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CLINICAL REVIEW

Diurnal and twenty-four hour patterning of human diseases: acute and chronic common and uncommon medical conditions

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SUMMARY

The symptom intensity and mortality of human diseases, conditions, and syndromes exhibit diurnal or 24 h patterning, e.g., skin: atopic dermatitis, urticaria, psoriasis, and palmar hyperhidrosis; gastrointestinal: esophageal reflux, peptic ulcer (including perforation and hemorrhage), cyclic vomiting syndrome, biliary colic, hepatic variceal hemorrhage, and proctalgia fugax; infection: susceptibility, fever, and mortality; neural: frontal, parietal, temporal, and occipital lobe seizures, Parkinson's and Alzheimer's disease, hereditary progressive dystonia, and pain (cancer, post-surgical, diabetic neuropathic and foot ulcer, tooth caries, burning mouth and temporomandibular syndromes, fibromyalgia, sciatica, intervertebral vacuum phenomenon, multiple sclerosis muscle spasm, and migraine, tension, cluster, hypnic, and paroxysmal hemicranial headache); renal: colic and nocturnal enuresis and polyuria; ocular: bulbar conjunctival redness, keratoconjunctivitis sicca, intraocular pressure and anterior ischemic optic neuropathy, and recurrent corneal erosion syndrome; psychiatric/behavioral: major and seasonal affective depressive disorders, bipolar disorder, parasuicide and suicide, dementia-associated agitation, and addictive alcohol, tobacco, and heroin cravings and withdrawal phenomena; plus autoimmune and musculoskeletal: rheumatoid arthritis, osteoarthritis, axial spondylarthritis, gout, Sjögren's syndrome, and systemic lupus erythematosus. Knowledge of these and other 24 h patterns of human pathophysiology informs research of their underlying circadian and other endogenous mechanisms, external temporal triggers, and more effective patient care entailing clinical *chrono*preventive and *chrono*therapeutic strategies.

Introduction

Many medical conditions exhibit profound day–night patterning in symptom intensity, with a large portion exacerbating nocturnally so as to disturb sleep onset and continuity, and occurrence of grave events. Knowledge of such patterns is necessary for appropriate patient care, including optimal timing of therapy, and accurate research of mechanisms and triggers of human disease. The subject of this and our companion paper in this journal issue [1] is diurnal and 24 h variation of acute and chronic medical diseases, conditions, and syndromes, and serious nonfatal and fatal events. Books devoted to human and clinical chronobiology were reviewed and PubMed and other relevant databases were explored, entering search terms of 'circadian rhythm in disease' or specific diseases or medical conditions paired with 'circadian', 'diurnal', 'nocturnal', or 'time-of-day'. Hospital reports were excluded, since life-extending care, medication schedules, and altered circadian time structure due to atypical light–dark and sleep–wake patterns in this environment are likely to give rise to non-representative findings [1]. Our thorough, although not entirely exhaustive, literature search uncovered >500 publications

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[1] This article is dedicated to Dr. Erhard Haus, a close colleague and internationally renowned pioneer of medical chronobiology, who passed away prior to its completion.

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Abbreviations

τ	period
AADD	alcohol addiction
ACTH	adrenocorticotropic hormone
AION	anterior ischemic optic neuropathy
AMI	acute myocardial infarct
AS	attempted suicide
ASPA	axial spondylarthritis
BC	biliary colic
BCH	bulbar conjunctival hyperemia
BDMS	bipolar disorder mood switches
BP	blood pressure
CDASD	Chagas' disease-associated sudden death
CH	cluster headache
CS	completed suicide
CV	cyclic vertigo
CVS	cyclic vomiting syndrome
CVH	cirrhotic variceal hemorrhage
DBP	diastolic blood pressure
FC	febrile convulsion
FFS	first febrile seizure
FLS	frontal lobe seizures
GERD	gastroesophageal reflux
GTP	guanosine triphosphate
HADD	heroin addiction
HH	hypnic headache
HPD	hereditary progressive dystonia
IOP	intraocular pressure
KCS	keratoconjunctivitis sicca
LOHS	length of hospital stay
MDD	major depressive disorder
MH	migraine headache
MM	meningococcal meningitis
MTLS	mesial temporal lobe seizure
NADD	nicotine addiction
NE	nocturnal enuresis
NID	neuroleptic-induced dystonia
NP	nocturnal polyuria
NTG	normal tension glaucoma
OA	osteoarthritis
OLS	occipital lobe seizure
PBC	pruritus of biliary cirrhosis
PD	parkinson's disease
PF	proctalgia fugax
PH	palmar hyperhidrosis
PHH	paroxysmal hemicranial headache
PLS	parietal lobe seizure
POAG	primary open angle glaucoma
PS	parasuicide
PUD	peptic ulcer disease
PUH	peptic ulcer hemorrhage
PUP	peptic ulcer perforation
RA	rheumatoid arthritis
RC	renal colic
RCES	recurrent corneal erosion syndrome
REM	rapid eye movement
RT	rectal temperature
SAD	seasonal affective disorder
SBP	systolic blood pressure
SLE	systemic lupus erythematosus
SS	Sjögren's syndrome
TAS	typical absence seizure
TH	tension headache
VAB	violent and aggressive behaviors
VM	vestibular migraine
VPR	vasopressin
WBC	white blood cell count

entailing >100 disease states/medical conditions. In keeping with journal guidelines, selected findings are reported in two articles of this journal issue, the first addressing temporal patterns in cardiac, vascular, and respiratory diseases [1] and this second one addressing various other diseases.

A vast array of methods was utilized to assess the temporal patterns reported herein, e.g., patient internet surveys, daily diaries, questionnaires, and self-assessments, plus time-of-day tabulations of: calls for ambulance service, symptom onset as stated by persons admitted to hospital emergency departments, grave incidents by enrollees in medical trials, and listed demise on death certificates. Generally, results were reported per clock-hour interval as group means in symptom intensity studies and number of incidents in acute event ones. This review communicates as group phenomena the clock-time manifestation of greatest and least intensity of symptoms and highest and lowest incidence of grave events.

Arthritis

Rheumatoid arthritis (RA)

RA is a chronic autoimmune disorder characterized by remodeling and deformation of the small joints, particularly the hands and feet. Prominent morning-time symptoms are hallmark, e.g., stiffness lasting ≥1 h in ~50% of recent-onset cases, inflammation, pain, compromised dexterity/strength, and fatigue [2–5], even in medicated patients [3–5]. Around-the-clock patient self-assessment studies, however, reveal symptoms actually worsen overnight, peaking ~02:00–04:00 h [6].

Osteoarthritis (OA)

OA, the most common form of arthritis, results from use-related degradation of the protective cartilage of joints, e.g., hip, knee, ankle, lower back, and neck. Typically, pain, inflammation, and other symptoms progressively escalate during diurnal activity generally being worse in the evening and night [7,8], although with time-of-day difference between individuals and affected joints [9]. Coexistence of both RA and OA usually manifests as a bimodal, morning/evening, peaked cycle of symptom intensity [10,11].

Axial spondylarthritis (ASPA)

Primary symptoms of ASPA, vertebral stiffness and pain, exhibit considerable diurnal variation, with major morning (06:00–09:00 h) and lesser evening (18:00–21:00 h) peaks [12,13].

Gout

Gout is a complex form of arthritis caused by accumulation in joints of uric acid crystals. Signs and symptoms of acute exacerbation – inflammation, tenderness, redness, and sharp pain – generally of the metatarsal-phalangeal joint of the big toe, but also, e.g., foot, ankle, knee, wrist, and elbow, flare at night (http://