CONTROL OF RESPIRATION

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DEPT OF PULMONARY MEDICINE

PGIMER

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 PaO_2 <3-4 mm Hg AND EVEN LESS FOR $PaCO_2$
- 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 Pa O2
- HENCE NOT AFFECTED BY CONDITIONS IN WHICH PaO2 (N)
  - MILD ANEMIA
  - CO POISONING

CHEMOTRANSDUCTION

- O2 BINDS CELL MEMB 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 PaO_2 AND H^+ CONCENTRATION (pH), $PaCO_2$
- 90% VENTILATORY RESPONSE TO HYPOXEMIA- CAROTID BODY
- 10% RESPONSE -FROM AORTIC BODIES
- VE INCREASED ↑ TIDAL VOLUME

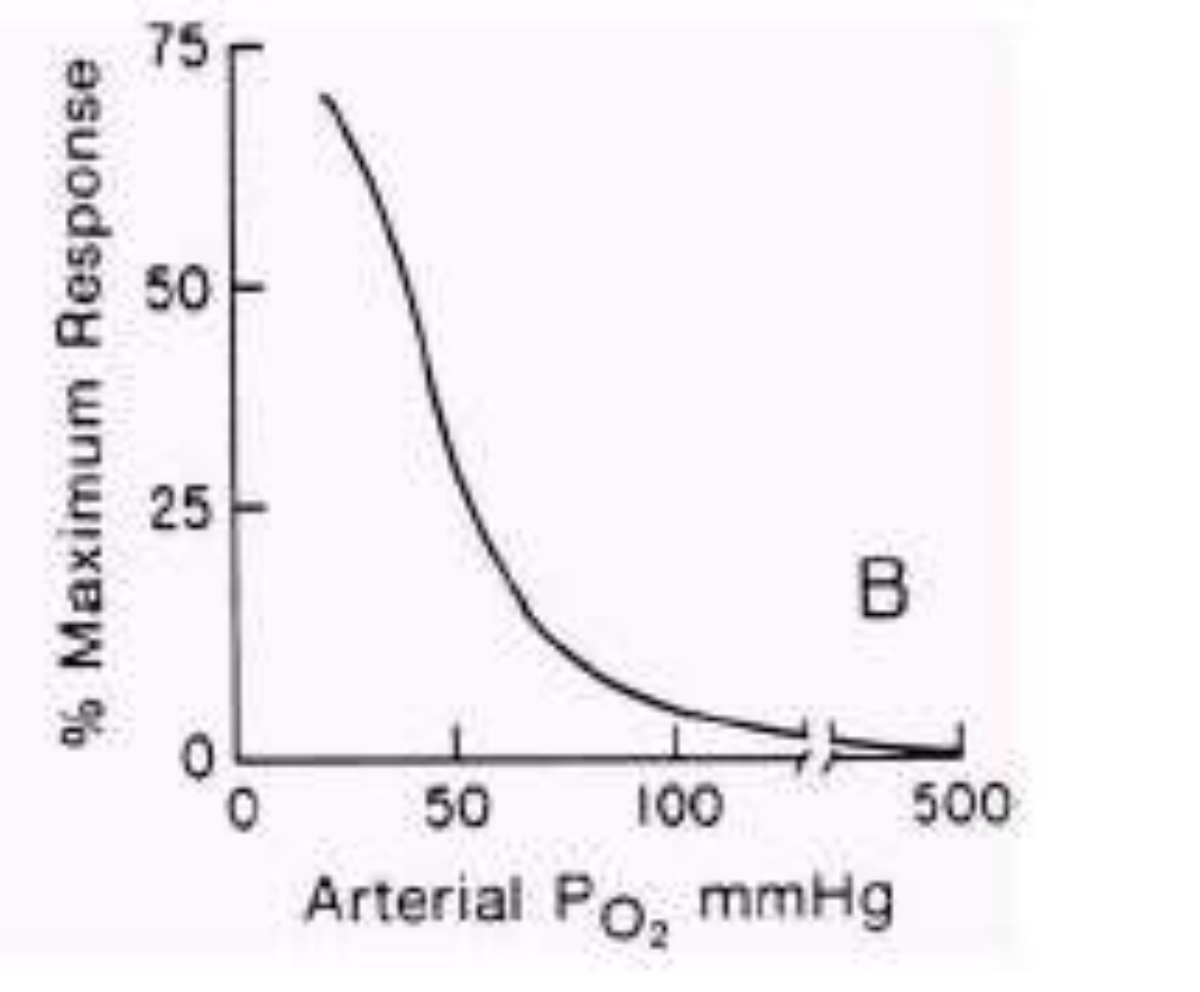
CHEMORECEPTORS

- 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

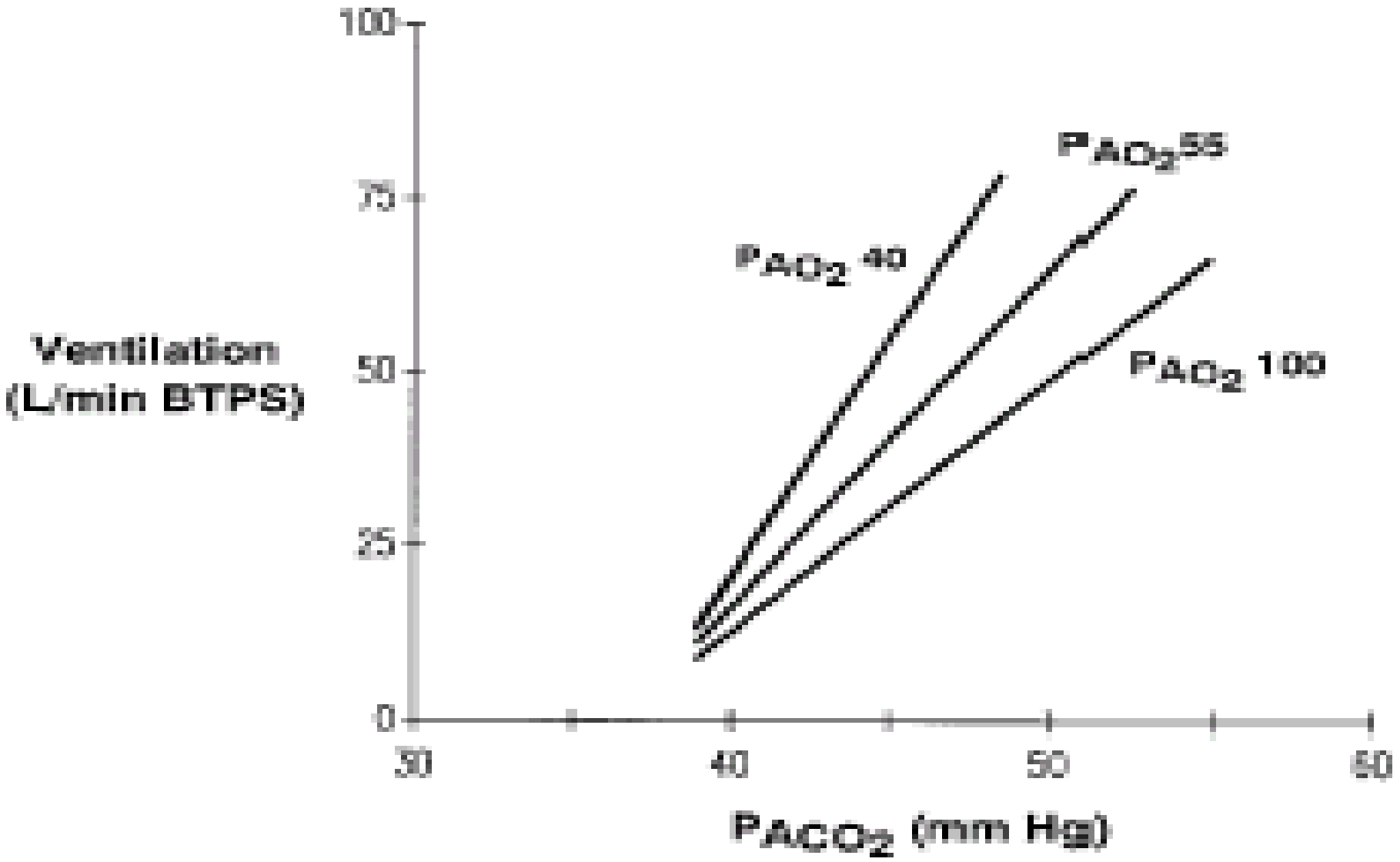
EFFECT OF Pa O2 ON CHEMORECEPTORS



EFFECTS OF PACO2

- VENTILATION INCREASES IN LINEAR MANNER WITH PaCO2
- **HYPOXEMIA** INCREASES THE SLOPE OF VENTILATORY RESPONSE TO PaCO2

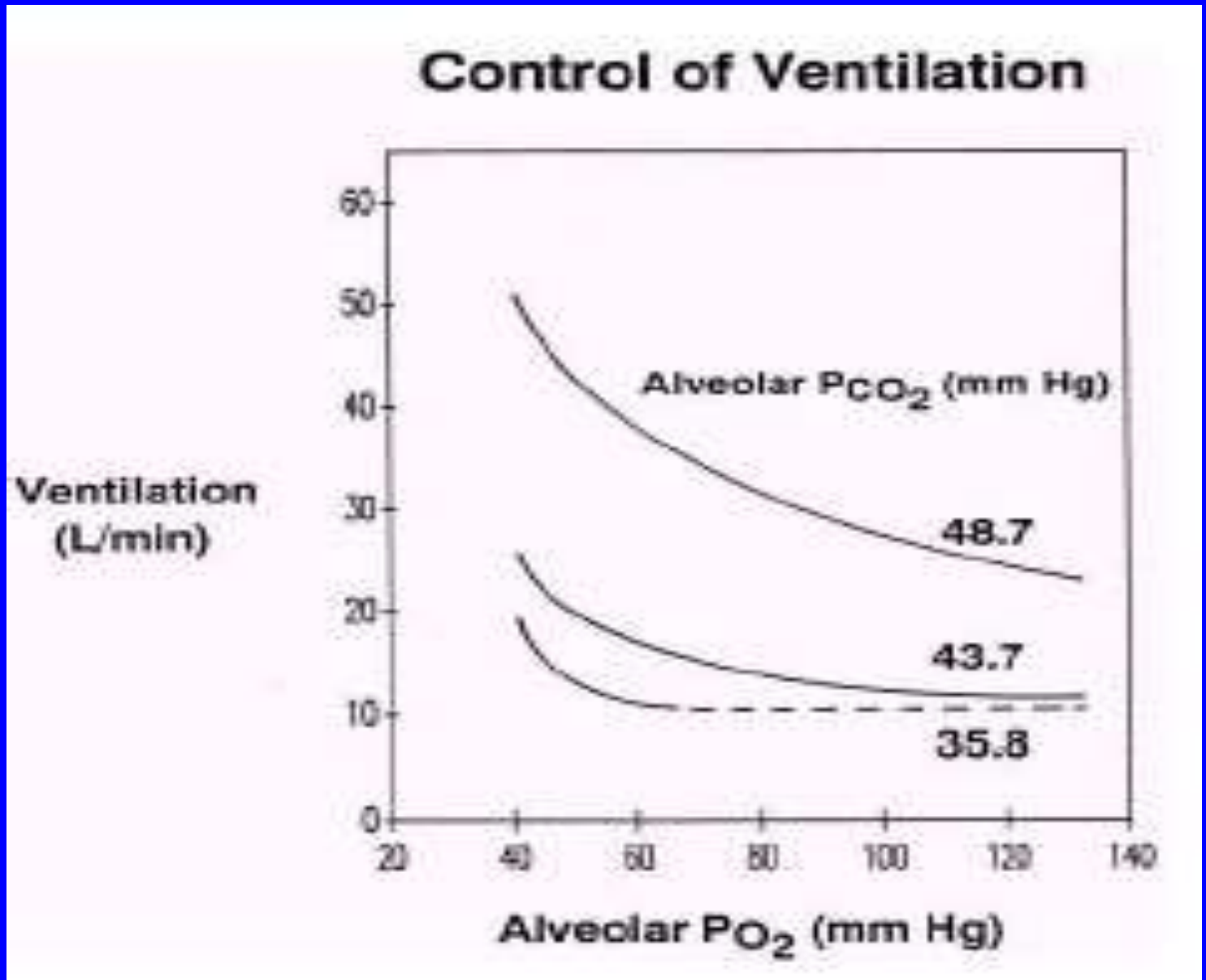
VENTILATORY RESPONSE TO ALV CO2



EFFECT OF PaO2

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

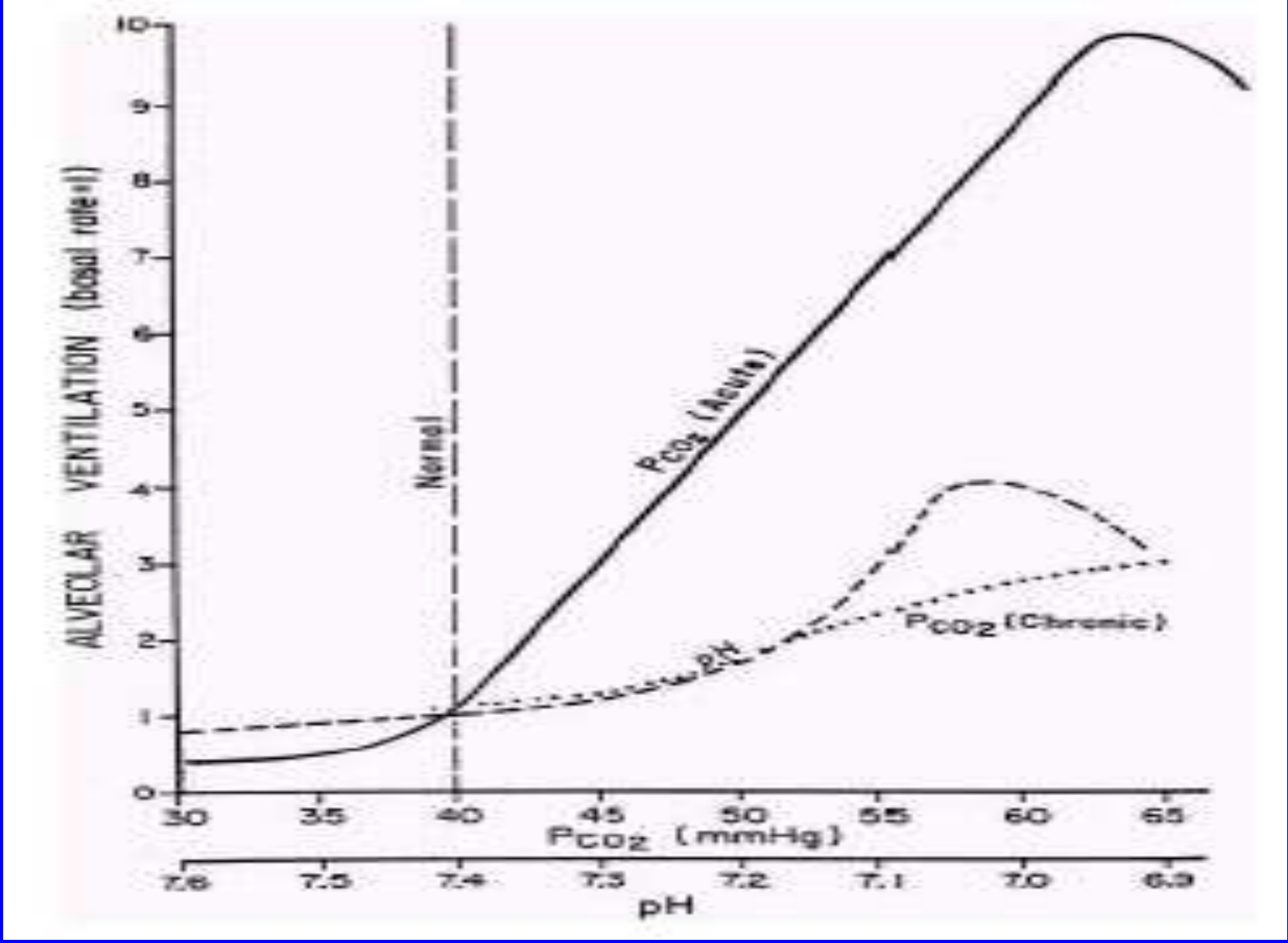
VENTILATORY RESPONSE TO ALV O2



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 🕓 2-4 mm Hg
- ELIMINATES VENTILATORY TO HYPOXIA AT REST AND EXERCISE
- 30% DECREASE IN RESPONSE TO HYPERCAPNIA

CASE

- 69 Y FEMALE COPD,CVA (OLD)
- CAROTID ENDARTERECTOMY 1YR
- ELECTIVE CE (R) DONE
- PREOP ABG ON R/A- 7.43/50/48/31
- DAY 3 EXTUBATED → O2 3L/MIN
- DAY5: SOMNOLENT AND CONFUSED
- ABG- 7.28/62/69/31
- BiPAP INITIATED → IMPROVED
- ABG-7.38/72/54/36

CO_2 NARCOSIS

COPD WITH HYPERCAPNIA & WORSENING RESP ACIDOSIS FOLL OXYGEN THERAPY

- LOSS OF HYPOXIC DRIVE
- WORSENING V/Q MISMATCH
  - ↑ PHYSIOLOGIC DEAD SPACE
  - ↓ CO_2 CARRYING CAPACITY AS OXYGENATION OF Hb IMPROVES

(HALDANE EFFECT)

RECEPTORS

- AIRWAY RECEPTORS
  - SLOWLY ADAPTING RECEPTORS (AIRWAY SMOOTH MSL)
  - RAPIDLY ADAPTING RECEPTORS (AIRWAY EPITH 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 OBSTRUCTN** ALLOWING HIGHER TV TO BE ACHIEVED

RAPIDLY ADAPTING RECEPTORS

- IRRITANT RECEPTORS (COUGH)
- CARINA AND PRINCIPAL BRONCHI
- NOXIOUS STIMULI-DUST,SMOKE
- CAUSES AUGUMENTED 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 SECRETIONS

EFFECT OF VAGOTOMY

- EXPT ANIMAL STUDIES
- VAGOTOMY ABOLISHES INCREASED RESP RATE AND MIN VENT (VE) WITH ASTHMA
- RAPID SHALLOW BREATHING PATTERN IN RESP TO BRONCHSPASM IS MEDIATED THROUGH VAGAL AFFERENTS

CHEST WALL RECEPTORS

- MECHANORECEPTORS - SENSE CHANGES IN LENGTH ,TENSION AND MOVEMENT
- ASCENDING TRACTS IN ANT ERIOR COLUMN OF SPINAL CORD TO RESP 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 MOVT
- INFLUENCE THE LEVEL & TIMING OF RESP ACTIVITY

CLINICAL SIGNIFICANCE

- SENSATION OF DYSPNEA WHEN INCREASED RESP EFFORT DUE TO "**LENGTH- TENSION INAPPROPRTATENESS**" - LARGE PLEURAL EFFUSION
- REMOVAL OF FLUID RESTORES THE END EXP MSL FIBRE LENGTH RESTORES THE LENTH TENSION RELATIONSHIP ⟶ RELIEF

CENTRAL CHEMORECEPTORS

- DENERVATION OF PERIPHERAL CHEMORECEPTORS - VENTILATORY RESPONSE TO CO_2 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 10 TH NERVES
- **CAUDAL** - LATERAL TO PYRAMIDS MEDIAL TO 12 TH 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 BLD STREAM
- ARTERIAL CO2 RAPIDLY PENETRATES **BBB**
- CONVERTED TO CARBONIC ACID
- H2C03 $\longrightarrow$ H + HCO3
- 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
- TRANSECTION BELOW PNEMOTAXIC CENTRE + VAGOTOMY INDUCES
- **APNEUSTIC BREATHING** HAS PROLONGED INSP TIME AND SHORT EXP 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 MOTORNEURONS 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** ↓ FUNCTION OF RAS LEADS TO RESPIRATORY DYSFUNCTION (SLEEP APNEA)

PHASES OF RESP RHYTHM

- BASED ON PHRENIC NERVE RECORDINGS
- INSPIRATION - LUNG INFLATION
- POSTINSPIRATORY INSP 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

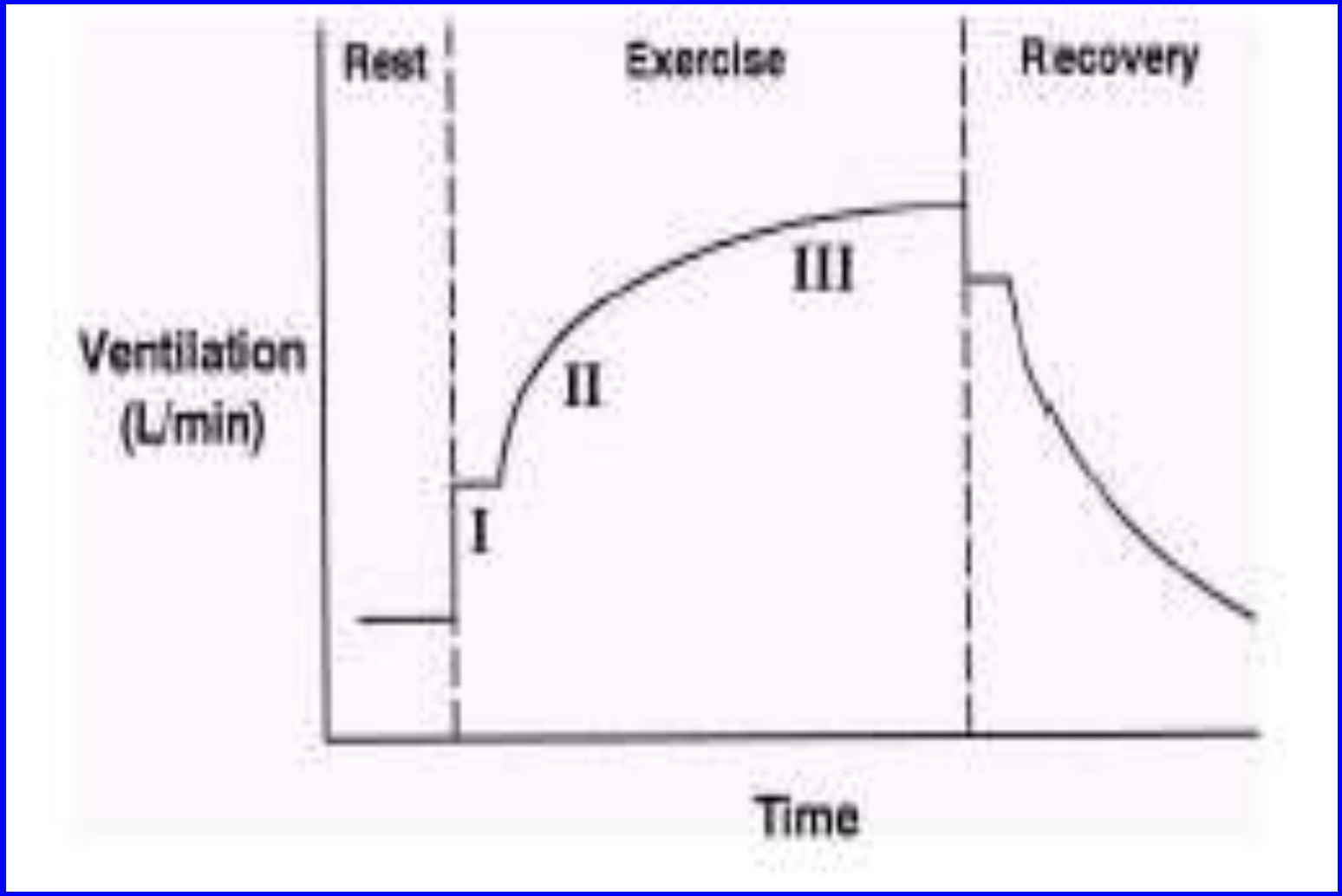
EXERCISE

- **PHASEI** - IMMED↑ VE WITHIN SECONDS,NEURAL IMPULSES MSL SPINDLES, JOINT PROPRIOCEPTORS
- **PHASE II**- WITHIN 20-30 SEC VENOUS BLD FROM MSL,SLOW AND EXPONEN ↑ 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 CONSUMTION> 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 $PaCO_2$
- USEFUL IN COPD AC EXCACERBTN
- OBESITY HYPOVENTILATION SYND

CONCLUSIONS

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