CONTROL OF RESPIRATION

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MEDICINE
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CONTROL OF RESPIRATION

- INTRODUCTION
- COMPONENTS OF RESP CONTROL
- SENSORS
- RESPIRATORY CENTERS
- RESPONSE TO VARIOUS STIMULI
- SPECIAL SITUATIONS
INTRODUCTION

• VENTILATION IS CONSTANTLY ADJUSTED TO MAINTAIN THE HOMEOSTASIS OF BLD GASES AND ARTERIAL pH

• VARIATIONS OF PaO2 <3-4 mm Hg AND EVEN LESS FOR PaCO2

• TO EXPEND MINIMAL ENERGY IN THE WORK OF BREATHING
SENSORS

• PERIPHERAL CHEMORECEPTORS
• CENTRAL CHEMORECEPTORS
• PULMONARY RECEPTORS
• CHEST WALL AND MUSCLE RECEPTORS
PERIPHERAL CHEMORECEPTORS

- CAROTID BODIES
- AORTIC BODIES (SIGNIFICANCE ?)
- BIFURCATION OF COMMON CAROTID
- BLOOD SUPPLY-EXTERNAL CAROTID
- VENOUS DRAIN-INT JUGULAR
- NERVE SUPPLY- IX NERVE
STRUCTURE

• 3 TYPES
  – TYPE I - GLOMUS CELLS
  – TYPE II - SUSTENTACULAR / SHEATH CELLS
  – SENSORY NERVE CELLS
CAROTID BODY

• RICH BLOOD SUPPLY (2L/100G/MIN)
• UTILIZES DISSOLVED O2 FROM BLOOD UNLIKE OTHER TISSUES
• SENSES CHANGES IN PaO2
• HENCE NOT AFFECTED BY CONDITIONS IN WHICH PaO2 (N)
  – MILD ANEMIA
  – CO POISONING
CHEMOTRANSDUCTION

- O2 binds cell membrand K+ channel
- Closing of K+ channel
- Depolarization of the cell
- Opening of Ca++ channel
- Neurotransmitter release
- Depolarizes the carotid sinus nerve
- Stimulates the medulla (DRG)
CHEMORECEPTORS

- RESPOND TO \( \text{PaO}_2 \) AND \( H^+ \) CONCENTRATION (pH), \( \text{PaCO}_2 \)
- 90% VENTILATORY RESPONSE TO HYPOXEMIA - CAROTID BODY
- 10% RESPONSE - FROM AORTIC BODIES
- VE INCREASED ↑ TIDAL VOLUME
CHEMORECEPTORS

• RESPONSE TO HYPERCAPNIA
  – 20-50% CAROTID BODIES
  – 50-80% CENTRAL CHEMORECEPTORS
EFFECT OF PaO2

- CHEMORECEPTORS CONTRIBUTES LITTLE TO EUPNEIC VENTILATION (10-15%)
- NO CHANGE CAROTID BODY ACTIVITY TILL PaO2 < 75mmHg
- VENTILATION MARKEDLY INCREASED WHEN PaO2 < 50mmHg
EFFECT OF Pa O2 ON CHEMORECEPTORS

![Graph showing the effect of arterial PO2 on maximum response percentage.](image)
 EFFECTS OF PACO2

• VENTILATION INCREASES IN LINEAR MANNER WITH PaCO2
• HYPOXEMIA INCREASES THE SLOPE OF VENTILATORY RESPONSE TO PaCO2
VENTILATORY RESPONSE TO ALV CO₂

Ventilation (L/min BTPS) vs. PACO₂ (mm Hg)
EFFECT OF PaO2

- **CO2 POTENTIATES** VENTILATORY RESPONSE TO HYPOXEMIA
- BOTH HYPOXEMIC AND HYPERCAPNIC RESPONSES DECREASE WITH AGEING AND EXERCISE TRAINING
VENTILATORY RESPONSE TO ALV O2

Control of Ventilation

Ventilation (L/min)

Alveolar P\textsubscript{CO\textsubscript{2}} (mm Hg)

Alveolar P\textsubscript{O\textsubscript{2}} (mm Hg)

Ventilation curves for different alveolar P\textsubscript{CO\textsubscript{2}} levels:
- 48.7 mm Hg
- 43.7 mm Hg
- 35.8 mm Hg
EFFECTS OF ↑ PaCO2

• **RAPID PHASE** - RAPID INCREASE IN VE WITHIN SECONDS DUE TO ↑ ACIDIFICATION OF CSF

• **SLOWER PHASE** - DUE TO BUILDUP OF H+ IONS IN MEDULLARY INTERSTITIUM

• **CHRONIC HYPERCAPNIA** - WEAKER EFFECT DUE TO RENAL RETENTION OF HCO3 WHICH REDUCES THE H+
EFFECT OF PaCO2 & pH ON VENTILATION
CLINICAL SIGNIFICANCE

- **BILATERAL CAROTID BODY RESECTION**
- **CAROTID ENDARTERECTOMY**
- REDUCES MIN VENTILATION (VE)
- RESTING PaCO2 \(\leq 2-4\) mm Hg
- ELIMINATES VENTILATORY RESPONSE TO HYPOXIA AT REST AND EXERCISE
- 30% DECREASE IN RESPONSE TO HYPERCAPNIA
CASE

- 69 Y FEMALE COPD, CVA (OLD)
- CAROTID ENDARTERECTOMY 1 YR
- ELECTIVE CE (R) DONE
- PREOP ABG ON R/A - 7.43/50/48/31
- DAY 3 EXTUBATED → O2 3L/MIN
- DAY 5: SOMNOLENT AND CONFUSED
- ABG - 7.28/62/69/31
- BiPAP INITIATED → IMPROVED
- ABG - 7.38/72/54/36
CO2 NARCOSIS

COPD WITH HYPERCAPNIA & WORSENING RESP ACIDOSIS FOLL OXYGEN THERAPY

– LOSS OF HYPOXIC DRIVE
– WORSENING V/Q MISMATCH
  ↑ PHYSIOLOGIC DEAD SPACE
– ↓ CO2 CARRYING CAPACITY AS OXYGENATION OF Hb IMPROVES
  (HALDANE EFFECT)
RECEPTORS

• AIRWAY RECEPTORS
  – SLOWLY ADAPTING RECEPTORS (AIRWAY SMOOTH MSL)
  – RAPIDLY ADAPTING RECEPTORS (AIRWAY EPITHELIUM CELLS)
  – SUPPLIED BY VAGUS AND MYELINATED NERVE FIBRES
SLOWLY ADAPTING RECEPTORS

- HERING BRUER INFLATION REFLEX -
  ↑ EXP TIME AND ↓ RESP RATE WITH LUNG INFLATION.
- ACTIVE ONLY IF TV>3L, PREVENTS OVERINFLATION
- PROLONGS INSP IN CONDITIONS OF AIRWAY OBUSRACTN ALLOWING HIGHER TV TO BE ACHIEVED
RAPIDLY ADAPTING RECEPTORS

- IRRITANT RECEPTORS (COUGH)
- CARINA AND PRINCIPAL BRONCHI
- NOXIOUS STIMULI - DUST, SMOKE
- CAUSES AUGMENTED BREATHS ‘SIGHS’ DURING (N) BREATHING TO PREVENT ATELECTASIS
- SENSATION OF DYSPNEA, CHEST TIGHTNESS, RAPID SHALLOW BREATHING IN ASTHMA
BRONCHIAL C RECEPTORS

- UNMYELINATED NERVE ENDINGS
- RESPONSIBLE FOR BRONCHOSPASM IN ASTHMA
- INCREASED TRACHEOBRONCHIAL SECRETIONS
- MEDIATORS - HISTAMINE, PROSTAGLANDINS, BRADYKININ
PULMONARY RECEPTORS

- **JUXTA CAPILLARY RECEPTORS**
  Located near capillary in ALV walls
- Responds to hyperinflation & mediators in pulm circulation
- Sensation of dyspnea in heart failure due to interstitial edema
J RECEPTORS

- PAINTAL ET AL (1970) PROPOSED J RECEPTORS FUNCTION TO LIMIT EXERCISE WHEN INTERSTITIAL PRESSURE INCREASES (J REFLEX)
- MECHANISM: INHIBITION OF RESP MOTOR NEURONS
PULM EFFECTS

• SAR- BRONCHODILATATION
  PREVENTS HYPER INFLATION
  (HERING BREUER REFLEX)

• RAR- BRONCHOCONSTRICTION
  TACHYPNEA

• J RECEPTORS
  BRONCHIAL RECEPTOR-
  BRONCHOCONSTRICTION
  AIRWAY SECRECTIONS
EFFECT OF VAGOTOMY

• EXPT ANIMAL STUDIES
• VAGOTOMY ABOLISHES INCREASED RESP RATE AND MIN VENT (VE) WITH ASTHMA
• RAPID SHALLOW BREATHING PATTERN IN RESP TO BRONCHOSPASM IS MEDIATED THROUGH VAGAL AFFERENTS
CHEST WALL RECEPTORS

- MECHANORECEPTORS - SENSE CHANGES IN LENGTH, TENSION AND MOVEMENT
- ASCENDING TRACTS IN ANTERIOR COLUMN OF SPINAL CORD TO RESPIRATORY CENTRE IN MEDULLA
MUSCLE SPINDLES

- SENSE CHANGES IN MSL LENGTH
- INTERCOSTALS > DIAPHRAGM
- REFLEX CONTRACTION OF MUSCLE IN RESPONSE TO STRETCH
- INCREASE VENTILATION IN EARLYSTAGES OF EXERCISE
GOLGI TENDON ORGANS

• SENSES CHANGES IN FORCE OF CONTRACTION OF MSL
• DIAPHRAGM > INTERCOSTALS
• HAVE INHIBITORY EFFECT ON INSPIRATION
JOINT PROPRIOCEPTORS

• SENSE DEGREE OF CHEST WALL MOV'T
• INFLUENCE THE LEVEL & TIMING OF RESP ACTIVITY
CLINICAL SIGNIFICANCE

• SENSATION OF DYSPNEA WHEN INCREASED RESP EFFORT DUE TO “LENGTH- TENSION INAPPROPRIATENESS” - LARGE PLEURAL EFFUSION

• REMOVAL OF FLUID RESTORES THE END EXP MSL FIBRE LENGTH RESTORES THE LENGTH TENSION RELATIONSHIP → RELIEF
CENTRAL CHEMORECEPTORS

• DENERVATION OF PERIPHERAL CHEMORECEPTORS - VENTILATORY RESPONSE TO CO2 PERSISTED

• LOCATED CLOSE TO VENTROLATERAL SURFACE OF MEDULLA

• SENSITIVE TO CHANGES IN H+ CONC IN CSF & MEDULLARY INTERSTITIAL FLUID
CENTRAL CHEMORECEPTORS

- **ROSTRAL** - Lateral to pyramids medial to 7th and 10th nerves
- **CAUDAL** - Lateral to pyramids medial to 12th nerve roots
- **INTERMEDIATE** - Not chemosens, afferent fibres from both zones converge → stim resp centres
CENTRAL CHEMORECEPTORS

- INCREASED INTENSITY AND RATE OF RISE OF INSP RAMP SIGNAL
- INCREASED FREQUENCY OF RESP RHYTHM
- SENSING OF pH CHANGES REQUIRES ENZYME CARBONIC ANHYDRASE
- IMIDAZOLE HISTIDINE IS THE SENSOR MOLECULE
MECHANISM

- H+ IONS ENTER CSF BY DIRECT DIFFUSION FROM BLOOD STREAM
- ARTERIAL CO2 RAPIDLY PENETRATES BBB
- CONVERTED TO CARBONIC ACID
  \[ \text{H}_2\text{CO}_3 \rightarrow \text{H}^+ + \text{HCO}_3^- \]
- H+ DIFFUSES INTO CSF
RESPIRATORY CENTERS
CEREBRAL CORTEX

- CAN OVER-RIDE / BYPASS LOWER CENTERS
- SPEECH, SINGING, COUGHING, BREATH HOLDING
BRAINSTEM CENTERS

• PNEUMOTAXIC CENTER
• APNEUSTIC CENTER
• MEDULLARY CENTERS
  – DORSAL RESPIRATORY GROUP
  – VENTRAL RESPIRATORY GROUP
PNEUMOTAXIC CENTER

- PONTINE RESP GROUP
- NUCL PARABRACHIALIS, KOLLIKER-FUSE NUCLEUS IN DORSOLAT PONS
- REGULATES TIMING OF RAMP SIGNAL BY STIMULATORY INPUTS TO DRG NEURONS
- HYPOXIA, HYPERCAPNIA, LUNG INFLATION STIMULATE RESP
RAMP SIGNAL

• NERVOUS SIGNAL TRANSMITTED TO INSPIRATORY MUSCLES AS A BURST OF ACTION POTENTIALS WHICH INCREASES IN A RAMP LIKE MANNER GENERATED BY THE DRG NEURONS
APNEUSTIC CENTER

- LOWER PONS
- FUNCTIONS AS “INSPIRATORY CUT OFF SWITCH” INHIBITS DRG
- TRAANSECTION BELOW PNEUMOTAXIC CENTRE + VAGOTOMY INDUCES
- APNEUSTIC BREATHING HAS PROLONGED INSPIRATION TIME AND SHORT EXPIRATION TIME
DORSAL RESP GROUP

– BILATERAL AGGREGATES OF RESP NEURONS
– DORSOMEDIAL MEDULLA
– ADJACENT TO NUCL OF TRACTUS SOLITARIUS
– MOST NEURAL ACTIVITY IS INSPIRATORY
– PUMP CELLS (P CELLS): ACTIVATION BY AFFERENTS IMPULSES FROM LUNG STRETCH LEADS TO HERING- BREUER INFLATION REFLEX
VENTRAL RESP GROUP

- ROSTRAL VENTROLATERAL MEDULLA
- LONGITUDINAL COLUMN OF NUCLEI
  - BOTZINGER COMPLEX
  - PRE-BOTZINGER COMPLEX
  - ROSTRAL VRG
  - CAUDAL VRG (N. RETROAMBIGUALIS)
INSPIRATORY DRG NEURONS

- Axonal projections to spinal cord motor neurons

- Lung inflation facilitates - I beta neurons inhibits - I alpha neurons

- Excitatory drive to phrenic and to lesser extent external intercostal motor neurons for inspiration
VENTRAL RESP GROUP

- BOTH INSP AND EXP NEURONS
- EXP NEURONS MAINLY (ROSTRAL AND CAUDAL AREA)
- INSP NEURONS ARE IN MIDDLE
- NUCL AMBIGUALIS CLOSE TO VRG INNERVATES THE LARYNGEAL AND PHARYNGEAL AIRWAY MUSCLES
- FOR RHYTMIC RESP CYCLE RELATED CONTRACTIONS
VENTRAL RESP GROUP

• BOTH I AND E NEURONS PROJECT TO SPINAL CORD

• BULBOSPINAL NEURONS INHIBIT PHRENIC MOTOR NEURONS ACTIVELY DURING EXPIRATION

• PRE BOTZINGER COMPLEX IS THE SITE FOR RESP RHYTHMOGENESIS

• OUTPUT INCREASES WITH EXERCISE AND OBSTR AIRWAY DISEASES
CHEYNE STOKES RESPIRATION

- PERIODIC BREATHING PATTERN WITH CENTRAL APNEAS
- BILATERAL SUPRAMEDULLARY LESION
- CARDIAC FAILURE
- HIGH ALTITUDE
- SLEEP
SPINAL CORD

- **DECENDING BULBOSPINAL FIBRES ARE IN THE VENTRAL AND LATERAL COLUMNS**
- **RESP NEURONS ARE IN VENTRAL HORN (CERV, DORSAL, LUMBAR SEGMENTS)**
- **EXP NEURONS - VENTROMEDIAL**
- **INSP NEURONS - LATERAL**
SPINAL CORD

• **ASCENDING SPINORETICULAR FIBRES CARRY PROPRIOCEPTIVE INPUTS TO STIMULATE RESP CENTRE**

• **BILAT CERVICAL CORDOTOMY**
  \[ \downarrow \text{FUNCTION OF RAS LEADS TO RESPIRATORY DYSFUNCTION (SLEEP APNEA)} \]
PHASES OF RESP RHYTHM

- BASED ON PHRENIC NERVE RECORDINGS
- INSPIRATION - LUNG INFLATION
- POSTINSPIRATORY INSPIRATION ACTIVITY (E1) - FOR BRAKING THE AIRFLOW TO MAINTAIN FRC
- EXPIRATION (E2) - ACTIVE EXPIRATION
SPECIAL SITUATIONS

- SLEEP
- EXERCISE
- HIGH ALTITUDE
- DRUGS
- RESP STIMULANTS
SLEEP

• ↓ RESPONSE TO HYPOXIA
  HYPERCAPNIA

• ↓ RESP TO MECHANORECEPTORS

• HYPOTONIA OF UPPER AIRWAY-
  OBSTR SLEEP APNEA

• HYPOTONIA OF SKELETAL & RESP
  MUSCLES - VENT DEPENDS ON
  DIAPHRAGM

• Pa O2 ↓ AND PaCO2 ↑ BY 4-8 mmHg
EXERCISE

• **PHASE I** - IMMEDIATE \(\uparrow\) VE WITHIN SECONDS, NEURAL IMPULSES MSL SPINDLES, JOINT PROPRIOCEPTORS

• **PHASE II** - WITHIN 20-30 SEC VENOUS BLD FROM MSL, SLOW AND EXPONENTIAL \(\uparrow\) VE (VENTILATION LAGS BEHIND CO2)
EXERCISE

• **PHASE III** - PULM GAS EXCHANGE MATCHES THE METAB RATE TO MAINTAIN STABLE O2, CO2, pH

• **PHASE IV** - BEGINS AT ANAOERBIC THRESHOLD, O2 CONSUMPTION > O2 DELIVERY AND LACTIC ACID ACCUMULATES.
VENTILATORY RESPONSE TO EXERCISE
DRUGS & RESPIRATION

• CAUSE RESP DEPRESSION - ↓ VE
  – INHALATIONAL ANAESTHETICS
  – NARCOTICS
  – BEZODIAZEPINES
  – ALCOHOL
  – ESP SEVERE COPD UNDER GA
     COPD INACUTE EXCACERBATION
  – NALOXONE, FLUMAZENIL IN DRUG OVERDOSE
RESP STIMULANTS

- DOXAPRAM
- PROGESTERONE
- AMINOPHYLLINE
- INCREASE VE AND REDUCE $\text{PaCO}_2$
- USEFUL IN COPD AC EXCERBTN
- OBESITY HYPOVENTILATION SYND
CONCLUSIONS

- ABNORMALITIES OF RESP DRIVE ARE OVERLOOKED IN CLIN PRACTICE
- BREATHING ABNORMALITIES MORE SEVERE DURING SLEEP AND CAN HAVE SERIOUS CONSEQUENCES