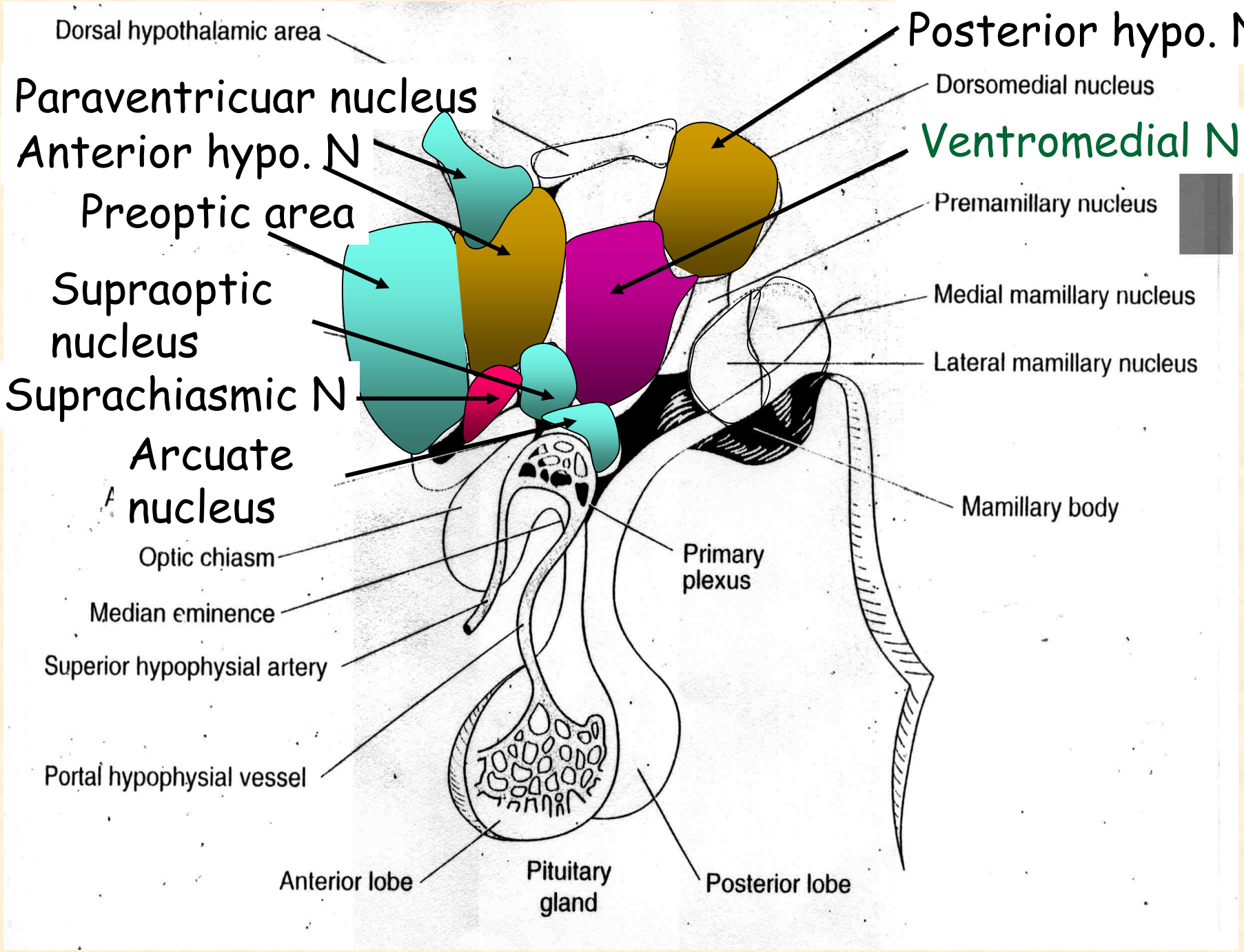
Hypothalamus

Prof. Niranga Manjuri Devanarayana

- Mass of grey matter nuclei
- Optic chiasma anteriorly
- Mammillary bodies posteriorly
- Internal capsule laterally
- 3rd ventricle superiorly


Dorsal hypothalamic area
Posterior hypo. N
Paraventricuar nucleus
Dorsomedial nucleus
Anterior hypo. N
Ventromedial N
Preoptic area
Premamillary nucleus
Supraoptic nucleus
Medial mamillary nucleus
Lateral mamillary nucleus
Suprachiasmic N
Arcuate nucleus
Mamillary body
Optic chiasm
Primary plexus
Median eminence
Superior hypophysial artery
Portal hypophysial vessel
Anterior lobe
Pituitary gland
Posterior lobe

Afferents

- Limbic system
- Cortex
- Lemniscus
- Brain stem
- Thalamus

Efferents

- Brain stem
- Spinal cord
- Hypothalamo-hypophyseal tract
- Thalamus

Neurotransmitters : Noradrenaline, Dopamine, Serotonin, Histamine

Functions of Hypothalamus

- Control of the endocrine system
- Temperature regulation
- Behaviour and emotions
  - Appetite and feeding regulation
  - Thirst regulation and drinking
  - Sexual behaviour
  - Rage and panic reactions
- Sleep & biological clock
- Autonomic nervous system

Objectives

- Endocrine functions of the hypothalamus
  - Hormones secreted from the hypothalamus and their functions
  - Role of hypothalamus is regulation of functions of other endocrine glands

- Outline role of hypothalamus is regulation of the following
  - Feeding
  - Drinking
  - Biological clock

Objectives cont..

- Regarding temperature regulation
  - State normal body temperature and describe its variations
  - Outline regulation of body temperature under physiological conditions
  - Outline pyrexia
  - Describe hyper and hypothermia

- Outline the consequences of hypothalamic disorders

Regulation of the endocrine system

Regulation of the endocrine system

Hypothalamus

↓

Hormones

↓ Via portal blood

Anterior pituitary

↓

Synthesis & release of pituitary hormones

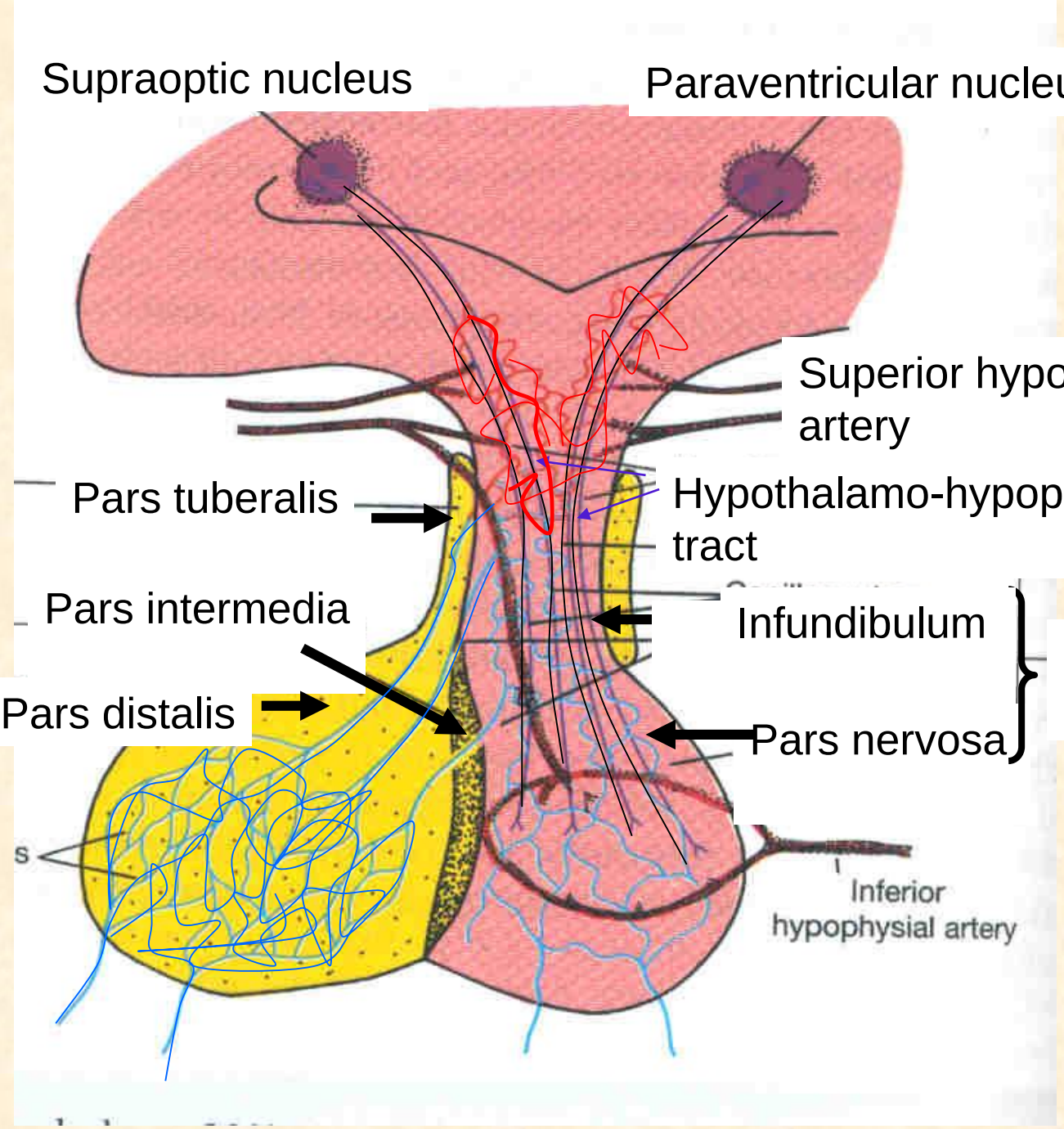
Hypothalamus

↓

Synthesis of Hormones

↓ Via neural connection

Released by the posterior pituitary (Oxytocin, Vasopressin)


Supraoptic nucleus
Paraventricular nucleus
Superior hypophyseal artery
Pars tuberalis
Hypothalamo-hypophyseal tract
Anterior pituitary
Pars intermedia
Infundibulum
Posterior pituitary
Pars distalis
Pars nervosa
Inferior hypophysial artery

Hypothalamic regulation of Anterior Pituitary

Corticotropin releasing hormone (CRH)

Thyrotropin releasing hormone (TRH)

Gonadotropin releasing hormone (GnRH)

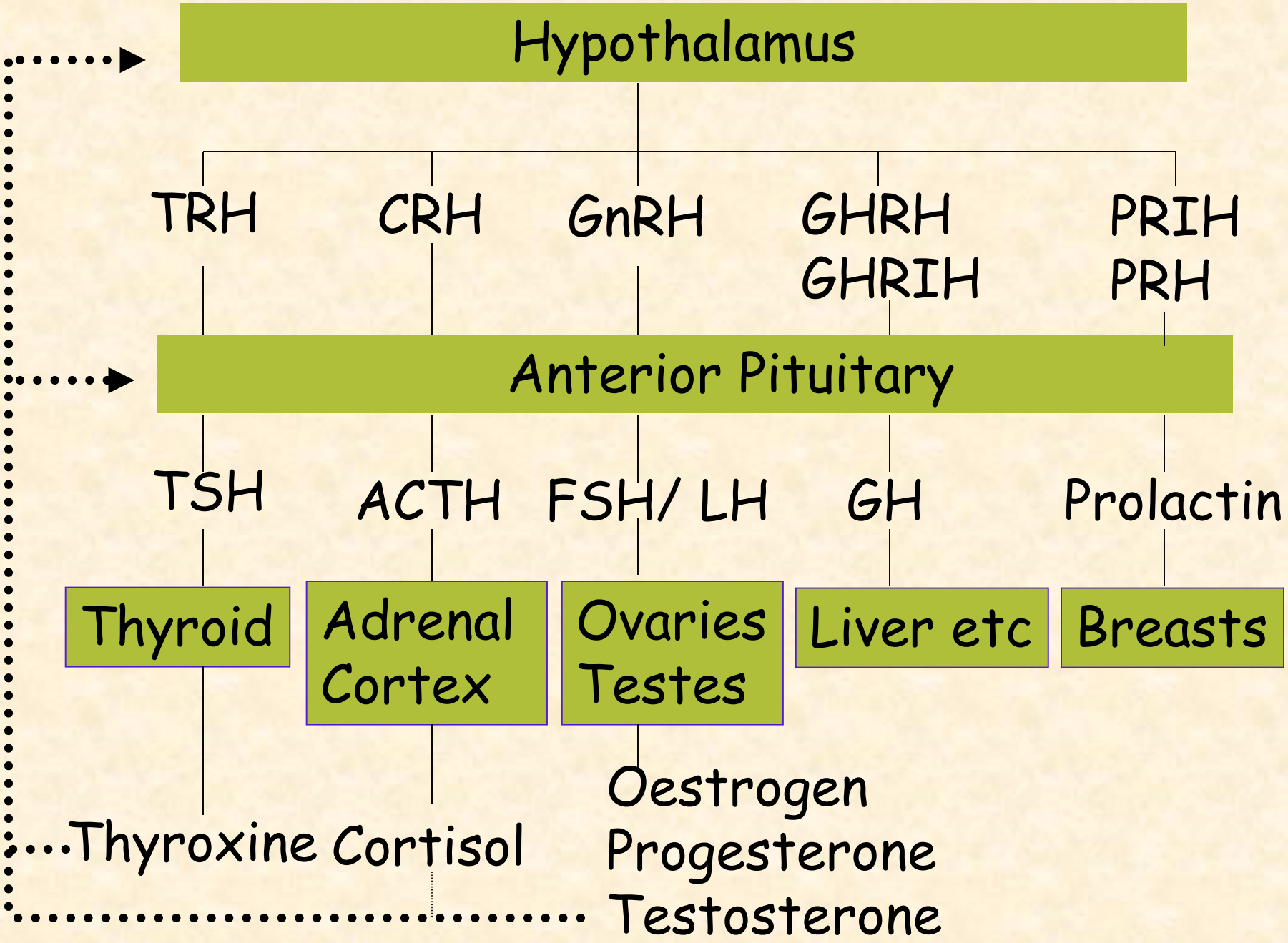
Growth hormone releasing hormone (GRH)
Growth hormone release inhibiting hormone (GIH)
"somatostatin"

* Prolactin release inhibiting hormone (Dopamine)
  Prolactin releasing hormone

Anterior Pituitary Gland

Hormones secreted:

1. Growth hormone (GH)
2. Adrenocorticotrophic hormone (ACTH)
3. Thyroid stimulating hormone (TSH)
4. Follicle stimulating hormone (FSH)
5. Leutinizing hormone (LH)
6. Prolactin (PRL)


Hypothalamus
TRH
CRH
GnRH
GHRH
GHRIH
PRIH
PRH
Anterior Pituitary
TSH
ACTH
FSH/ LH
GH
Prolactin
Thyroid
Adrenal Cortex
Ovaries Testes
Liver etc
Breasts
Thyroxine
Cortisol
Oestrogen
Progesterone
Testosterone

Regulation of behaviours

1. Regulation of feeding

Regulation of Feeding

Long term → Weight regulation

Short term → Meal size adjusted

Mechanisms of stimulating/ inhibiting feeding

1. Lipostatic hypothesis

Food intake increases
Energy expenditure reduces

↓

Fat deposition

↓

Increased secretion of Leptin ⋯⋯▶ Reduced Food intake
Increased energy expenditure

2. Gut peptides

Gastrointestinal hormones (eg. CCK) and peptides act on hypothalamus to inhibit or stimulate appetite

- Peptide YY
  - Secreted from small intestine when caloric intake is high
  - Decreases food intake
- Ghrelin
  - Involved in short term control of food intake
  - Secreted by gastric mucosa when stomach in empty
  - Increases appetite and food intake and decrease fat utilization

3. Glucose:

Raised blood glucose

↓

Increased satiety centre glucose utilisation

↓

Satiety centre activated

↓

Inhibit feeding centre

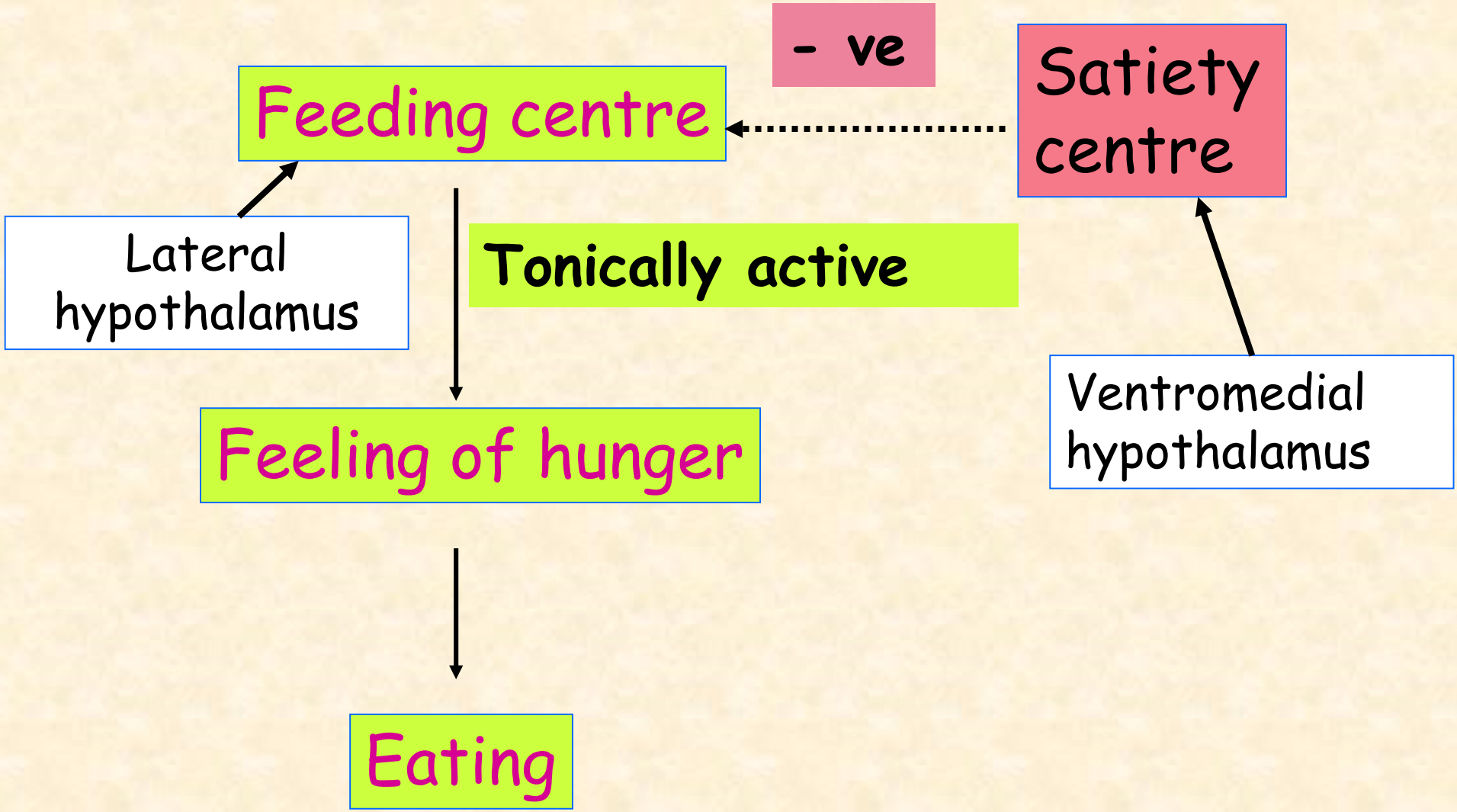
Other mechanisms

- Cold weather increases appetite
- Gastro intestinal distension reduces appetite
- Brown fat

Leptin

- Coded by the Ob gene
- Secreted by adipose tissue
- Leptin
  - Involved in long term regulation of body weight
  - Decreases appetite and food intake
  - Increases basal metabolic rate and energy expenditure
  - Increases peripheral fat utilization
- Mutations of the Ob gene or the leptin receptor cause obesity

Hypothalamic regulation of feeding

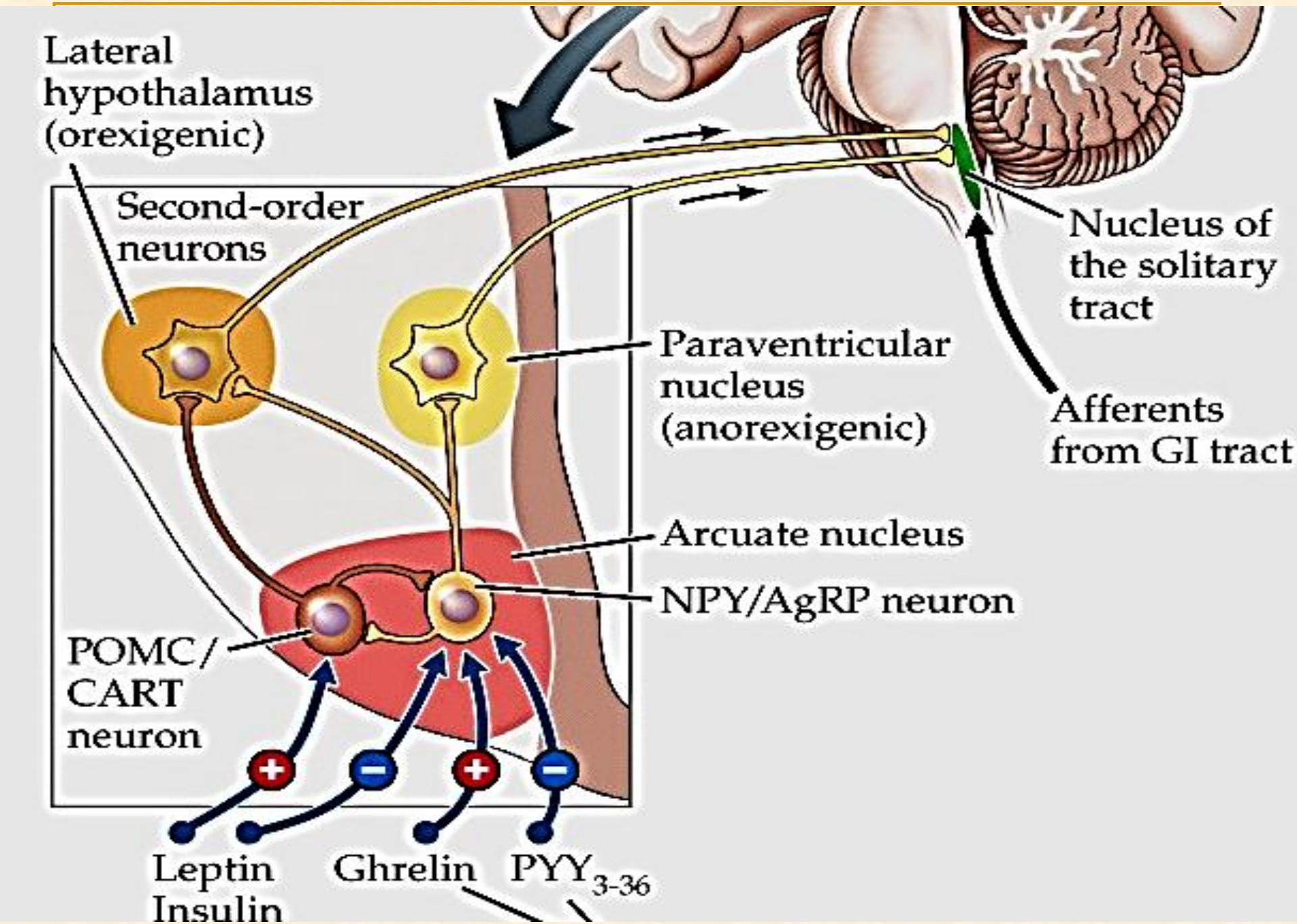


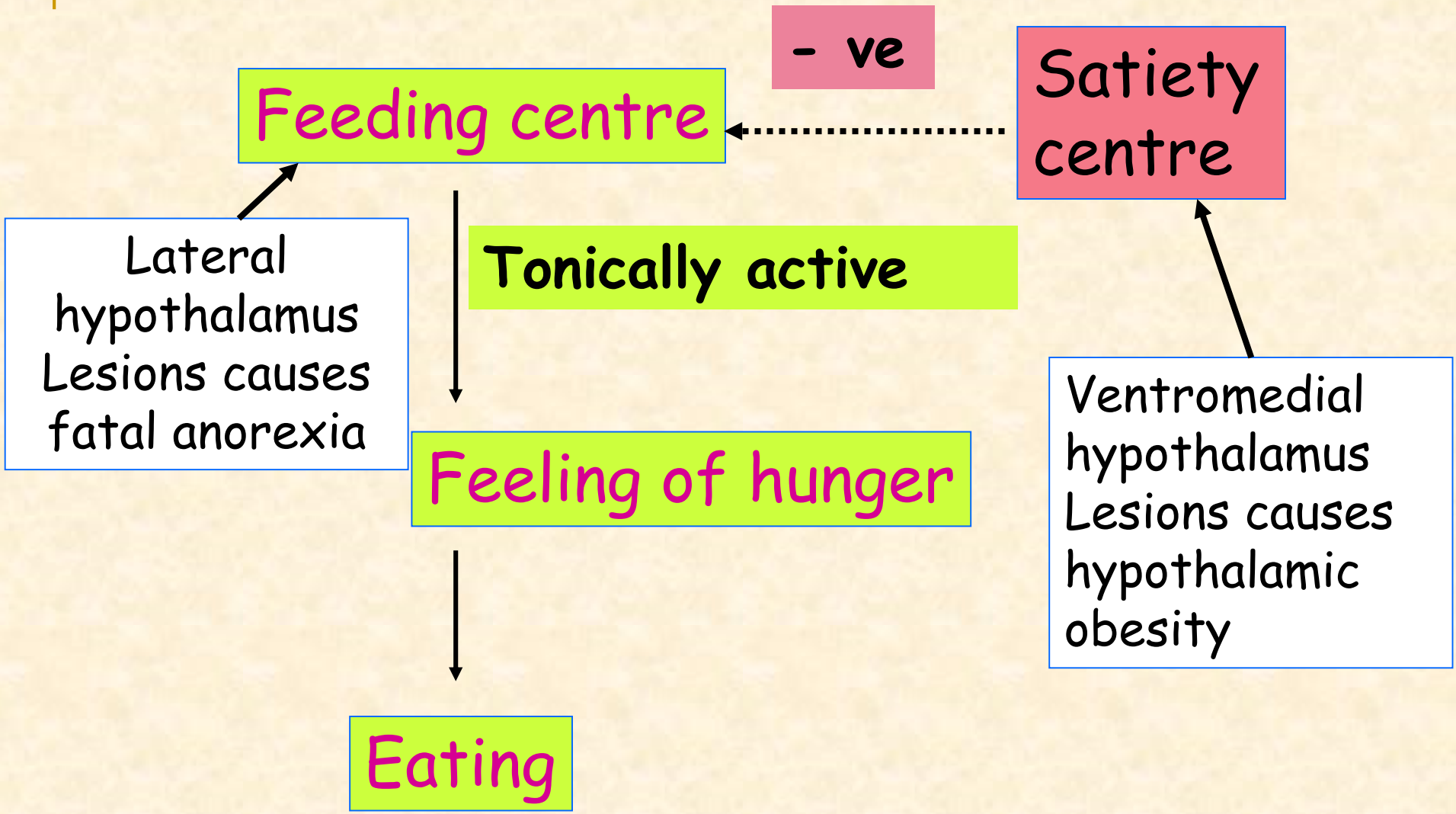
Hypothalamic regulation of feeding cont…

Arcuate nucleous contains two main sets of neurons secreting

1. Neuropeptide Y / (Agouti related peptide)
   - Promote feeding

2. Melanocortins / cocaine-amphetamine regulated transcript
   - Decrease food intake


Lateral hypothalamus (orexigenic)
Second-order neurons
Nucleus of the solitary tract
Paraventricular nucleus (anorexigenic)
Afferents from GI tract
Arcuate nucleus
NPY/AgRP neuron
POMC/ CART neuron
Leptin
Insulin
Ghrelin
PYY3-36


- ve
Satiety centre
Feeding centre
Lateral hypothalamus Lesions causes fatal anorexia
Tonically active
Feeling of hunger
Ventromedial hypothalamus Lesions causes hypothalamic obesity
Eating

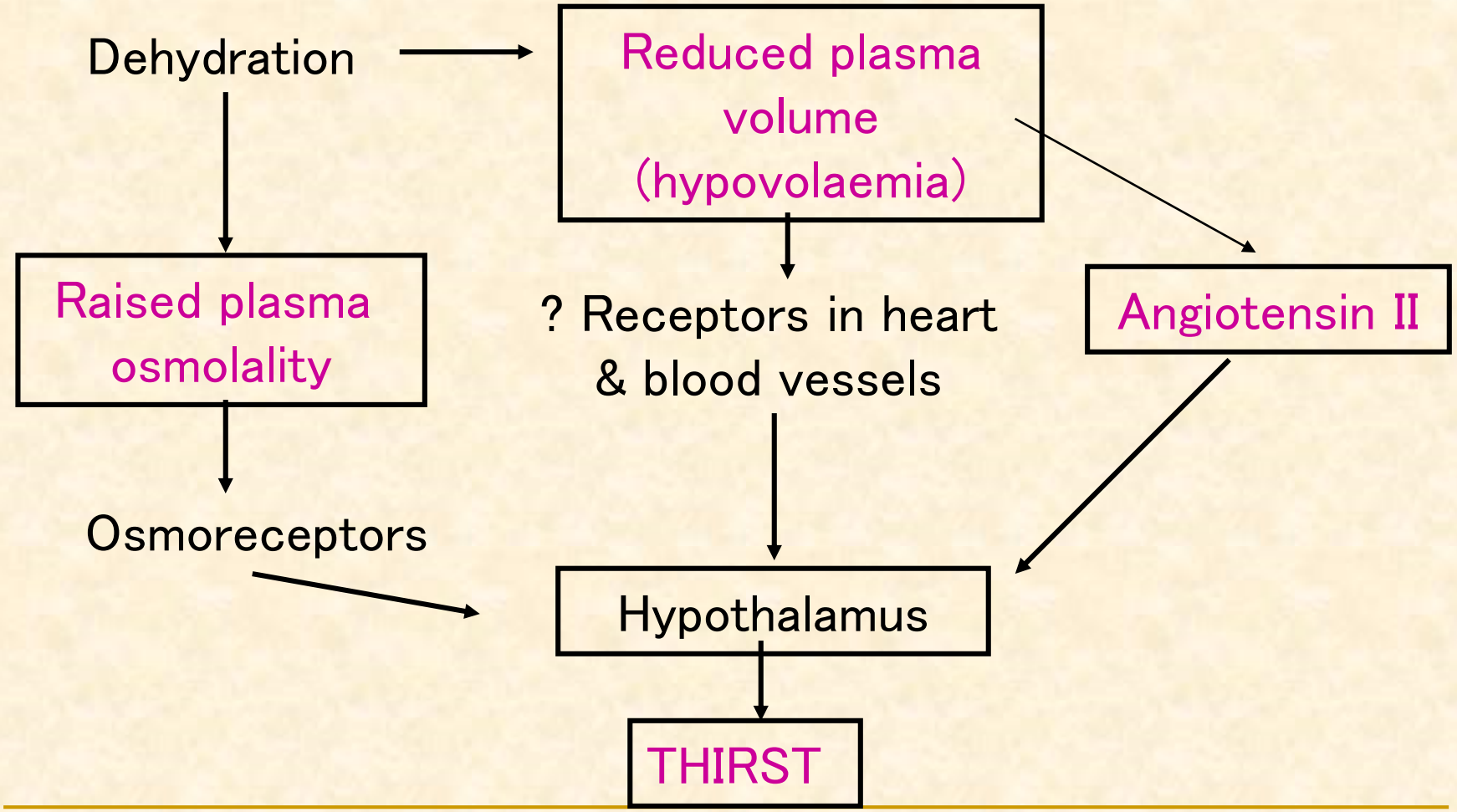
2. Thirst and drinking

Thirst and drinking

- Regulated by
  - Hypothalamus
  - Local factors (dry mucous membranes)
  - Psychological factors

- Osmoreceptors in hypothalamus
  - sensitive to the osmolality of the ECF
  - Dehydration → raised plasma osmolality

Regulation of drinking



Biological clock

Biological clock

- Circadian rhythms are controlled by hypothalamus (suprachiasmic nucleus)
- Includes the sleep- wake cycle, hormonal secretions, temperature changes during the day

Temperature regulation

Temperature regulation in living organisms

- **Homeothermic animals**
  - Body temperature maintained at a constant level irrespective of environmental temp
  - E.g. birds and mammals

- **Poikilothermic animals**
  - Do not have constant body temperature
  - Varies according to environmental temp
  - E.g. reptiles

Body Temperature

- Normal Body Temperature (NBT) oral - 98.6^0F (37^0C)
- Range of NBT - 96.4^0F to 99.1^0F (35.8^0C – 37.3^0C)

- Rectal Temp - 0.6^0C (0.5^0F to 1^0F) above the Oral temp
- Rectal Temp reflects the internal body Temp (Core Body Temp) better

- Core Body Temp remain almost constant – 37.8^0C (100^0F)

- Skin Temp is variable - 29.5^0C – 33.9^0C (85.1^0F-93^0F)

Temperature Homeostasis

- Keep the body temp within a very narrow range
- Temperatures above this:

  denature enzymes and block metabolic pathways
- Temperatures below this:

  slow down metabolism and affect the brain.

Physiological variations in the Temperature

- Age – higher in children, lower in old age
- Sex – less in females due to low BMR
- Diurnal variation – early morning 1^0C less than in the afternoon
- After meals – increase by 0.5^0C
- Exercise – increase due to heat production
- Sleep – decrease by 0.5^0C
- Emotion – increases with emotions
- Menstruation cycle – increases immediately after ovulation (0.5-1^0C) and decreases during menstrual cycle (0.5^0C)

Heat Balance

- Heat balance maintains the body temp
- Balance between heat production & heat loss (Heat Balance)
- Heat Balance
  - Heat production= Heat loss
- Heat production is called thermogenesis
- Heat loss is called as thermolysis

Heat Production (Thermogenesis)

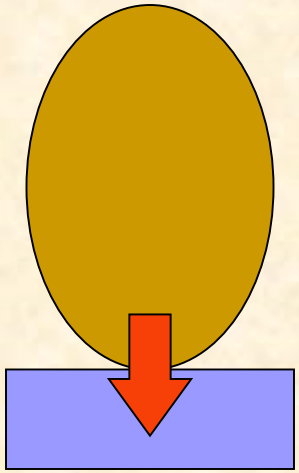
- Metabolic activities
  - Metabolism of food
- Activity of skeletal muscles
  - Shivering
  - Physical activity and Exercise
- Hormonal activity – accelerate BMR
  - Epinephrine &Norepinephrine
  - Thyroxine
- Brown Fat-
  - Source of considerable heat production
  - Abundant in infants
- Radiation of heat from the environment

Heat Loss (Thermolysis)

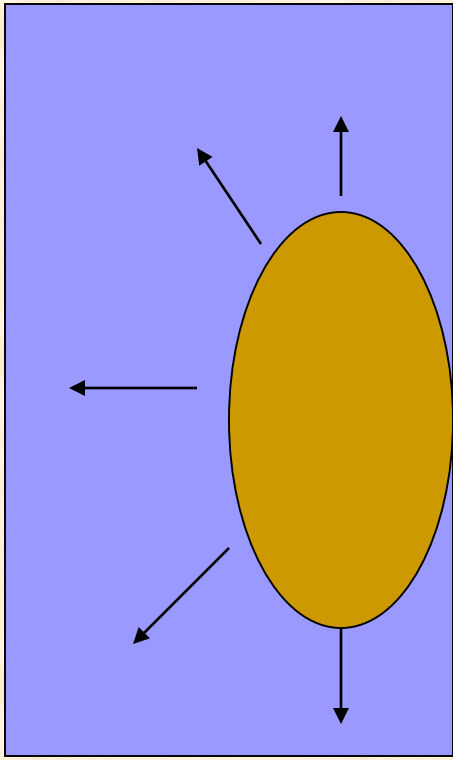
- Radiation
- Conduction
- Convection
- Evaporation
- Perspiration
- Respiration
- Loss through urine & feces

Heat loss

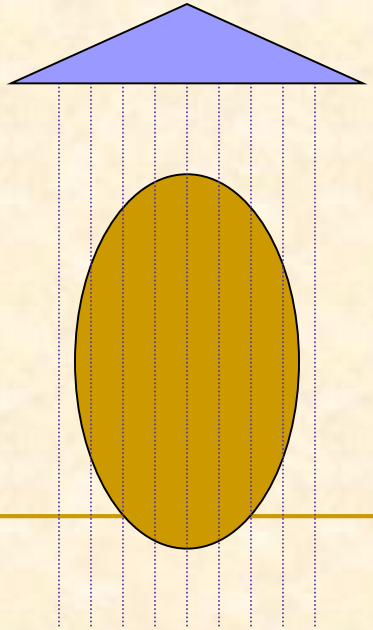
Conduction



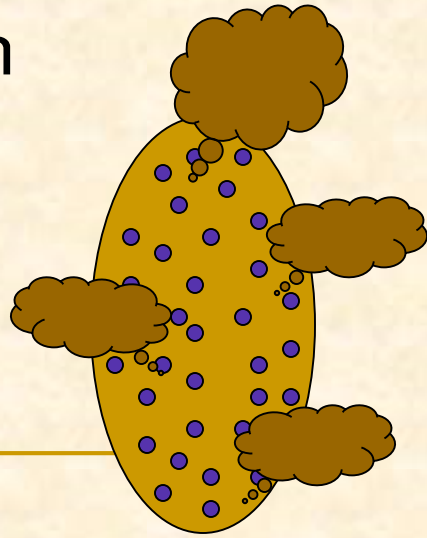
Radiation



Convection



Evaporation



Radiation

- Physical transfer of heat between the body and the environment by electromagnetic waves
- 65% of heat transfer
- Modified by insulation (clothing, fat layer), cutaneous blood flow

Convection

- Energy transfer between the body and a gas or liquid
- Affected by temperature gradient, motion at the interface, and liquid
- Not usually a major source for heat loss or dissipation, but this increases with wind chill and body motion

Conduction

- Direct transfer of heat energy between two surfaces
- Responsible for only a small proportion of heat loss under normal circumstances
- Increases significantly with immersion in cold water

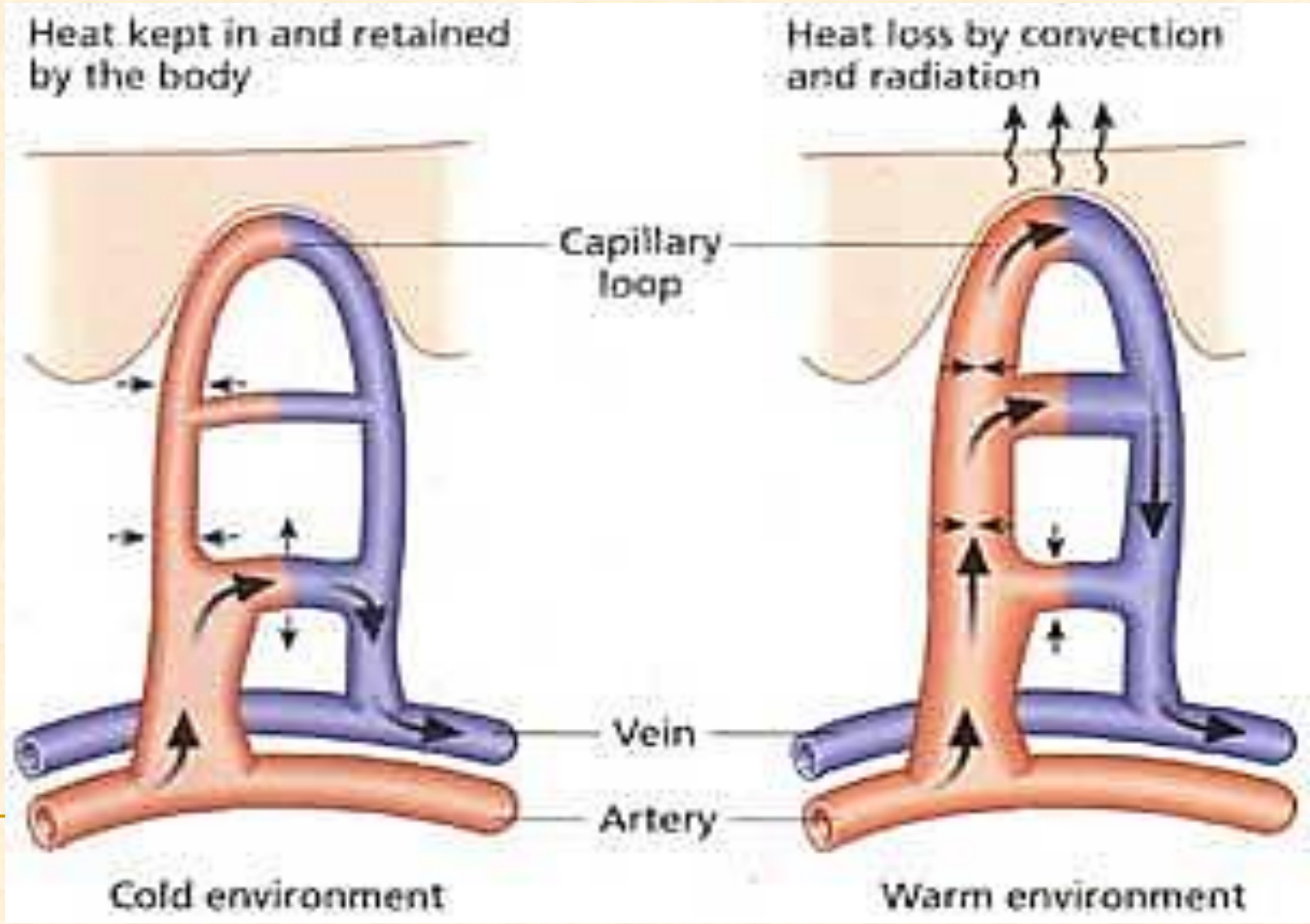
Evaporation

- Most important source of cooling under extreme heat stress
- 25% of heat loss in temperate/cool conditions… may be increased significantly by sweating, increased respiratory rate
- Affected by relative humidity and clothing

Cutaneous factors involved in temperature regulation

1. Cutaneous blood flow
   - Approximately 8.6% of cardiac output
   - Cutaneous vasodilatation to deliver blood to skin surface
2. Sweating
   - Evaporation of sweat uses heat
   - More heat lost when humidity is low
3. Erection of hair

Vasoconstriction and Vasodilatation



Sweating

- Evaporation of sweat uses heat– sweating causes more heat loss when humidity is low
- Sweat glands stimulated by sympathetic cholinergic stimulation
- Sweat contains water and NaCl
- What is the mechanism involved in producing sweat?

Thermoregulation

- Temperature is regulated by nervous feedback mechanisms
- Thermoregulatory centers are located in the **Hypothalamus**
- Thermoregulatory regulatory responses include

  Autonomic

  Somatic

  Endocrine

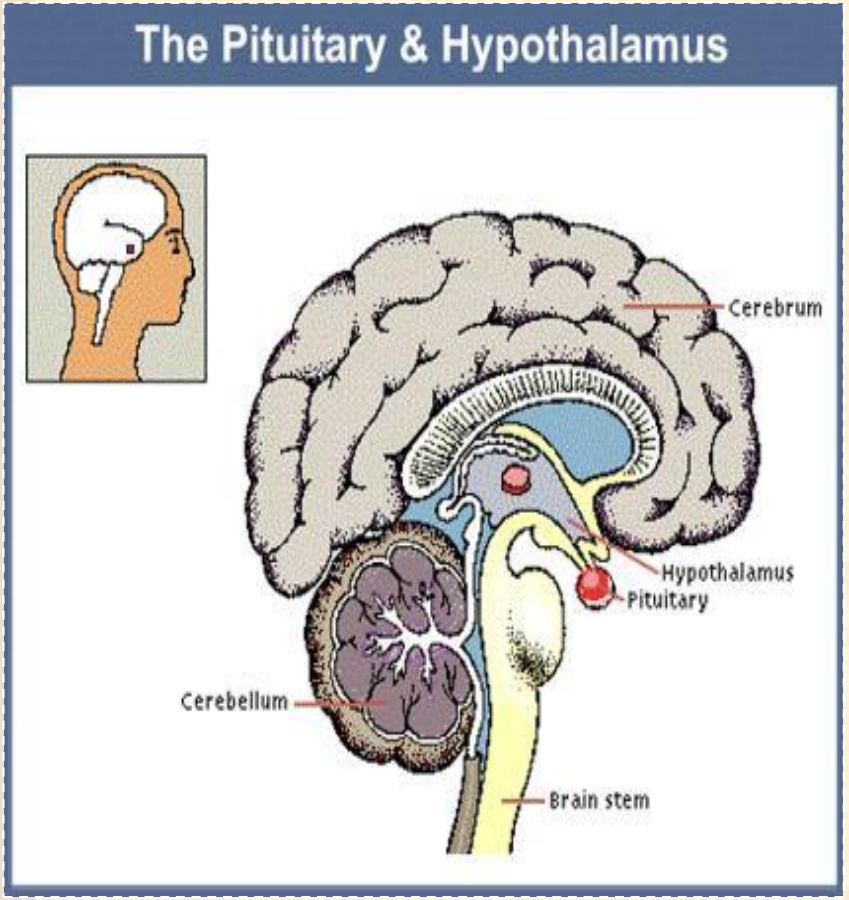
  Behavioural changes

Feedback system

- 1) Receptor - thermoreceptor
  - Sensor that responds to changes (stimuli)
  - Cutaneous sensors – skin - detect external temp
  - internal sensors – CNS, viscera – detect core temp
- 2) Control Center - hypothalamus
  - Sets range of values
  - Evaluates input and
  - Sends output
- 3) Effector- main skin and skeletal muscles
  - Receives output from control centre
  - Produces a response

Body Temperature Control System

- Hypothalamus
  - Acts as a thermostat
  - Receives nerve impulses from **cutaneous thermoreceptors**
  - Thermoreceptors - Cold &Heat



- Hypothalamus- also has thermoreceptors called **central thermoreceptors**
- These detect changes in blood temperature

Hypothalamic centers for regulation of temperature

Heat loss center

- Situated in preoptic nucleus of anterior hypothalamus
- Has heat sensitive neurons
- Stimulation results in cutaneous vasodilatation and sweating
- Lesions increase the body temp.

Heat gain center

- Situated in posterior hypothalamus
- Stimulation causes shivering
- Removal or lesions leads to fall in body temp

Thermoregulatory regulatory responses to cold

1. **Promotion of heat production**
   - Shivering – center in posterior hypothalamus
   - Non shivering thermogenesis – children by brown fat
   - Increase voluntary activity
   - Increased metabolic reactions – sympathetic NS

   E.g. Increase TSH and Catecholamine

2. **Prevention of heat loss**
   - Vasoconstriction – sympathetic nervous system
   - Horripilation – raised hair causes insulation
   - Behaviours - Curling up, warm cloths, stand near fire/heat

Thermoregulatory regulatory responses to heat

1. **Promotion of heat loss**
   - Vasodilatation – decreased sympathetic activity
   - Sweating – increase evaporation heat loss
   - Increased respiration
   - Behaviours – open posture

2. Prevention of heat production
   - Anorexia
   - Behaviours - Apathy – minimum activity, seek cool paces and avoid heat sources
   - Decrease TSH secretion and adrenalin

Changes in body temperature

↓

Stimulation of (cold) receptors
e.g. skin, spinal cord, deep tissues and hypothalamus

↓

Afferents to posterior hypothalamus

↓

Hypothalamic interpretation
(Compared with set point for body temp)

↓

There are threshold core temperatures for main temperature regulating mechanisms
When threshold is reached, the relevant mechanism get activated

↓

Make adjustment to maintain normal body temperature

In cold weather

Reducing heat loss

- Vasoconstriction → Reduces skin blood flow & heat loss
- Mechanisms:
  - Increased sympathetic output (via hypothalamus)
  - Increased sensitivity of skin vessels to circulating catecholamines

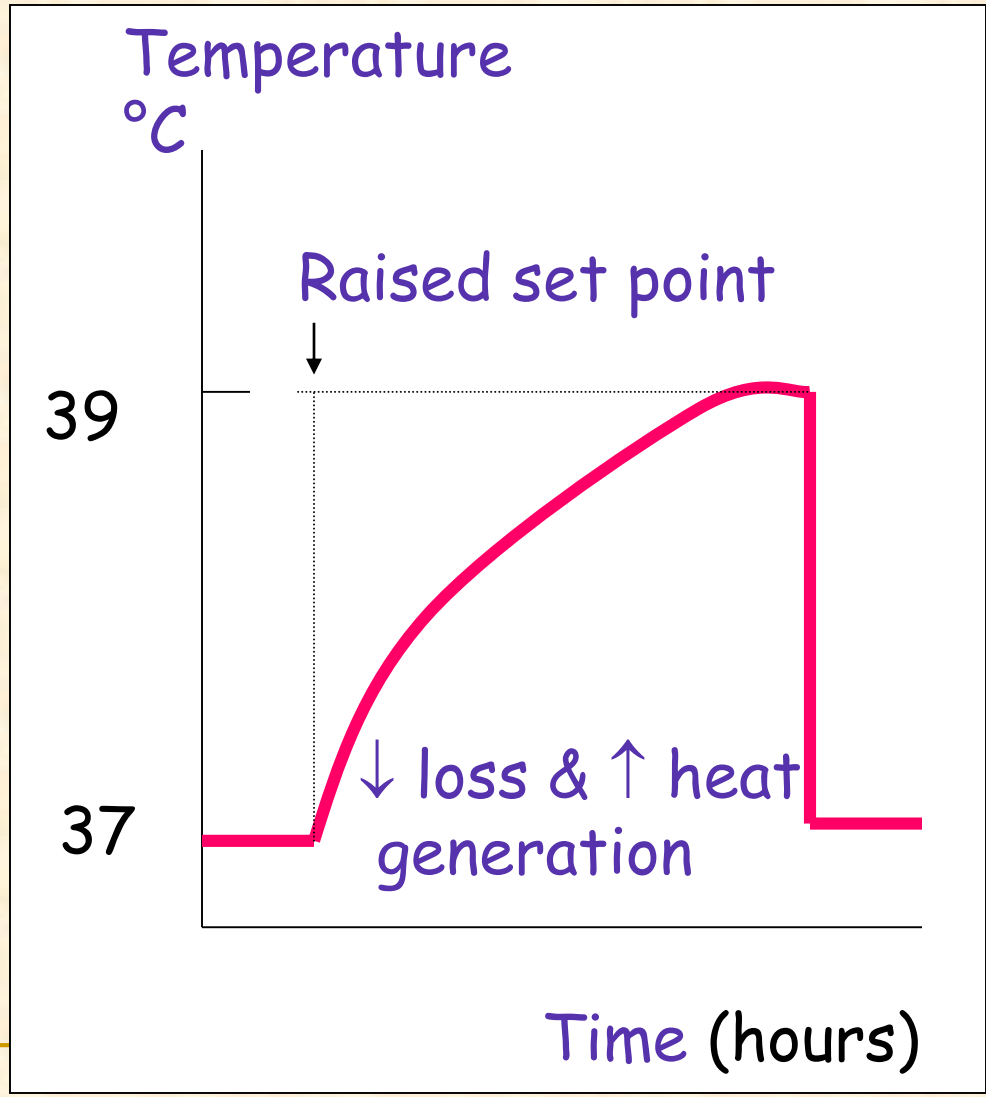
Increased heat generation

- Shivering
- Horripilation (piloerection, goose bumps, Erection of hair)
- Behaviour changes
  - Hunger – eat
  - ↑ activity

Home work: What are the mechanisms that get activated in warm weather?

Fever (Pyrexia)

- Hypothalamus reset from its normal to a higher point
- Body then has to maintains its temperature at this higher level



Infection (Endotoxin from bacteria)

Inflammation etc

Stimulation of cytokine production

Preoptic area of hypothalamus secretes Prostaglandins

Raise temperature set point

Fever

Hyperthermia

- Core body temperature > 38^{o}C

- Spectrum of heat-related illnesses
  - Heat cramps
  - Heat exhaustion
  - Heat stroke

Causes

- Increased heat load
  - Heat absorption from environment
  - Exertional
  - Metabolic heat
- Diminished heat dissipation
  - Obesity, anhidrosis, drugs
- Sepsis

Predisposing factors for heat stroke

Increased Heat Production	Decreased Heat Loss
Environmental heat stress	Environmental heat stress
Exertion	Cardiac disease
Fever	Peripheral vascular disease
Hypothalamic dysfunction	Dehydration
Drugs (sympathomimetics)	Anticholinergic drugs
Hyperthyroidism	Obesity
	Skin disease
	Ethanol
	β Blockers

Signs and Symptoms

- Heat cramps
  - Cramps in big muscles – spasms
  - Normal temperature, mentation
  - Caused by dilutional hyponatremia (hypotonic fluid replacement)

Signs and Symptoms, cont..

- **Heat exhaustion**

  Circulatory failure brought about by excessive sweating, cutaneous vasodilation which leads to hypovolaemia, decreased cardiac out put and mean arterial pressure

  - Weakness, dizziness, headache, syncope
  - Nausea, vomiting
  - Temperature 39-41.1^{o}C
  - Normal mentation
  - Profuse sweating

Signs and Symptoms, cont..

- **Heat Stroke**

Heat reduction mechanisms fails due to extremely high temp – hypothalamic control is lost

Causes – Exertional, hot & humid environment, alcohol (disable the thermostat)

- Mortality of 10-20% with current treatment
- Coma, seizures, confusion
- No sweating
- Temperature >41.1^{o}C
- Classic triad: hyperpyrexia, CNS dysfunction, anhidrosis

Treatment

- ABC’s!!!
- Cooling
- Remove to cool environment!
- Correct fluid and electrolyte imbalances

Hypothermia

- Core body temperature less than 35°C
  - Mild: 34-36°C
  - Moderate: 30-34°C
  - Severe: < 30°C

Causes of hypothermia

- Decreased heat production
  - Endocrine, insufficient fuel, neuromuscular inactivity
- Increased heat loss
  - Accidental/immersion hypothermia, vasodilatation, skin disorders, iatrogenic
- Impaired thermoregulation
  - Central (metabolic, drugs, CNS)
  - Peripheral (spinal cord injury, neuropathy, diabetes, neuromuscular disorders)

Predisposing factors for hypothermia

Age extremes
- Elderly
- Neonates

Outdoor exposure
- Occupational
- Sports-related
- Inadequate clothing

Drugs and intoxicants
- Ethanol
- Phenothiazines
- Barbiturates
- Anesthetics
- Neuromuscular blockers
- Others

Endocrine-related
- Hypoglycemia
- Hypothyroidism
- Adrenal insufficiency
- Hypopituitarism

Neurologic-related
- Stroke
- Hypothalamic disorders
- Parkinson's disease
- Spinal cord injury

Multisystem
- Malnutrition
- Sepsis
- Shock
- Hepatic or renal failure
- Burns and exfoliative dermatologic disorders
- Immobility or debilitation

Hypothermia when severe

- Reduces body temp – impairs CNS functions
  - Hypothalamic regulatory centre get depressed
- Eventually impair organ functions
  - E.g. Heart – pace makers

Frost bite

- Actual freezing of tissue (may or may not have hypothermia)
- Affect mainly the extremities
  - E.g. limbs, nose, ears etc.
- When severe – results in necrosis, gangrene and eventual loss of tissues
- Rewarming can minimize damage, if not severe

Disorders of hypothalamus

Damage to the hypothalamus

- Alteration of temperature regulation
- Abnormal eating behaviour
- Altered sleep - wake cycle
- Abnormal drinking behaviour
  especially reduced thirst
- Autonomic dysfunction