Chrono-Pharmacology

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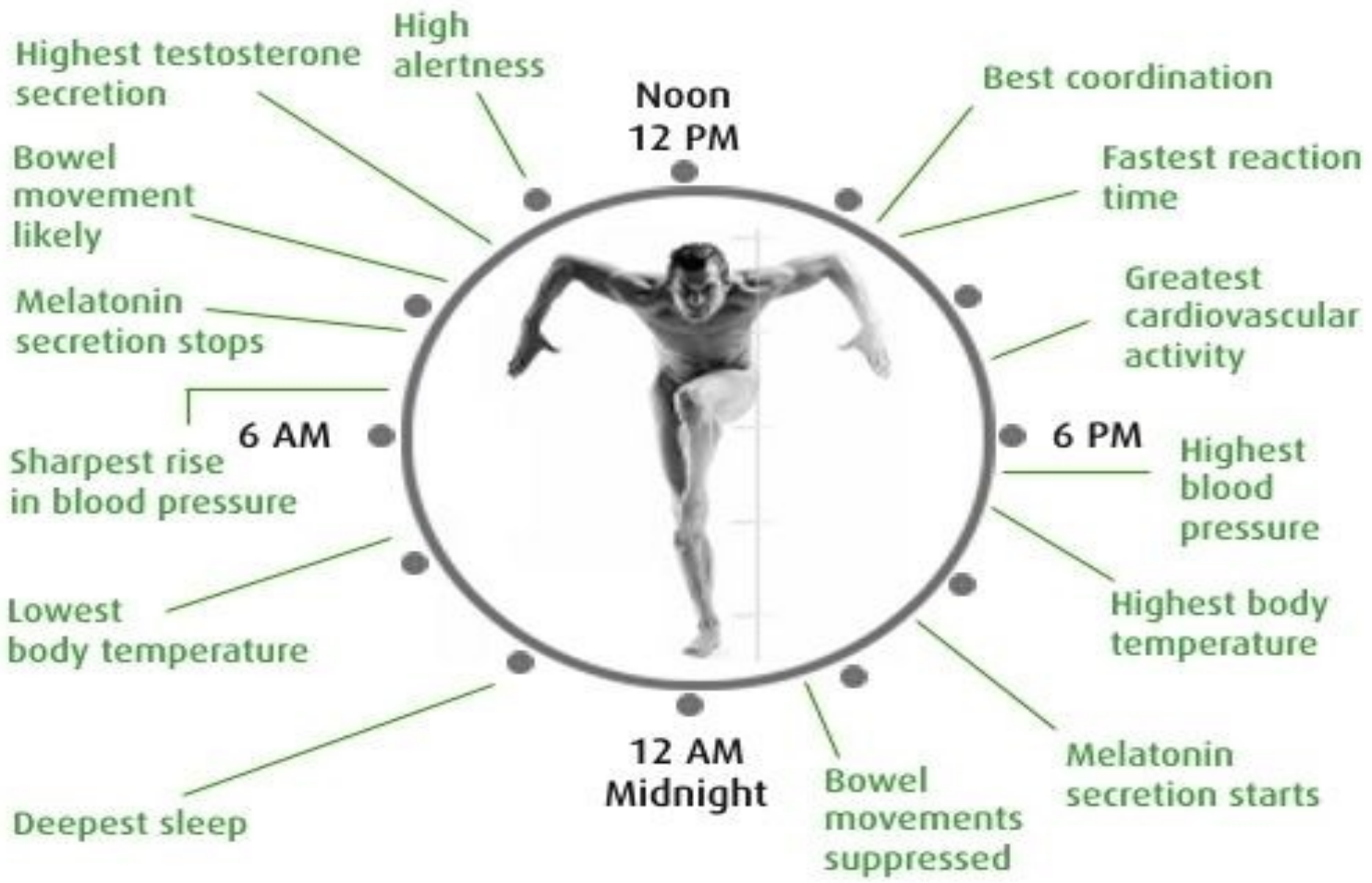
Introduction

Medications used in best time for enhance their therapeutic value



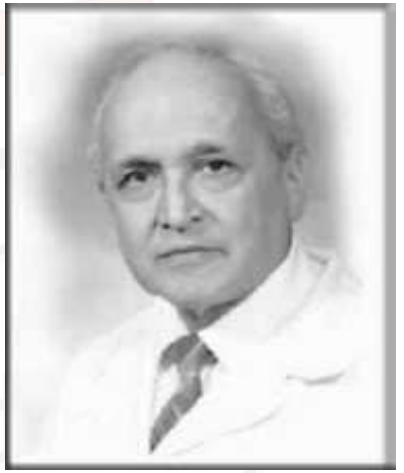
History

Jean-Jaques d'Ortous de Mairan

- described circadian rhythms of plants in the 18th century

Franz Halberg

- He coined the term '**Circadian'** in 20th century.
- (circa – about or approximately; dian-day or about 24 hour).
- Considered as one of the founders of
- Modern Chronobiology.



Definitions

Chronobiology:

- Chronos – Time; Bio-Life; Logos- Study
- It is the branch of sciences dealing with the "*Biological rhythm*" and their mechanism in the living organism is called **Chronobiology**

Biological Rhythm:

- It is the determined rhythmic biological process or function within a defined time period.

Definitions

Biological Rhythm:

- A biological rhythm is a self-sustaining oscillation with the duration of time between successive repetitions (i.e; the period) being rather non-varying under normal conditions.
- **Circadian**: Lasting for about 24 hours. "Sleep wake cycles"
- Infradian: Cycles longer than 24 hours. "Menstrual cycle"
- Ultradian: Cycles shorter than a day. "Neuronal firing time"
- Seasonal: Seasonal affective disorders.

Definitions

Chronopharmacology

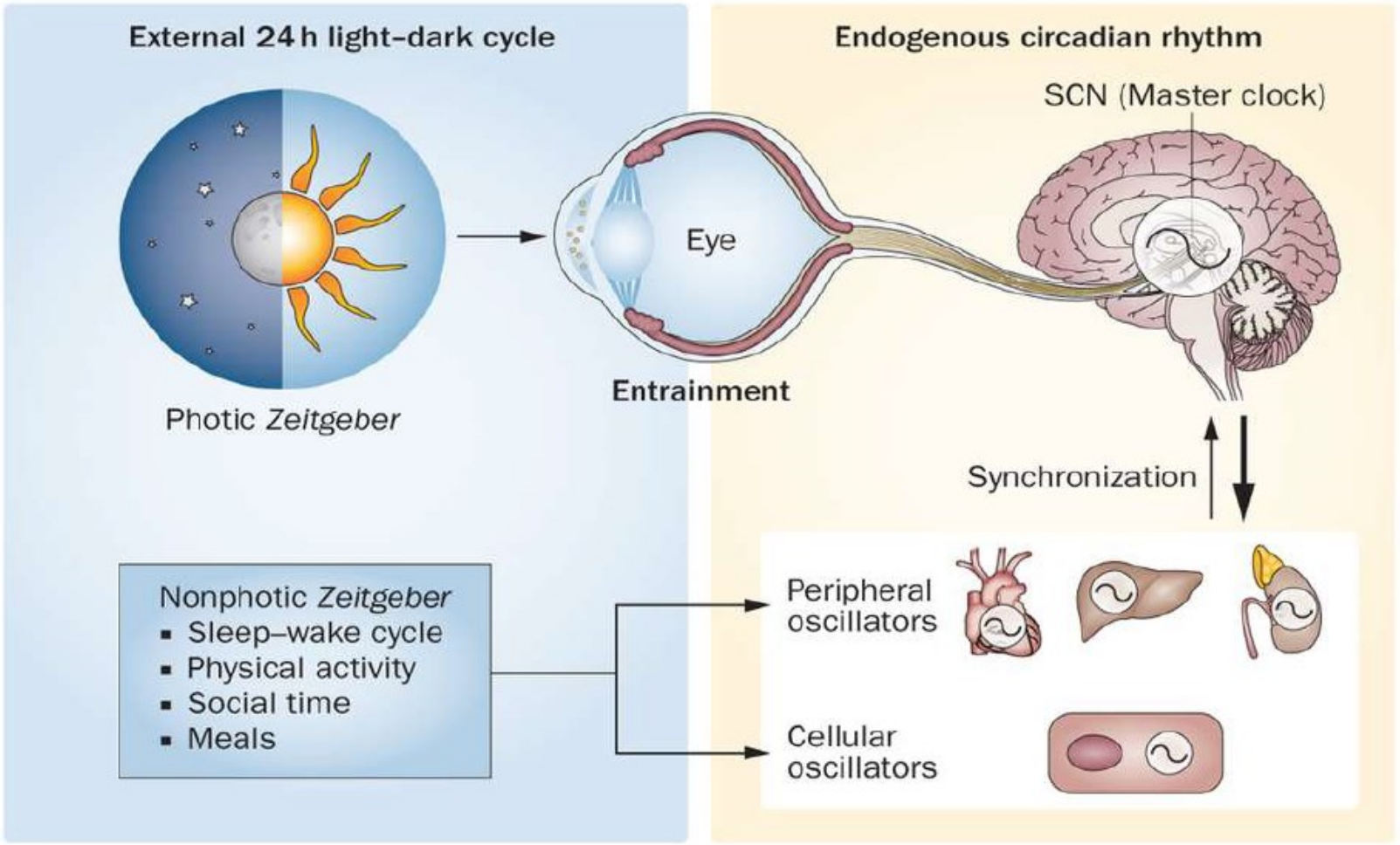
- Chronos – Time; Pharmacon- Drug; Logos- Study
- It is the branch of sciences dealing with the pharmacological action of a drug in relation to biological rhythm. It is concerned with the effects of drugs upon the timing of biological events and rhythms.
- Aim: Enhance the therapeutic efficacy, optimization of drug effects & minimization of adverse effects by using timing medications in relation to biological rhythm.

Circadian Rhythm

- Oscillations in the biological, physiological & behavioral functions of an organism with a periodicity of 24 hrs
- Circadian rhythms are particularly important in medical sciences and right time use of a medicine.
- A circadian clock (24 h clock) in the NS coordinates daily physiological cycles.
  - sleep/wake
  - Digestion
  - temperature
  - Hormones
  - Cardiovascular activity

Circadian Rhythm

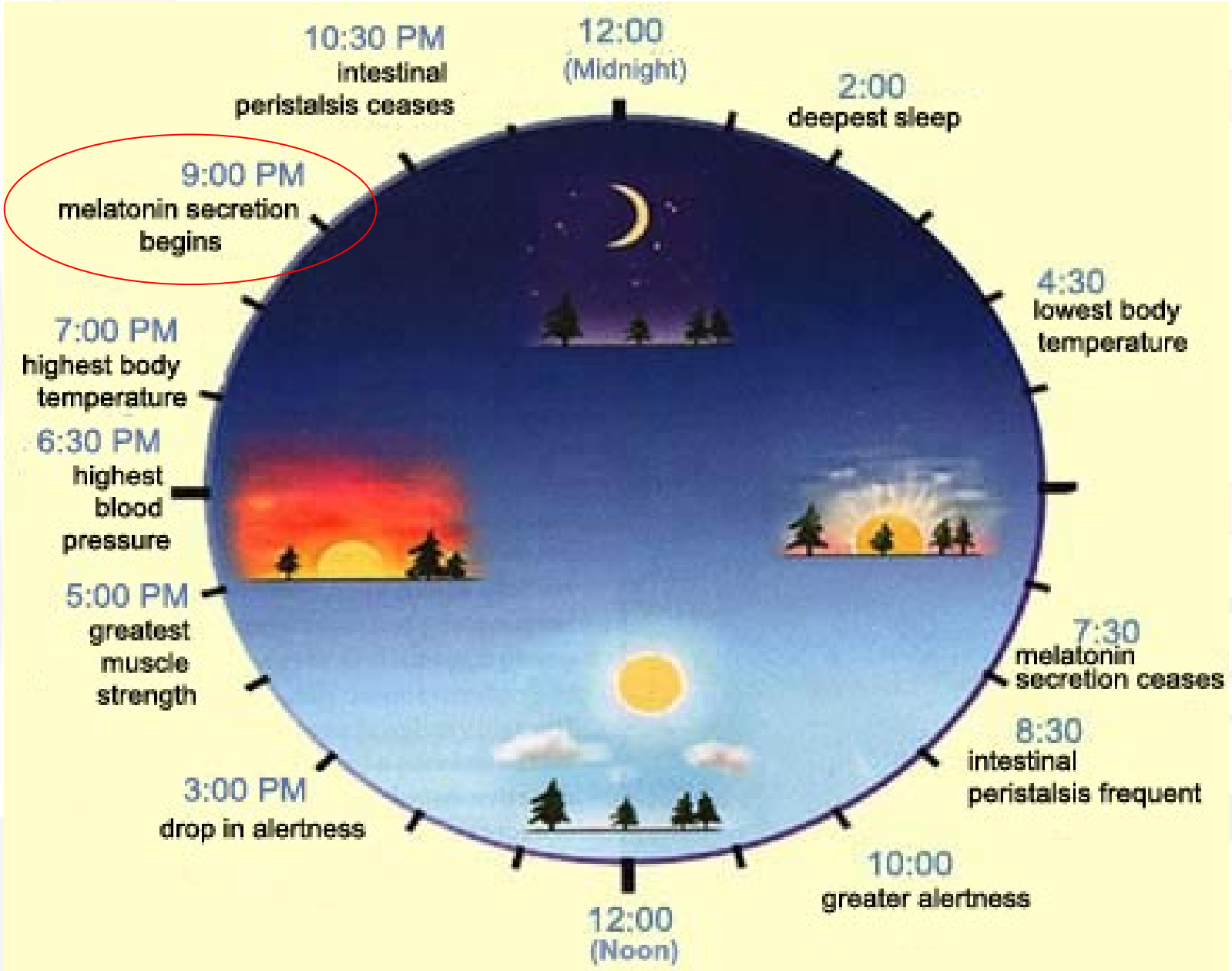
Regulation: External cues which reset the circadian clock = ***ZEITGEBERS (German words- Timer)*** = synchronizers



Circadian Rhythm

- In the mammals, an internal biological clock is located in the suprachiasmatic nucleus (SCN) of the hypothalamus, delivering its message of time throughout the body.
- It is responsible for circadian rhythms and annual and seasonal rhythms.
- SCN uses its connected ANS for spreading its time-of-day message, either by setting the sensitivity of endocrine glands (i.e., thyroid, adrenal, ovary) or by directly controlling an endocrine output of pineal gland (i.e., melatonin synthesis)

Circadian Rhythm



Chronopharmacolgy

- It is the branch of sciences dealing with the pharmacological action of a drug in relation to biological rhythm

- Chrophysiology—Chronopathophysiology—Chronopharmacology

Subdivision:

- **Chronotherapeutics**
- **Chronokinetic**
- **Chronotoxicity**
- Chronesthesy
- Chronergy

Chronopharmacolgy

- **Chronotherapeutics:** Study of effective therapy relation to biological rhythm of a disease
- **Chronokinetic:** It deals with the study of the temporal changes in the pharmacokinetics (ADME) of the drugs with respective time.
- **Chronotoxicity:** it may be defined as the changes in an organism's sensitivity to toxicants in relation to time.
- **Chronesthesy:** The rhythmic changes in susceptibility or sensitivity of a target system to a drug.
- **Chronergy:** Rhythmic changes of both the desired [effectiveness] and undesired [toxicity, tolerance] effects on the organism as a whole

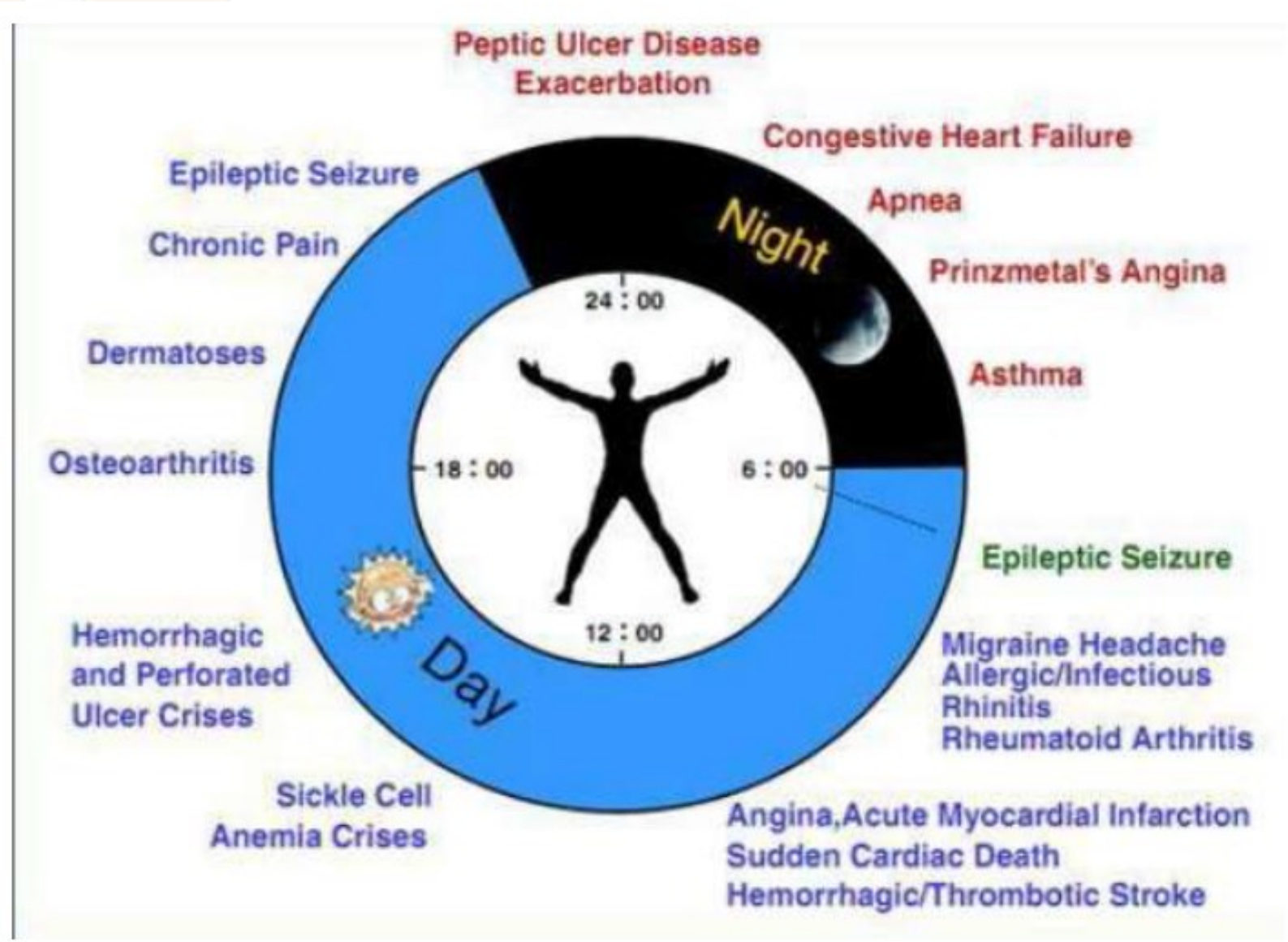
Chronopharmacolgy

Chronotherapeutics (Chronotherapy)

- Effective therapy relation to biological rhythm of a disease (Chrono-pathophysiology)
- It refers to treatment method in which drug availability is timed to match rhythm of diseases in order to optimize the therapeutic outcomes and minimize side effects

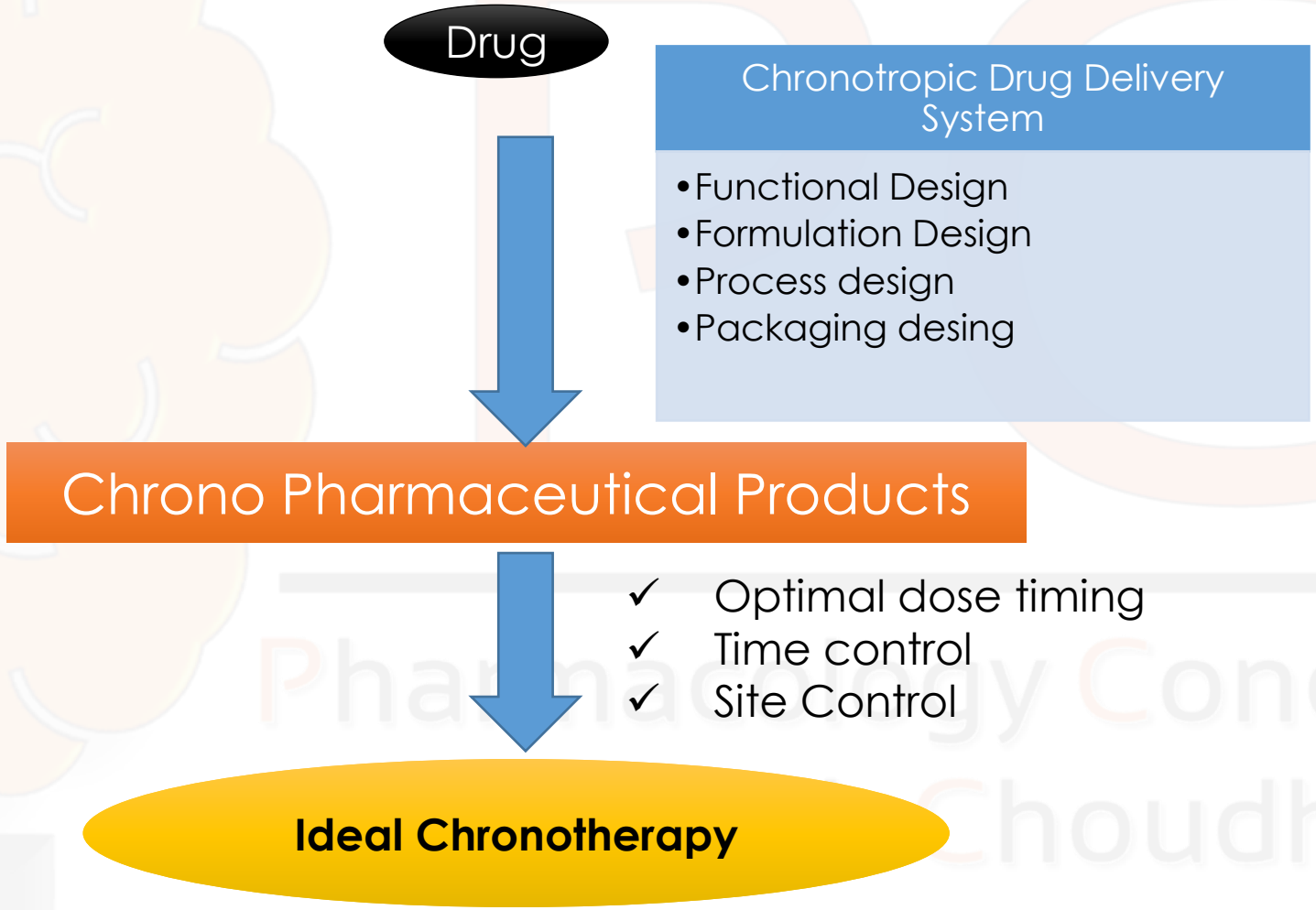
Advantages: Prevents over dosage; Appropriate usage of drug; Reduce side effects

Chronopharmacolgy



Chronopharmacolgy

Chronopharmaceutics: Development of chrono drug delivery system



Chronopharmacolgy

Chrono drug delivery system

- SODAS-Spheroidal oral drug absorption system
- CODAS- Chronotherapeutics oral drug absorption system
- Chronomodulating infusion pumps
- TIMERx
- CONTINER

Chronopharmacolgy

Application of Chronopharmacology:

- Asthma therapy
- Hypertension
- Oncology
- Strokes
- Sleep apnea
- GI tract disorders
- Allergies

Chronopharmacolgy

Asthma Therapy:

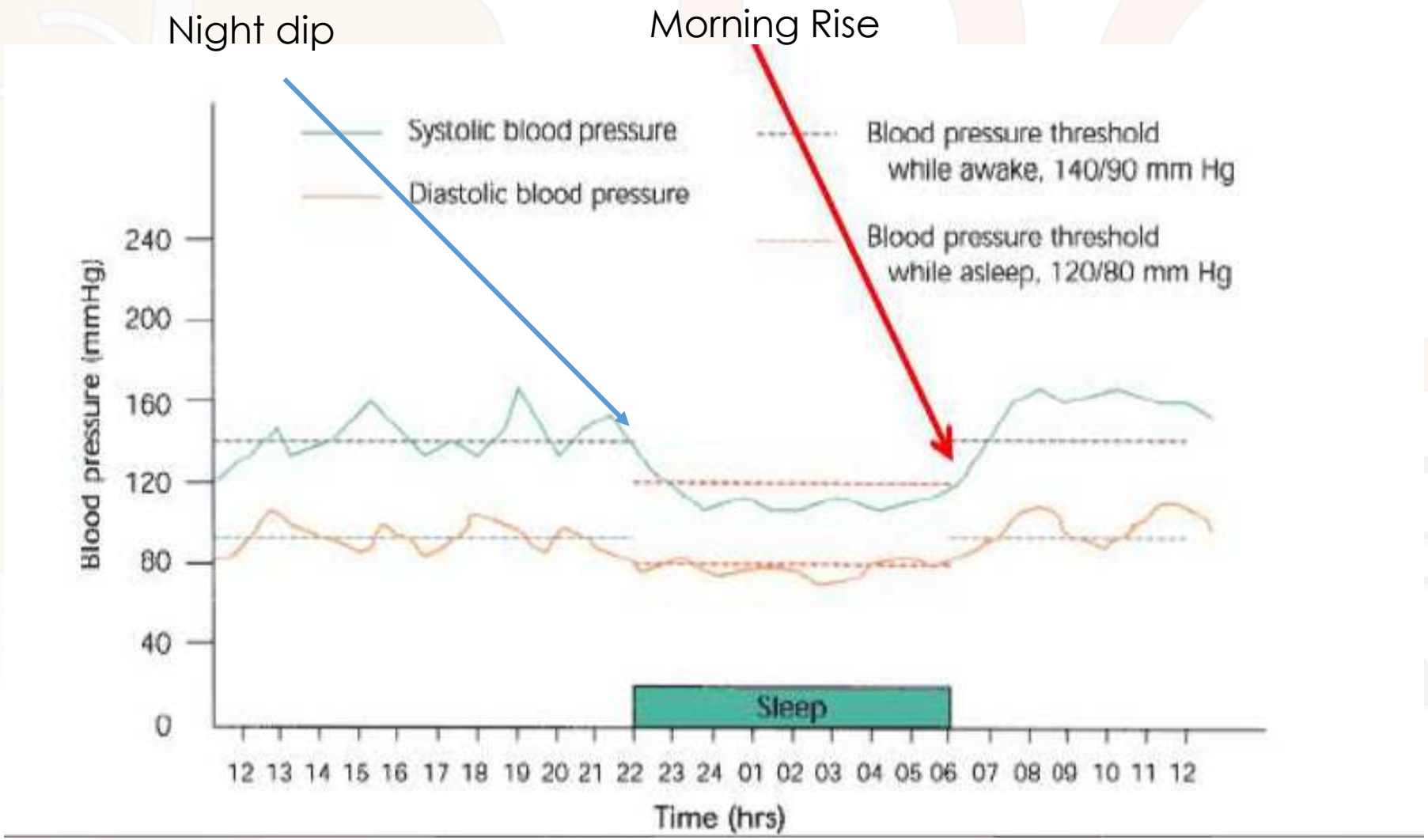
- Asthmatic attack is more common between 2 AM to 6 AM
- The risk of asthmatic attack is almost 70 times higher in patients at 04:00-05:00 AM in the morning, compared with the afternoon
- Increased bronchoconstriction at night due to…
  - ↑Parasympathetic tone
  - ↓ Adrenaline
  - ↓ Cortisol at midnight
  - ↑Sensitivity to irritants and allergens at night
  - exacerbations of allergic rhinitis & asthma

Asthma Therapy:

- Chronopharmacotherapy for asthma is aim to getting maximum beneficial effect from bronchodilators during the early morning
- E.g., **Sustained release long acting theophylline** taken once a day in the evening causes theophylline blood levels to reach their peak and improve lung function during the difficult early morning.

Chronopharmacolgy

Hypertension Therapy: Blood pressure pattern in a day



Hypertension Therapy:

- A new COER (Controlled onset extended release system) verapamil use in HTN It is formulated as a pill with a shell that dissolves slowly. Taken at bed-time, this exerts peak effects btw 5 am and noon & no mid-night dip in B.P is seen.

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