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HOW SMART PEOPLE CAN OVERCOME JET LAG

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FOREWORD

As a smart person, would you be prepared to waste some of your precious time or take certain risks just for a business trip? Would you be prepared to put up with sleep deprivation, and be less efficient during an important meeting or a crucial financial transaction and thereby run the risk of losing huge amounts of money? Would you be prepared to give up your days off in a delightful place for the simple reason that there is a significant time difference between your hometown and your holiday destination? Of course not!

In that case you would (almost) be ready to try out anything to overcome or at least to alleviate the symptoms brought on by jet lag. The problem is knowing which is the best and safest method to use.

When Professor LE BON asked me to write this foreword, I was a little puzzled. The use of the Pharmacopeia is the domain of specialists and requires many precautions. If someone is ready to assume the responsibility for potential health risks, and you give him what he requires in the form of a ready-made recipe, even with all the necessary explanations and regardless of his intelligence, he runs a risk.

An interesting comparison can be made between military operations and civilian activities. It is common in military operations to be faced with situations such as sleep deprivation, fatigue (both physical and cognitive), changes in biological rhythms, reduced performance and stress. In these circumstances, solutions have been prepared, and in each country, rules have been established which provide safe measures for soldiers to combat these conditions. The problem is very simple: one must find a balance between, on the one hand, an assessment of the risk – and ultimately that of death (for example, taking a pill which will makes the person realise the very dangerous situation he is in), and on the other hand, a reasonable risk from the side effects linked to a controlled form of medication. In a war situation, decisions often have to be taken very quickly. In civilian activities, the stakes are not the same: it is not a life-or-death situation but simply a problem of efficiency related to the patient's health in the short- or long-term. As a doctor, I cannot approve this use of medication. The cure must not be worse than the disease.

Nevertheless, scientific progress helps us to deal with new situations which do not incur great risks. I think that every person should be responsible for their own health and act according to their own ethics. However, to be able to take these kinds of decisions, people must be well-informed and be provided with comprehensive information. Those concerned should know precisely the risks associated with the actions which have been recommended. They should also know themselves inside-out. In the army, soldiers tend to be young, in very good

physical shape, and used to a heavy workload. Smart people may be young or old, with or without metabolic or any other disease which may hinder their recovery. Each person ought to recognise his own vulnerabilities in the face of environmental constraints and act accordingly.

This is the first book to detail the different measures smart people who are subject to the effects of jet lag can take to alleviate it. Twenty-three different situations are outlined in this book, one for every time-zone, as well as the options which are suggested to help to find the safest and most efficient solution. I think that this book is a new and original contribution in the struggle against jet lag.

I wish this book every success in the hope that it will be used reasonably by smart people.

Major-general (2°S) Didier Lagarde
French Forces Biomedical Research Institute
France

PREFACE

In my opinion, anyone who claims that there is a universal and simple cure for jet lag is naive, misinformed or dishonest. There is no such cure. No remedy, application or device is yet capable of eliminating it completely, especially if you take into consideration the fact that jet lag differs whether you travel eastwards or westwards and depends on the number of times zones you cross.

I am confident though, that finding a cure is only a matter of time. Tomorrow, or within five or twenty years, a way to adapt immediately to time zone shifts will be invented, patented and distributed. Soon, jet lag will be a thing of the past. But what can be done in the meantime? There is, as just mentioned, no universal cure and the problem is more complex than it looks, but there are a lot of things that can already be done to help you overcome jet lag if you are affected by it.

Jet lag seems to bother people to varying degrees. To some, like me unfortunately, it repeatedly harms work and holidays if nothing is done about it. Other, more fortunate people seem to adjust almost seamlessly to even several time zone shifts, going to work practically as soon as they land, as though nothing had happened. The majority however are somewhere in between.

As I am fond of travelling, I started to explore the scientific remedies that are presently proposed. No-nonsense measures can do a lot of good with little effort. Bright light and melatonin shorten the adaptation time. Sleeping pills help you obtain enough sleep and stimulants help you stay well awake when needed.

I rapidly realized though that there are as many optimal strategies against jet lag as there are time zones (minus one of course if you remain in the same one). Designing specific "treatments" or "remedies" for each of them increases their effectiveness by a good notch.

I thus started with the available evidence-based medicine on the matter, in order to learn what could really help. I then extrapolated from that to adapt these remedies to each possible time zone shift. I did this on the basis of common sense, on my own experience as a traveller and on reports by a few patients who trusted me. Thus this sometimes goes beyond proven science, as many of the remedies described have not been field-tested at all or not sufficiently. I wish that they had been or I wish that I could participate in their testing, but this would require resources I do not have, as well as a lot of time.

These remedies only work if you use them wisely, opting for the best one intelligently and

progressively. The graduated response strategy I suggest here is for you to try the simple tricks and no-nonsense reasoning first. I then propose trying bright light and melatonin. If these do not prove effective enough, you could try sleeping pills. Caffeine can be very effective against sleepiness, especially if you wean yourself from it a week before departure. If nothing works enough and you want to venture a little more into the field of stimulants, then you may consider modafinil.

All in all, I believe that these combinations can already and safely solve the vast majority of jet lag-associated problems. This book will bring to a wider audience this knowledge which can still be improved. I hope that your feedback will help me to refine it for a future edition.

Don't forget this is a threesome party, as you will have to convince your doctor to prescribe you the sleeping pills and stimulants.

My hope is that this book will help people who love or need to travel and continue to be handicapped by jet lag.

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My deep respect and gratitude are also addressed to Didier Lagarde, who did not hesitate to write the Foreword of this book.

I want to thank Jim Murphy, who patiently taught me how to write in an academic manner.

And I am immensely grateful to Ian P. Jones, who made my English look like it was my mother tongue. Ian has in fact done much more than that, offering countless essential suggestions on the content, details and layout of this book.

CONFLICT OF INTEREST

The authors confirm that they have no conflict of interest to declare for this publication.

CHAPTER 1

Introduction

Abstract: This section describes the phenomenon of jet lag and the symptoms associated with it, which vary not only from person to person, but also according to how many times zones are crossed, and in which direction. Two main lines of research are described: the first endeavours to accelerate the adaptation process; the second helps to fight insomnia and sleepiness between arrival and adjustment to the new time zone. Homeostatic and circadian influences on sleep and vigilance are explained on the basis of Borbély's Two-Process Model. The benefits of specifying the remedies for each time zone shift are explained. A strategy of graduated response to jet lag is suggested, from the safest to the most effective. Limitations of these proposals are detailed.

Keywords: Adaptation, Adjustment, Chronobiology, Circadian, Homeostatic, Jet lag, Sleep debt, Sleep inertia, Sleepiness, Time zone, Two-Process model, Vigilance.

"*... you may arrive at your destination exhausted, feeling mentally and physically out of sorts and performing poorly at things usually done well. That can take the edge off business acumen or leave a traveller guilt-ridden for "wasting" precious, costly vacation time.*"

Jane Brody [1].

"*... a sense of mild disorientation when arriving at my destination. I often feel as if I was operating in a light fog, almost as if there was a translucent cloth over my eyes. Things do not seem quite right even if nothing feels really wrong either*".

Donald McEachron [2].

THE PROBLEM

Jet lag is a phenomenon that to varying degrees annoys the millions of people who travel across time zones each year. It is the result of a mismatch between the local time at your destination and your rather robust internal body clock, which stubbornly remains set at your home time, at least for a few days. Then you will often have more or less adjusted to local time just as you are about to return home – only to suffer from the reverse problem on arrival.

Jet lag manifests itself mostly through an urge to sleep during inconvenient parts of the day and through long battles against insomnia or early awakening. Although it spontaneously and gradually goes away and usually only has benign consequences, jet lag can seriously ruin your holidays or hamper your reactions in difficult negotiations. Perhaps, you could not avoid missing the early parts of conventions in the US (or dozed off during them) because you flew from Japan, or struggled during the late sessions because you landed a day or two before from Europe? Perhaps, you regret having signed a poorly negotiated contract in Hamburg or waking up at 3 am in your Honolulu hotel, finding it nearly impossible to sleep anymore when you know you should do in order to be fit the next day for your basketball match.

As nature makes us somewhat different from each other, some of us are just slightly bothered by jet lag, whereas others are severely affected, to the extent of doing almost anything to avoid transmeridian trips in the future. The majority are somewhere between these extremes and I am ready to bet that sensitivity to jet lag, just like almost every biological variable, follows the usual statistical (Gaussian) distribution. Also, some of you are early birds and some are night owls, some need a lot of sleep whereas a few lucky ones are fully in shape with just four hours a day. These factors and many others play a part here too. There does not appear to be a difference in sensitivity linked to gender or ethnic origin.

As long as the earth keeps spinning round and our genome is not modified, the bad news is that jet lag is here to stay. Probably, some day we will be able to turn our body clock forward or back and reset it immediately to our new time zone, but such a procedure has yet to be discovered. Presently, the natural process of

adjustment to new time zones is slow (from a day or two to more than a week). So what can we do in the meantime?

THE SCIENTIFIC APPROACH

To fully understand jet lag, we need to integrate two components, as was proposed in 1982 by A. Borbély [3]. The propensity to sleep at any given moment is the result of two forces. The first is homeostatic and intuitive: the longer you have been without sleep, the more you need it. The second is cyclical and more complex: a body clock, located deep inside your brain (the suprachiasmatic nuclei), helps you to sleep on a regular basis, not in a piecemeal way. As its influence repeats its pattern every day, it is called circadian (about a day). In a "normal" situation, your cyclical body clock pushes you to sleep at night (and to some extent in the afternoon) but definitely not in the evening. When you travel away from your home time zone, the homeostatic component functions as usual but the cyclical component gets out of phase and urges you to sleep at odd times. Although the relative strength of the two components has not been compared precisely in jet lag, I would tend to place them at roughly fifty-fifty.

There are also two main pathways followed by scientists to counter jet lag. Most studies have been performed by chronobiologists and have as their main goal to speed up the adjustment of the body clock to the new schedule, mostly using timed exposure and avoidance of bright light, as well as the timed use of the hormone melatonin. At the present time, chronobiologists have often succeeded in accelerating and thereby reducing the adjustment process, but I feel that their recommandations still make for a slow and not fully satisfactory result, especially when many time zones are crossed. Although I believe the chronobiologists will some day have the final word and will help us reset our body clock as soon as we land (and thus enable us to overcome jet lag), this still appears a distant perspective.

The second school of research is more pragmatic. Here we start from the point of view that we want to be as fully operational as we can and as soon as possible. So the body clock is more or less left to itself and allowed to take its time without much interference. The aim is to counter insomnia and fatigue or sleepiness with

CHAPTER 2

A Bit More on the Nature of Jet Lag?

Abstract: If you better understand what is at stake in jet lag, you will be better able to adjust harmoniously. Jet lag is reasonably well explained scientifically today. Rapid changes of time zones disturb the functioning of your body clock, which remains stubbornly set on departure time for a while. This can make sleep shallow or non-existent for substantial parts of the night while vigilance is less than optimal during parts of the day. Flying west seems easier than flying east. Jet lag can in some cases be a more serious medical nuisance.

Keywords: Body clock, Circadian, Circadian clock, Core body temperature, Evening-type, Fatigue, Homeostatic, Jet lag, Morning-type, Sleepiness, Travel fatigue, Vigilance.

"The circadian clock is normally synchronized to the solar light-dark cycle and promotes alertness during the day and sleep at night. The pathophysiology involves a temporary misalignment between the circadian clock and the local time."

Robert L. Sack [1]

BODY CLOCK

The American Academy for Sleep Medicine (AASM), in the 2nd edition of its International Classification of Sleep Disorders (2005) [2] defines jet lag (circadian disorder, jet lag type), as a disorder "related to a temporal mismatch between the timing of the sleep-wake cycle generated by the endogenous circadian clock produced by a rapid change in time zones". In other words, it results from crossing time zones too rapidly for the circadian clock to keep pace.

Like other mammals, human beings have a circadian clock, a paired group of nuclei in the base of the hypothalamus – the suprachiasmatic nuclei. They receive information from the retina about external light. These data allow for a daily-based correction and synchronization with the daily cycle of light and dark. The suprachiasmatic nuclei are considered together to represent the "master clock" of the brain, synchronizing a series of hormones (such as melatonin, cortisol and growth hormone), behaviours and other more specialized body clocks (core body temperature, rapid eye movement sleep, for instance).

The actions of the suprachiasmatic nuclei monitor the change from day to night. They have a useful stabilizing function on the body's biological rhythms but they are slow to react to changes in lighting schedules, so that after time zones have been crossed rapidly, the endogenous signals for sleep and wakefulness do not match the local light-dark and social schedules. The suprachiasmatic nuclei may also be influenced by other time-givers, such as meals, daytime physical activity or social factors. Some of the biological cycles adjust in a few days, while others, such as the core body temperature, take even more time [3].

Core body temperature is one of the best markers of your body clock. It is important as it has been linked with sleep and its rapid eye movement (REM) and non-rapid eye movement (NREM) components. "The ease of getting to sleep and staying asleep depends not only on previous wake time, but also on associations with the circadian rhythm of core temperature. Sleep is easiest to initiate when core temperature is falling rapidly or is at its lowest and most difficult when body temperature is rising rapidly or is high. Waking is the opposite of sleep initiation, because it occurs when core temperature is rising or is high. Sleep is favoured when body temperature is low or rapidly descending, as at the end of a normal evening" [4].

JET LAG SYMPTOMS

Jet lag symptoms are frequent. Rogers and Reilly [5] indicated that 74% of surveyed travellers reported some form of jet lag. Of these respondents, 50% reported above-average tiredness and fatigue and 28% indicated some disruption in normal sleeping patterns. 5% reported difficulties in concentration, while 5%

reported eating problems. Gisquet [6] reported 80% of sleep disorders among travellers: difficulty in falling asleep, insomnia, premature awakening and daytime sleepiness. Among very frequent travellers such as flight personnel and international business executives, the disorder may be recurrent or even chronic [1].

The most obvious jet lag symptoms for the majority of travellers are the inability to sleep during destination night and to remain alert during destination day. It also includes difficulty in concentrating, clumsiness, difficulty with memory, general weakness, dizziness and lethargy [7]. General malaise, dysphoric mood, headaches and gastrointestinal disorders (indigestion, loss of appetite, bowel irregularities) have also been described but cause less harm, however you could notice your bowel functioning at the old schedule for a while.

Symptoms logically vary according to the time of day where assessments are made (overlap or not with home schedules) and as a function of the number of time zones crossed, eastwards or westwards. Morning-type people may find it more difficult to adjust when travelling westwards and evening-types have more trouble when travelling eastwards [8]. People with more rigid sleeping habits suffer more [9]. Short sleepers logically adjust easier. Age over 60 results in greater difficulty in adjusting to jet lag [10]. Gender does not make a significant difference [11].

EAST, WEST, HOW MANY TIME ZONES CROSSED?

As could be expected, jet lag symptoms are generally worse the more time zones you cross. Although crossing one to four time zones is not universally considered jet lag, I propose here that you do so for the sake of consistency. As said before, if your normal sleep schedule is partly included in night-time at destination (more or less from plus or minus one to seven or eight hours), there is at least some overlap with your usual sleeping hours: you will either have difficulties in keeping on sleeping (westwards, Group A) or in falling asleep (eastwards, Group C) but you will have some sleep at least. Once you cross more than seven or eight time zones (from plus or minus seven or eight to the maximum of twelve, the full antipodes – Group B), you need to sleep at times when your body does not even want to and

CHAPTER 3

No-Nonsense Measures

Abstract: There are many practical things you can do to reduce the burden of jet lag: fast psychological adjustment, exercise, judicious timing of meeting schedules, judicious timing of naps, optimizing your activities in short stay durations, exerting self-discipline, preflight rescheduling and in some cases, sleeping in two parts.

Keywords: Discipline, Exercise, Launch window, Nap, Powernap, Preflight rescheduling, Psychological adjustment, Sleep debt, Sleep inertia, Split sleep, Stay duration.

"Keep your eyes on the stars, but remember to keep your feet on the ground."

Theodore Roosevelt

In this chapter, I will summarize a few considerations or measures you can take at practically no risk.

FAST PSYCHOLOGICAL ADJUSTMENT

Change your wristwatch as soon as you get on the plane and follow the destination schedules (meals, *etc.*) as soon as you land. These new time givers may help your body clock to adjust faster (to what extent has not been measured scientifically). But this cannot do any harm.

By the way, this is a big difference with shift work. People forced to work in shifting schedules have time clues working *against* them, as they obviously know for instance that they are working when everybody else is asleep. Here, everything external acts in favour of adjustment and continuously shows you the right way.

To avoid lengthy adaptations to jet lag, adjust as fast as you can, using personal discipline – even if you are on holiday... Well, that's up to you, obviously!

EXERCISE

You can hardly sleep while taking physical exercise. And physical exercise keeps your body alert for an hour or two. It is usually recommended to do some physical exercise to adjust to your new schedules. It could be especially recommended at those times of the day when you would be more prone to sleepiness. However, it is not recommended to undertake physical exercise less than two hours before bedtime if you expect to find it hard to fall asleep (eastwards flights).

NAPS

Sleeping partly during daytime is the rule for babies, infants and many children. It is also the case for adults in many parts of the world: by shifting some of the main sleep load from night-time to naptime (siestas), working hours are adjusted to more favourable weather conditions. The circadian clock seems less rigid in the afternoon than in the morning or the evening and may allow for individual variations that become the usual circadian pattern in the long run.

Naps may produce surprisingly powerful waking effects. Sleeping just a few minutes during the daytime may considerably reduce the urge for sleep that was present immediately before and made concentration difficult. Napping more than 20-25 minutes however can paradoxically be less pleasant and induce a slight degree of drowsiness (because of sleep inertia, as we have seen above) sometimes for hours. Longer naps also pull some sleep pressure off from the coming night, and thus may delay your adaptation to local time.

If there is a good indication for a nap, its optimal duration should thus be somewhere between 15 to 25 minutes. This is probably linked to the sleep stages that occur during the nap. Very light sleep (stage 1 sleep) is probably not very useful for recovery. Stage 2 sleep includes loss of awareness of the external world and seems to be quite beneficial. Stage 3 (deeper sleep) is even more effective but may have the negative impact of sleep inertia. REM sleep is normally an exception in naps, but could happen when your body clock is still set to your

home time, as REM sleep also depends on your circadian clock. We should thus focus on achieving some stage 2 sleep: it will happen spontaneously if you manage to lose awareness during the nap. To make what is commonly called a powernap, you just need to set a timer or an alarm clock for 15 to 25 minutes. Your mobile phone will be perfect for that matter.

Beware that, if you have a strong sleep debt or if the nap timing corresponds to sleep time at home, it may be difficult to wake up after the programmed 15 to 25 minutes. Naps are thus a double-edged sword and make for a difficult issue, which will be discussed for every time zone.

LAUNCH WINDOW

In spaceflight, a launch window is a time period during which a particular vehicle (rocket, space shuttle, *etc.*) must be launched in order to reach its intended target. If the rocket is not launched within the "window", it has to wait for the next opportunity.

Using this as a metaphor, there are times where you have travelled across several time zones and the destination daytime overlaps with your home daytime. It is a moment where jet lag symptoms should be minimal – although they may not have disappeared, especially if you have accumulated a sleep debt. The launch window is large when few time zones are crossed. It will be shorter – and split into two parts – when you cross the globe. Knowledge of the launch window(s) may be crucial to plan and do the important things you want to at your destination, be it museum visits, family or business meetings, or political negotiations. It will of course be easier to choose your meeting times if you are a powerful CEO than if you are looking for a job.

For every time zone, I will show you a chart with your biological time and your destination time. I will also give you the most favourable times to be active once there (launch window open) and the times when you should avoid activities (launch window closed).

You can also check a website dedicated to finding the optimal meeting times (such as World Clock Meeting Planner).

CHAPTER 4

Accelerating the Phase Adjustment

Abstract: Ideally, we would want to turn our body clock forward or back and reset it to local time as soon as we land. The jet lag problem would disappear instantly and you could throw this book away. Unfortunately, no such mechanism has yet been found. However, the adjustment process can already be speeded up using bright light and melatonin.

Keywords: Adaptation, Adjustment, Body clock, Bright light, Chronobiotic, Circadian, Circadian clock, Ear, Evening-type, Fatigue, Latitude, Longitude, Melatonin, Morning-type, Season, Sleepiness, Supra-chiasmatic nuclei.

"Life is the continuous adjustment of internal relations to external relations."

Herbert Spencer [1]

THE NATURAL WAY IS FINE BUT SLOW

Your body clock adjusts spontaneously and seamlessly to your destination time. The only problem is that the change is slow and your holidays or business stay abroad may be too short for its full and timely implementation.

As has been mentioned earlier here, it takes about one day by time zone when you fly eastwards and two-thirds of a day when you fly westwards to adjust for sleep and vigilance. Flying from London to Shanghai (eight time zones' difference) may hence demand eight days until jet lag symptoms become almost undetectable – the reverse course from Shanghai to London would take between 5 and 6 days. Hormones such as cortisol may take up to 3 weeks to fully adjust but this is not translated into obvious clinical symptoms and it probably does not matter much

[2]. Reducing this adjustment time and minimizing the symptoms is the goal of this chapter.

Adjusting the body clock is a natural and complex process, based on the reception of time-givers (also called time-cues or zeitgebers). The most important of them is exposure to light above a certain threshold of physical intensity (bright light being apparently far more effective than dim light, although the issue is not closed). As mentioned before, other time-givers also play a less important part: social activity, meals, psychological adjustment, physical activity, *etc.*

HOW TO INTERACT WITH THE BODY CLOCK?

Bright light has a direct time-setting action on the body clock supra-chiasmatic nuclei. It also inhibits the production of melatonin [3]. Melatonin in turn helps to adjust the body clock to the external day/night 24-hour cycle. There are receptors for melatonin in the body clock, which allows exogenous artificial melatonin to act on it.

Exposure to bright light on the one hand and melatonin on the other hand are two complementary ways that can be used to push your body clock and adjust faster to the destination time. Please note that bright light should also be *avoided* in certain conditions, to prevent the unwanted opposite effect. Bright light especially needs to be administered at precise timings, for every different kind of jet lag difference (see the time zone sheets further on).

The time zone sheets are designed for people whose usual sleep schedules are between 10:00 pm (22.00) and midnight for sleep initiation and 6:00 am to 8:00 am for wake up. If your sleep patterns fall outside this range, you should adjust the directions accordingly (see also chapter 8). For instance, if you tend to be a night-owl and go to bed later than this, then you should add extra time to all instructions. If you tend to be a morning-type early bird and are used to going to sleep earlier than that, you should subtract the difference. As being early birds or night-owls seems to be genetically determined [4], it is likely that sooner or later you will use the same pattern again anyway, once you have settled into your new time zone.

Although a bit neglected in the scientific literature, the issues of seasons and latitude (north-south) inescapably increase the level of complexity. Although daylight duration is very similar in the summer and the winter when you live close to the equator, it varies considerably when you live closer to the north or south poles. There, as seasons change without interfering much with sleep duration, and as most people don't sleep behind opaque curtains or blinds, we must postulate some kind of mechanism which adjusts the body clock progressively to longer or shorter durations of external bright light and varying durations of melatonin secretion. It is likely that the other time-givers, such as meals and social life, help to achieve this adaptation.

So, if you fly from your home in Singapore (practically at the equator) to Vladivostok (43°N), you will have several more hours of exposure to daylight than at home in the summer, and several fewer in the winter. It is even more striking when you change hemisphere, as seasons are inverted when you cross the equator. Suppose for instance that you fly from Berlin (52°N), in the midst of the European winter, to Cape Town (33°S), which will be enjoying the South African summer. The sun will set at around 05:30 pm (17.30) at home, and five hours later, at 10:30 pm (22.30) when at destination. This does of course not mean that you should begin to sleep five hours later, since you are in the same time zone.

What I want to insist on here is how complex it may be to determine the best timing for the administration of melatonin and bright light. In the Time Zone Sheets, we only take into account the east-west dimension and just do as if there was no north-south difference. But the greater the north-south difference, the less unpredictable the reaction will be, as this area needs more research.

BRIGHT LIGHT

Bright light is the main time-giver to the body clock. Its effects (phase-response curve) on the body clock were modelled thirty years ago [5]. Exposure to bright light in the morning should have the effect of advancing circadian rhythms: it would help you to sleep earlier (useful when you fly eastwards). Exposure to bright light in the evening should do the opposite, retarding the circadian rhythms and helping you to sleep later (useful when you fly westwards).

CHAPTER 5

Sleeping When Your Body Does Not Seem to Want to

Abstract: Sleepiness mainly comes from a deficit in sleep quantity or quality. From a homeostatic perspective, obtaining enough sleep of good quality is the most determining factor. The circadian perspective explains why your body clock contradicts your wish to sleep at appropriate times once at destination. It may make it difficult to fall asleep (Group A), to wake up (Group C), or both (Group B). Here is what you can do about it, using sleeping pills if needed (benzodiazepines and others).

Keywords: Alcohol, Benzodiazepine, Dosage, Fatigue, GABA-A, Legal status, Melatonin, Non-benzodiazepine, Side-effects, Sleep debt, Sleep hygiene, Sleepiness, Z-drug.

"The most important factor in adapting to time zone changes is to preserve sleep."

Josephine Arendt [1]

SLEEP DEBT

The effect of lacking two hours of sleep may be compared to drinking two or three 33 cl (12 oz) bottles of beer, whereas a sleep loss of four hours is similar to drinking five or six bottles [2]. Sleep debt has also been found to parallel alcohol intoxication [3]. But you will only have a full measure of what is meant here if you travel to the antipodes and do not sleep at all during the night. On top of this, if the situation repeats itself night after night, you accumulate sleep debt and the situation only becomes worse – until it gets better when your body clock finally

adjusts to its new time zone. As you can imagine, you will not be in top shape to take decisions, negotiate, visit or simply enjoy your new environment. What can you do to help you sleep when it seems you just can't?

THE GOLDEN RULES OF SLEEP HYGIENE

First check your sleep hygiene. I doubt that it can solve a problem that is of a different nature, but it does no harm. The recommandations by the American National Sleep Foundation (sleepfoundation.org) include:

a. Avoid *stimulants* (*e.g.* caffeine, nicotine, even chocolate) too close to bedtime;
b. Avoid *alcohol* too close to bedtime;
c. Avoid *exercise* too close to bedtime (better in the morning or the afternoon)
d. Avoid *upsetting conversations and activities* before going to bed (really scary movies ...);
e. Avoid *large meals* or dietary changes;
f. Take r*elaxing exercise*, like yoga before bed to help initiate a restful night's sleep;
g. Follow a r*elaxing bedtime routine;*
h. Make sure you have a *pleasant and relaxing sleep environment* (comfortable bed, room not too cold or too hot, too humid or too bright, too noisy, *etc.*).

MISCELLANEOUS NON-DRUG METHODS

Bio-feedback, stimulus-control, sleep restriction, cognitive therapy and cognitive behavioral therapy are other useful methods to treat common insomnia but it would take us too far to develop them here. Again it is to be emphasized that jet lag insomnia is due to phase delay and occurs to people who sleep perfectly well in normal circumstances, so these techniques may not be very useful or sufficient here. Sleep restriction would certainly not be a good idea in the present context.

Having sex is seldom mentioned in sleep guidelines, but is not usually advised against either, which should be good news!

DRUGS OF ALL KINDS

There is nothing more restorative than plain, normal, drug-free sleep. But there is

also little doubt that sleep induced by sleeping pills is more restorative than insomnia.

Over the centuries, humans seem to have experimented with all kinds of compounds including opioids, alcohol, cannabis and many others to obtain sedation (reducing excitation and anxiety), alter consciousness or induce sleep (among other effects). In addition to these, many such compounds are now produced artificially from raw chemicals.

If there is one advantage of medications over non-regulated or over-the-counter substances, it is that their effects (main and side) have been studied far more rigorously. Medications need approval under strict legislation and have to demonstrate at least one useful action superior to the placebo effect. Their production is strictly supervised and controlled. This means that you know what you are getting and it will always be the same – the chemical equivalent of the fast-food restaurant. For these reasons, in order to obtain predictable sleep-inducing effects, I believe that you will be better off relying on recognised medications than on less-regulated products.

Amongst all the pharmacological classes that may induce sleep, I only describe here in some detail the benzodiazepines ("benzos" in short). They should be effective and their side-effects are well known and limited when used on a short-term basis. There are other valuable compounds that have their pros and cons but, except in specific cases, or when the subject suffers from alcohol or drug dependency, I don't see major benefits of using the other medication classes. Your doctor may nevertheless have a different view and I see no theoretical objection to using drugs outside the benzo group. You may also want to use medications other than benzos if you want to safeguard yourself against any legal issues, since the use of benzos is more restricted in some countries (see legal status below).

Unfortunately, no drug is perfect and whatever their origin, from those considered "fully natural" to those chemically produced in laboratories, compounds inevitably have one or the other side-effect. Side-effects are a minor nuisance to some but may be more substantial to others, as they vary from person to person and also depend on the dosage, as well as the patient's health, age, weight, gender,

CHAPTER 6

Staying Awake When Your Body Only Seems to Want to Sleep

Abstract: This chapter reviews the importance of fatigue (sleepiness) as a cause of distress and accidents. It insists on the fact that the best way to avoid it is to sleep enough and well. It presents the stimulants that could help you fight sleepiness if nothing else has worked (caffeine, modafinil).

Keywords: Accident, Abuse, Caffeine, Energy drink, Fatigue, Legal status, Modafinil, Sleep debt, Sleepiness, Withdrawal.

"What did the Chernobyl and Three Mile Island nuclear accidents, the space shuttle Challenger explosion, and the Exxon Valdez grounding have in common? Answer: fatigue. Accidents like these are especially dramatic examples of what can happen when humans become fatigued. But each year thousands of other less spectacular accidents occur across a range of activities, a by-product of a 24/7 world where sleep loss and circadian disruption are the norm for many individuals".

Mark Rosekind [1]

SLEEPINESS AND STIMULANTS

When your body clock tells you to sleep and you are in the morning, the middle of the day or early evening at your destination, you may find it difficult and sometimes impossible to enjoy your stay or do exactly what you want to do. Sleepiness may be very difficult, often hard to resist and if somehow you succeed, you are not at your best.

For the sake of consistency, I am using the terms “fatigue” and “sleepiness” interchangeably in this book, although we are mostly dealing here with sleepiness. Fatigue is a more complex and less well-explained phenomenon, not necessarily related to sleep [2].

The burden on human activities and the heavy load of casualties caused by fatigue, whether military, civil or personal, have been very convincingly described in Caldwell and Caldwell's Fatigue in Aviation [3] (to be re-issued soon). This great book also discusses in detail the various ways used by the military to counteract fatigue, among them being the use of stimulants and sleeping pills (see also [4]).

As mentioned in the previous chapter, the first thing is to make sure that you have an adequate number of hours of sleep behind you at all times. If you don't, homeostatic pressure (sleep debt) will add to the circadian issue, as we have seen in the Introduction. So the first thing to do is to sleep enough (see preceding chapter).

Use of stimulants must be seen as a last resort, after you have tried everything described in the previous chapters. Never use stimulants (other than caffeine) without first making sure that you have slept properly, if necessary by taking sleeping pills. Not following this rule could be dangerous as you would exhaust yourself without allowing yourself to recuperate. To delve here into the intricacies of sleep function(s) and sleep regulation would be to go too far. In summary, it does not seem especially dangerous to shift sleep by a few hours but it would surely be hazardous to suppress sleep by artificial awakening using stimulants.

Stimulants (caffeine, modafinil) have been recommended in jet lag situations for short (2 or 3 day) stays, since melatonin and bright light do not have time to speed up your adaptation [5]. I believe that they can also be useful for intermediate durations, especially if you cross many time zones and if melatonin and bright light are not effective enough for you.

Unfortunately, both caffeine and especially modafinil have a rather long duration of action (5-8 hours for caffeine, 5-10 hours for modafinil). This does no harm when sleepiness due to jet lag manifests itselfs in the morning or the afternoon

(Groups B and C). But this long action makes them trickier to use when sleepiness is felt in the evening (Group A) and you need to sleep a few hours later. The problem is easy to understand: if you take caffeine or modafinil too early, only the tail end of their action will hit the sleepiness, perhaps ineffectively. If you take them too late, or if you take too much, you may be wide awake during the evening but you could also find falling asleep more difficult. Consequently, we aim at an intermediate point in the curve.

For flights of a few time zone shifts westwards (*e.g.* time zone shifts from W+3 to W+7), it would be best to use shorter-acting compounds, most of whose action will disappear by the time you go to bed. They could also be useful in eastwards flights when the sleepiness induced by your body clock lasts from 1-5 hours (*e.g.* time zone shifts from E-2 to E-5). In fact, such short-acting medications already exist, for instance those used by hyperactive children. They are even more powerful than modafinil or caffeine. They could be used in small dosages against jet lag westwards, starting as late as 6 pm (18.00). Surveys have even shown that some supposedly very smart people, such as readers of the scientific journal Nature, already use them to combat jet lag [6]. Unfortunately, the legal status of these drugs is restricted (Schedule II or their equivalent in most countries) and I certainly cannot recommend them for off-label use here. The use, possession and above all distribution of even a few pills of a Schedule II drug may in fact land you in legal trouble and get you sent to jail in some countries.

CAFFEINE

Description

A mild stimulant from the xanthine family, it is arguably the most widely used psychoactive drug in the world. You find it in coffee of course, but also in tea, cocoa, chocolate, soft drinks, energy drinks, in some medications and over-the-counter preparations.

Its absorption is irregular, varies from person to person, and is influenced by food intake. Peak effects are observed after one hour, while residual effects can be perceived from 5 to 8 hours afterwards [7], and even more when pregnant or when taking hormonal contraceptives.

CHAPTER 7

In the Plane

Abstract: This chapter presents the differences between travel fatigue and jet lag, and what you could do in the plane.

Keywords: Homeostatic, Sleep-inducing, Jet lag, Preventive sleep, Prophylactic sleep, Travel fatigue.

"Airplane travel is nature's way of making you look like your passport photo".

Al Gore

TRAVEL FATIGUE (WITHOUT JET LAG)

Travel fatigue is general tiredness, disorientation and headache caused by a disruption in routine, time spent in a cramped space with little chance to move around, a low-oxygen environment, and dehydration caused by limited food and dry air. Travel fatigue can occur *without crossing time zones*, and it often disappears after a single night of high-quality sleep [1].

The design and size of seats, the angle of recline and the light environment of the cabin all play a role. Meals presented in the middle of biological night are undesirable [2]. I would add some generally pointless announcements by airplane crew, every now and then, in four languages in a row, sometimes very loud. Inconsiderate fellow passengers and noisy small children may constitute additional handicaps (I just fear the day when people will be able to use cellphones in the quieter airflights of the future). At least, we have lost yesterday's tobacco smoke for those who remember it! Sleep in the main cabin of a long-haul flight is thus likely to be fragmented to say the least. Travelling business or first

class has obvious advantages in terms of general comfort conditions but the cost of this makes it only a solution for the happy few.

But then travel fatigue is not limited to aviation. Travelling hundreds of miles by car, coach, train or boat in the summer to reach your holiday destination can be just as exhausting, especially if air conditioning is not available, the road is bad and traffic is not fluid.

So a distinction must be made between travel fatigue and jet lag, as many people confuse them. Travel fatigue is present, to a varying degree, whatever you do when trips are long and the conditions are average (or worse). Jet lag only hits you when you cross several meridians, even if you have had a very good flight. Travel fatigue is readily solved, as mentioned above. Jet lag takes days to get over, and so it is interesting to decide what you can do about it already while travelling.

WHEN JET LAG IS ADDED TO TRAVEL FATIGUE

So, if you don't travel across meridians (east-west), you only suffer from travel fatigue. As it will soon be quickly overcome, you just need to survive the travelling as best as you can, enjoy it if possible and then relax after arrival.

When jet lag is superimposed, I often hear of two contradictory strategies. There are no scientific surveys to my knowledge to tell you which is the best. The first seems more popular but the second sounds more logical.

The first strategy is to resist sleep as much as you can, watch movies, talk to friends, make new acquaintances, play games, listen to audiobooks, and get a chance for once to read The Economist from cover to cover, read good books or silly magazines, *etc.* This way your homeostatic drive to sleep (sleep debt) is maximized and should help you to enter and *stay asleep* once you are at your destination. The only problem is that this advantage will not last, whereas jet lag will, which is why the second option is probably better in most cases.

The second strategy is to try and sleep as much as you can in the plane, avoiding meals if necessary. This way, your homeostatic sleep drive will be reduced but you will arrive charged with some kind of “prophylactic” (preventive) sleep in the best case (usually still less than needed, but certainly more than in the first

scenario). Use eye covers, earplugs, noise-reducing headphones, blankets, pillows and relaxing music if it helps. If you skip meals, be sure to carry with you some form of light snack and water or soda (purchased after airport security of course). Tell the airflight attendant that he or she should not wake you up if possible. You will fall asleep more easily during the periods when your body clock tells you to sleep or nap (which may not be helped by the particular flight organisation). Then you can also use sleeping aids to increase your time asleep: choose a short-acting agent unless you have a really long flight, where medium-range ones could be more adequate – as long as you take them enough hours before landing! Try to combine sleep aid and body-clock periods, for instance a short-acting sleeping pill that will be relayed by the body clock later in the night. Also remember to use your time to walk a bit in the aisles, to help prevent deep vein thrombosis. Unfortunately, there are just far too many kinds of flights to give more precise advice here.

In general, avoid alcohol and drink water or caffeine-free sodas. Alcohol may wake you up as a rebound effect when you would want to sleep more. It can also make some people more irritable and agressive during the flight and nobody needs that.

On the circadian side, it could also be a good time to use melatonin if you are flying eastwards. Check if the timing for melatonin absorption indicated in the Time Zone Sheet *of your destination* occurs during your flight (that will be easier if you adjust your wristwatch or smartphone to your destination time in advance). Using bright light (and avoidance of it) is obviously more complicated due to the conditions, but nevertheless it cannot do any harm (eye covers, a light visor).

CHAPTER 8

How to Use the Time Zone Sheets (TZS)

Abstract: The Time Zone Sheets in the next chapter explain what to do in each jet lag situation, from West +1 to East -1. This chapter tells you how to find the one that corresponds to your particular trip (outward and return). It also discusses how to fine-tune your choice of Time Zone Sheet as a function of geography rather than political borders and of your own usual sleep habits.

Keywords: Daylight saving, Evening-type, Fine-tuning, Morning-type, Return trip, Time zone map, Time zone sheet, World clock.

"When an actor plays a scene exactly the way a director orders, it isn't acting. It's following instructions. Anyone with the physical qualifications can do that".

James Dean

How to Find your TZS?

As it is easy, effective and accurate to check on the Internet for the time difference existing between two cities, there is no need to develop charts here. I presently mostly use World Clock [1], which gives all the details you need (including the precious meeting planner I mentioned earlier). But there are other excellent websites available and I cannot list them all here.

The only pitfall, but it is important enough to insist on, is that *you don't go in the wrong direction!* And this is not very intuitive, even counterintuitive for many people, including myself. Is flying from Cape Town to Beijing +6 or -6 hours? (It is actually -6). If you use the wrong set of instructions, you may find yourself worse off than doing nothing. So, pleased double-check! For this reason, I always put the west or east wind rose (for instance W+7; E-3, *etc.*).

Olivier LE BON

If it is any help and if you have a basic knowledge of geography, remember that if the sun sets earlier somewhere, then people living there are already later in that day, so your clock will need to be delayed by so many hours. As a rule of thumb, going *eastwards*, you will thus feel you have *lost* hours of your life, and so use a *negative* sign. Going *westwards*, people may still be asleep when you arrive; they are earlier in their day, so you feel you have *gained* hours and use a *positive* sign.

World time zone maps are fascinating to look at, and you quickly realize that there are major differences between actual time zones and time zone outlines of countries or groups of countries. This is the result of political and practical reasons. China for instance, covers more than 3 time zones and yet uses only one official time (GMT +8). India for instance covers time zones GMT +5 and GMT +6 and has chosen to use only one time zone in between: GMT +5.5. Time zone differences by half hours are also observed in parts of Australia, Iran and Venezuela, for example. I apologize to the citizens of or travellers to those countries, since I only propose TZS by the hour, not half-hour. The TZSs will therefore need a little fine-tuning (see below).

Taking account of daylight saving time is a problem that can be solved by consulting Internet time zone sites. These are updated on a daily basis, so that this is no longer a major issue. But some fine-tuning may however be advised in specific cases.

Fine-tuning: Official Time and Actual Time Zones

The TZSs presented below give suggestions based on a city-to-city official time scheme. As mentioned above, political reasons and daylight saving may distort the geographical reality.

To begin with a negative example, if you travel from a city in the west of China and fly to a city in the east of India, I would logically, basing myself on Beijing (GMT +8) and Delhi times (GMT +5.5), recommend something between TZS E-2 and E-3. Actually, both are at more or less the same longitude and you should in fact do nothing special against jet lag! On the contrary, if you fly from Madrid (GMT +2) in the summer, to a city in the northern Russian Urals (GMT +3), I would logically recommend TZS E-1, when you will in fact cross 4 or 5 time

zones.

Consequently, you may want to be more precise and base yourself on actual geography rather than on official time. If you want to check for that using time zone maps, count how many zones you actually cross and adjust correspondingly.

Early Birds (Larks) and Night Owls (Morning-types, Evening-types)

As mentioned earlier, not everybody goes to sleep at the same time at home. There are a host of reasons for that: genetic, professional, personal, *etc.* As mentioned earlier, most of you will rather quickly use the same schedule at your destination as at home, mostly for the same reasons.

In order to simplify the suggestions made in the TZSs below, I assume a normalized 11 pm (23.00) bedtime and 7 am wake-up time. If you are used to going to sleep at 10 pm (22.00) and waking up at 6 am, you should subtract one hour from the suggestions made. If your habit is rather to sleep from 1 am to 9 am, then add an extra two hours to the time patterns.

On the Way Back

Let us suppose you have just done a round trip and are on the way back. Then, just follow the instructions – changing the sign of your destination (W+8 becomes E-8 for instance).

The duration of the adaptation time (in days) is estimated on the basis of a steady state, that is we suppose that your body clock is stable (jet lag-wise) before leaving. If your stay abroad is more than a week long, the estimated duration is still valid on the way back. Just follow the instructions! But if your trip is of a shorter duration, you will adjust more easily and in less time on the way back. In that case, you could take the recommended measures for a shorter time than you would do otherwise. To give an estimate, I would say that for a 2-3 day trip, you could cut the duration of the adaptation by half. But they are so many possibilities that it is simply not possible to be more precise.

CHAPTER 9

Time Zone Sheets (TZS): A Journey Around the World

Abstract: 23 jet lag situations, from West +1 to East -1, are described here. I begin with the specific problems that may be encountered in each case, as well as a list of specific solutions. These solutions start with no-nonsense measures; go on to speeding up the adjustment using bright light and melatonin; then to sleeping pills; and, if nothing else works, to strong doses of caffeine and stimulants. I suggest you use a graduated, step-by-step response and to go to the next level only if you have an insufficient result. I will end with a few comments based on my own experience over the years as a traveller.

Keywords: Bright light, Caffeine, Fatigue, Launch window, Medium-duration sleeping pill, Melatonin, Modafinil, Sleeping pill, Nap, No-nonsense measure, Power nap, Practical, Preflight rescheduling, Short-duration sleeping pill, Sleepiness.

"Anytime I feel lost, I pull out a map and stare. I stare until I have reminded myself that life is a giant adventure, so much to do, to see".

Angelina Jolie

Warning: I do not recommend the separate purchase and use of this chapter. Time Zone Sheets need to be used intelligently and with caution. Therefore, they are really parts of the whole book, as the explanations are a key element for their proper use.

W+1

Olivier LE BON

Examples: Daylight saving time (changing to wintertime); New York to Chicago (USA)

Time zone chart (Fig. 1)

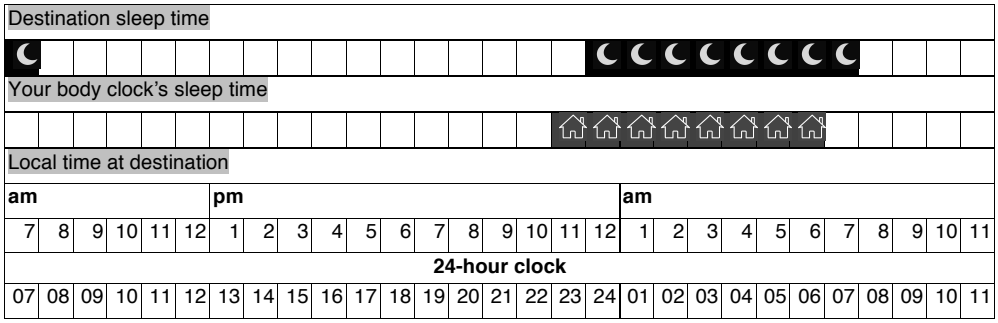

Fig. (1). The time of day in am/pm and as a 24-hour clock is shown in the bottom lines. The black rectangles with the little moons show the duration of normal sleep period at your destination. The grey rectangles with the little houses indicate the duration of the sleepiness induced by your body clock, still set to your home place. In this chart, sleepiness arrives one hour too soon and leaves one hour too soon.

Group A: There is an overlap between your body clock and the destination time. The problem is to *remain awake* late in the day and to *stay asleep* early in the morning.

Symptoms: You will feel abnormally sleepy around 10 pm (22.00) and find the end of your night somewhat shallow.

Adaptation: Should last 1-2 days.

My adaptation difficulty rating (maximum 5):

No-nonsense measures

Preflight rescheduling: You could gradually delay your bedtime by about one hour a few days before the switch. Then you will already have adjusted before arrival. Avoid important meetings late in the evening.

Personal comments

Since it is usually easier to go to bed an hour later than an hour sooner, this time zone difference should not cause a big problem. Once at my destination, I would just go to sleep a little earlier than I would normally, around 10 pm (22.00). I would then allow myself to sleep a little longer in the morning. This way, I may even recover a bit of my usual sleep debt! It won't last, as there is a good likelihood that within a day or two I will go to sleep at my usual sleep time.

W+2

Examples: Canberra to Perth (Australia); Seoul (South Korea) to Beijing (China) (NB: check the daylight saving time on both sides and adjust the times accordingly)

Time zone chart (Fig. 2)

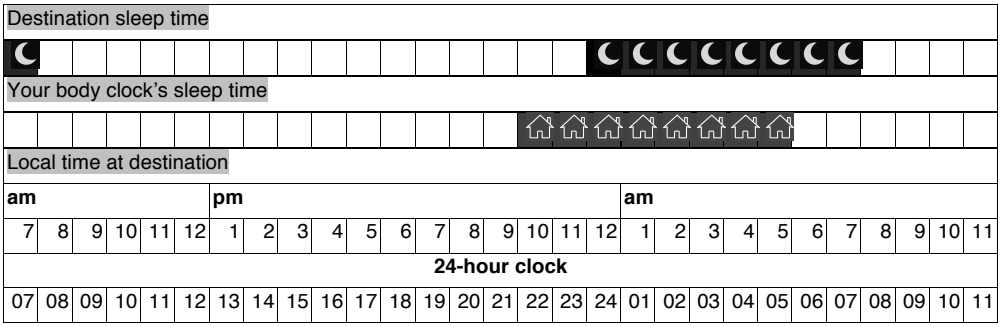

Fig. (2). The time of day in am/pm and as a 24-hour clock is shown in the bottom lines. The black rectangles with the little moons show the duration of normal sleep period at your destination. The grey rectangles with the little houses indicate the duration of the sleepiness induced by your body clock, still set to your home place. In this chart, sleepiness arrives two hours too soon and leaves two hours too soon.

Group A: There is an overlap between your body clock and the destination time. The problem is to *remain awake* late in the day and to *stay asleep* until the morning.

Symptoms: You may feel groggy from 9 pm (21.00) to bedtime at 11 pm (23.00). You should then fall asleep without too much difficulty. But you may very well

CHAPTER 10

How You Can Help to Advance the Science of Jet Lag

Abstract: The present suggestions are an extrapolation of evidence-based medicine. They have not been extensively field-tested. By completing a survey, you can help me to refine the suggestions for future editions of this book.

Keywords: Comments, Feedback, Future editions, Jet lag, Online, Science, Survey.

Many instructions presented in this book are, as indicated in the Introduction, proven science, practical suggestions or an extrapolation of what is currently known about jet lag. I have given you the best solutions I have been able to think of but they have not all been field-tested, *let alone* in a scientific way.

If you would like to help me to improve these solutions in the future, please take the time to answer the online questionnaire by following the link below, whether you feel they have helped greatly, a little or not at all. I will then be able to examine what has really proven useful and what has not and share this information with fellow scientists. I hope that together, we will help to progress this field.

www.jetlagsmart.org

Olivier LE BON

Annex: Example of Drug Scheduling

The US Drug Enforcement Administration of the Department of Justice

DRUG SCHEDULES

Drugs, substances, and certain chemicals used to make drugs are classified into five (5) distinct categories or schedules depending upon the drug's acceptable medical use and the drug's abuse or dependency potential. The abuse rate is a determinate factor in the scheduling of the drug; for example, Schedule I drugs are considered the most dangerous class of drugs with a high potential for abuse and potentially severe psychological and/or physical dependence. As the drug schedule changes-- Schedule II, Schedule III, *etc.*, so does the abuse potential-- Schedule V drugs represents the least potential for abuse. A Listing of drugs and their schedule are located at Controlled Substance Act (CSA) Scheduling or CSA Scheduling by Alphabetical Order. These lists describes the basic or parent chemical and do not necessarily describe the salts, isomers and salts of isomers, esters, ethers and derivatives which may also be classified as controlled substances. These lists are intended as general references and are not comprehensive listings of all controlled substances.

Please note that a substance need not be listed as a controlled substance to be treated as a Schedule I substance for criminal prosecution. A controlled substance analogue is a substance which is intended for human consumption and is structurally or pharmacologically substantially similar to or is represented as being similar to a Schedule I or Schedule II substance and is not an approved medication in the United States. (See 21 U.S.C. §802(32)(A) for the definition of a controlled substance analogue and 21 U.S.C. §813 for the schedule).

Like all medications, there are both benefits and risks associated with the use of these compounds. The benefits and risks should be considered by the prescribing doctor and the person before a decision is made.

Schedule I

Schedule I drugs, substances, or chemicals are defined as drugs with no currently accepted medical use and a high potential for abuse. Schedule I drugs are the most dangerous drugs of all the drug schedules with potentially severe psychological or physical dependence. Some examples of Schedule I drugs are: heroin, lysergic acid diethylamide (LSD), marijuana (cannabis), 3,4-methylenedioxymethamphetamine (ecstasy), methaqualone, and peyote.

Schedule II

Schedule II drugs, substances, or chemicals are defined as drugs with a high potential for abuse, less abuse potential than Schedule I drugs, with use potentially leading to severe psychological or physical dependence. These drugs are also considered dangerous. Some examples of Schedule II drugs are: Combination products with less than 15 milligrams of hydrocodone per dosage unit (Vicodin), cocaine, methamphetamine, methadone, hydromorphone (Dilaudid), meperidine (Demerol), oxycodone (OxyContin), fentanyl, Dexedrine, Adderall, and Ritalin.

Schedule III

Schedule III drugs, substances, or chemicals are defined as drugs with a moderate to low potential for physical and psychological dependence. Schedule III drugs abuse potential is less than Schedule I and Schedule II drugs but more than Schedule IV. Some examples of Schedule III drugs are: Products containing less than 90 milligrams of codeine per dosage unit (Tylenol with codeine), ketamine, anabolic steroids, testosterone.

Schedule IV

Schedule IV drugs, substances, or chemicals are defined as drugs with a low potential for abuse and low risk of dependence. Some examples of Schedule IV drugs are: Xanax, Soma, Darvon, Darvocet, Valium, Ativan, Talwin, Ambien, Tramadol.

Schedule V

Schedule V drugs, substances, or chemicals are defined as drugs with lower potential for abuse than Schedule IV and consist of preparations containing limited quantities of certain narcotics. Schedule V drugs are generally used for antidiarrheal, antitussive, and analgesic purposes. Some examples of Schedule V drugs are: cough preparations with less than 200 milligrams of codeine or per 100 milliliters (Robitussin AC), Lomotil, Motofen, Lyrica, Parepectolin.

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SUBJECT INDEX

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Olivier LE BON

As well as pursuing an already long career as a clinical psychiatrist and Head of the Department of Psychiatry at Tivoli Hospital (La Louvière, Belgium), Olivier LE BON, MD, PhD, is a lecturer (maître d'enseignement) at the Université Libre de Bruxelles (Belgium). In collaboration with colleagues from Europe as well as North and South America, he has studied several fields of psychiatry, neurophysiology and sleep, publishing more than 80 scientific papers. The subject of his PhD was biological cycles and in particular the alternance of REM and NREM sleep cycles in humans, rats and mice. He pioneered research on the role of ultra-slow wave sleep in clinical fields, such as chronic fatigue. He has also published significant papers in the fields of alcoholism, addiction and personality. He is a globe-trotter, too, having visited more than 60 countries around the world.