9th National Seminar on Travel Medicine

17 November 2011

Jet Lag

14.30-14.50

JET LAG

Prof F. Van Gompel, – ITG Antwerpen

The NEW ENGLAND JOURNAL of MEDICINE

CLINICAL PRACTICE

Jet Lag

Robert L. Sack, M.D.

This Journal *feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the author's clinical recommendations.*

N Engl J Med 2010;362:440-7.

NEJM february 4 2010 jet lag casus

- A 57-year-old physician is planning a trip from Europe to the US to attend a scientific conference.
- Time difference = 6 hours

- His previous trip to the US was complicated by
  - sleepiness during meetings
  - difficulty falling asleep and remaining asleep at night

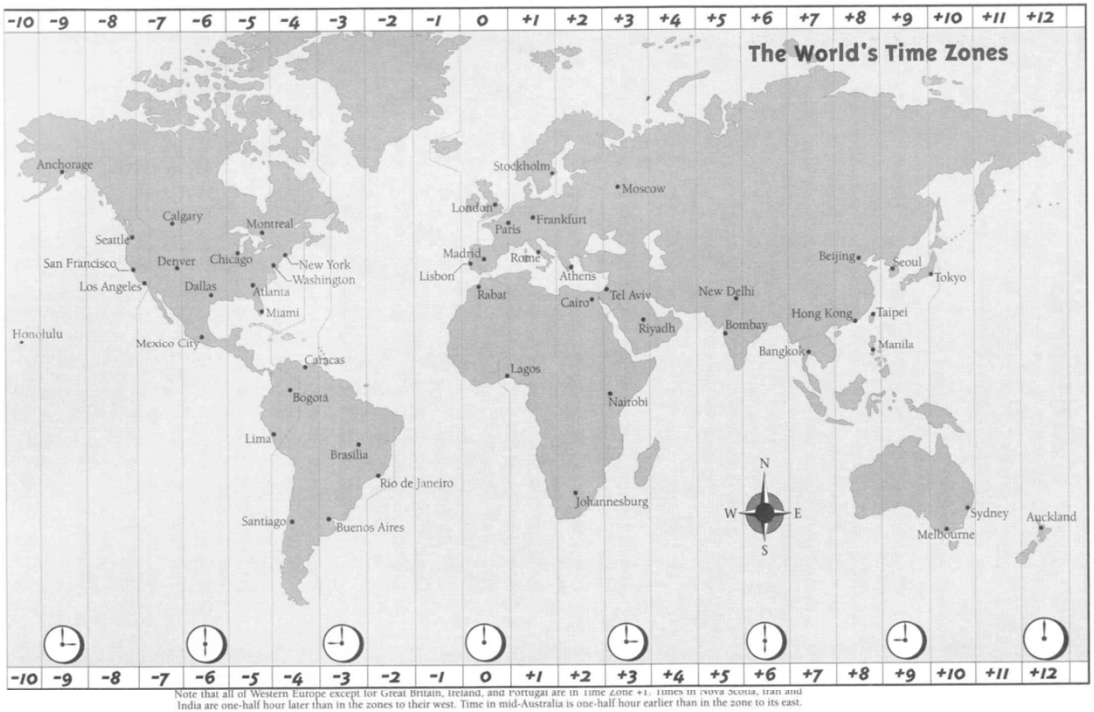
- He wants to know what he can do to avoid jet lag. What would you advise?

In the case of the traveler described in the vignette, I would recommend that,

- **On his arrival at his destination = WESTward = 6 hours longer,** I would advise him
  1. to seek exposure to bright **light** in the **evening**
  2. to take a low dose of **melatonin** (*0.5 mg*) if he awakens **before 5 a.m**.
- **After his return = EASTward = 6 hours shorter** , I would recommend that
  1. he walk in the bright sun**light** each **morning** and
  2. drink a **caffein**ated beverage each **morning**.

I would also recommend that

1. he take **melatonin** *(3 mg)* (the dose that is most commonly available) at **bedtime**, for 3 to 4 days to accelerate phase shifting = advancing.
2. If melatonin alone is insufficient to facilitate sleep, the addition of a **hypnotic** agent may be justified.

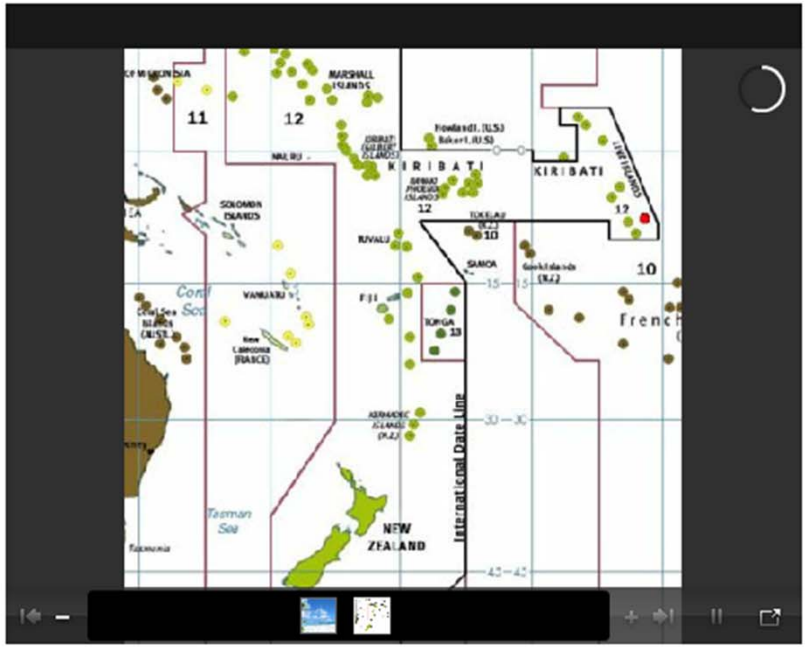


Note that all of Western Europe except for Great Britain, Ireland, and Portugal are in Time Zone +1. Times in Nova Scotia, Iran and India are one-half hour later than in the zones to their west. Time in mid-Australia is one-half hour earlier than in the zone to its east.

Tokelau springt over datumgrens

vrijdag 07 oktober 2011 om 15u45

De Zuid-Pacifische eilandengroep Tokelau stapt over naar de westkant van de internationale datumgrens. Samoa deed onlangs hetzelfde.



De Tokelau-eilanden, bestaande uit drie atollen met zo'n 1.400 inwoners, zijn een overzees gebiedsdeel van Nieuw-Zeeland ten noorden van Fiji, ongeveer halfweg tussen

Jet lag = a recognized sleep disorder

- Results from crossing *several* time zones *too rapidly* for the **circadian clock** to keep pace
- The pathophysiology = temporary *misalignment* between the **circadian clock** and **local time**
- The circadian clock is located in the suprachiasmatic nucleus of the hypothalamus)

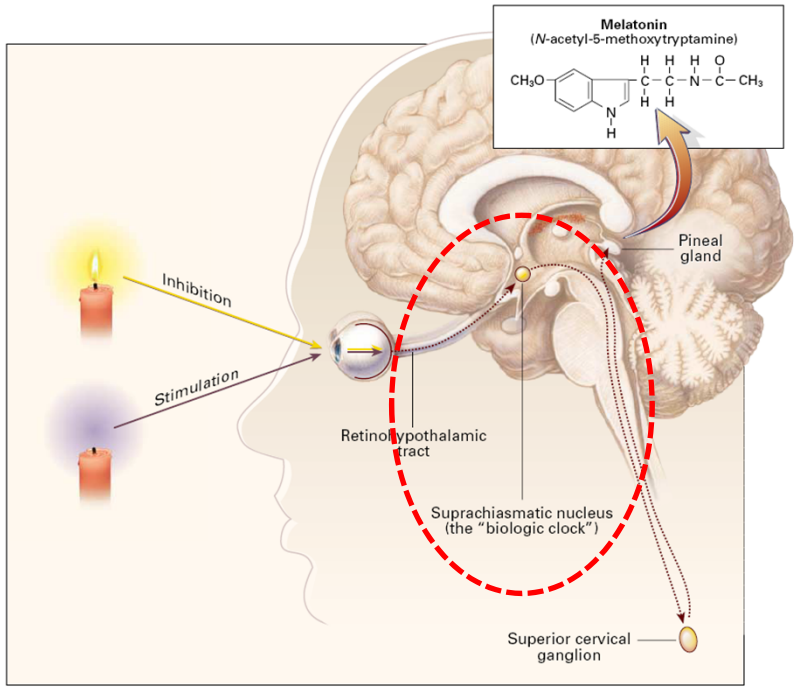


Figure 1. Physiology of Melatonin Secretion.

The **circadian / body clock** is

- normally *synchronized* to the **solar light–dark cycle**
- promotes alertness during the day and sleep at night

- ***slow*** *to reset*, so that after time zones have been crossed,

  the endogenous signals for sleep and wakefulness

  do not match the

  local light–dark and social schedules**.**

The **symptoms** of jet lag are

- insomnia and daytime sleepiness
- but can also include
  - dysphoric mood
  - diminished physical performance
  - cognitive impairment
  - gastrointestinal disturbances “Gut-lag”
- usually medically benign and self-limited
  - it may occasionally cause serious misjudgments in business or professional dealings

often compounded by **nonspecific travel fatigue**

- as a consequence of
  1. prolonged immobility
  2. irregular sleep times and mealtimes
  3. dehydration
  4. other factors associated with long-distance air travel, irrespective of the crossing of time zones

- occurs with long-distance travel,
  whether or not times zones are crossed

- can be reversed within a day or two
  with adequate diet, rest, and sleep

←→ symptoms of **jet lag** persist until the circadian system is realigned.

The intensity and duration of the symptoms of jet lag are related to several factors :

1. **Number** of time zones crossed
2. **Direction** of travel
   - it is more difficult to travel east than west because the endogenous period of the body clock is typically longer than 24 hours and it is therefore easier to lengthen the day than to shorten it;
3. **Sleep loss** during travel
4. Availability of **local time cues**
   - Exposure to natural light at the destination is the most important factor for re-entrainment of the circadian clock, but it varies with the location, the time of year, and the activity of the traveler;
   - Exposure to bright light at the "wrong" phase of the circadian cycle can inhibit re-entrainment of the circadian clock.
5. **Ability to tolerate** circadian misalignment
   - individual differences
   - tolerance appears to decrease with increasing age

Table 1. Factors That Contribute to Jet Lag.

Factor	Contribution to Jet Lag
No. of time zones crossed	The degree of circadian misalignment is proportional to the number of time zones crossed; nonspecific travel fatigue occurs with long-distance travel whether or not times zones are crossed and often compounds symptoms of jet lag.
Direction of travel	For most people, it is more difficult to travel east than west because the endogenous period of the body clock is typically longer than 24 hours and it is therefore easier to lengthen the day than to shorten it; however, some people, especially "morning types" (whose endogenous period may be shorter than 24 hours), may find eastward travel easier.
Sleep loss during travel	Sleep loss is almost inevitable with overnight travel, but it may be attenuated with business-class or first-class seating; acute sleep loss can be made up with adequate sleep after arrival, but symptoms of jet lag will probably persist until circadian realignment has occurred.
Availability of local time cues	Exposure to natural light at the destination is the most important factor for re-entrainment of the circadian clock, but it varies with the location, the time of year, and the activity of the traveler; exposure to bright light at the "wrong" phase of the circadian cycle can inhibit re-entrainment of the circadian clock.
Ability to tolerate circadian misalignment	There are individual differences in the ability to tolerate phase misalignment, but in general, tolerance appears to decrease with increasing age.

3 treatment strategies

1. promoting ***realignment*** **of the circadian clock** with
   - the use of **appropriately timed exposure to light**
   - the administration of **melatonin**
   - or **both**
2. planning the optimal **duration and timing of sleep**
3. using **medication to counteract** the symptoms of
   - *insomnia*
   - *daytime sleepiness*

- can be combined in practice.

1. Therapeutic Resetting of the Circadian Clock

It has been estimated that the circadian clock resets an average of

- **90minutes** later each day after a **westward** flight
- **60 minutes** earlier each day after an **eastward** flight
  - Used indicator of circadian timing =
    - the daily cycle in core body temperature
    - the timing of melatonin secretion
- In principle, ***realignment*** **can be accelerated** by **recruiting** **the clock-resetting mechanisms** that, under ordinary circumstances, fine-tune the circadian system :

1. Therapeutic Resetting of the Circadian Clock

1. A. Optimizing **Light** Exposure

1. B. **Melatonin** Administration

1. A. Optimizing Light Exposure

1. A. Optimizing Light Exposure

- There is general consensus that
  the timing of exposure to light
  is the most important time cue
  for synchronizing circadian rhythms
  in humans (as it is in most species)

1. A. Optimizing Light Exposure

!!! However, current treatment recommendations for resetting the circadian clock
that are based on the timing of light exposure
rely heavily on **models** of circadian regulation that have been developed from **laboratory studies (simulations)**
---- must be considered to be **provisional**, pending additional testing in randomized clinical trials !!!!

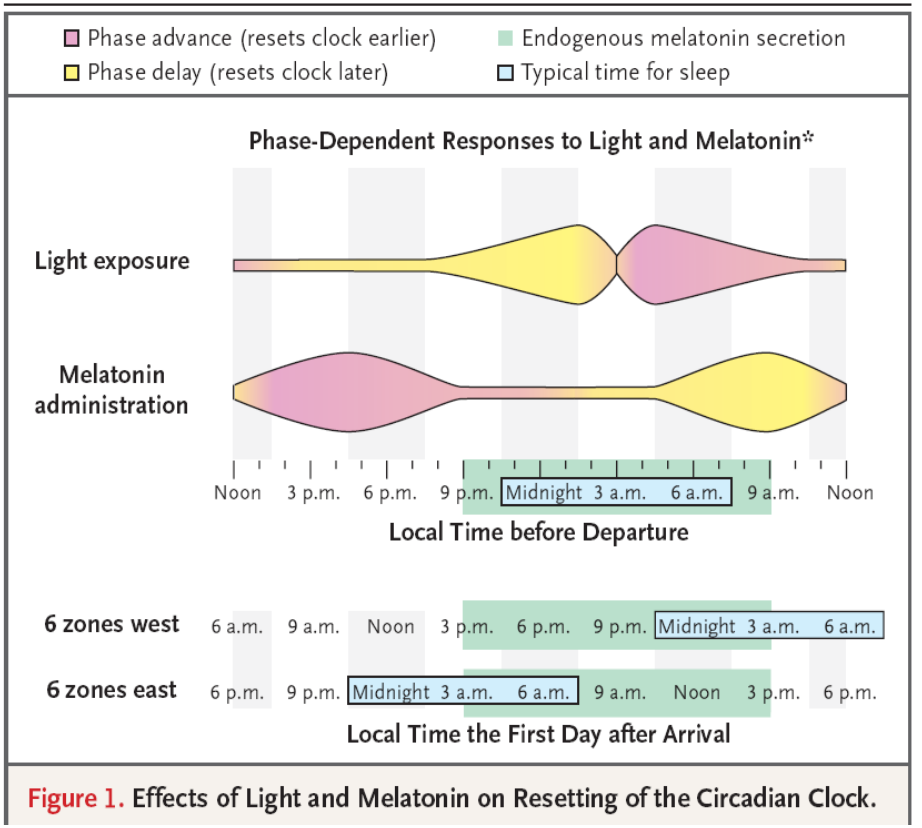
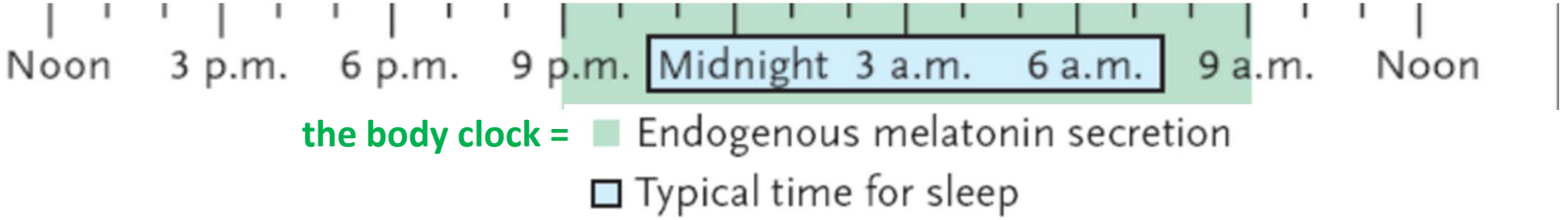


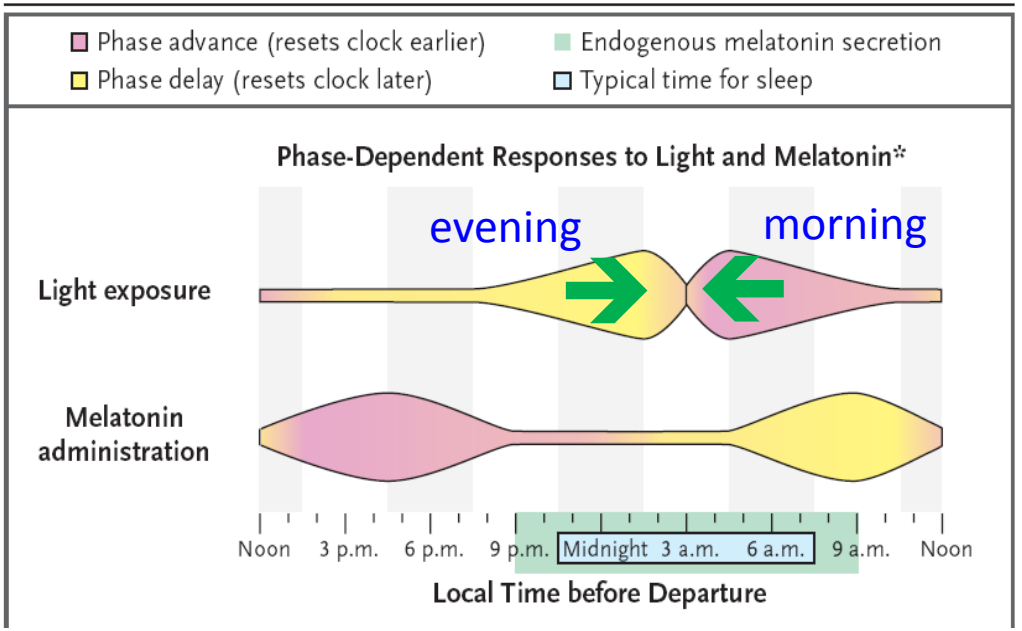
Figure 1. Effects of Light and Melatonin on Resetting of the Circadian Clock.



Exposure to light in the evening ➔ shifts **the body clock** to a later time = phase delay

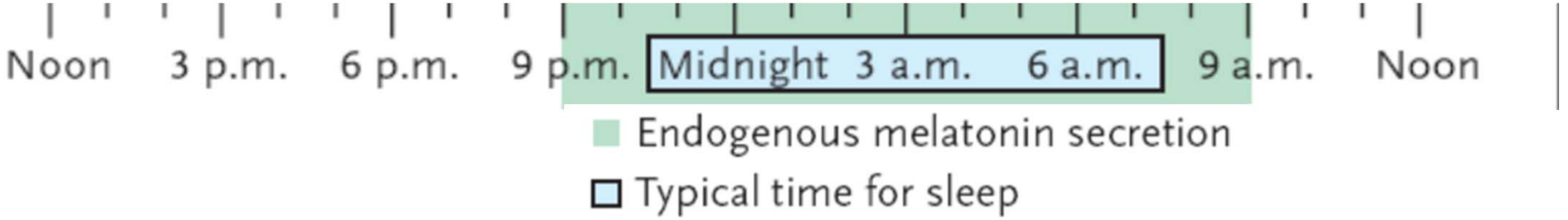
Exposure to light in the morning ➔ shifts **the body clock** to an earlier time = phase advance

= compensating for any drift away from a 24-hour cycle



at some point during the night, there is a **crossover point** that separates

- "evening responses"
- "morning responses"



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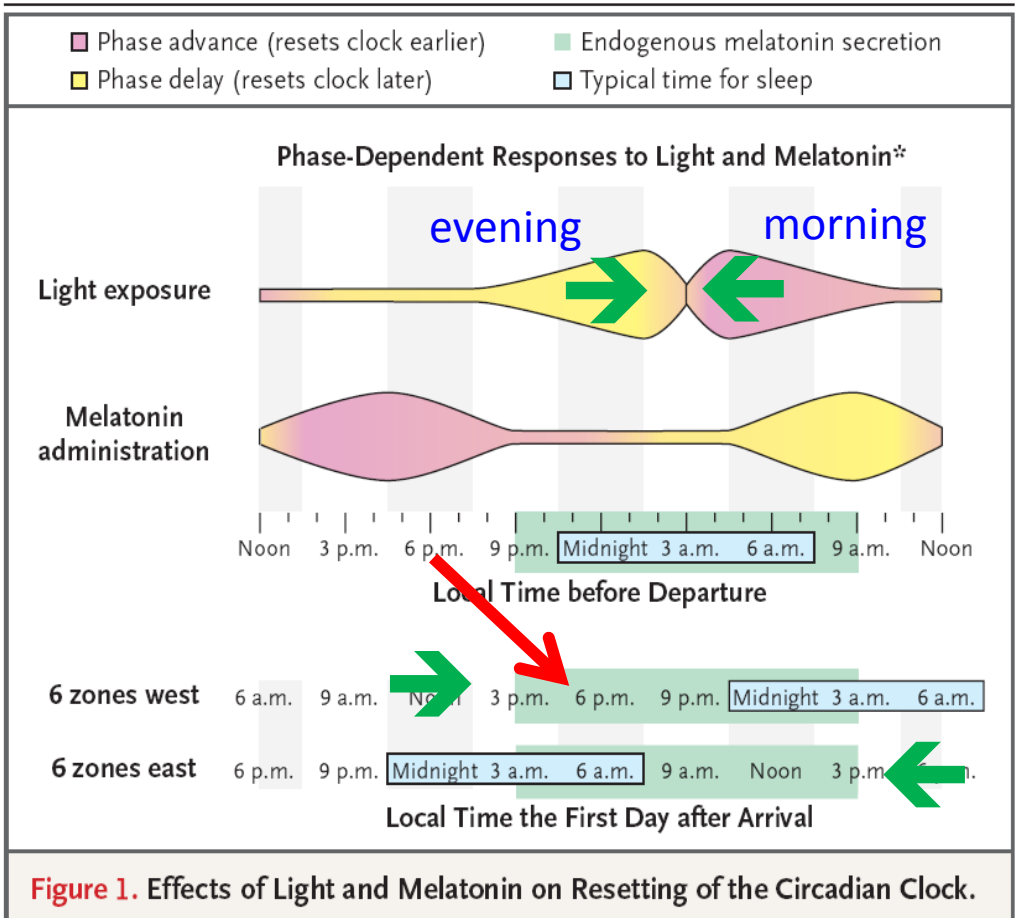

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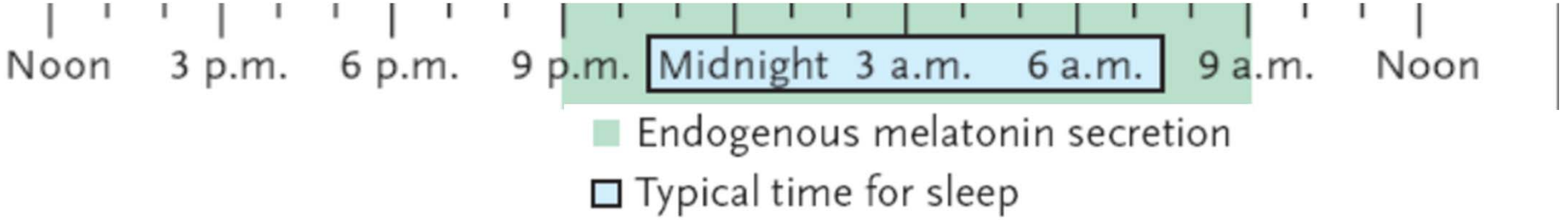

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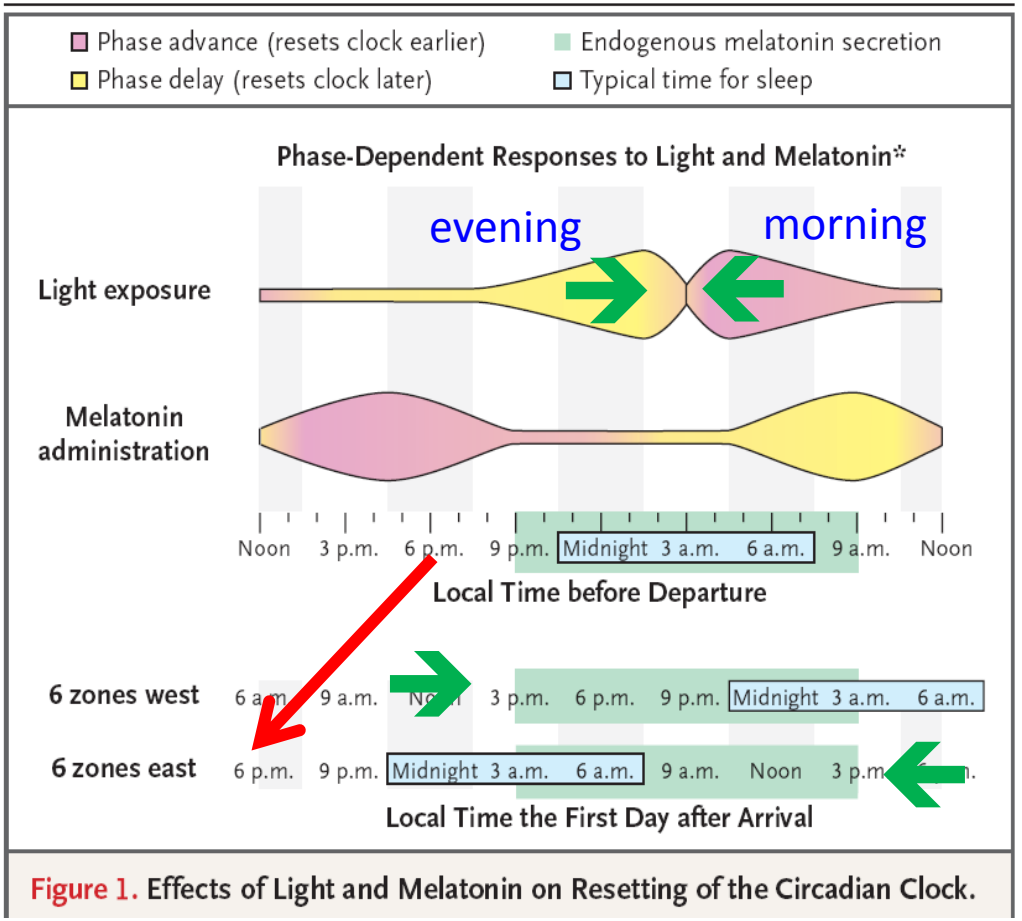


Figure 1. Effects of Light and Melatonin on Resetting of the Circadian Clock.

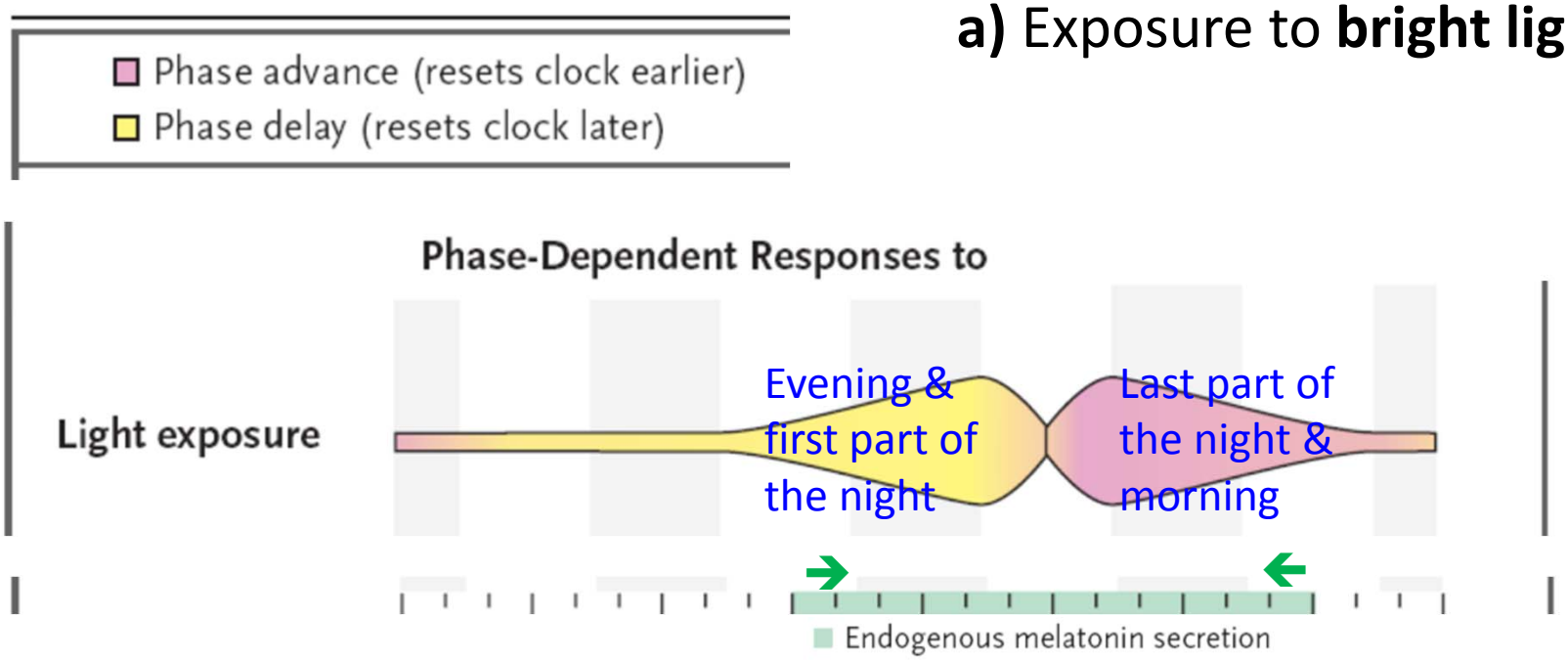
1. A. Optimizing Light Exposure

- The timing of sleep does not, in itself, reset the clock;
- however, because people **normally sleep in the dark with their eyes closed,** sleeping limits the exposure to light and therefore plays an important role in the regulation of the circadian clock.
- Unplanned exposure to natural daylight in the new location generally facilitates the adaptation of the circadian clock to local time
- the intensity and availability of light will **vary** according to the
  - time and season of travel
  - the local weather
  - the brightness of interior illumination
  - the activity and sleep schedule of the traveler.

- These factors can result in considerable **variability** in the direction and speed of re-entrainment.

a) A traveler may be able to accelerate re-entrainment by **intentionally seeking out bright light at the optimal times of the day**.

- for travel across ***up to (≤) 8 time*** *zones*
  a simple recommendation is
  to seek exposure to bright light
  - in the morning after eastward travel
  - in the evening after westward travel

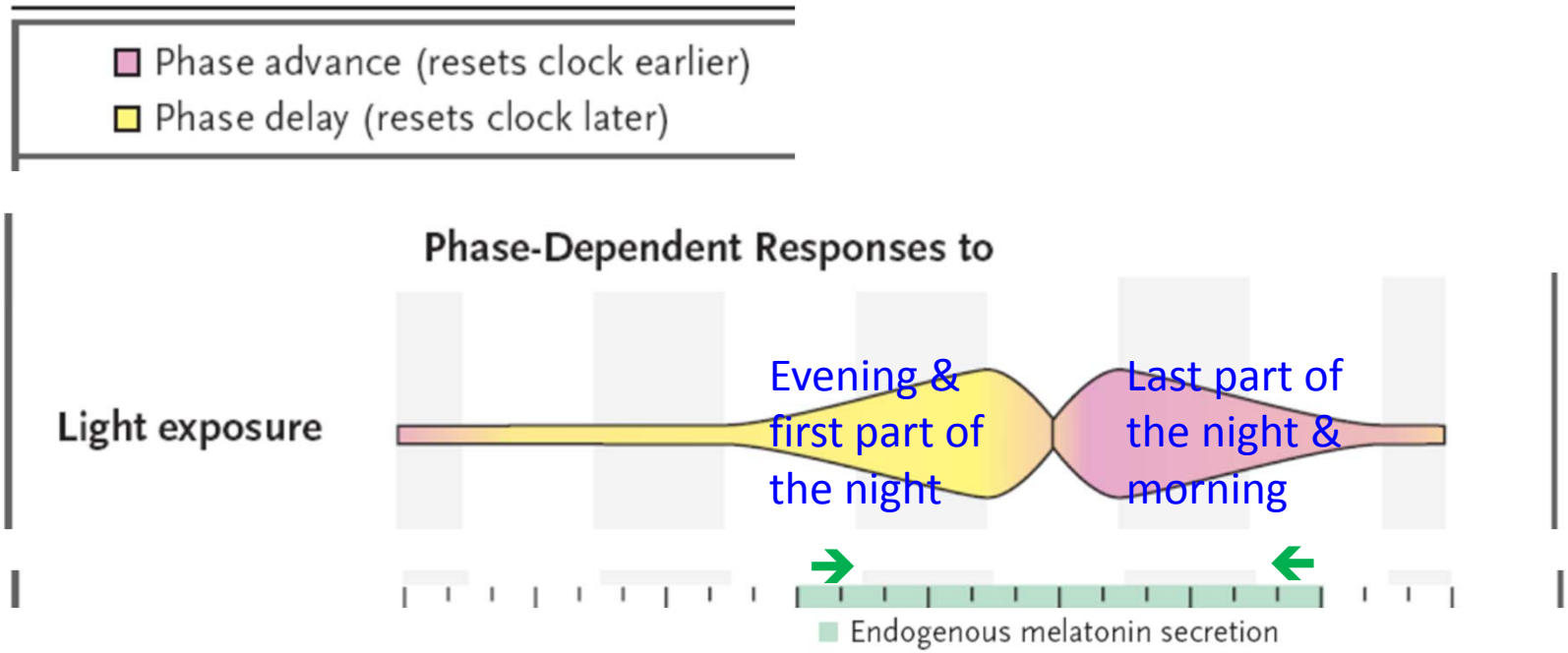


a) Exposure to **bright light**

Exposure to **bright light**

- in the **evening** and the first part of the night would reset the endogenous clock later (= phase delay) ➔ after WESTward travel

- in the last part of the night and the **morning** would reset the endogenous clock earlier (= phase advance) ➔ after EASTward travel



b) It may be useful to **avoid light** when exposure would impede adaptation

- for travel across ***eight or more time*** *zones*
  staying indoors ……. may be indicated for
  - the first few hours of daylight after eastward flights
  - a few hours before dusk after westward flights

1. A. Optimizing Light Exposure

- If avoiding bright light is impractical, **wearing low-transmittance sunglasses** may be a useful alternative, as suggested by studies that have simulated shift work

- After a few days, the circadian system will have shifted sufficiently that avoidance of light can be discontinued

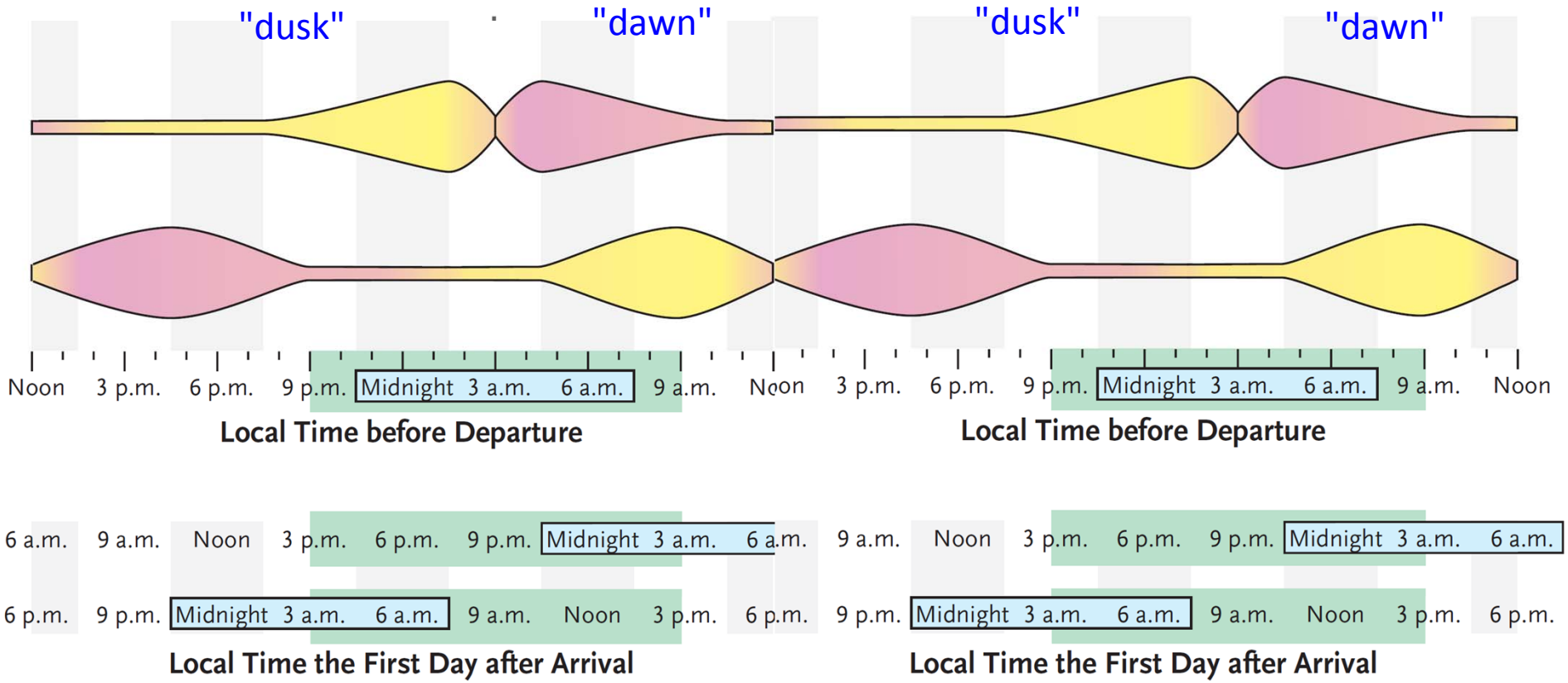
1. A. Optimizing Light Exposure

- More specific recommendations for exposure to and avoidance of light are provided in the Supplementary Appendix

For westward travel (to reset the circadian clock later)								
Time zones crossed	Seek Light			Avoid Light			Take melatonin	
3	17:00	to	23:00	3:00	to	9:00	4:00	
4	16:00	to	22:00	2:00	to	8:00	3:00	
5	15:00	to	21:00	1:00	to	7:00	2:00	

For eastward travel (to reset the circadian clock earlier)								
Time zones crossed	Seek Light			Avoid Light			Take melatonin	
3	9:00	to	15:00	23:00	to	5:00	19:00	
4	10:00	to	16:00	0:00	to	6:00	20:00	
5	11:00	to	17:00	1:00	to	7:00	21:00	
6	12:00	to	18:00	2:00	to	8:00	22:00	
7	13:00	to	19:00	3:00	to	9:00	23:00	

Some experts recommend that all flights that cross <u>more than (>) 8 to 10 time zones</u> be treated as if they were westward …



…… <u>after eight or more time zones have been crossed</u>, sunlight that would ordinarily be interpreted by the circadian system as **"dawn"** may now be interpreted as **"dusk"** (and vice versa).

Areas of Uncertainty

- Additional field studies that use state-of-the-art measures of the circadian phase are needed to elucidate the natural course of circadian re-entrainment after time-zone displacement and the factors that mediate it, such as exposure to natural light, baseline circadian phase before departure, age, and sex.
- Randomized, controlled trials are needed to test the efficacy of planned exposure to or avoidance of light.
- The optimal treatment for travelers who cross 8 to 12 time zones remains perplexing, since some studies have shown that re-entrainment can occur by either advances or delays
- The recommendation for treating all such travel as if it were westward travel needs to be tested in field studies.

1. B Melatonin Administration

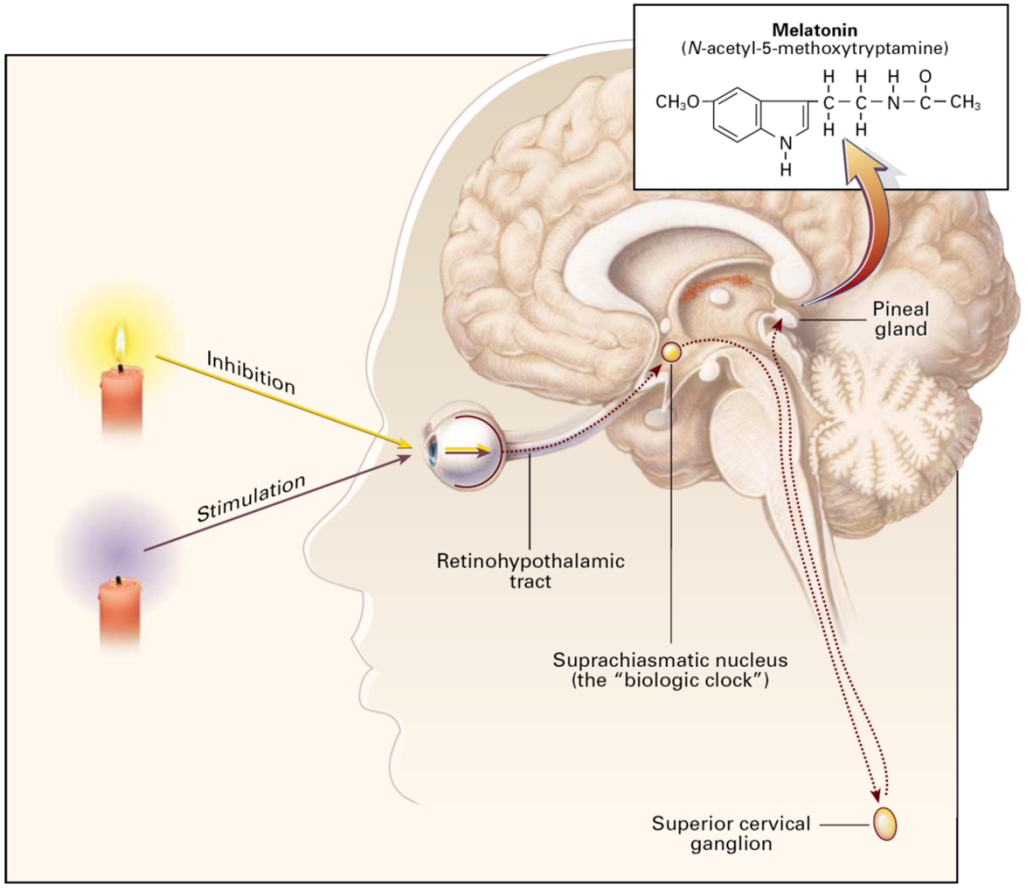
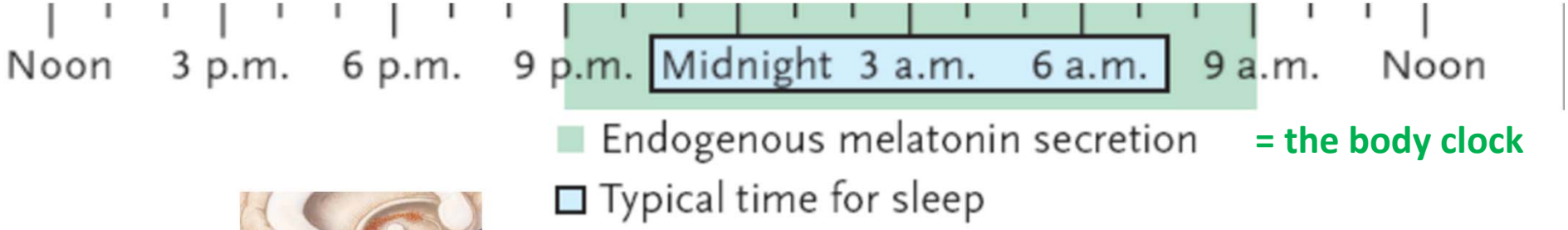


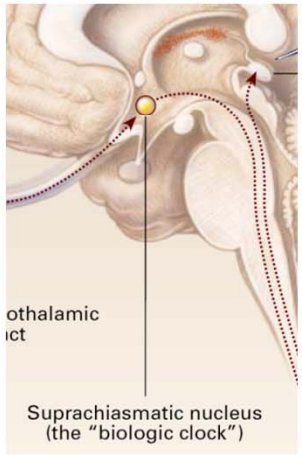
Figure 1. Physiology of Melatonin Secretion.

1. B Melatonin Administration

- a hormone
- secreted for about 10 to 12 hours at night
- synchronized to the light–dark cycle by the circadian clock.



= the body clock

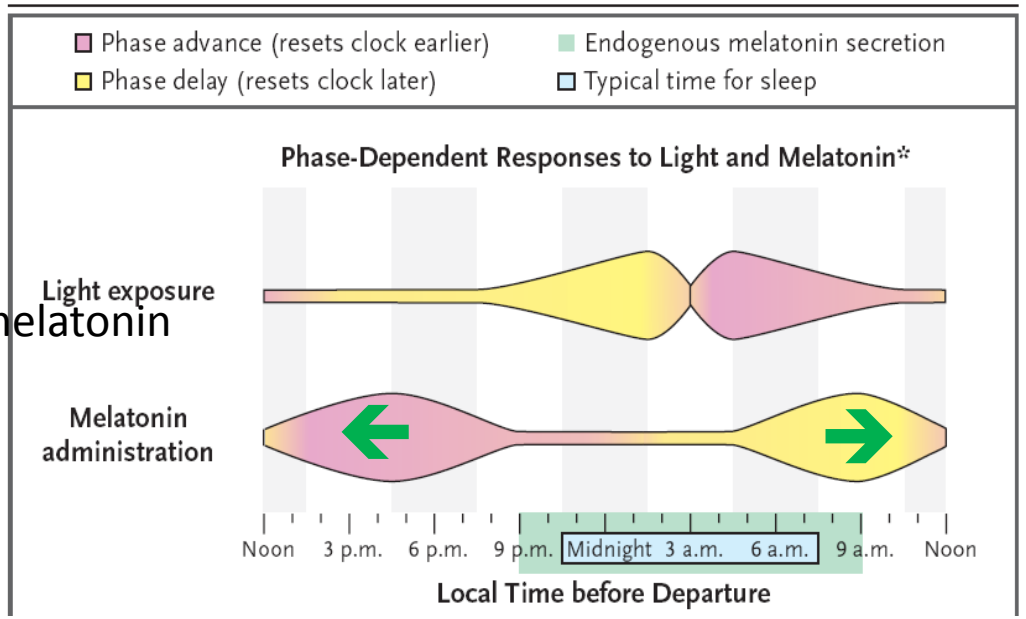


- = a darkness signal
- with opposite effects (*to the effects of exposure to light*) on circadian timing :

1. B Melatonin Administration

- when melatonin is taken **in the evening** (before the onset of its endogenous secretion) ← it resets the **body clock** to an earlier time = phase advance

- when melatonin is taken **in the morning** (after endogenous levels have fallen) → it resets the **body clock** to a later time = phase delay



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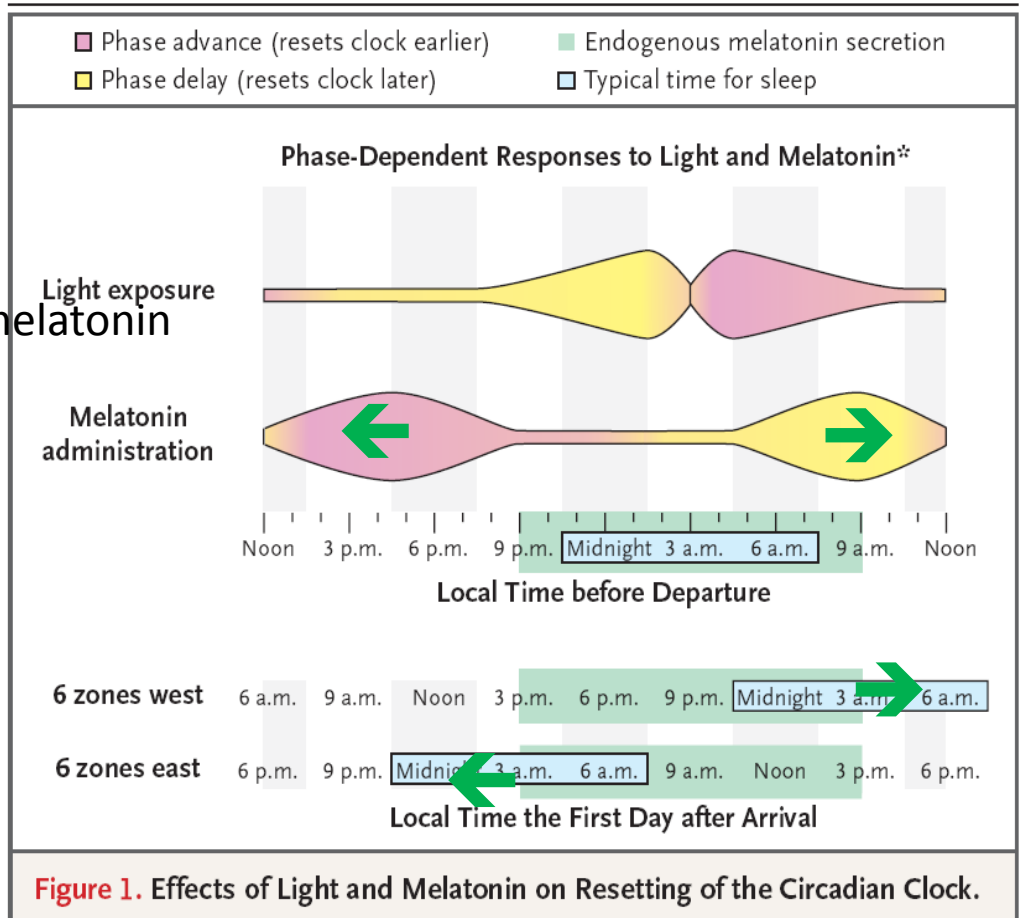
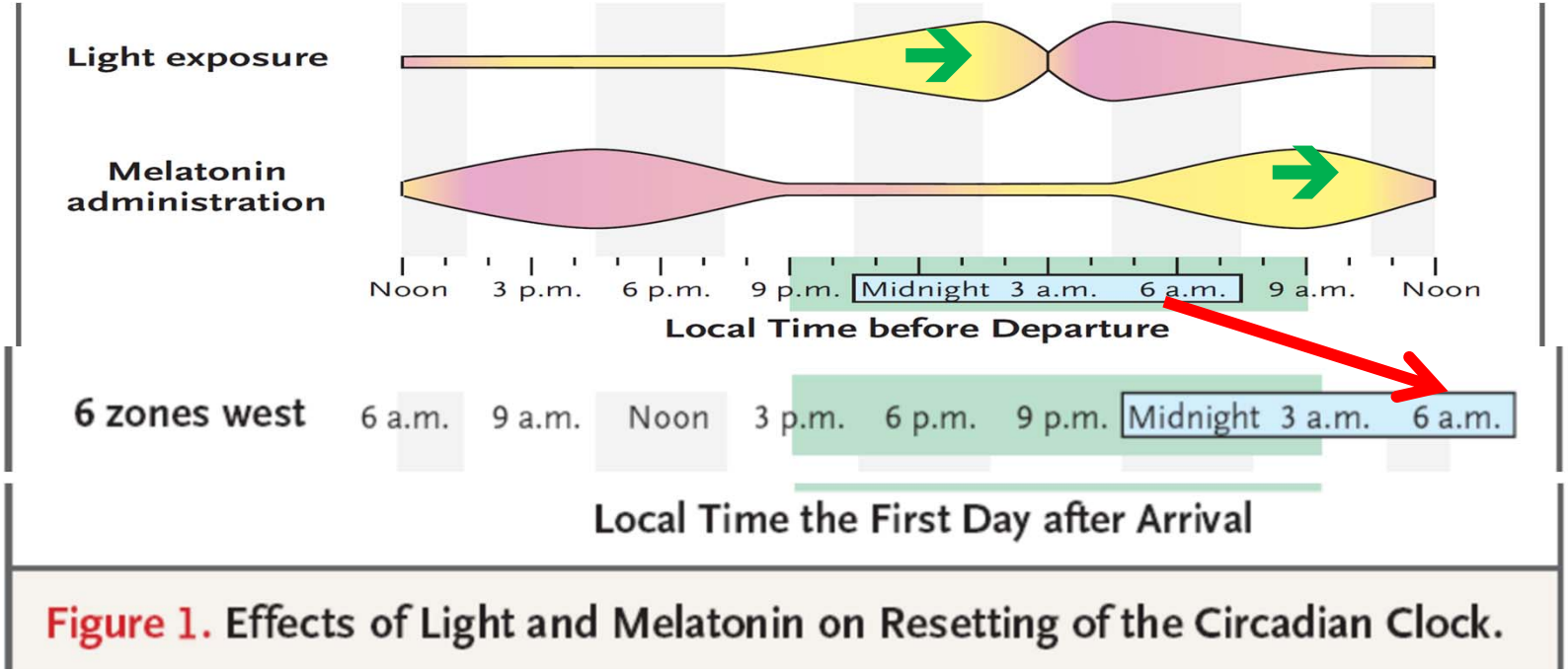


Figure 1. Effects of Light and Melatonin on Resetting of the Circadian Clock.

For westward travel (to reset the circadian clock later)							
Time zones crossed	Seek Light			Avoid Light			Take melatonin
3	17:00	to	23:00	3:00	to	9:00	4:00
4	16:00	to	22:00	2:00	to	8:00	3:00
5	15:00	to	21:00	1:00	to	7:00	2:00
6	14:00	to	20:00	0:00	to	6:00	1:00
7	13:00	to	19:00	23:00	to	5:00	0:00
8	12:00	to	18:00	22:00	to	4:00	23:00
9	11:00	to	17:00	21:00	to	3:00	22:00
10	10:00	to	16:00	20:00	to	2:00	21:00
11	9:00	to	15:00	19:00	to	1:00	20:00
12	8:00	to	14:00	18:00	to	0:00	19:00



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For eastward travel (to reset the circadian clock earlier)							
Time zones crossed	Seek Light			Avoid Light			Take melatonin
3	9:00	to	15:00	23:00	to	5:00	19:00
4	10:00	to	16:00	0:00	to	6:00	20:00
5	11:00	to	17:00	1:00	to	7:00	21:00
6	12:00	to	18:00	2:00	to	8:00	22:00
7	13:00	to	19:00	3:00	to	9:00	23:00
8	14:00	to	20:00	4:00	to	10:00	0:00
9*	15:00	to	21:00	5:00	to	11:00	1:00
10*	16:00	to	22:00	6:00	to	12:00	2:00
11*	17:00	to	23:00	7:00	to	13:00	3:00
12*	18:00	to	0:00	8:00	to	14:00	4:00

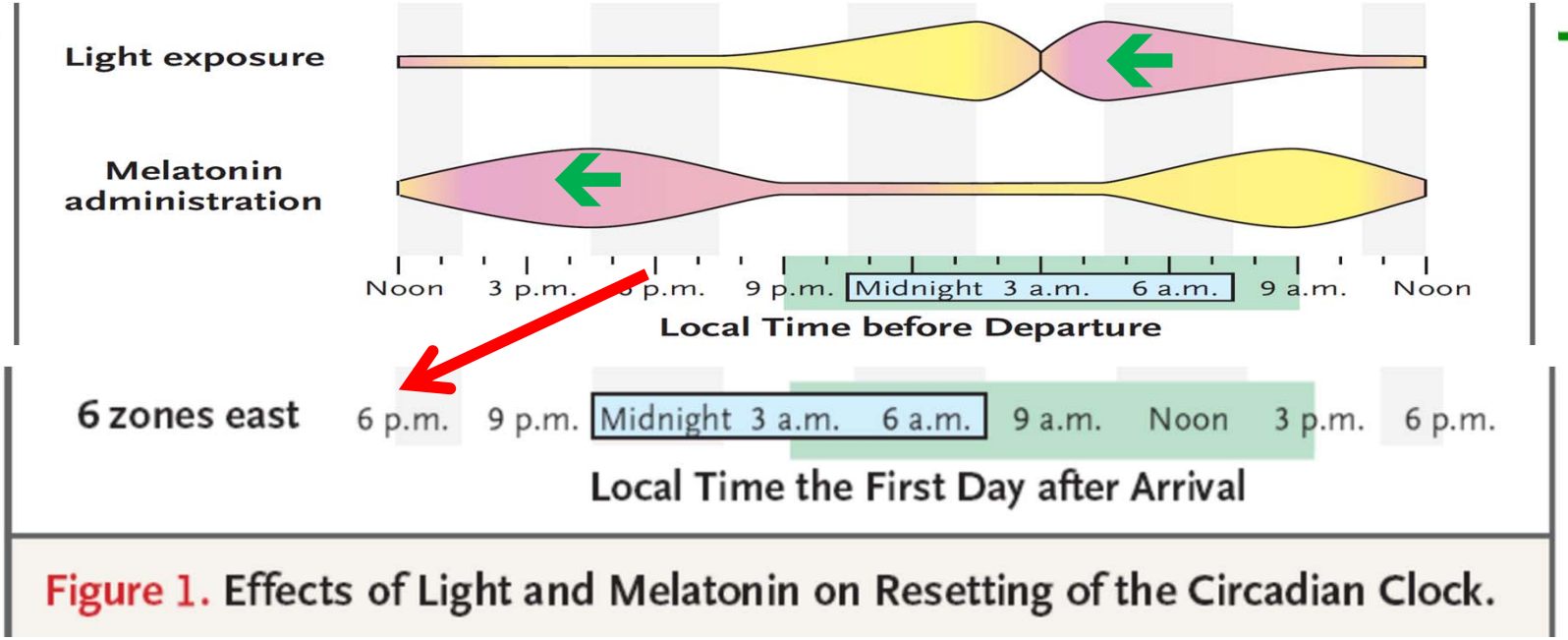


Figure 1. Effects of Light and Melatonin on Resetting of the Circadian Clock.

1. B Melatonin Administration

- The administration of melatonin is the most extensively studied treatment for jet lag.
- Most of the benefits of melatonin with respect to jet lag are probably related to its **clock-resetting effects** (*via the receptors on the suprachiasmatic nucleus)*
- but melatonin may also have some direct **hypnotic activity**, especially at higher doses (*1 mg or more*).

1. B Melatonin Administration

Of **11 double-blind, placebo-controlled trials**

- **8 showed** a **significant benefit** of melatonin with respect to symptoms of jet lag as rated by the study participants
  - 2 of the studies that did not show a benefit of melatonin may have been underpowered
  - 1 involved subjects whose baseline circadian phase may not have been appropriate

1. B Melatonin Administration

meta-analysis of **four** trials

- using a **100-point visual-analogue scale**
  (*with higher scores indicating more severe jet lag*)
  estimate the magnitude of the benefit from
  melatonin (administered at a dose of 5 or 8 mg)

- the **weighted mean average global jet-lag score**
  was **significantly lower** ($P<0.001$)
  after treatment with melatonin
  than after receipt of a placebo
  - after eastward travel, the scores were **31** and **51**, resp.
  - after westward travel, the scores were **22** and **41**, resp.

1. B Melatonin Administration

- The results of several **field studies** of melatonin administration
  that have monitored the circadian phase
  have provided some support
  for the assumed correlation between
  - the reduction of symptoms
  - accelerated realignment of the circadian clock,
- but this association requires further investigation.

1. B Melatonin

- Timing ?
- Short-acting !
- Dosing ?
- Anticipatory intake before departure ?
- Combination with hypnotic agent ?

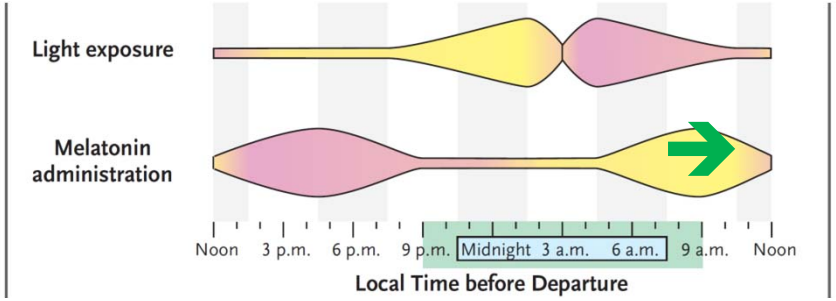
R/ Melatonine 3 mg
Dt 60 gel
S/ 1 gelule ‘s avonds

Deze bereiding is niet terugbetaald

- *Areas of uncertainty*

1. B Melatonin - TIMING

- In a majority of studies of melatonin, the hormone was administered **at bedtime after an eastward flight**.
- However, **at bedtime after a westward flight** (*that crosses fewer than (<) 6 to 8 time zones*) may **not be the optimal time** to take melatonin, since the administration of melatonin has the **least phase-shifting effect when it overlaps with endogenous secretion.**
- It may be preferable to take a low, short-acting dose (0.5 mg or less) **later in the night**.



1. B Melatonin - SHORT- ACTING

It may be preferable to take a low, **short-acting** dose (0.5 mg or less) later in the night.

1. B Melatonin - DOSING

- The most common dose of melatonin that was used in the randomized trials was **5 mg**

- 1 trial compared **5-mg** with a **0.5-mg** dose,
  - the efficacy of the two doses was **similar**
  - although subjects rated the **5-mg** dose as more sleep-promoting.

1. B Melatonin – “ANTICIPATORY”

- In several of the studies, melatonin was given for a few days **before departure**, at a time that coincided with bedtime at the destination,

  but it remains unclear whether anticipatory treatment provides a substantial advantage over treatment that is initiated after arrival at the destination.

1. B Melatonin COMBINED

- A single trial melatonin was compared with
  - Zolpidem (hypnotic agent administered at a dose of 10 mg)
  - Zolpidem combined with melatonin

❑ Zolpidem alone seemed to be the most effective in reducing self-rated symptoms of jet lag

❑ the combination was associated with

- a higher incidence of daytime sleepiness
- confusion

Areas of Uncertainty

- The **optimal dose** of melatonin is uncertain.

- For the purpose of resetting the circadian clock, **the timing** of the administration of melatonin (relative to the phase of the circadian clock) is probably *more important than the dose*, but this requires further study.

  Additional studies are needed to provide data on the optimal timing of the administration of melatonin *after westward travel, when a bedtime dose may not be optimal*.

- Clinical trials are warranted to evaluate the **new melatonin agonists** that may have clock-resetting effects and to assess the benefits and risks of combining different agents to treat the syndrome of jet lag.

2. Strategic Scheduling of Sleep

2. Strategic Scheduling of Sleep

a) **try to maintain the sleep–wake schedule** from home after arrival at the destination
   - – **simple** way to minimize jet lag
   - – especially in the case of **short trips**
   - – often **incompatible** with desired social activities or business obligations.

b) (((**Anticipatory : shifting** one's sleep schedule by 1 or 2 hours **toward congruence with** the destination time zone **before departure** may shorten the duration of jet lag.)))

2. Strategic Scheduling of Sleep

- combination of
  - **rescheduling of sleep**
  - **artificial exposure to light**
- has been shown in simulation studies to
  - augment phase-shifting
  - reduce symptoms of jet lag
- **requires considerable planning and discipline**

2. Strategic Scheduling of Sleep

- **First-class or business-class accommodations** that facilitate sleep will probably reduce the travel-fatigue component of jet travel.
- However, most travelers will be sleep-deprived after an overnight flight and will require extra (recovery) sleep on the first day or two after arrival.
- On subsequent days,
  - **short naps** are effective in reducing daytime sleepiness,
  - longer daytime naps
    - undermine nighttime sleep
    - reduce exposure to the re-entraining effects of light
- Even with adequate nighttime sleep, daytime sleepiness **may persist until the circadian system is realigned**.

Areas of Uncertainty

- Data on the effects of other, nonpharmacologic interventions for jet lag are scarce.
  - A single study of the **Argonne diet** (alternating days of "feasting" on high-protein breakfasts and lunches and high-carbohydrate dinners with days of caloric restriction) showed some benefit in reducing the symptoms of jet lag but lacked an appropriate control group.
  - Exercise has also been proposed to reduce the symptoms of jet lag but has not been studied in clinical trials, and even **strenuous exercise** has modest effects on circadian rhythms.

3.Pharmacotherapy

3.A Hypnotic Agents

3.B Agents That Promote Alertness

3.A Hypnotic Agents

- **after arrival** : a short course of hypnotic medication has been shown in randomized trials to reduce insomnia related to jet lag.
  - **zolpidem STILNOCT®** (10 mg at bedtime) for 3 to 4 nights after eastward travel across five to nine time zones significantly improved total sleep time and sleep quality while reducing awakenings from sleep.
- **during an overnight flight** : the use of a hypnotic agent may also be helpful, since a traveler may have difficulty sleeping while seated in a cramped, semi-recumbent airplane seat.
  - Because there is limited opportunity to sleep during a flight, a hypnotic medication that has only a 2- to 3-hour duration of action (e.g., **zaleplon SONATA®**) is preferred.

" Z-drugs "

- The effects of other nonbenzodiazepine hypnotics (eg, **zopiclone**) on jet lag are likely to resemble those of **zolpidem** and **zaleplon**.

3.A Hypnotic Agents
potential adverse effects :

- **amnesia and confusion**
  - triazolam = HALCION : dramatic global amnesia reported in several cases where used to promote sleep during jet travel.

  If not previously taken = take a test dose at home

- the immobility induced by a hypnotic medication might be expected to further increase the already elevated risk of **deep-vein thrombosis** associated with air travel.

3.B Agents That Promote Alertness & counteract the daytime sleepiness

- Increased consumption of **caffeine**
  - In a double-blind, controlled trial, slow-release caffeine (300 mg) increased alertness and reduced other symptoms of jet lag after eastward flight across seven time zones.
  - The primary risk of caffeine consumption is an **exacerbation of the insomnia** associated with jet lag.

3.B Agents that promote alertness & counteract the daytime sleepiness

Armodafinil

- FDA approved only for the treatment of narcolepsy
- recently shown to improve wakefulness after air travel across six time zones (from the eastern United States to France) at 7 a.m. for 3 consecutive days after arrival
  - reduction in self-rated daytime sleepiness
  - increase in alertness
  - (measured by the time it took for the subjects to fall asleep during scheduled daytime nap trials, performed on the first 2 days after arrival).
- a higher incidence of headache, nausea, and vomiting

3.B Agents That Promote Alertness & counteract the daytime sleepiness

Modafinil = PROVIGIL ®

- a drug that is closely related to armodafinil,
- could be expected to have similar effects,
- although it has not been evaluated in a clinical trial.

In the case of the traveler described in the vignette, I would recommend that,

- **On his arrival at his destination = WESTward = 6 hours longer,** I would advise him

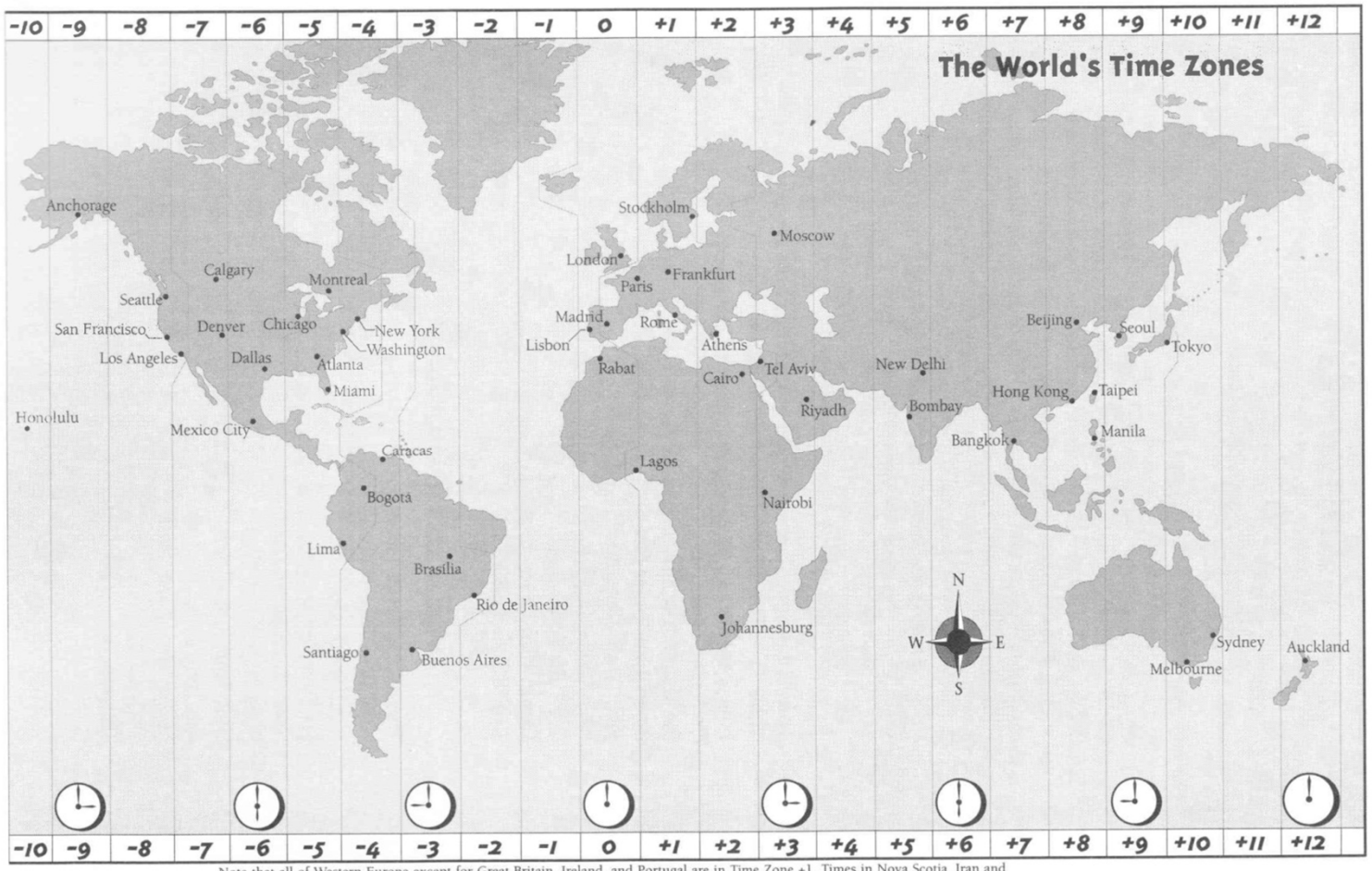
  1. to seek exposure to bright **light** in the **evening**
  2. to take a low dose of **melatonin** (*0.5 mg*) if he awakens **before 5 a.m**.

In the case of the traveler described in the vignette, I would recommend that,

- **After his return = EASTward = 6 hours shorter** , I would recommend that
  1. he walk in the bright sun**light** each **morning** and
  2. drink a **caffein**ated beverage each **morning**.

I would also recommend that

1. he take **melatonin** (*3 mg*) (the dose that is most commonly available) at **bedtime**, for 3 to 4 days to accelerate phase shifting = advancing.
2. If melatonin alone is insufficient to facilitate sleep, the addition of a **hypnotic** agent may be justified.



Note that all of Western Europe except for Great Britain, Ireland, and Portugal are in Time Zone +1. Times in Nova Scotia, Iran and India are one-half hour later than in the zones to their west. Time in mid-Australia is one-half hour earlier than in the zone to its east.

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Extra slides

Ramelteon =melatonin receptor agonist

FOLIA mei/mai 2009

- Voor **ramelteon, een agonist van de melatonine-receptoren**, werd er een aanvraag ingediend voor een vergunning voor het in de handel brengen in de Europese Unie voor de behandeling van slapeloosheid, maar deze werd **geweigerd** omwille van het gebrek aan evidentie van doeltreffendheid.

- **Le rameltéon , un agoniste des récepteurs de la mélatonine**, a fait l'objet d'une demande d'autorisation de mise sur le marché européen pour le traitement de l'insomnie, mais celle-ci a été **refusée** en raison du manque de preuves d'efficacité.

FOLIA sept 2010

- **Agomelatine** is een **antidepressivum** met een nieuw werkingsmechanisme: agomelatine inhibeert de heropname van noradrenaline of serotonine niet, maar **is een agonist ter hoogte van de melatoninereceptoren** en een antagonist ter hoogte van bepaalde serotoninereceptoren. De resultaten van de studies in verband met de doeltreffendheid van agomelatine zijn niet eenduidig,

- **L'agomélatine** est un **antidépresseur** présentant un nouveau mode d'action: il n'inhibe pas la recapture de la noradrénaline ou de la sérotonine, mais il **exerce un effet agoniste sur les récepteurs de la mélatonine** et un effet antagoniste au niveau de certains récepteurs sérotoninergiques. Les résultats des études concernant son efficacité ne sont pas univoques

REVIEW

CME CREDIT *EDUCATIONAL OBJECTIVE:* Readers will suggest strategies to lessen jet lag and shift work disorders

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Jet lag and shift work sleep disorders: How to help reset the internal clock

ABSTRACT

Jet lag sleep disorder and shift work sleep disorder are the result of dyssynchrony between the internal clock and the external light-dark cycle, brought on by rapid travel across time zones or by working a nonstandard schedule. Symptoms can be minimized by optimizing the sleep environment, by strategic avoidance of and exposure to light, and also with drug and behavioral therapies.

KEY POINTS

Symptoms include daytime anergia, alternating complaints of insomnia and hypersomnia, emotional disturbances, and gastrointestinal distress. The severity depends on the degree and the duration of dyssynchrony, as well as on innate factors such as age and whether the patient is an "early bird" or a "night owl."

Drug treatment addresses sleep-related symptoms (eg, somnolence, insomnia) and attempts to hasten circadian reacclimation.

Exposure to bright light in the hours leading up to the patient's minimum core body temperature tends to push the internal clock later in time, whereas bright light in the hours immediately afterward pushes the clock earlier in time.

FOR PEOPLE WHO MUST TRAVEL long distances east or west by air or who must work the night shift, some relief is possible for the grogginess and disorientation that often ensue. The problems arise from the body's internal clock being out of sync with the sun. Part of the solution involves helping reset the internal clock, or sometimes, preventing it from resetting itself.

This review will focus on jet lag sleep disorder and shift work sleep disorder, with an emphasis on the causes, the clinical assessment, and evidence-based treatment options.

WHEN THE INTERNAL CLOCK IS OUT OF SYNC WITH THE SUN

Circadian rhythm sleep disorders are the result of dyssynchrony between the body's internal clock and the external 24-hour light-dark cycle. Patients typically present with insomnia or excessive somnolence. These disorders may represent an intrinsic disorder, such as delayed or advanced sleep-phase disorder, or may be the result of transmeridian air travel or working nonstandard shifts.[1]

Sleep and wakefulness are conceptually governed by two processes, "process S" and "process C."[2] The homeostatic drive to sleep (process S) is proportional to the duration of sleep restriction, and it becomes maximal at

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Seminar

Lancet 2007; 369: 1117–29

Jet lag: trends and coping strategies

Jim Waterhouse, Thomas Reilly, Greg Atkinson, Ben Edwards.

The number of travellers undertaking long-distance flights has continued to increase. Such flights are associated with travel fatigue and jet lag, the symptoms of which are considered here, along with their similarities, differences, and causes. Difficulties with jet lag because of sleep loss and decreased performance are emphasised. Since jet lag is caused mainly by inappropriate timing of the body clock in the new time zone, the pertinent properties of the body clock are outlined, with a description of how the body clock can be adjusted. The methods, both pharmacological and behavioural, that have been used to alleviate the negative results of time-zone transitions, are reviewed. The results form the rationale for advice to travellers flying in different directions and crossing several time zones. Finally, there is an account of the main problems that remain unresolved.

Lancet 2007; 369: 1117–29

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Effect of long-haul flights

> "I do not suffer from jet lag, only with difficulties in sleeping"
>
> *(Comment from an Olympic athlete after flying from UK to Australia)*

Long-haul flights are associated with negative feelings after arrival that constitute travel fatigue.[2–4] Panel 1 shows the main symptoms and causes. The effects are due to time spent in an environment that is cramped and offers little opportunity for exercise, a restricted choice of food, dehydration due to dry cabin air,[7] and cabin hypoxia, which increases fatigue and changes the daily profiles of some variables.[8] Concern has been (although the reason for this finding is unclear),[15] and depends on the direction of the time-zone transition—flights to the east are associated with more jet lag than flights west.[16] Sleep and circadian rhythms are also disrupted in aircrew,[17–19] thus, experience of time-zone transitions does not act as a protection, although many aircrew members change their sleep behaviour to keep jet-lag difficulties to a minimum.

Role of the body clock

To understand and cope with jet lag, we should be aware of the basic properties of the body clock, and the roles of this structure in healthy people. The suprachiasmatic nuclei, paired groups of cells either

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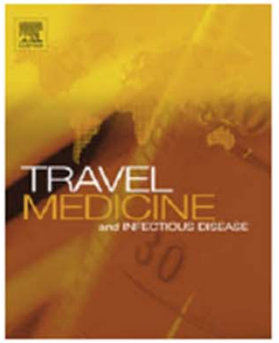

Jet lag and other sleep disorders relevant to the traveler

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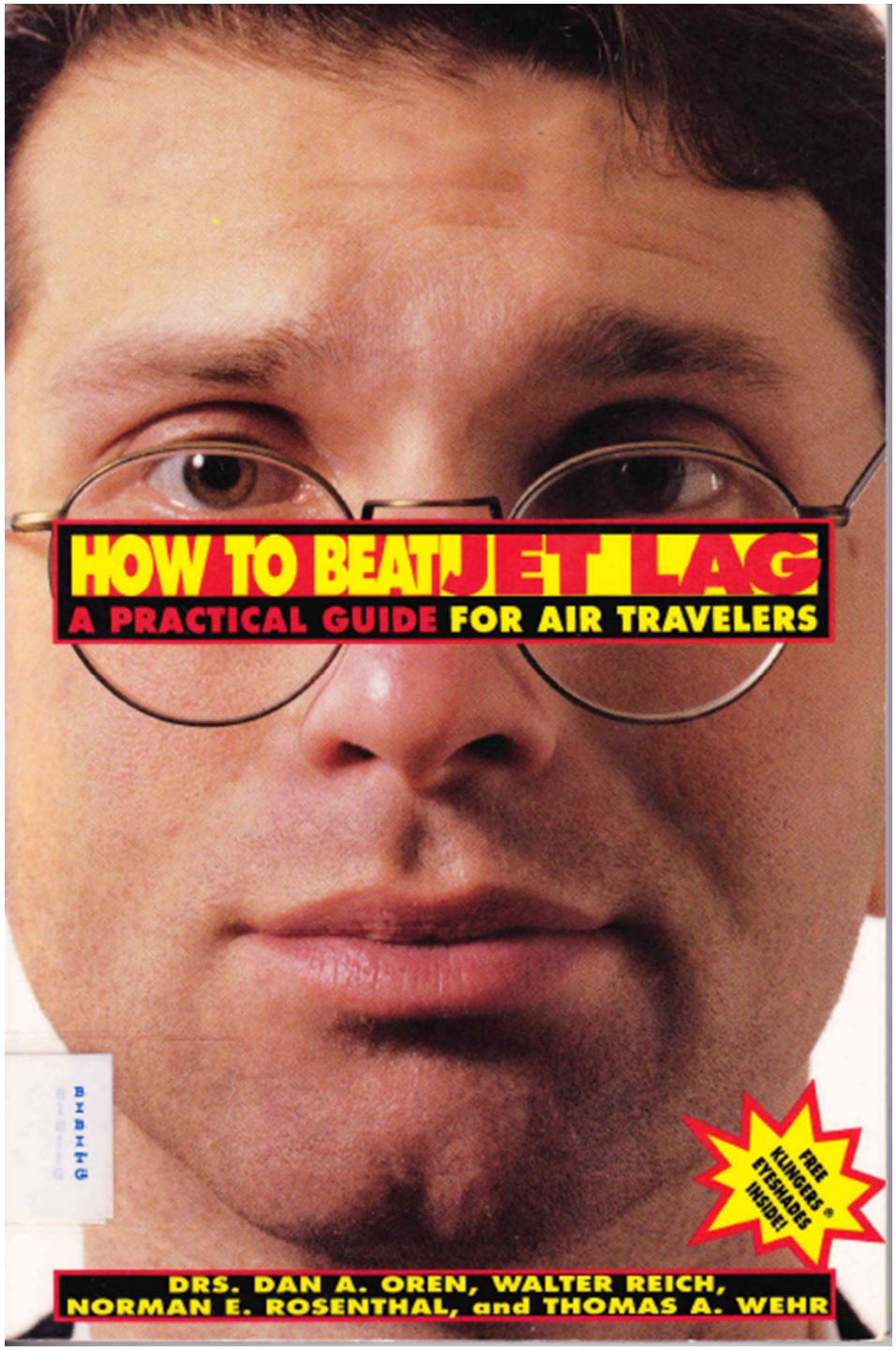

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INCLUDES TIME ZONE MAP

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Travel/How To

Lichtdouchen / Lichttherapieapparaten voor de professionele en home-care behandeling van winterdepressie, winterblues, PMS (Pre Menstrueel Syndroom), slaapstoornissen en jetlag, thuis en in het ziekenhuis.

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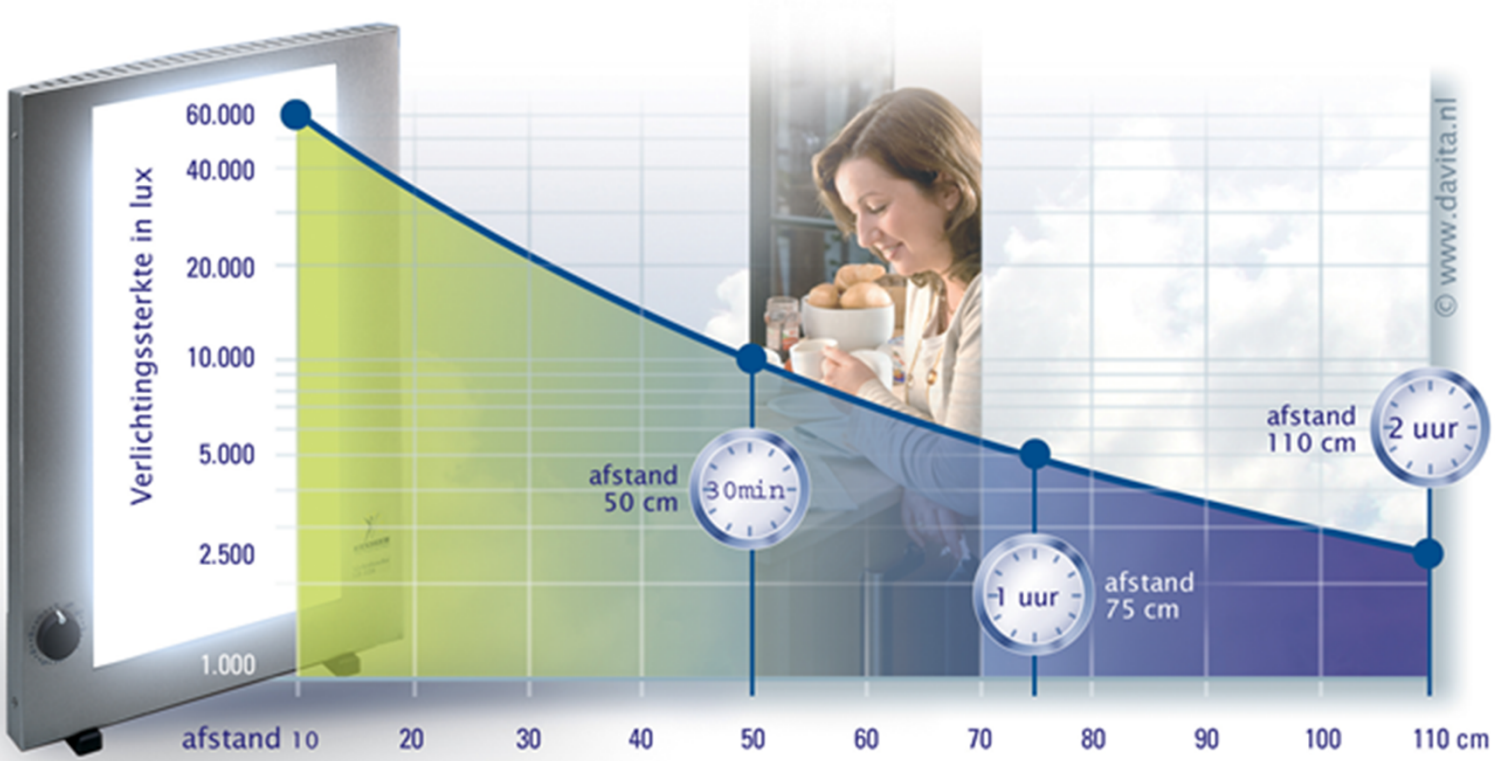

Bron: Evaluatierapport van het DAVITA Lichttherapieapparaat LD 220

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Voor de behandeling van winterdepressie