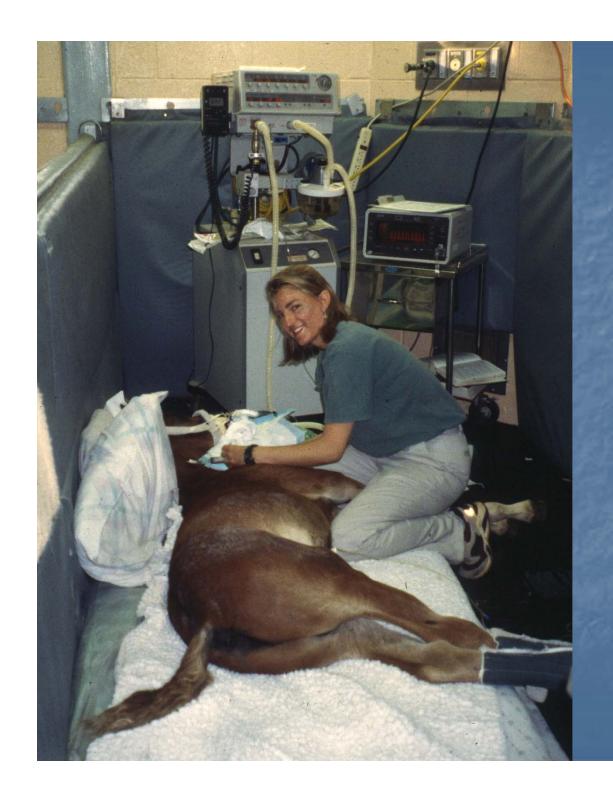
- Heat and moisture must be added
 - Drying and cooling causes mucosal injury
 - Response of the trachea
 - Proliferation of goblet cells
 - Production of discharge
 - Becomes desiccated, tenacious
 - Obstruct airway/endotracheal tube
- Active humidifiers
 - External water source
 - Electrical powered heating elements
 - Intratracheal temperature > 35C
 - Water content > 40 mg/L



Preconditioning Ventilator Gases

- Passive Humidifiers HME filters
 - Trap heat and moisture from exhaled breath
 - Effective with average foal
 - Antimicrobial filter
- Limitations of HME filters
 - Large foals (>70 kg)
 - Large minute volumes
 - Add a cold active humidifier
 - Hypothermic patients
 - Airway discharge
 - Obstruct the filter dangerous situation





Cold Cascade Humidifier in line

Monitoring During Ventilation

- Arterial blood gas (ABG)
- Capnography
- FIO₂
- Tidal Volume/Minute Volume
- Airway pressure
- Compliance/Resistance
- Endotracheal tube





Capnography

- Endotracheal cuff integrity
- Ventilator leaks
- ETCO₂ depends on
 - PaCO₂
 - Cardiac output
 - Alveolar dead space ventilation
 - Pulmonary perfusion
 - Airway time constants (Rz)
 - CO2 production (metabolic rate)
 - Bicarbonate therapy
- Changing V/Q relations
- Other valuable information



Case 1 Problems

- $ETCO_2 = 0$
- Long inspiration
- Flow meter shows a dramatic ↓TV
- Common problem
 - Have foal sitter monitor cuff
 - Often slow leak
 - Bad valve use hemostat or clamp
 - Leaking cuff replace endotracheal tube



HD	9	HD	9

pH 7.304 7.443

Pco₂ 76 52

Po₂ 115 111

SAT 97.5 98

Cont 16.0 16.3

HCO₃ 38 36

BE +9.6 +10.8

FIO₂ 0.35 0.35

ETCO₂ 72 52

Mode PS PS

PS 20 12





Weaning from Ventilation

- When?
 - Consider as soon as begin ventilation
 - Goal: keep ventilation period short
- Indications
 - Cardiovascular stability
 - Metabolic stability
 - Sepsis Controlled
 - Original problem has resolved/improved
- No reliable predictor foal is ready



Case 1 Weaning

- 1st weaning challenge HD 6
 - Off the ventilator
 - Good breathing efforts
 - ETCO2 increased
 - Foal became cyanotic (on INO2)
 - Aerophagia increased abdominal size
 - 10 minute trial
- 2nd weaning trial HD 8
 - After 22 minutes Paco₂ 48 → 60

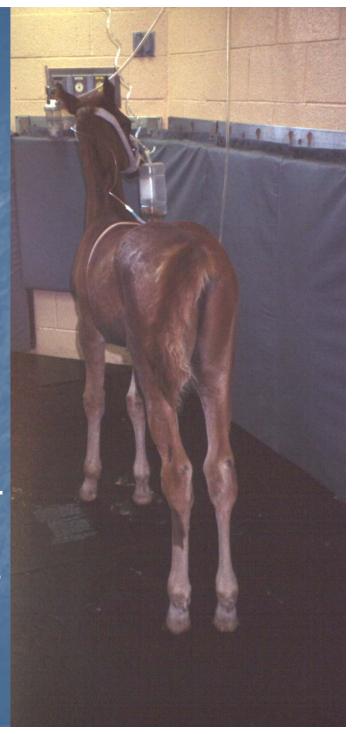


3rd Weaning Attempt

	HD 10	3 pm	6 pm	3 am	6 am	HD 14
рН	7.443	7.365	7.394	7.338	7.031	7.420
Pco ₂	52	55	50	64	129	49
Po ₂	111	72	184	79	49	120
SAT	98	91	99	92	60	98
HCO ₃	36	32	31	34	34	32
BE	+10.8	+5.4	+5.5	+6.7	-1.3	+7.0
FIO ₂	0.35	8 lpm	10 lpm	8 lpm	0.5	4 lpm
ETCO ₂	52				84	
Mode	PS	off	off	off	PS	off

Outcome

- Successful weaning HD 14
- Standing day 15
- Dysphagia
 - HD 22 able to swallow water
 - HD 23 able to swallow solids
- Hospital Discharge HD 30





Case 2 Clinical Problems

- Septic Shock
- Bacteremia/Sepsis
 - Pantoea agglomerans
- Neonatal Encephalopathy
 - Somnolent, facial nerve paresis
 - Seizure-like activity
- Neonatal Enteropathy
 - Fetal diarrhea, dysmotility
- Neonatal Nephropathy
- Other problems
 - Urachitis, hepatomegaly
 - Linear dermal necrosis, patent urachus
 - Angular limb deformity



Adm 1 hr

pH 7.339 7.349

Pco₂ 60 58

Po₂ 44 144

SAT 77 100

Cont 13 15

HCO₃ 32 32

BE +5.6 +5.9

INO₂ RA 10 lpm



Neonatal Encephalopathy

- 4 hours
 - Respiratory effort decreased
 - Apneustic breathing (breath holding)



	Adm	1 hr	4 hr	5 hr
рН	7.339	7.349	7.284	7.354
Pco ₂	60	58	82	62
Po ₂	44	144	80	250
SAT	77%	100	97	100
Cont	13.3	14.9	15.4	16.4
HCO ₃	32	32	34	35
BE	+5.6	+5.9	+10.5	+8.2
INO ₂	RA	10 lpm	10 lpm	15 lpm



Caffeine for Central Hypoventilation

- Naturally occurring methylxanthine
 - Theophylline, aminophylline
- Mechanism of action
 - Mild, direct general CNS stimulant
 - Increases respiratory center output
 - Increases chemoreceptor sensitivity to CO₂
 - Cardiac stimulate increases cardiac output
 - Increases renal blood flow
 - Mild diuretic

Caffeine for Central Hypoventilation

- Pharmacokinetics
 - Well absorbed from the GI tract



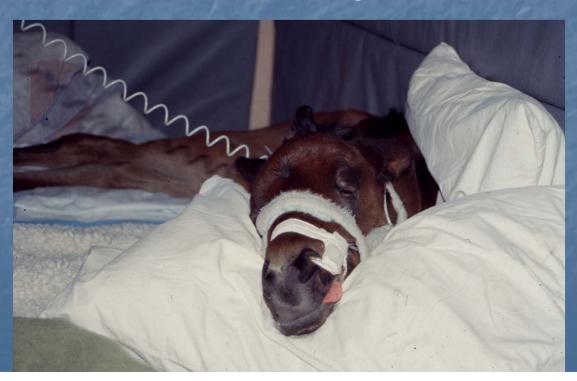
- Good levels in foals given per rectum
- Metabolized in the liver, excreted in urine
- Plasma half-life is long in neonates (40 230 hr)
- Dosage caffeine base PO or PR
 - Loading 10 mg/kg may repeat 2-3X
 - (Maintenance 2.5 mg/kg SID)
 - 2 mg caffeine citrate = 1 mg caffeine base

Caffeine for Central Hypoventilation

- Response monitored through ABG
- High therapeutic index
 - Effective blood levels 5-20 μg/ml
 - Toxic levels > $40 50 \mu g/ml$ in humans
 - Safer than aminophylline
- Adverse effects
 - Hyperactive more difficult to manage
 - Tachycardia have not seen

Case 2 Neonatal Encephalopathy

- 10 hours
 - Apneic respiratory pattern
 - 40 second apneic period
 - Cluster breathing in-between



	Adm	1 hr	4 hr	5 hr	10 hr	12 hr
рН	7.339	7.349	7.284	7.354	7.276	7.451
Pco ₂	60	58	82	62	85	45
Po ₂	44	144	80	250	105	141
SAT	77%	100	97	100	100	100
Cont	13.3	14.9	15.4	16.4	16.1	15.5
HCO ₃	32	32	34	35	40	32
BE	+5.6	+5.9	+10.5	+8.2	+11	+7.4
INO ₂	RA	10 lpm	10 lpm	15 lpm	10 lpm	10 lpm

Case 2 Neonatal Encephalopathy

- 12 hours
 - Periods of somnolence and nonresponsiveness
 - Apneic respiratory pattern with cluster breathing
 - Facial nerve paresis
 - Right ear lower and slower to respond
 - Ears are not synchronized
- 21 hours
 - Seizure-like activity
 - Opisthotonus
 - Tonic/Clonic marching activity
 - Treated with intravenous phenobarbital

27 hr 29 hr

pH 7.313 7.269

Pco₂ 75 85

Po₂ 118 119

SAT 100 100

Cont 14.5 14.7

HCO₃ 38 39

BE +10.4 +10.3

INO₂ 10 lpm 10 lpm





Ventilate

- Goals
 - Increase alveolar ventilation
 - Maintain FRC
- Mode: IMV/PS with PEEP/CPAP
 - TV = 460 ml (8.5 ml/kg)
 - PIP = $18 \text{ cmH}_2\text{O}$
 - PS initially set at 9 cmH₂O
 - Normal lungs
 - PEEP/CPAP = $4 \text{ cmH}_2\text{O}$
 - Normal lungs
 - Peak flow = 60 lpm
 - RR = 24
 - Foal's rate 33
 - $FIO_2 = 0.4$



	27 hr	29 hr	31 hr	36 hr		
рН	7.313	7.269	7.353	7.428	mode	SIMV
Pco ₂	75	85	67	50	TV	460 ml
Po ₂	118	119	96	164	PF	60
SAT	100	100	99	100	RR	36
Cont	14.5	14.7	13.9	14.4	PEEP	4
HCO ₃	38	39	38	33	PS	9
BE	+10.4	+10.3	+10.9	+8.3	P _{peak}	28
	10 lpm	10 lpm	0.4	0.5	P _{plat}	18
ETCO ₂			54	46		
Cont HCO ₃ BE FIMO ₂	14.5 38 +10.4	14.7 39 +10.3	13.9 38 +10.9 0.4	14.4 33 +8.3 0.5	PEEP PS P _{peak}	4 9 28

Weaning

Began asking when? within 12 hours

After 21 hours – PS trial

	48 hr	52 hr	57 HR	60 hr	48 hr	52 hr
рН	7.447	7.473	7.392	耐力性	SIMV	PS/CPAP
Pco ₂	45	40	54	50	460 ml	520-75
Po ₂	242	91	252	95	60	
SAT	100	100	100	B9. 7	36	22
Cont	14.5	14.1	14.3	REED	4	4
HCO ₃	31	29	33	B2	9	6
BE	+7.2	+6.0	+7.7	P-Z-4	21	
	0.5	0.35	10 lpm	B _p lam	16	
ETCO ₂	42	38				

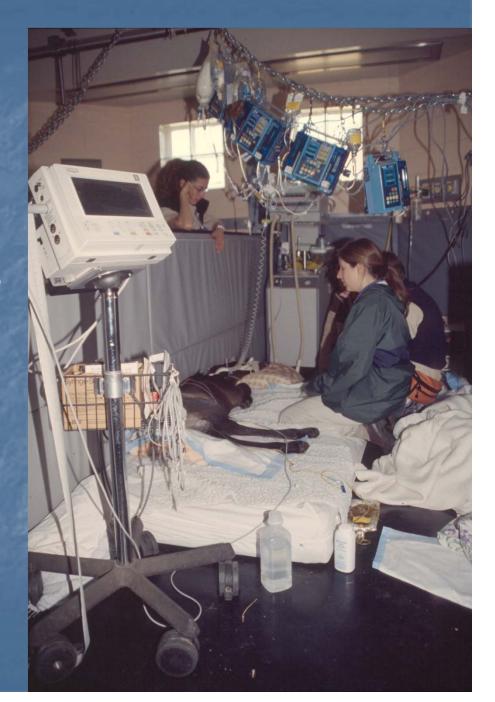




- Admission 8 hr old
- Septic shock Streptococcus bacteremia
 - Minimally responsive
 - Hypothermic (36.8 C)
 - Hypotonia
 - Pupils were pinpoint, iris edema
 - Inappropriately low heart rate
 - Cold legs, and poor peripheral perfusion
- Admission lab work
 - Leukopenic (WBC = 528 cells/ul)
 - Hypoglycemia required 20 mg/kg/min to get > LO

Case 3 Therapy

- Intranasal oxygen
- Shock doses of fluids
- Plasma
- Antimicrobials
- Ventilation
- Dobutamine
- Norepinephrine



Benefits of Mechanical Ventilation

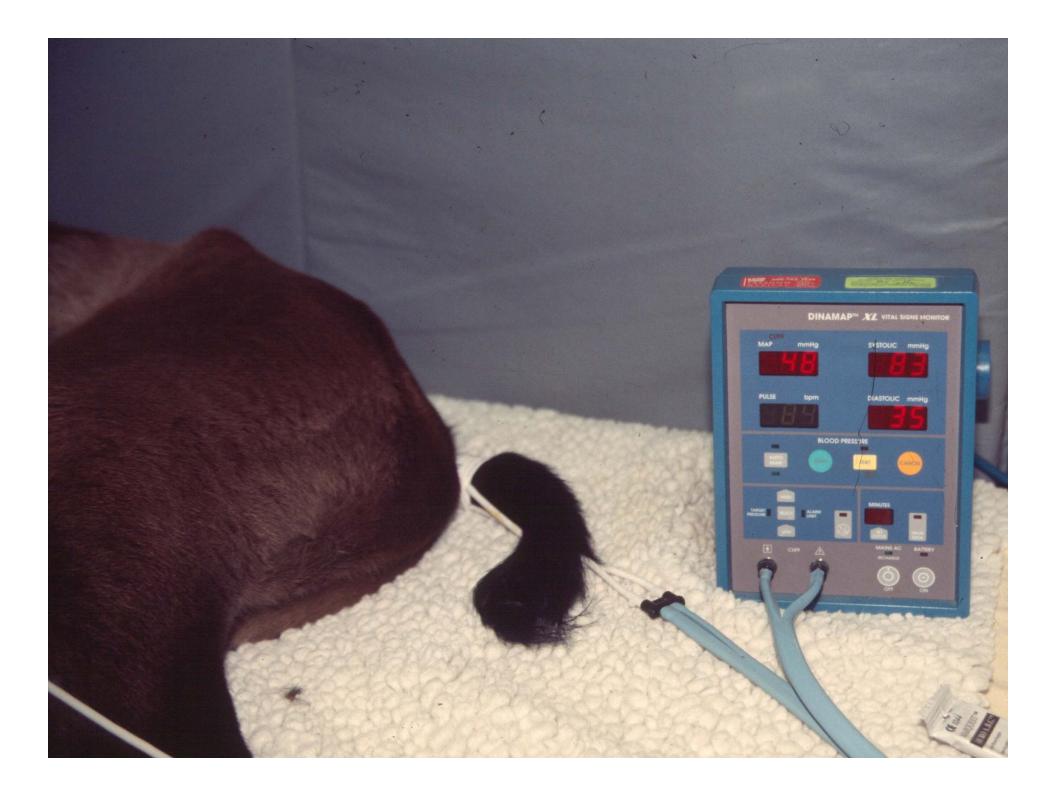
- Traditional
 - Improve gas exchange
 - Improve V/Q matching
 - Decrease shunt fraction
- Benefit of decreasing work of breathing
 - Normal quiet breathing
 - Inhalation active process
 - Requires energy
 - 3% 5% O₂ consumed
 - Exhalation is a passive
 - Requires no energy, O₂

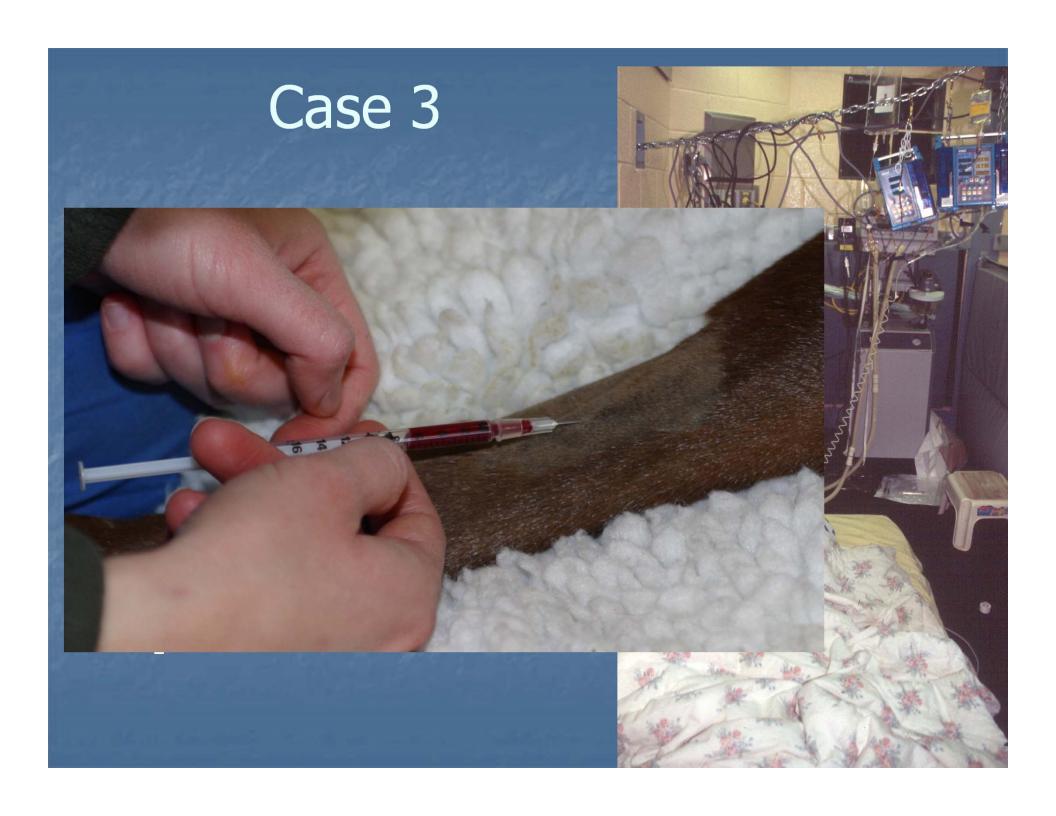
Benefits of Mechanical Ventilation

- Pulmonary failure 2ndary to septic shock
 - Respiratory distress
 - Work of breathing
 - O₂ required up to 50% of available O₂
 - Diverts perfusion resources
 - Accessory muscles recruited
- Relieving work of breathing
 - Redistribution of O₂
 - Redistribution of perfusion
 - Sparing energy resources
- Ventilation foals with septic shock
 - Improve perfusion, increase BP
 - Improved glucose balance









Ventilate

- Goals
 - Decrease the work of breathing
 - Correct pulmonary hypertension
 - Maintain FRC
- Initial settings
 - Mode: PS with CPAP
 - PS initially set at 18 cmH₂O
 - Based on easy of breathing and resulting TV
 - PEEP/CPAP = $8 \text{ cmH}_2\text{O}$
 - $FIO_2 = 1.0$
- Set by foal
 - TV = 180 ml (7 ml/kg)
 - PIP = 32 cm H_2O
 - RR = 48



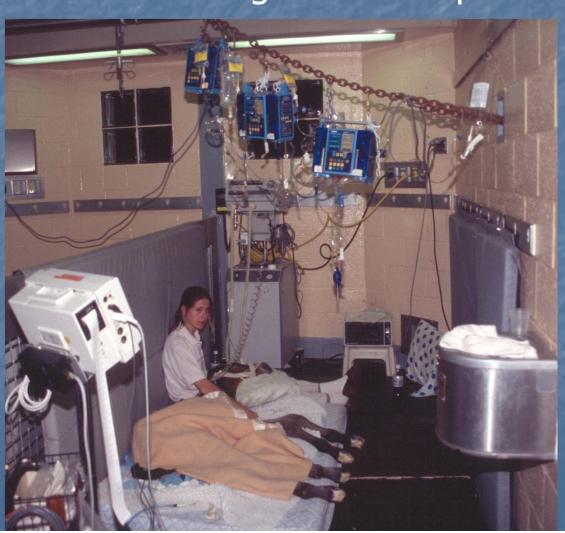
	Adm	1 hr	1.5 hr	Mode	PS
рН	7.220	7.072	7.073	TV	180
Pco ₂	65	70	62	RR	48
Po ₂	22	20	248	PEEP	8
SAT	27.7	21.2	99.6	PS	18
Cont	5.1	3.4	14.9	P _{peak}	32
HCO ₃	27	20	18		
BE	-1.7	-9.6	-11.3	NO	20 ppm
FIO ₂	0.21	1.0	1.0		

	3.75 hr	4 hr	5 hr	6 hr	Mode	PS
pН	7.000	7.062	7.089	7.061	TV	220
Pco ₂	96	92	84	98	RR	30
Po ₂	73	25	146	96	PEEP	10
SAT	86.3	29.4	97.8	92.3	PS	20
Cont	11.4	4.1	14.1	13.2	P _{peak}	32
HCO ₃	24	26	26	28		
BE	-7.5	- 4.6	- 4.6	- 3.1	NO	200 pppm
FIO ₂	1.0	1.0	1.0	0.50		

Case 3 ADV

	1 hr	1.5 hr	3.75 hr	4 hr	5 hr	6 hr
Pco ₂	70	62	96	92	84	98
ETCO ₂	34	34-54	46-64	33	43-56	25-33
ADV	51%	13-45%	33-52%	64%	33-49%	66-75%

Multifocal necrotizing interstitial pneumonia



- Sequela to many cases of ALI
- Increased pulmonary vascular resistance
 - Inflammatory mediators
 - Severe hypoxemia

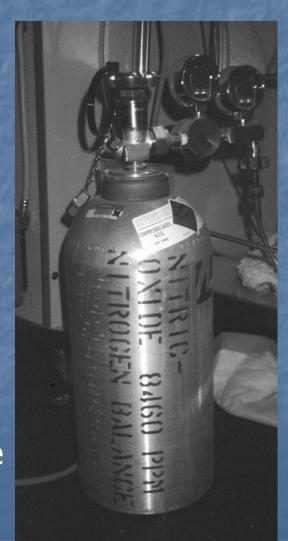
- Neonate
 - Right to left shunting
 - Foramen ovale
 - Ductus arteriosus
 - Reversion to fetal circulation
 - Adaptive advantage
 - Achieve adequate systemic cardiac output
 - Neonate's unique ability
 - Exist in a hypoxemic state
 - Regain CO by shunting
 - Survive pulmonary hypertension without systemic ischemia

- 1.0 F_{IO2} trial
 - Pao₂ < 100 torr after 15-20 min</p>
 - Shunt fraction > 30%
 - Cause of the hypoxemia extrapulmonary
 - Large cardiac shunt
 - PPHN

- Pulmonary hypertension
 - Failure to make the birth transition PPHN
 - Imbalance of vasodilators and vasoconstrictors
 - Nitric oxide and endothelin
 - Regression to fetal circulation PPHN
 - Perinatal hypoxemia
 - Cytokine showers
 - Secondary
 - Pulmonary disease
 - Septic shock
 - ALI

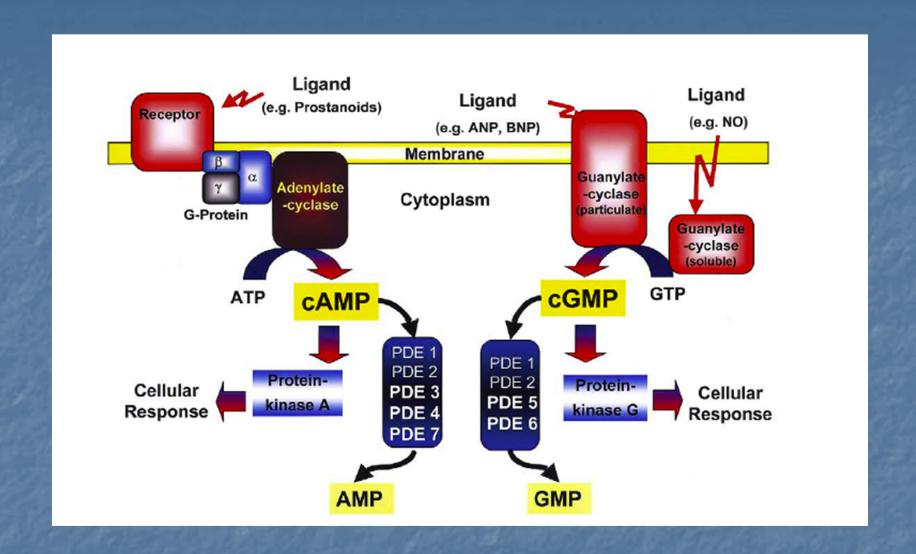
Pulmonary Hypertension Therapy

- Traditional therapy
 - Maximize exposure to O₂
 - Ventilation with 100% oxygen
 - Alkalinize arterial pH
 - Mild hyperventilation
 - Treatment with bases
 - Maintain systemic blood pressure
 - Counterbalance the pulmonary pressure
 - ALI will counteract these approaches
- Inhaled NO therapy
 - 5 to 20 ppm
 - Immediate effect
 - Significant pulmonary toxicity possible
 - Free radicals



Pulmonary Hypertension Therapy

- NO Mechanism of action
 - Vasodilation
 - Increasing cGMP levels
 - Relaxation of the pulmonary vasculature
- Type V phosphodiesterase inhibitors
 - Selectively prevent cGMP destruction
 - Endogenous nitric oxide
 - Pulses of exogenous nitric oxide
 - Currently available
 - Sildenafil
 - Vardenafil
 - Tadalafil



From: Ghofrani HA, et. al. J Am Coll Cardio 44(7):1488-96, 2004

