



# NEWSLETTER

*Special Issue, 1998*

*World Federation of Sleep Research Societies*

<http://www.wfsrs.org/newsletter/specialissue>



Michel Jouvet



Allan Rechtschaffen



Elio Lugaresi

In this special issue, we wish to acknowledge the role of three major figures who have definitively marked the sleep field across the century: Michel Jouvet, Elio Lugaresi and Allan Rechtschaffen, the Lyon-Bologna-Chicago "magic triangle". Each one of us is aware of the scientific achievements of these great pioneers and how important their contributions to the understanding of the mystery(ies) of sleep have been. The point here is not so much to tell this truth once more, but to share among all of us some special times that we have experienced with them. You will notice that these pieces are extremely diverse, as a reflection of their individual personalities.

Joëlle Adrien

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## TABLE OF CONTENTS

FROM THE EDITOR.....	2
MESSAGE FROM THE PRESIDENT.....	2
MICHEL JOUVET.....	3
Biography.....	4
Commemoration.....	5
Colleagues Recall.....	8
ELIO LUGARESÌ.....	17
Biography.....	18
Commemoration.....	19
Colleagues Recall.....	24
ALLAN RECHTSCHAFFEN.....	27
Biography.....	28
Commemoration.....	29
Colleagues Recall.....	32
SCRAPBOOK.....	42
THIRD INTERNATIONAL CONGRESS.....	46

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## FROM THE EDITOR

In this special issue, we wish to acknowledge the role of three major figures who have definitively marked the sleep field across the century: Michel Jouvet, Elio Lugaresi and Allan Rechtschaffen, the Lyon-Bologna-Chicago “magic triangle”.

Each one of us is aware of the scientific achievements of these great pioneers and how important their contributions to the understanding of the mystery(ies) of sleep have been. The point here is not so much to tell this truth once more, but to share between all of us some special times that we have experienced with them. You will notice that these pieces are extremely diverse, as a reflection of their individual personalities.

*Joëlle Adrien*

WFSRS



## MESSAGE FROM THE PRESIDENT

It is my opinion, and hope, that this issue of the WFSRS Newsletter will become a classic for three reasons. First, I hope that it will serve as a tutorial for young investigators on how to become renowned and respected while retaining one's humanity and sense of humor. Second, I see it as a blueprint on how to succeed as a researcher while maintaining the highest moral and ethical standards. Finally, I see it as a reflection of the best of our field, which is the embodiment of the characteristics of our leaders and those whom we hold in the highest esteem—Michel Jouvet, Elio Lugaresi, and Allan Rechtschaffen.

As I read the descriptions of Michel, Elio, and AI, I was impressed not only by what was said, but perhaps even more by what was not said. All were described as exhibiting humbleness and a lack of desire for self glorification. Not one of these leaders of our field was portrayed, even indirectly, as being egocentric, unfair, inappropriately demanding, etc. All championed the young people that worked with them and strongly supported their careers. None were so devoted to their own hypotheses that they were not open to contradictory ideas or data. All changed their scientific positions numerous times, but always according to the data. Not one of them was difficult to work with. All had a terrific sense of humor. Two of the three relished gourmet food and admired the finest of wines (sorry AI, but no one's absolutely perfect!).

All these characteristics communicate to me the simple fact that one can succeed, one can even rise to the top of one's field, while having a sense of humor, while being completely honest and while eating good food and drinking superb wine.

Thus, there are certainly many lessons to be learned by reading and re-reading this issue of the WFSRS Newsletter, and I hope that young people and established investigators as well read it as a morality piece and research map of what it is possible to attain in a given field, while being the very best that one can be.

*Michael Chase*

WFSRS

# MICHEL





## BIOGRAPHY OF MICHEL JOUVET

**Date of Birth:**  
November 16, 1925

**First University Position and Date:**  
1961-Associate Professor in Experimental Medicine  
Claude Bernard University  
Lyon, France

**Most Recent University Position:**  
Professor Emeritus  
Claude Bernard University  
Lyon, France

### Representative Awards:

- Prix Bing (Swiss Academy of Medical Sciences) (1966)
- Intra-Science Award, Intra-Science Research Foundation (1981)
- Prix de la Fondation pour la Recherche Médicale (France) (Foundation for Medical Research) (1983)
- Distinguished Scientist Award of the Sleep Research Society (USA) (1989)
- Gold Medal of the CNRS (1989)
- Simone et Cino del Duca World Award (1991)
- Fyssen Foundation International Prize (1997)

### Service Contributions:

Honorary President, Founding Congress of the World Federation of Sleep Research Societies (1991)

### Representative Publications:

- Jouvet, M. and Michel, F. Recherches sur l'activité cérébrale au cours du sommeil. C.R. Soc. Biol. Paris 152:1167-1170, 1958.
- Jouvet, M. Diagnostic électro-sous-corticographique de la Mort du Système Nerveux Central au cours de certains comas. EEG and Clinical Neurophysiology 11:805-806, 1959.
- Jouvet, M. Telencephalic and rhombencephalic sleep in the cat. In the Nature of Sleep. CIBA Foundation Symposium, Churchill, London, 1961.
- Jouvet, M. Recherches sur les structures et les mécanismes des différentes phases du sommeil physiologique. Arch. Ital. Biol. 100:125-206, 1962.
- Jouvet, M. Paradoxical Sleep: A Study of its Nature and Mechanism. Progress in Brain Research (Sleep Mechanisms) 18:20-62, 1965.
- Jouvet, M. Biogenic amines and the states of sleep. Science 163:32-41, 1969.
- Jouvet, M. The role of monoamine and acetylcholine-containing neurons in the regulation of the sleep-waking cycle. Ergebnisse der Physiologie 64:166-307, 1972.

### The following reflect either the first finding in the field or a significant pioneering construct or theory:

- ▶ Description of the EEG signs of cerebral death (1959).
- ▶ Description of muscle atonia during paradoxical sleep (1959).
- ▶ Demonstration that physiological sleep is composed of two different states: Telencephalic sleep (slow wave sleep) and rhombencephalic sleep (paradoxical sleep) (1961).
- ▶ Description of the ontogeny and phylogeny of sleep in animals (1961-1962).
- ▶ Description of "oneiric behaviors" after lesion of the Pons (1965).
- ▶ Origin and pathways of PGO activity (1970).



## Commemoration of Michel Jouvet

### The Discoverer of Paradoxical Sleep and Many Other Things about the Physiology of Vigilance

by Dr. Jean-Louis Valatx  
Laboratoire de Médecine Expérimentale  
Université Claude Bernard  
Lyon, France

The first time I met Michel Jouvet I was a medical student. In November 1959, as I was very interested by the neurophysiology course, I was looking for a laboratory working on brain research. Within the physiology department, there were cardiovascular and thermoregulation sections. An assistant told me about a very new research section run by Michel Jouvet, fondly called "the poet of the lab" because he was beginning to study sleep and dreams, a research field considered as very subjective at that time. The assistant introduced me to Jouvet who was implanting a cat. He said to me, "Come when you want". The first afternoon I went to his laboratory, he said "come and see", then we entered a darkened room where an EEG apparatus was standing in front of a big cage with a one-way window. He said, "Observe the behavior of the cat inside the cage and write all you see on the EEG chart". I remained a couple of hours to discover arousal, slow waves and sleep with eye, vibrissae and ear movements. The following day I started to make up electrodes with Danièle Mounier, his future wife. In other departments, students used to wait for several weeks before beginning research work. This personal recollection emphasizes the remarkable pedagogy of Michel.

Another trait of his personality is to focus his attention on what other persons would consider as not important, e.g., the discovery of paradoxical sleep. After his stage in the Magoun laboratory (1955), being an admirer of Pavlov, Jouvet started a series of experiments to study the respective role of the reticular formation and the neocortex in conditioned reflexes (MD, thesis, 1956). For this purpose, with

François Michel, he carried out experiments on decorticated or decerebrate cats implanted with multiple subcortical electrodes. They thus discovered two important things. Firstly the total ablation of the neocortex suppressed slow-wave activity in the thalamus (1958). Despite the absence of slow waves, sleep behavior was still

### The poet of the lab...

observable. Secondly, in decerebrate cats presenting hypertonia of neck and limbs, they observed by chance that this hypertonia ceased periodically for a few minutes. They inserted electrodes in the neck muscles to objectively examine this hypotonia which was associated with eye movements and "spindle-like" activity in the reticular formation. They also observed that the arousal threshold was higher than during the hypertonic state. Jouvet was very intrigued by this phenomenon: to be sure it was not a surgical artefact, they tried to find it in intact animals. They observed that this phenomenon not only existed but was also associated with a "waking"-like cortical activity already observed by Bill Dement in 1958. At that time since "fast activity" was synonymous with waking, it was a contradiction to observe an aroused brain while the body was profoundly asleep. He thus developed the concept of paradoxical sleep which was the beginning of the modern history of sleep.

From that moment, all his research work was focused on sleep mechanisms.

In order to prove that paradoxical sleep was a new state of the brain—occurring during sleep—but distinct from slow-wave sleep, Jouvet and his coworkers presented many new data in favor of the existence of two states of sleep, namely slow-wave sleep (SWS) which depends upon telencephalic structures, and paradoxical sleep (PS) which depends upon the rhombencephalon (pons and medulla oblongata). For this purpose, Jouvet never hesitated to import or develop new techniques allowing him to further the understanding of sleep mechanisms, such as microelectrodes, histochemistry, neurochemistry, voltametry or molecular biology, without forgetting the simplest technique, the visual inspection of behavior.

For many years, these promising experiments were made possible thanks to several grants obtained from the U.S. Air Force with the help of Colonel James P. Henry.

### The concept of paradoxical sleep was the beginning of the modern history of sleep.

The duality of sleep was supported by different but complementary approaches. A synthetic review was put forward during the international symposium organized in Lyons by the CNRS in 1963. From the discussion which followed, it became evident that the theory of two states of sleep was accepted by the international physiological community together with the now widely accepted hypothesis that slow-

wave sleep involves the neocortex and paradoxical sleep the rhombencephalon. Jouvets theory was subsequently published in many reviews in English. I will briefly summarize the main and original results obtained by Jouvet.

### 1. Physiological experiments

Everything remained to be discovered concerning paradoxical sleep. The main questions were: Was it a brain or peripheral phenomenon? Was it a common phenomenon shared by all mammals and vertebrates? What was its evolution from birth to adulthood?

**Localization of structures responsible for PS.** The first description of PS in a decerebrate cat was crucial for answering this question. The main results from a large series of brain transections and ablations were described in a paper published in Archives Italiennes de Biologie (1962) which is most frequently cited. In this paper, Jouvet demonstrated the pontine origin of paradoxical sleep and proposed a relationship with cholinergic mechanisms (both facts are still valid today). For that, his most famous experiment was the "pontine preparation", an animal in which the entire forebrain in front of the colliculi was removed including the hypothalamus and pituitary gland. Such a drastic operation was made possible thanks to his clinical neurosurgical experience. These pontine animals still presented all the characteristics of PS except, of course, cortical desynchronization.

But, what was the influence of the periphery? Thanks to the friendly collaboration of other sections of the physiology department, many ablations or sections of spinal cord, sympathetic ganglia, vago-aortic, tenth, eleventh or twelfth nerves, adrenals, etc., were carried out and showed that PS was still present in all these preparations. Thus, PS was a true central phenomenon.

The localization of neurons responsible for each parameter of PS (atonia, PGO waves, eye movements,

cortical activation) was progressively specified. Lesioning the pontine system for muscular atonia led to the disclosure of a very dramatic behavior that occurs only during *paradoxical sleep without atonia* i.e., attack, lookout, flight, rage, grooming, feeding, drinking without any goal. This "oneiric" behavior was illustrated in a film shown during the International Physiological Congress in Tokyo (1965) and subsequently confirmed by Henley and

### Everything remained to be discovered concerning paradoxical sleep.

Morrison. The discovery of this behavior resulted in the opening-up of a new field since dreaming can be objectively studied in the cat.

**Phylogeny of sleep.** In a series of articles summarized in 1964, Jouvet and his coworkers described the phylogenetic evolution of paradoxical sleep. Using polygraphic techniques, they were the first people to study in laboratory conditions the sleep-wake cycle in fishes, reptiles (tortoise, python, caiman) and birds. He concluded that PS does not exist in poikilothermic animals (fishes, amphibians, reptiles) while, in contrast, SWS and PS exist in homoiothermic animals (birds, mammals). While he was studying the sleep of the lamb, a young professor of the veterinary school of Lyons, Ruckebusch, came to the laboratory and learned

### Pontine animals presented all the characteristics of PS except cortical desynchronization...

the polygraphic techniques before starting his famous work on the sleep of herbivores and ruminants.

**Ontogeny of sleep.** In parallel with its phylogenetic evolution, I worked with Danièle Jouvet on the ontogenetic

evolution of sleep and we discovered that PS was much more frequent in newborn mammals (rat, kitten, lamb) or even *in utero* by chronic recording of the guinea-pig fetus. The fact that the rapid eye movements are seen before the opening of the eyelids and that paradoxical sleep appears before SWS confirmed the duality of the states of sleep and led to the hypothesis that PS might be related to some "programming" mechanism of the brain. The results obtained, as early as 1961-1964, were confirmed later and are still valid today.

**Genetics of sleep.** Searching for a function for PS, Jouvet asked me to study inbred strains of mice to determine the relationship between learning and PS. Surprisingly, with Kunio Kitahama we observed large differences in sleep durations between strains. A genetic study of sleep was then undertaken in parallel with that of learning. Results showing a genetic determinism for EEG frequencies and sleep durations were published in *Nature* (1972). Then a similar

### PS does not exist in poikilothermic animals...SWS and PS exist in homoiothermic animals.

determinism was evidenced for the number of eye movements during PS. This genetic approach was continued with the study of some mutant rats and transgenic mice. From these results (ontogeny, oneiric behavior and genetics), Jouvet suggested in 1972 that paradoxical sleep is involved in iterative genetic programming of the brain.

### 2. The monoaminergic theory of the sleep-wake cycle

Elaboration of this theory started in 1963 with the alterations of sleep observed after reserpine injection by J. Matsumoto during his stay in the laboratory. Then, as soon as the work of Dalhstrom and Fuxe (1964) on the brain localization of monoamine neurons by the Hillarp's histofluorescent method was published, Jouvet made his intuition effective about the role of monoamines in sleep mechanisms. Lesioning the area of the locus coeruleus led to a strong reduction of PS. Then, lesioning the serotonergic (5-HT) neurons located in the raphe system caused total insomnia

for several weeks. By using PCPA (5-HT synthesis inhibitor) and 5-HTP bypassing the inhibition, Jouvet confirmed the role of 5-HT in slow-wave sleep regulation. At the same time (1965), he imported the histofluorescence technique by sending a technician to Fuxe's laboratory. He then created the biochemistry section of his laboratory for the dosage of monoamines. This section later became an independent laboratory directed by J.F. Pujol. In 1969, Jouvet proposed the monoaminergic theory (serotonin for SWS, acetylcholine for PS and catecholamines for waking) which was published in *Science* and is a citation classic. Then, when new results showed that 5-HT neurons were only active during waking, he did not hesitate to revisit his theory.

The monoaminergic theory led to a radical new paradigm in the field of sleep-waking mechanisms since "wet" neurophysiology (monoamines) was entering the field of "dry" neurophysiology (electrophysiology).

In developing this new approach, Jouvet and his group (principally Raymond Cespuglio) developed new methods for the *in vivo* study of certain neurochemical factors, e.g., electrochemistry with special carbon microelectrodes for measuring monoamines, nitric oxide (NO), energetic metabolites (glucose, lactate) and, more recently, laser optochemistry for NADH.

In 1973, observing by chance the suppressive effect of chloramphenicol (an antibiotic inhibiting protein synthesis) on sleep, he developed experiments showing the role of certain peptides in sleep regulation.

Recently, Jouvet focused his attention on the waking system. He showed that the role of waking structures established many years ago by electrocoagulation lesioning should be revisited by using ibotenic acid, a neurotoxin causing only the degeneration

of neurons. Such a lesion of the mesencephalic reticular formation and/or posterior hypothalamus does not alter wakefulness. These results led to the concept of a waking network composed of multiple redundant structures. Among them, the histamine system mainly studied by J.S. Lin was shown to play an

### Paradoxical sleep is involved in iterative genetic programming of the brain.

important role. Moreover, Jouvet elucidated the basic mechanisms of the action of modafinil, a new arousing drug with a possible hypnotic role, used for the treatment of hypersomnia and narcolepsy.

Very recently, Jouvet found a new model to study hypersomnia by injecting muscimol (a GABA agonist) into the periaqueductal grey (PAG). Depending on the infusion site, SWS or PS can be triggered continuously for several hours. This approach in combination to c-fos immunocytochemistry seems to be more promising than sleep deprivation for elucidating the functions of both states of sleep.

In summary, Jouvet and his school opened up an entirely new domain in neurosciences by discovering that paradoxical sleep (which is most likely related to dreaming) was a new

### The monoaminergic theory led to a radical new paradigm in the field of sleep-waking mechanisms

state of the brain (totally different from waking and slow-wave sleep). In discovering oneiric behavior, they also pioneered the objective study of the unconscious and of a possible oneiric function.

It should also be noted that in 1959 Jouvet was the first to describe all the polygraphic criteria for assessing brain death, a seminal discovery that helped in

the development of organ transplantation. At the same time, his coma classification was very useful for physicians.

Jouvet's leading role in the fields of integrated physiology, psychology and pharmacology is well known and testified by the number of 1) M.D. and Ph.D. theses (n=100) done under his direction, and 2) sleep researchers from all around the world who came and worked in his laboratory. Among them, Ralph Berger, J. Allan Hobson, Allan Rechtshaffen, Barbara Jones, Dennis McGinty, J. Matsumoto, T. Maeda, Kunio Kitahama, Kazuya Sakai, P. Putkonen, Carlyle T. Smith, Raul Laguzzi, D. Megirian, J.X. Zhang, and J.S. Lin.

For those who work or have worked with him, everybody has experienced the engaging personality of Michel Jouvet. It is a permanent pleasure to discuss with him new results thanks to his

### Jouvet opened up an entirely new domain in neurosciences by discovering that paradoxical sleep was a new state of the brain...

accurate insights and his understanding and ability to see new developments in a given research result. Moreover, when confronted with results contradictory to his theory, he discusses every inch of the study and then either suggests new experiments to refine the interpretations or accepts them if they have been correctly obtained. Some hours or days later, he finds how to incorporate these results into his theory or how to modify his theory.

Very few scientists are capable of standing back, getting the problem into perspective and relevant to their own work. Jouvet's interest in the history of sciences has led him to write a piece of fiction—*The Castle of Dreams*—showing that most of the "contemporary" observations on sleep and dreams could have been made in the XVIIIth century.



by  
Joëlle Adrien, Ph.D.  
CHU Pitié-Salpêtrière  
INSERM  
Paris, France

## About Michel Jouvet...



by  
Odile Benoit, M.D., Ph.D.  
Laboratoire D'Etude du Sommeil  
INSERM  
Paris, France

What I want to tell about Michel Jouvet originates from rather deep memories, beginning as a familiar image, which eventually became the universally-known outstanding scientific figure. When I was in high school, my best friend used to tell me about her older brother who was studying sleep in cats with Michel Jouvet in Lyon. At that time, I thought it was a rather strange thing to be doing. Later on, as a college student, I attended my friend's brother's thesis presentation. This was the very first time I met Michel Jouvet, and from then on he became—although he was unaware of it—a familiar companion. This resulted from the fact that, as a student in psychophysiology at the Faculté des Sciences de Lyon, I had joined a laboratory where the late Danièle Jouvet, Michel's wife, was investigating the field of sleep ontogeny.

I first met Michel Jouvet in Lyon, while I was a medical student. He was "Interne des Hopitaux de Lyon", puis "Chef de Clinique". I worked under his supervision in different Departments such as infectious diseases, neurology and neurosurgery. At the same time, we were also working in the Department of Physiology at the University, directed by Professor H. Hermann. Both of us were interested by neurophysiology. In 1955, when Michel Jouvet came back from the United States, we decided to start research on auditory conditioning and developed experiments on "chronic animals". We were as motivated as we were naive, and we had to learn, by ourselves, every aspect of that methodology. Often the University doors were closed when we finished the experimental sessions and we had to jump over the high gates! To find cats for research was also a hard job and sometimes we tried to catch the wild cats in the hospitals! It was fascinating to work with Michel Jouvet and I am indebted to him for my deep interest in research. I moved to Paris in 1956. Michel Jouvet's interest in sleep research began a few months later, while he was working with Francois Michel and later with Danièle Mounier.

From that time on, I always found wise and kind advice when I consulted Michel Jouvet. In 1971 he was an examiner at my thesis and was somehow surprised by the important changes in the neuronal firing of thalamic neurons as a function of sleep states, which meant that paradoxical sleep modifies all the brain functioning!

He always raises enthusiasm,  
controversies and new ideas...

As with many of us, I am sure that international sleep research would not have been so active without Michel Jouvet. He always raises enthusiasm, controversies and new ideas about sleep, paradoxical sleep in particular. I hope his retirement does not mean that he will quit doing sleep research.

Michel Jouvet—a rather weird  
character...a mythical figure...  
a role model.

During this period, I was lucky enough to share with Danièle the exciting time when she discovered that the less mature the brain, the greater the proportion of "active" sleep that is present (the term "seismic" sleep was used then, which gave a better image of what we could observe). Of course, Danièle was very often referring to Michel's inspired ideas, which actually led me to the fascinating possibility of paradoxical sleep being the very first manifestation of life, and thus playing a fundamental role as an interface between nature and nurture. This was the beginning of my dedication to ontogeny, which was followed by a few great years in Howie Roffwarg's laboratory in New York.

Finally, after this long period of indirect contacts with Michel, I had the joy and honor to have him as a jury member for my Ph.D. thesis, and since then to have frequent discussions with him. With this short story, I want to express my gratitude to Michel Jouvet for his decisive contribution to my interest in the field, firstly in my high school student's mind as—I must confess—a rather weird character, secondly as a mythical figure, and progressively as a role model. Today, I wish to give him a very special tribute for never disappointing this expectation, and, on the contrary, for having always stood several steps ahead from where I thought he had reached.



by  
Alexander Borbély, M.D.  
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University of Zürich  
Zürich, Switzerland

Michel Jouvet has been the towering European figure in sleep research in the past four decades. His discoveries and concepts contributed significantly to the progress and fascination of the field. The work performed by him and his collaborators is so prolific that mentioning some selective examples does injustice to the rest. The first description of paradoxical sleep in the cat was a momentous achievement which triggered a host of studies in other animals. His own exploration together with Danièle Jouvet-Mounier of the phylogenetic aspects of sleep is still a classic in the field and a source of invaluable information. An exciting discovery with far reaching consequences was the identification of the pontine generating mechanisms of paradoxical sleep. The subsequent studies with Sastre revealed that selective lesions of the descending inhibitory centers in the pons results in an animal which exhibits motor and emotional activity during this sleep state.

The comprehensive monoamine theory of sleep was published in 1972 and influenced sleep research during the following years and decades. It was the first major and masterly synthetic scheme in which neuroanatomy, neurophysiology and the emerging discipline of neurochemistry were integrated. This theory gave rise to a large number of studies in which specific aspects were tested and further elaborated. Not all experiments confirmed the original claims. However, the fate of a fruitful theory is its continuous evolution as new data arise. Dr. Jouvet himself contributed to this process by reinterpreting the role of serotonin in sleep.

...Danièle Mounier's phylogenetic  
study of sleep  
is still a classic in the field...

Michel Jouvet's research laboratory will fortunately persist after his retirement because several able and renowned senior scientists together with enthusiastic and creative young colleagues will continue the study of sleep in Lyon. However, knowing the master's insatiable quest for new insights, it is unlikely that formal retirement will mean the cessation of research. Michel Jouvet's encyclopedic knowledge, his unique integrative mind and his wide interests will be needed by his friends and colleagues in the years to come.



by  
Michael H. Chase, Ph.D.  
Department of Physiology  
University of California  
at Los Angeles  
Los Angeles, California, U.S.A.

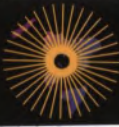
My earliest recollection of Michel Jouvet was in association with Raul Hernández-Peón and the epic debates of the early 1960s regarding the neurophysiological and neurochemical bases for sleep state control, whether sleep was one or two states, and the relative importance of serotonergic vs. cholinergic systems. At that time and for succeeding decades, Michel has come to

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promoting sleep research on a global basis.

epitomize the best within the field of sleep research; throughout his entire research career he has been the singularly most important force in promoting sleep research on a global basis—first, by virtue of his incredibly keen scientific acumen; and secondly, by the prestige in which he is held, throughout the world, by sleep researchers, investigators in other biomedical disciplines, administrators, politicians, writers, etc.

I have been blessed to have had scores of interactions with Michel over the years. These interactions were centered principally, but not exclusively, on the conferences and congresses that I've organized in which he participated significantly. He has unhesitatingly and unselfishly given of his time and energies to assist me in my endeavors, for which I am eternally grateful. What I've also come to recognize is that while his willing participation in these activities has often come at the price of personal discomfort or difficult scheduling problems, he has always been there for me, personally, and for the field, in general.

Like every other human endeavor, there are politics in sleep. But somehow, for over 30 years, Michel has been able to be at the forefront of sleep research, while never becoming allied within the field with one faction, camp or political persuasion. Incredible as it may seem, he has stood head and shoulders above the fray while being admired and respected by all. Research questions and his pursuit of the answers are the sole reason for his participation in the field—and it shows. It shows in Michel's incredible array of research accomplishments, which others have



## Michel Jouvét

others have detailed in this *Newsletter*. Rather than reiterate what has already been said, I would like to highlight his unique ability to be a spokesperson, role model and "hero" for the field. He has retained the respect and admiration of sleep researchers for decades.

I believe that Peretz Lavie had it right when he highlighted Michel's telegram in response to problems of a political nature vis-à-vis the Israel venue for the European Congress of Sleep Research (see Peretz's contribution in this *Newsletter*). I repeat this here because it cannot, in my opinion, be repeated often enough. "Friends, I'll be in Jerusalem in September 1988 even if I am the only participant in your meeting!" For Michel, it was not politics, it was simply research.

Michel also has an incredible sense of humor, in general, but also about himself and the problems that he is tackling. He is always playful with scientific concepts and ideas but underneath, of course, there is a rock hard seriousness. I believe that it is his humor that has prevented him from becoming entrenched and narrow-minded; rather it has allowed his vision to reach and exceed all scientific horizons of knowledge.

I remember the first time that I visited his laboratory and I brought with me what I thought was a superb California wine; it was graciously accepted and commented upon most favorably. I knew that I was bringing "coals to Newcastle". Nevertheless, he appeared to enjoy the concept of a Californian presenting such a gift to the field's premier connoisseur of French wines. I sincerely hope he enjoyed my gift (as long as he didn't use it to cook with!). I also remember interacting with Danièle (his first wife) and the many people with whom he has been associated over the years, all of whom uniformly reflect his characteristics of honesty and dedication to scientific research. He is as creative in his research endeavors as he is in all of his other pursuits, in his magnificent house, in his historical collections and in his fictional and nonfictional writings, etc.

I will always be grateful to Michel for the warmth and friendship that he has extended to me personally, and for the knowledge that I can always count upon him to be a true friend.



by  
René Drucker-Colín, M.D., Ph.D.  
Universidad Nacional  
Autónoma de México  
Mexico City, Mexico

My acquaintance with Michel Jouvét started much before my first personal meeting with him, mainly because as a student of Hernández-Peón, his name was consistently present in our laboratory. I finally had the opportunity and the honor of meeting Michel in the early 70's in Mexico City, where he came to give a talk within the context of a Mexico-France Scientific Program. Then, I asked him whether he could look at a paper I had recently written and give me his opinion before I submitted it for publication. What struck me most about Michel Jouvét was that, despite his scientific greatness, he was totally unpretentious and carried the simplicity and joviality of

the greats. Since then, he has been one of the few scientists who I have truly admired and who has made a profound impression on me as a person and in my research.

Sometime in the 80's, Dr. Jouvét again visited Mexico and I



*...despite his scientific greatness, Michel is totally unpretentious and carried the simplicity and joviality of the greats.*



had the opportunity of having him visit my laboratory and spend a couple of days discussing a variety of things. When I visited Lyon, with, at the time, my 15 year-old daughter, his hospitality became a thing to remember. I believe that a scientist of Dr. Jouvét's capacity and ability should not be allowed to retire, because there are still many ideas he can provide that can be fruitful for sleep research. In a way, I have always been sorry that the distance between Mexico and Lyon has prevented me from having a closer interaction with this scientist who, in my mind, undoubtedly has made sleep research the important field it is today. I salute a great man and I am proud to think of him as a friend.



by  
Jean-Michel Gaillard, M.D.  
Institutions Universitaires  
de Psychiatrie  
Vandoeuvres, Switzerland

Michel Jouvét has been a scientific reference as well as a model of prime importance in my whole professional activity. He is one of those persons that life sometimes gives you the privilege to meet.

Over the years, many contacts with him allowed me to appreciate the features of his scientific thinking. He can be placed in the tradition of the natural philosophy of the eighteenth century. He is impermeable to the fashion; he has the capacity to see the implications of experimental results largely beyond the horizon line; he likes to draw attention to the unconventional aspects of a problem. His wide culture is fed by abundant reading in



*...one of those persons that life sometimes gives you the privilege to meet.*



domains very remote from his specialty (he is also a collector of ancient books) and he uses this information in his conceptualization of the current question of interest. His natural philosophy will be a valuable object of study for the next generation of historians of science.

I remember particularly one week we spent together in August 1971 in Warsaw. We were both attending the satellite symposium on "Adrenergic Mechanisms of the Congrès des Sciences Physiologiques". Since I was not fluent in English, I presented my communication in French. The only one who could understand what I said was Jouvét. He was very kind to the young scientist that I was and we spent a lot of time together.

At this moment, Jouvét was very preoccupied by the function



*According to Michel,  
"The crucial 'manip' (experiment)  
has not yet been done."*



of paradoxical sleep, and he had not yet elaborated his famous theory on the reprogramming of genetic information by paradoxical sleep in the formation of behaviors. In the very characteristic way of his natural philosophy, he started from the observation that the regulation of paradoxical sleep is so precise that it must have been designed by the forces of evolution for some important purpose, not adequately accounted for by the existing theories. These discussions were for me a fantastic learning experience of scientific thinking: how to integrate experimental data into a conceptual framework so that the ways and means of nature are consistent with each other, as well as how to design experiments within this framework. I still hear him saying "The crucial 'manip' (experiment) has not yet been done."

One of the most significant contributions of Jouvét comes from his experiments on the brain serotonergic structures in sleep. However, at the end of the sixties, he also proposed that noradrenaline played an active role in paradoxical sleep. At the time of this Congress, various results were starting to appear here and there, suggesting antagonism between noradrenaline and paradoxical sleep; namely, that noradrenergic structures had to become silent for the occurrence of paradoxical sleep. This is still the dominant concept today.

Stimulated by these exchanges with Jouvét, my co-workers and I started a series of pharmacological experiments on this question. The data collected in the following 15 years suggested to me that the early formulation of Jouvét, although too schematic, was in the correct direction. Some kind of noradrenergic (or catecholaminergic) activity is necessary for the generation of paradoxical sleep.

Finally, Michel, addressing myself directly to you, I want to thank you heartily for your friendship during all these years.



by  
Barbara E. Jones, Ph.D.  
McGill University  
Montreal, Quebec, Canada

Michel Jouvét, Neurologist, Neurophysiologist, and Renaissance man, having grown up in a rich intellectual milieu in Lyon, France, was early captivated by the mysteries of the mind-body transformation that occurs over the course of the sleep-wake cycle. In 1959, he was the first to establish criteria for brain death ("mort du cerveau") described in cases where the body could be maintained alive and healthy yet all somatic and visceral reactivity was lacking and, as he demonstrated, all electrical activity in the brain had ceased.



*...Michel extracted from the brain its secrets concerning the generation of sleep-wake states and dreams.*



He went to California to train with Magoun in neurophysiology and to learn first hand about the ascending reticular activating system and its importance for maintaining waking and consciousness. But he was even more intrigued by the powers of sleep. He knew well from his wide reading, which extended back to writings of early Hindu scholars recorded in the Upanishads, that sleep was not simply a monolithic state of rest for the brain but rather comprised of different states for brain, mind and body. Stimulated by the findings of Aserinsky, Kleitman and Dement in humans, Jouvét was to demonstrate the existence of an activated state of sleep with rapid eye movements in the cat, which he was to call paradoxical sleep ("sommeil paradoxal"). This term captivated the essence of this enigmatic and, as Jouvét demonstrated, distinct third state of the mammalian organism. He went on to extract from the brain its secrets concerning the generation of sleep-wake states and dreams.

Having participated in the Resistance in France as a young man during the war, he was imbued with military strategy, hence, perhaps his systematic "search and destroy" approach to locating the nerve centers for waking, slow wave sleep and paradoxical sleep. Using transections, electrolytic lesions, and neurotoxic lesions, he delineated the major neuronal centers and pathways critical for each of the three states. He dissected the systems controlling paradoxical sleep and was able to disenable the circuitry that normally inhibits movement during this state to reveal the occurrence of dreams in cats by their enactment. But he realized early on that the neural systems that control the state of the organism do not simply function by rapid neural



transmission, but utilize neurotransmitters with prolonged action, thus as the term evolved, neuromodulators.

After monoamines and acetylcholine were discovered in the brain, Jouvet embarked on a systematic mapping of the neurons containing these chemicals and systematic testing of their involvement in the sleep-waking cycle. He was thus to reveal the importance of noradrenergic and dopaminergic neurons for waking and serotonergic neurons for slow wave sleep. He also brought forward evidence that cholinergic neurons play an important role in paradoxical sleep.

In 1972, he provided a complete map and a coherent scheme of the neuronal systems and chemical modulators underlying the sleep-wake cycle published in *Ergeb. Physiol. Biol. Chem. Exp. Pharmacol.*, that has served as a landmark reference and Citation Classic (Current Contents, 1992) in Neuroscience. In addition to being recognized worldwide for his achievements, he was also recognized in France first by being named, at a young age in 1968, Professor (Faculté de Médecine et Universitaire Claude Bernard, Lyon), and subsequently by being appointed, still at a relatively young age, in 1977 to the Académie de Sciences (Paris).

As a young graduate student in the United States in the late 1960's, I rapidly became interested in the physiology of sleep and as rapidly drawn to the path-breaking research by Jouvet. Elated by a positive response from him to my letter asking whether I could pursue studies in his lab, I set off for Lyon, where in addition to learning about French cuisine, Europe, the war and military strategy, I was swept up in that great period of discovery, as well as revolution, in 1968. A wonderful beginning for a student, and an inspiration for a lifetime for a researcher.

Yet, after the 1960's and 70's, the magical veil of sleep remained, and wizard though he was, Jouvet could not remove it. Fundamental secrets eluded him. He explored neuroactive peptides to ultimately show what appeared to be ancillary roles



...Michel has traveled the globe looking for clues in special corners of the world and the animal kingdom.



in modulating sleep-wake states. Even genes he probed for clues. He returned to basic physiology to examine the importance of thermoregulation and metabolism. And he continued in his quest to understand penile erection that occurs in all mammals during paradoxical sleep and may have been noted and depicted, as he maintains, even by the early cave dwellers and artists of Lascaux. He has traveled the globe looking for clues in special corners of the world and the animal kingdom. Following retirement in 1997 as Director of the "Laboratoire de Médecine Expérimentale", "Études des États de Vigilances" (ou aussi "...d'Onirologie Moléculaire"), he embarked in the winter of 1998 on a sea voyage to the Antarctic to look for

sea mammals and sea birds which have developed special adaptations to sleep. So although retired as Director, he has not retired as Scientist and will continue like his 18th century hero, Le Conte in his best-selling novel, *Le Château des Songes* (*Chateau of Dreams*, 1991), in the search for the infinite secrets of sleep.



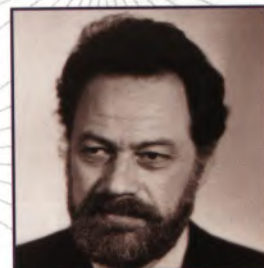
...like his 18th century hero,  
Le Conte in his best-selling novel,  
*Le Château des Songes*  
(*Chateau of Dreams*, 1991), Michel  
will continue in his search  
for the infinite secrets of sleep.



He has contributed greatly and will continue to contribute by communicating the complexity and mystery of sleep and revealing many, but not all, of its secrets.

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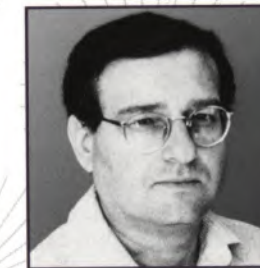


by  
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Academy of Sciences  
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#### A PENSION... FOR A CAT!

Every sleep researcher knows now about the life and adventures of *Hugues la Scève*, the hero of Jouvet's novel *Le Château des Songes*. But only a few of them are aware of the history of Michel Jouvet himself, although his personal life is interesting enough and full of various events, both comic and dramatic. Here you see such a story which I once heard from him.

At the beginning of the sixties, Michel, who was younger than forty, experienced the peak of his creating activity. He was full of energy, working a lot, his studies were progressing at a tremendous rate, and each month the experiments on cats brought unexpected and fascinating results. Michel lived with his first wife Danièle in old Lyon in one of the romantic *quartiers* described later in *The Castle of Dreams*. It was one of the happiest periods of his life. There was only one problem which shadowed his fortune: early each morning an unknown cat appeared under his windows and cried horribly, preventing the



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#### Michel Jouvet—A Man of Science

The increased specialization of scientific research has created a breed of scientists who know more and more about less and less. Thus, to become a leading expert in a field, one has to narrow his or her research interests to sometimes ridiculously minuscule dimensions. Recently, I attended a seminar given by a leading expert of pineal neurophysiology who was astonished to learn that the pineal is also implicated in reproduction, and even more so its role in sleep regulation. When Michel Jouvet told me about his retirement, my first reaction was "What do you mean retiring? Men like you have nothing to do with retirement!"

Over twenty years ago, I met Michel for the first time in a winter resort high in the Swiss Alps, in a seminar organized by the European Brain Research Organization. At that time I was a young scientist struggling for his own sleep career in Israel. I had a great interest in ultradian rhythms, and I spent days and nights chasing 90-minute rhythms in almost any system that could be measured. Many at that time thought that I was chasing the Loch Ness Monster! But there, high up in the Alps, I met one of the high priests of sleep research, who was ready to listen and discuss my fantasies on ultradian rhythms. However, he listened not only to me, but also listened and discussed science with every young man that approached him. A marvelous feeling for a young investigator.



...high up in the Alps, I met one of  
the high priests of sleep research...



most sweet paradoxical sleep hours of the tired sleep researcher! Each morning, half-dressed, Michel ran after this cat in the yard, but the next morning the situation inevitably was repeated. Michel did not know who the owner of the cat was and to whom to complain. Finally, Danièle lost her patience: "Will you do something? You are a specialist, aren't you?" Then Michel decided to take a radical route: despite the vain running after the cat, the next time when hearing her cry, he came out with a fish and a big bag, put the bag with the cat into his car, and brought it to the lab.

The cat appeared to be quite domestic, healthy and fat. It was good enough for science. Therefore, several days later when the cat's owner appeared in the laboratory together with a policeman, the cat had already been operated on for polygraphic recordings. Later Michel recognized that one of his neighbors had seen him catching the cat and had informed the owner whom he knew. A policeman showed Michel a declaration of the cat's owner with a resolution of the Quarter's chief of police: "Return the cat to the owner in its initial state".

What to do? Michel took off all the electrodes and sutured the scalp back over the cranium. The cat received a course of antibiotic injections and several days later it appeared as before, without any sign of trauma. Nevertheless, the owner was not satisfied and decided to apply to a court. Michel was very worried though he tried not to show it. The matter was that in addition to the electrodes, the cat had also been subjected to a small neurosurgical procedure: a bilateral lesion of the oculomotor nuclei. After this operation, the cat's eyes could move independently, like a chameleon lizard. Fortunately, the cat's owner did not notice it.

But this fact could be opened in court! A special expert was invited by the judge to estimate the degree of injury made by the scientist to the innocent cat. This expert was a retired veterinary surgeon who was permanently called in to participate in various cases related to horses, dogs, cats and other domestic animals. To win this person to his side, every claimant would invite him to restaurants, so that he was permanently drunk. He looked continuously at the cat but as his own eyes could not be coordinated successfully either, he did not notice anything special!

Nevertheless, he declared with a pathos to the judge that the scientist had produced not physical, but psychological suffering to the cat because it was subjected to an operation against its will! As a result, Michel pleaded guilty and was ordered to pay a pension for this particular cat for the rest of its life in the amount of the cost of food (at that time it was about \$5-6 (US) per month). Fortunately, the cat was not so young and in a couple of years expired.

However, this story could have led to very dramatic consequences for all of the science of sleep. The matter is, in accord with French law, every citizen condemned by a court (it does not matter for what) has to be registered into a special *Conduite d'Etat*. And all persons whose names appeared in its pages were forbidden to hold any state job. For Michel, that automatically implied the loss of his university position and the impossibility of doing research and educational work in the future. He applied enormous efforts and all of his authority to prevent the inclusion of his name into this book. Ever since he has become very cautious and never again committed any such mischief. And he only uses cats supplied by special companies!

Throughout the years, in many annual sleep meetings where we met, I learned that Michel is a compassionate person, a lover of people, old books, good conversation and good wine and food. But true friendship can be tested only during trying times. Ten years later, I took upon myself to organize the 1988 European Congress of Sleep Research. When I volunteered to do that I did not anticipate the emotional outbursts that would surround the meeting, or the sleepless nights that awaited me. Planning any major event in a country like Israel, that witnesses a war with its neighbors every few years, is a risky business. Nevertheless, the hundreds of scientific meetings that have taken place in Israel over the years and the millions of tourists that visit the country, proves that this is not an impossible task. The first distressing signs appeared about a year before the planned time of the meeting. Letters suggesting a change in the venue of the meeting





because of the "political situation" in Israel started to be circulated among members of the Society. The most disturbing aspect of these letters was that they were not concerned about the safety of the participants, but protested the meeting because of the political attitudes of the Israeli government. What was even more painful was that some came from old and close friends. These were difficult times. How can one proceed with preparations in view of what appeared to be an almost organized effort to boycott it. Then came the first light. It came in February 1988, in the form of a

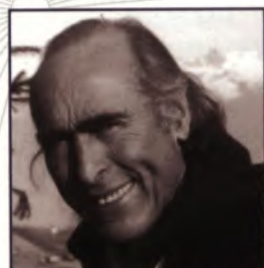


...a truly "renaissance" man...



telegram from none other than Michel Jouviet. It comprised only one sentence: "Friends, I'll be in Jerusalem in September 1988 even if I am the only participant in your meeting!" This was the turning point, and soon after that, encouragement and support poured in from many others. I will never forget the moment of receiving that telegram.

With the retirement of Michel Jouviet a friend and a truly "renaissance" man is leaving the sleep stage.



by  
Mauro Mancia, M.D.  
Department of Physiology  
University of Milan  
Milan, Italy

My memories of Michel Jouviet take me back to the years of my early "scientific youth", when I was working as an assistant of Professor Giuseppe Moruzzi at the Institute of Physiology at the University of Pisa. At that time the laboratory had become a "Mecca" for sleep researchers, and together with Frederic Bremer's laboratory in Brussels, it was at the forefront of scientific research and one of the most committed neurophysiology laboratories in Europe.



It was a kind of sleep whose characteristic features were paradoxically similar to wakefulness...



The laboratory in Pisa was regularly frequented by a group of young and older European and American researchers. I still remember the visits that P. Dell from the University of Marseilles, J. Magnes from the University of Jerusalem, and some eminent Nobel Prize winners, such as Lord Adrian, used to pay to the laboratory. When Lord Adrian came for a visit, Moruzzi, who was particularly fond of the architectural treasures of Villa Manzi, always took him sightseeing to admire the villas in the area of Lucca. I can recall perfectly Michel Jouviet's visits to the laboratory in the 1950's, when he was still a novice in search of his own identity as a scientist, as were we.

When I arrived in California in 1959, I met Francois Michel, who was at that time a close collaborator of Dr. Jouviet's and he told me interesting anecdotes about his life in California and about his interest in a phase of sleep which was then mysterious to me. It was a kind of sleep whose characteristic features were paradoxically similar to wakefulness, although the animal was behaviorally asleep. This is how the history of the physiology of REM sleep began in the 1960s, and it is an interesting history in many respects. Data revealing the presence of this phase of sleep in animals and in man already existed in the literature. However, the prevailing theory at the laboratory of Physiology at the University of Pisa was that the *synchronization* of EEG rhythms was the only electrophysiological equivalent of sleep. This bias led us to neglect this new phase of sleep. This was not true of Michel Jouviet, whose studies represented a sharp break from the old conceptions of sleep. He ventured into the unknown world of paradoxical sleep, trying to determine its neurophysiological mechanisms. In Sherrington's wake, he carried out a series of experiments consisting of the sectioning of



...animals behaved as if they were driven by the fantasies of the dream...



the brainstem at different levels so as to identify the structures responsible for REM sleep (which were found to be located in the pons) and the ones responsible for ascending phenomena (EEG desynchronization, eye movements) and for descending phenomena (postural atonia) of REM sleep.

Jouviet's neurophysiological observations drew the attention of the scientific community, particularly neurophysiological and psychophysiological researchers, to REM sleep. Many laboratories in the world started to carry out research aimed at studying the physiological, tonic and phasic aspects of REM sleep. In the meantime, psychophysiologicals began studying mental activity in the different phases of sleep, particularly REM sleep. Interest in REM sleep increased when Dr. Jouviet and Dr. Delorme discovered that a lesion in the locus coeruleus induced an oneiric acting-out. By observing the animals' motor activity and emotional response, they noticed that the animals behaved as if they were driven by the fantasies of the dream that appeared during REM sleep. Dr. Jouviet subsequently widened his investigation on the neurochemical mechanisms of sleep, particularly of REM sleep, by demonstrating the role of serotonin

and acetylcholine in inducing and maintaining these phases of sleep. Besides his great scientific merits, internationally acknowledged with four honorary degrees, five international awards and two golden medals, one of which was awarded by the University of Padua and the other by the CNRS, Michel Jouviet is a person endowed with great humanity, deep knowledge and unquestionable charm. A helpful friend with whom it is possible to disagree on theoretical matters, but also a person it is always enjoyable to talk to, and exchange opinions with, while sitting comfortably at a table in a restaurant, sipping a good glass of Bordeaux.



by  
Majid Mirmiran, M.D., Ph.D.  
Department of Physiology  
Netherlands Institute  
for Brain Research  
Amsterdam, The Netherlands

I am delighted to write in jubilant celebration of Michel Jouviet, the consummate sleep scientist, and to briefly acknowledge his research legacy as he assumes a status of retirement which means that he is personally in charge of his schedule. He is clearly one of the most gifted scientists in the field of sleep and the mere mention of his name brings to mind discoveries about sleep and his pivotal role therein. As a young physician in training, he wrote his dissertation on the discovery of REM sleep for the French School of Medicine. Following this achievement he became Director and excelled for his entire career as Director of the historic Department of Experimental Medicine at Claude



His artistic views accentuated his scientific view of the close intimacy between sexuality and REM.



Bernard University in Lyon. In France he was awarded the most prestigious honor for scientists, "The Gold Medal", for his life long research achievements in the physiology of sleep.

As a young scientist, I was inspired and guided by research from his laboratory which was published by Michel and his first wife Danièle Mounier which showed the importance of REM for brain maturation. Later in my own work, I was able to demonstrate that by suppressing REM in the neonatal rats, brain growth was reduced, sexual behavior decreased, anxiety and depression increased, individual differences diminished and brain plasticity was lessened (Mirmiran, 1995). However, in spite of Michel's encouragement and urging, I could not single out the "function" for REM. I remember how impressed I was when I first visited his private office in the back of the laboratory. His original work on the brainstem REM generator started in the fifties, on the so-called "pontine cat". To my surprise all of his records,

including his first experiments, were nicely kept in files covered by nude photographs of beautiful women. His artistic views accentuated his scientific view of the close intimacy between sexuality and REM. He even had the forethought to save brain specimens from the fifties for modern immunocytochemical techniques to come in the eighties. I wagered that although the generator for REM is in the pons, a hypothalamic factor(s) is very likely required for triggering and maintaining REM.

Among the countless theoretical and experimental contributions he made to our field, I would like to cite the one which has remained his (and mine too) lifetime enigma viz., the function of REM. Michel hypothesized that an endogenous genetic programming of the brain occurs during REM sleep (Jouviet, 1980). In this fascinating view, REM is indeed responsible for individual differences throughout life. In other words, it preserves and is your identity. Jouviet explicated this complex theory by offering that the genetic read-out, which is mostly related to "forward experience", is not necessarily adaptive to the latent historical being of the individual. In this case, the periodic programming may or may not be in accord with the processing of new information. In some cases, it may facilitate the acquisition of new information, but in others (different individuals or other occasions for the same individual) it may have no effect or even destroy traces of certain memories. This view, although not exclusive, differs from the view of Sigmund Freud, i.e., that dreams fulfill our wishes (in the modern jargon of neurobiology: activation of neuronal systems that are disproportionately activated during wakefulness). However, as a developmental neurobiologist, I feel strongly that since REM occurs in the fetal and neonatal period before any substantial waking experiences, it may (independent of wakefulness) shape the individual's identity before much experience occurs in the journey of one's life.

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by  
Allan Rechtschaffen, Ph.D.  
Sleep Research Laboratory  
University of Chicago  
Chicago, Illinois, U.S.A.

One of the great joys of a professional lifetime in sleep research has been the great people I've met, and one of the greatest of these has been Michel Jouviet. We all know of his pioneering research accomplishments: the discovery of the anatomical center of REM sleep, the role of brain amines in sleep regulation, and hundreds of other studies. He was for many years the heart and soul of neuroanatomical and neurochemical sleep research and produced such a large volume of solid studies as to create respectability for all of us. In addition to his research accomplishments, he created a large and dynamic laboratory—bringing sleep research out of the attics and basements—and trained a large cadre of younger investigators to continue the tradition. All of this was done with creative verve;

at annual meetings, all ears were attentively tuned to "What is Jouvet reporting this year?"

I have the good fortune to have a personal relationship with



...At annual meetings, all ears were attentively tuned to "What is Jouvet reporting this year?"



him. I could not believe my good fortune when he accepted our invitation to the first (or was it the second?) meeting of APSS in 1961 (or was it 1962—neither of us remember). His presentation of new discoveries about the neuroanatomy of REM sleep was the single most dramatic, exciting scientific report I have ever experienced. It prompted me to get into the neurophysiology of sleep, which I learned by spending the next summer in his laboratory. He was a marvelous host (I will never forget Lyon) and an inspiring teacher. I had never before or since seen anyone with such an organic feel for what the subject was doing. As we watched the cats, Michel would talk about what it was feeling, what forces were struggling within it, what the cat was trying to do. For Michel Jouvet, neurophysiology is a living, palpable process. Too bad that this intimacy has to be edited out of professional publications.



...in 1961 (or was it 1962), Michel's presentation of new discoveries about the neuroanatomy of REM sleep was the single most dramatic, exciting scientific report I have ever experienced.



In later years, we did not get to spend much time together, but I loved to sit next to him at meetings. As we listened to a succession of papers, he would signal approval with just a subtle nod of the head and protusion of the lower lip, or disapproval with a raised eyebrow and slight shrug of the shoulder. These small Gallic gestures instantly told me about the scientific worth of the presentations; there wasn't much more that needed to be said. And I remember one day in the sixties when Bill Dement was driving Michel and me to Yosemite for an overnight stay. Michel cautioned, "Drive carefully Bill; we have an accident, there goes sleep research." I felt I did not deserve to be included in that trio, but that is beside the point now. The remark illustrates the kind of friendship and mutual respect that we enjoyed. We wish the same for our successors.



by  
Howard Roffwarg, M.D.  
Department of Psychiatry  
University Medical Center  
Jackson, Mississippi, U.S.A.

When confronted with the unwelcome reality of Michel Jouvet's retirement, a myriad of emotions and memories burgeon forth, too many to even mention in the couple of paragraphs permitted here. But one emotion must be expressed quickly and definitely—gratitude: *unfailing gratitude* that the study of sleep had trapped the fascination of this scientific giant who towered over the neurophysiology of sleep for four decades; *inestimable gratitude* for his incandescent imagination, but also for the perspicacity and insight that helped order our concepts of a never-before recognized state of the CNS, guided our studies of sleep's constitution, sources and dynamics, and transformed our understanding of the functioning of the brainstem; *profound gratitude* for the charisma of his teaching and public presentations, but also for his patience in dealing with all of us whom he either influenced, nurtured, excited or otherwise drew to the study of sleep. I wager that not one laboratory researcher of sleep walks the Earth who has not been propelled forward, enriched or challenged by Michel's seemingly limitless fund of information about the brain, his "feel" for how it works, and his innovative and sometimes daring experimental approaches (encompassing every brain-study technique) to uncovering the nature and mechanisms of the mysterious states we study.

Allow me to relate a memory from 1965. I had wanted to spend a few months in Jouvet's laboratory learning implantation techniques. It was not possible in 1965 because I only had a long summer and he was to be away most of it. He arranged for me to work with his wonderful colleague, Francois Michel, who hosted me at the Faculte des Sciences in Lyon. I had a superb experience with Francois, splitting the brainstem and trying to make sense of what had been done to sleep and waking. Michel

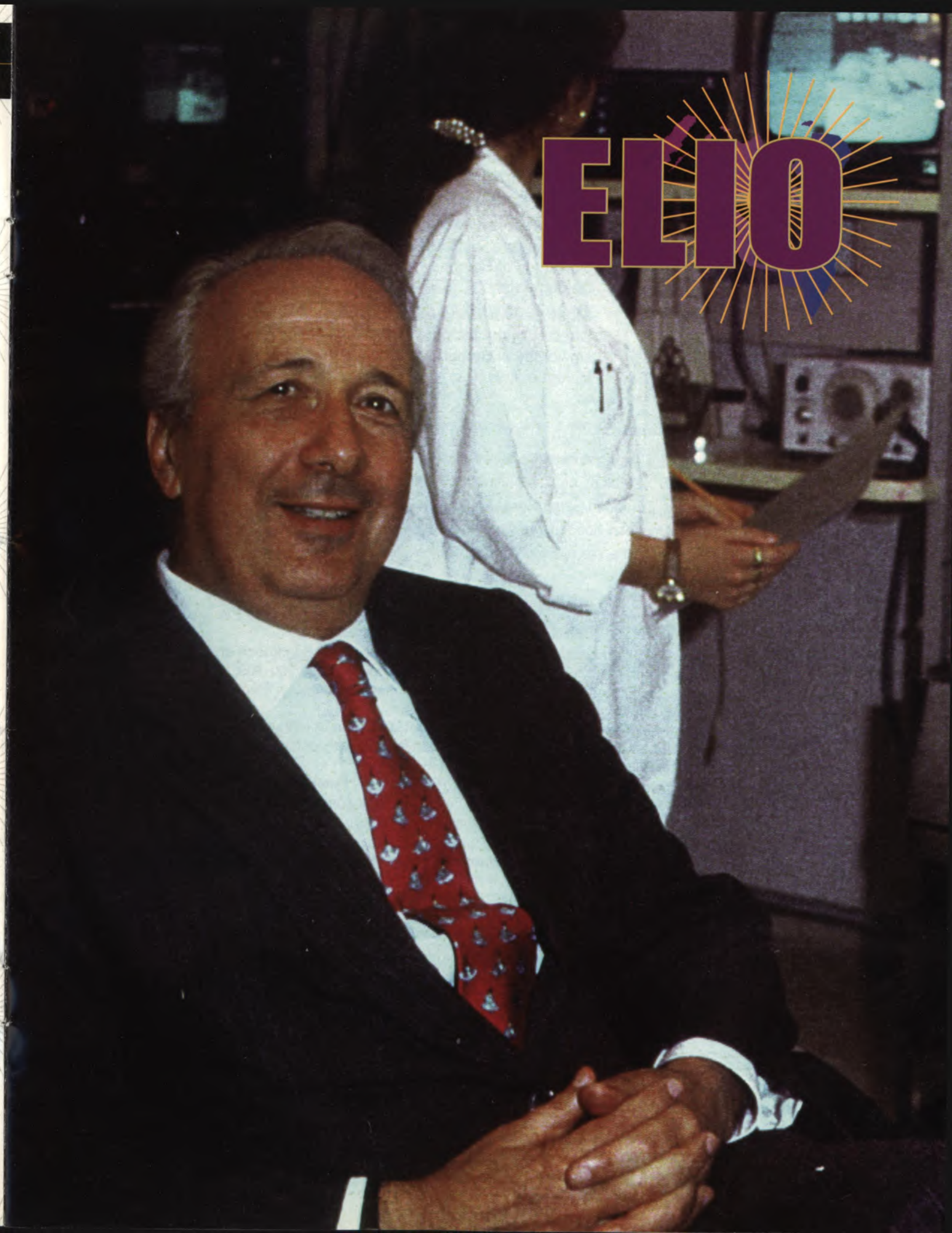


Michel Jouvet never stopped trying to "get it right".



returned shortly before my summer ran out and we had a chance to talk at some length. He told me that often he could only arrive at his laboratory in the late morning because he was not able to sleep for most of the night. I noticed some drawings on his desk, his "theorie des paniers", different attempts at a series of baskets that stood for centers in the brain. He told me that when he could

See About Michel Jouvet, page 41



ELIO



## BIOGRAPHY OF ELIO LUGARESİ

### **Date of Birth:**

July 1, 1926

### **First University Position and Date:**

Full Professor of Neurology (1969-present)  
University of Bologna  
Bologna, Italy

### **Most Recent University Position:**

Director of the Institute of Clinical Neurology (1975)  
University of Bologna  
Bologna, Italy

### **Representative Awards:**

- American Association of Sleep Disorders Centers Special Award for Distinguished Service (1983)
- Ottorino Rossi Award for Neurology of "C. Mondino" Foundation, University of Pavia (1995)
- Pisa Sleep Award of the European Sleep Research Society (1996)
- Potamkin Prize of the American Academy of Neurology (1997)
- Giuseppe Moruzzi Award of the World Federation of Clinical Neurophysiology (1997)

### **Representative Publications:**

- Lugaresi, E., Coccagna, G. and Mantovani, M. Hypersomnia with Periodic Apneas Plenum Press, 1977.
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### **The following reflect either the first finding in the field or a significant pioneering construct or theory:**

- ▶ Description of Fatal Familial Insomnia.
- ▶ Laboratory study of naps.
- ▶ An electroclinical description of epilepsy with ecstatic seizures (so-called Doestoevsky Epilepsy).
- ▶ Polysomnographic investigation into Restless Legs Syndrome demonstrating the presence of involuntary periodic limb movements they termed "Nocturnal Myoclonus".
- ▶ Research into snoring and sleep apnea.



## Commemoration of Elio Lugaresi

### **Elio Lugaresi: A Tribute**

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Professor Elio Lugaresi will soon be retiring as Director of the Institute of Clinical Neurology at the University of Bologna in Bologna, Italy, a position which he has held for almost a quarter of a century. He will, however, be continuing as Director of the Post-Graduate School of Neurology and in a research capacity. This is an excellent time and opportunity to celebrate his remarkable and continuing contribution to clinical neurology and, in particular, to our fields of sleep medicine and sleep research.

Elio Lugaresi graduated from the School of Medicine at the University of Bologna in 1952 and then undertook graduate training from 1952-58 at its Neurological Institute, which he currently directs. This was interrupted by one year (1956-57) as a postgraduate fellow with Henri Gastaut at the latter's world renown EEG laboratories in l'Hôpital de la Timone in Marseilles, France. Gastaut, I know as a fact, was very impressed with this young Italian "assistant étranger" and their professional interactions, mutual respect and warm friendship lasted throughout the remainder of his life. After this training Dr. Lugaresi rapidly became Chief of Inpatient Neurology (1958) in his institute then, at the remarkably young (especially for European academic medicine at the time) age of 43 years, he was named Professor of Neurology (1969), and later Director of the Institute and Director of the Postgraduate School of Neurology (both in 1977). He has also been director of the School of Neurophysiopathology Technicians of his university since 1975 and was founder and first editor (1975-81) of the *Italian Journal of Clinical Neurophysiology*. In brief, his career at

Europe's oldest university has definitely been "fast track".

The full extent of Dr. Lugaresi's many contributions to sleep medicine is not widely known. Influenced by his training with Gastaut and by the epoch, his research, especially initially, has had a decidedly clinical neurophysiological slant. In the late 1950's and early 1960's he published a remarkable series of articles in the major Italian and French

**This is an excellent time to celebrate Elio's remarkable and continuing contribution to clinical neurology and sleep medicine and sleep research.**

neurological journals. These papers include the first recordings both of Restless Legs Syndrome and of what we now call periodic movements in sleep, but which at the time was referred to (after Sir Charles Symonds) as "nocturnal myoclonus". There were also several important publications on the evolution of different forms of epilepsy during sleep. All of these early studies make rewarding reading and a number warrant translation in order to make these early discoveries more widely available. Like other groups in Europe working in the field, his polygraphic sleep recordings routinely included a very full range of measures including 6-8 EEG leads, EOG, submental EMG, EKG and multiple peripheral EMGs. This was at a time when sleep medicine in North America had not really begun and where much less comprehensive recordings were the rule.

In 1963 Dr. Lugaresi sent a young colleague, Carlos Alberto Tassinari, to study with Gastaut at the Centre St. Paul for Epileptic Children, where by chance I had begun my own training the year before. With Bernard Duron (a fortuitous

combination of neurologist, neurophysiologist and pulmonologist), Tassinari was involved in the discovery of the obstructive nature of sleep apnea in so-called Pickwickian patients, which was published with Gastaut in 1965. At the time we in the Marseilles laboratories did not recognize the full importance of this finding and thought that the laboratory's research on epilepsy and sleep, on the parasomnias and on myoclonus had greater promise! In the late 1960's

Lugaresi first heard Jung and Kuhlo present their 1965 findings on sleep apnea (not shown by them as due to upper airway obstruction) in

Pickwickian patients at an Alpine EEG meeting organized by Gastaut. He also already knew the details of the Marseilles research showing the existence of upper airway obstructions from Tassinari.

Dr. Lugaresi returned from the Alpine meeting having decided to mount a research program on this new finding which was initiated with the help of the wife of his colleague Giorgio Coccagna. She was an anaesthetist working with a team of heart and lung specialists at the local general hospital. Her anaesthetic expertise permitted the Bologna team to collect our field's first data on the ventilatory and hemodynamic aspects of obstructive sleep apnea including eventual nocturnal and diurnal systemic hypertension and its reversal by treatment (tracheostomy, later CPAP). In 1972 Dr. Lugaresi organized an international meeting (later published) held in Rimini, Italy, where sleep researchers (Lugaresi, Coccagna, Tassinari, Duron and Kurtz), all neurologists, for the first time presented their findings to European and North American lung specialists. Over the next few years much further work was done on

the topic in collaboration with his colleagues, especially Coccagna, Mantovani, Berti Ceroni and Cirignotta, which together comprise a remarkable series of papers on snoring and on sleep apnea. These documented more extensively the negative hemodynamic and ventilatory effects of obstructive apneas, and the very close clinical and physiopathological links between, and the virtual identity of, chronic heavy snoring and the obstructive sleep apnea syndrome. The Bologna group also published early careful studies on central apnea and on central alveolar hypoventilation (Ondine's curse). This pioneering research on sleep apnea largely predates and certainly was more extensive than that of the Stanford school.

Not all the early European contributions were from Bologna. Daniel Kurtz in Strasbourg and Betty Schwartz in Paris also began their studies soon after reports of the discovery of sleep apnea; and Bernard Duron moved to Amiens to continue his research in the area. But there is no question that the contribution organized and led by Lugaresi and summarized in his 1978 book *Hypersomnia with Periodic Apneas* co-authored with Coccagna and Mantovani was the outstanding one after the actual discovery of sleep apnea. Along with a later enlarged group of collaborators including also Mondini, Montagna, Tinuper and others, many subsequent contributions were made on obstructive sleep apnea, snoring as a risk factor for cardiovascular disease, the epidemiology of medical sleep disorders, and related topics.

Throughout his career Elio Lugaresi has shown a remarkable ability to recognize what is important in his data, make the discovery and then, not just pass on to another topic, but create a sustained program of research. This is repeatedly exemplified in his series of papers on nocturnal paroxysmal dystonia, idiopathic recurring stupor and Fatal Familial Insomnia, all three of which represent major later contributions to clinical medicine. He has shown that nocturnal paroxysmal dystonia comes in at least two varieties with different

physiopathogeneses and treatment. Idiopathic recurring stupor (or coma) was found to be due to an accumulation of endogenous benzodiazepine-like substances (endozepines) and to be

**There is no question that the contribution organized by Lugaresi was the outstanding one after the actual discovery of sleep apnea.**

successfully treatable by agents that block the benzodiazepine receptors.

Fatal Familial Insomnia (FFI) was shown by Lugaresi and Gambetti and their colleagues to be a hereditary autosomal dominant disease characterized by a remarkably complete insomnia, hyperactivity of the sympathetic nervous system and progressive attenuation of autonomic and neuroendocrine circadian fluctuations. In collaboration with Gambetti, Lugaresi found it to be due to a selective degeneration of the dorsomedial and anteroventral thalamic nuclei, i.e., the limbic thalamus. Much of the intense international interest in this condition has reflected the fact that it provides strong

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further support for human sleep being an active state requiring the integrity of specific structures for its generation. More recently the group discovered that FFI is a prion disease. Over the last decade Dr. Lugaresi's research has focused on further demarcating the clinical, neurophysiological, neuropsychological, endocrine and autonomic aspects of this fascinating condition, which are summarized in a book he has edited. This research has led to major revisions of our understanding of the regulatory mechanisms of the human sleep/wake cycle and other circadian rhythms.

**His research has led to major revisions in our understanding of the regulatory mechanisms of the human sleep/wake cycle and other circadian rhythms.**

The contribution of Elio Lugaresi to clinical neurology has not, however, been limited to the field of medical sleep disorders. He provided one of the first electro-clinical studies of so-called absence status or petit mal status in which a continuous generalized EEG discharge is associated with impaired consciousness and with amnesic automatic behavior. With his colleague Baruzzi, he did significant early work on serum anticonvulsant drug levels. Lugaresi has researched the variety of stimulus induced ("reflex") epilepsy triggered by mental arithmetic, card games and chess and has shown the importance of focused strategic thought in its genesis. Other studies describe the negative prognostic import of so-called drop attacks (atonic epileptic seizures) in the evolution of partial epilepsies. And Dr. Lugaresi has provided one of the few electro-clinical studies of epileptic seizures with ecstasy (so-called Dostoevsky epilepsy). There are also numerous papers and co-edited books on the evolution and prognosis of the epilepsies and on migraine headaches and epilepsy. In all, Elio Lugaresi has published some 500 journal articles, authored three books (two in Italian), and been an editor of another five volumes. His

vast contribution has been made, essentially, without the support of research grants, thereby underlining the essential roles of perspicacity, motivation, organization and leadership over mere money, important as the latter is for our increasingly expensive technologies.

As a personal note, during a sabbatical year spent in 1984-85 with Dr. Lugaresi, I had a better opportunity to get a "measure" of this colleague who had been a friend since the early 1960's. He had kindly invited me to the first

international congress on sleep medicine which he organized in Bologna in 1967 (unfortunately I was unable to attend) as well as to a later major conference in Venice on the prognosis of epilepsy, and over the years had thoughtfully sent me copies of his published books as they appeared. My recollections of this pleasant year include his strong visionary leadership of the Institute, the extreme care with which he prepares for his clear and dynamic presentations at major congresses, his remarkable performances at neurology grand rounds where, as Chairman, he was expected to be the first to diagnose all cases, his warm friendship



## Commemoration of Elio Lugaresi

### Remembrances of an Old Pupil

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Everything had been decided. I would become a psychiatrist, obtain a position in one of the three mental hospitals in my home town near Bologna, open an office in the family home next to my father's and see the remaining unhospitalized patients, despite those mental institutions. My mother, of course, was delighted with the plan: one of the children would stay around the house for the time being. So, I was waiting on that day in 1961 in the library of the University of Bologna Department of Neurology and Psychiatry (at that time Neurology and Psychiatry were combined) to be received by the Chairman as was customary at that time, and make the formal request to be admitted as a resident in the Psychiatry Division of the Department.

As I waited, I became aware of a young man in a white lab coat sitting at the library table behind a pile of scientific journals; he asked me who I was and what

and generosity towards my wife and I, and, more prosaically, his wonderful wood panelled office with its collection of memorabilia and hunting trophies. Lugaresi's life-long passion outside of medicine has in fact been hunting or, as he has put it, "relaxing in good company in marshes waiting for the ducks to appear". He has hunted in marshes from Hungary to Tasmania.

Elio Lugaresi's eminence has been reflected in his many journal editorial responsibilities and in his honorary membership in eight scientific and medical societies (Italian, French, Spanish,

I was doing. It was the second time I had met Professor Elio Lugaresi. I had previously encountered Dr. Lugaresi, at that time Chief of the Neurological Division, when as a medical student, I attended his neurology laboratory sessions. Among the students he had the reputation of being the best teacher, yet also friendly, at least according to the standards of Italian university professors of the time. After my

**Among the students he had the reputation of being the best teacher.**

answers, he asked me whether I wanted to publish papers and become known. To my positive answer, he replied that psychiatrists do not publish much and that I should ask the Chairman to commence my residency in the Neurological Division of the Department. My objection that I had planned to become a psychiatrist was quickly countered with the argument that the stay in Neurology Service would have been only the beginning sequence in my training and that I would subsequently rotate into

German and American). He has received the American Association of Sleep Disorders Centers' special Award for Distinguished Service (1983), the Rossi Award for Neurology of the "C. Mondino" Foundation of the University of Pavia (1995), the European Sleep Research Society's Pisa Award (1996), the American Academy of Neurology's Potamkin Award (1997) and the World Federation of Clinical Neurophysiology's Giuseppe Moruzzi Award (1997).

We are all privileged indeed to have this remarkable person as a colleague.

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literature on Werdnig-Hoffmann was followed by a search on all muscle diseases of the young, which resulted in tables chronicling each reported case, and then drafts and drafts of the paper. Of course, my summer vacation was cancelled for that year. When Dr. Lugaresi came back, I gave him, with great trepidation, the manuscript which was returned to me a few days later reduced to one tenth of the original length. But it now included many things that I wanted to say but couldn't express and many others that I did not think of saying but should have. So, the paper 'Le amiotrofie neurogene infantili a decorso protratto: il problema del loro inquadramento nosologico in rapporto all malattia di Werdnig-Hoffmann' was published in *Rivista Sperimentale di Freniatria e Medicina Legale delle Alienazione Mentali* in 1965 (Lugaresi et al., 1965b), subsequently, in a more concise version in the *Journal of Neurological Sciences* (Lugaresi et al., 1966) the following year and then included in a list of selected papers on clinical neurology published that year.

**There is ample proof of Elio Lugaresi's incredible dedication to science, but also and especially of his achievements as a teacher and mentor.**

shadow of a doubt the diagnosis of a "particular form of Winiwarther-Burger."

About ten years later, Dr. Lugaresi phoned to tell me that our atypical case of Winiwarther-Burger had been listed in a review, as one of the most typical cases of Sneddon's syndrome, which had been originally reported in the *British Journal of Dermatology* shortly after we finished our manuscript (Sneddon, 1965). And that is how Dr. Lugaresi and I missed the first chance to discover a new disease, and perhaps made Dr. Ludo van Bogaert, the discoverer of so many neurological conditions, miss it too.

In 1984, when I was already at Case Western Reserve University in Cleveland, Dr. Lugaresi called me. "I have the brain of a member of a family affected by a new disease. He could not and did not sleep during the last six months of his disease" was the message describing this patient's history. "Look in the hypothalamus and brain stem for lesions" were the professorial instructions. Thus, the work on Fatal Familial Insomnia (FFI) with dysautonomia and thalamic atrophy began (Lugaresi et al., 1986). It took me month after month to try to produce a perfect neuropathological examination in the difficult task of matching the clinical study, possibly one of the most complete neurological studies in modern neurology, carried out by Dr. Lugaresi and his team, Drs. Pasquale Montagna, Pietro Cortelli, Agostino Baruzzi, and other collaborators. A number of other papers followed that definitely established the individual clinical features of FFI, its mutation on the prion protein gene, the role of codon 129 in the expression of the FFI phenotype, the

studying the histopathology and having discussions with Dr. Lugaresi, we settled for an atypical form of Winiwarther-Burger disease. The case, of course, was presented to Dr. Ludo van Bogaert, who after examining the slides at the microscope for what seemed like a few minutes (to me at least who had spent months on them), confirmed beyond a

characterization of the protease resistant prion protein and addressed many more topics. The number of trips made from Bologna to Cleveland and from Cleveland to Bologna or to other parts of the world increased. This travel was in addition to almost daily telephone consultations with Professor Lugaresi, who in the meantime had become Chairman of the Neurological Institute of the University of Bologna, discoverer of a number of other neurological conditions, a world renowned sleep expert, and recipient of numerous honors and awards.

Now, almost 40 years and 40 papers after that eventful encounter in the library, I see this story not only as another proof of Elio Lugaresi's incredible dedication to science, but also and especially as the ultimate achievement of a teacher and mentor who nurtured a productive working relationship for so long and in a way that allowed the student to become a colleague and then a friend, as the science kept progressing, getting better and better.

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## Commemoration of Elio Lugaresi

### Elio Lugaresi: A Tribute

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In 1972, I met two giants in the field of sleep medicine: Yasuo Hishikawa and Elio Lugaresi. Both were neurologists and clinical neurophysiologists. In 1963, Dr. Hishikawa reported that narcoleptics had abnormal sleep onset REM periods at the same time that Allan Rechtschaffen and colleagues were demonstrating it. He was also directing a team of young researchers at Osaka University who would first describe what became known as "REM Behavior Disorder", while Elio Lugaresi was soon to be the director of the Institute of Neurology at Bologna University.

I was a young researcher and had just passed my specialty board in Neurology and completed my diploma at the science faculty. I believed, based on the work of these two researchers, that a new specialty of medicine called "internal medicine during sleep" could be created. A scientific meeting dedicated to hypersomnia with periodic breathing was held in Rimini in 1972. Between presentations and a visit to the mosaic of Ravenna, I had a chance to appreciate the scientific openness of Elio, who encouraged me to express my ideas on sleep disordered breathing. Elio Lugaresi was already a dominant figure in 1972. A friend of Henri Gastaut, he organized and co-chaired the XVth European Meeting on Electroencephalography in Bologna in 1967. The meeting was entirely dedicated to the "abnormalities of sleep in man." Many themes, familiar to all researchers to date, were identified at that meeting, from the interaction between thermoregulation and sleep states, to the Restless Legs Syndrome. Lugaresi and his colleagues already pointed out that Restless Legs Syndrome was a cause of insomnia and that periodic leg movements and restless legs were not completely identical.

Starting in 1967, Dr. Lugaresi regularly organized meetings in Bologna that pushed the field of sleep medicine towards new frontiers. In 1972, research in obstructive sleep apnea and its association with the Pickwickian syndrome led to the blossoming of the "obstructive sleep apnea syndrome." He dedicated the meeting in 1983 to "the epidemiology of sleep disorders and long term follow-up studies", a theme that American researchers and the U.S. National Institutes of Health took back as a primary interest in the 1990's. In 1994, he dedicated another one of the by now famous Bologna meetings to the molecular biology of sleep medicine and prion diseases, which led to Nobel recognition 3 years later.

**Based on the work of Yasuo Hishikawa and Elio Lugaresi, a new specialty of medicine called "internal medicine during sleep" was created.**

Despite over 100 journal articles, Dr. Lugaresi believed more in books than in journal articles, and many of his works have not received the emphasis that they deserve. The first description of abnormal breathing during sleep as an independent cause of hypertension, even in the obese population, was by Elio Lugaresi in association with Georgio Coccagna. The epidemiological study performed in the Republic of San Marino examined insomnia, the prevalence of sleep walking, daytime sleepiness, and usage of hypnotic drugs in the general population.

In 1986, Dr. Lugaresi and his colleagues published in the *New England Journal of Medicine* that Fatal Familial Insomnia, a syndrome discovered and described in Bologna, was associated with a selective degeneration of the anterolateral and dorso-medial nuclei of the thalamus and resulted in a disorder of the autonomic nervous system leading to

agrypnia and death. This autosomal dominantly inherited disease was shown to be related to an abnormal isoform of the prion protein. Pierluigi Gambetti, a long-time friend of Elio, and Rossela Medori, one of his students, were very much involved with the characterization of the prion protein gene mutation leading to fatal familial insomnia. These major findings must not eclipse his initial description of paroxysmal nocturnal dystonia or his discovery of the repetitive coma-like events linked to endozepines. The contributions of Elio Lugaresi to our field have been matched by very few. Many of his findings have not yet been integrated by researchers and specialists in the field of sleep medicine. But Elio Lugaresi, a humanist and a professor in the oldest University in the western world, who as a child of Romagna knew what a good meal and a good wine should be, has opened many avenues that will be easier for others to follow. Fortunately for us, if administrative decisions force Elio Lugaresi to retire, his imaginative mind will still be leading the field for years to come.

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by  
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I first embarked on my adventure in the field of sleep medicine together with Elio Lugaresi in the early sixties. When I reached the Institute of Clinical Neurology at Bologna University to specialize in neuropsychiatry the only thing I knew about sleep was what my physiology professor had taught me a few years previously: sleep was a passive phenomenon which comes about, as Moruzzi had specified, when the activating reticular substances, tired of being bombarded all day long by sensory and sensorial stimuli, decided to take a rest.

I soon learned that the notion of sleep had changed radically during my last years as an undergraduate. A new kind of sleep, called REM sleep, had been discovered, attracting the interest of neurophysiologists and clinicians alike, and they soon undertook the first polygraphic recordings which disclosed the pathophysiological mechanisms responsible for narcolepsy.

However, the main field of interest in the new hypnology discipline focused quite rightly on what is deemed the most widespread and well-known sleep disorder of them all: insomnia. At that time, Elio was very friendly with Henri Gastaut and knew that his laboratory in Marseilles was already performing polygraphic recording and sleep staging.

On my return, an ideal opportunity arose to record a strange patient, a friar exasperated by a severe form of insomnia which everyone laughed about. As soon as he retired to bed, he would feel an unbearable sensation in his legs which forced him to move his limbs frenetically until in the end he was forced to get up and run and jump about the room. We recognized in this patient the symptoms described by Ekbom in a paper published in *Neurology* in 1960 entitled Restless Legs Syndrome (RLS) and we set about investigating him as a model for insomnia. Alongside the usual parameters used to classify sleep stages, I decided to add to the polygraphic monitoring an EMG recording of two leg muscles (the anterior tibialis) to document the motor restlessness recounted by the friar.

During the first half of the night, everything went as planned: the patient complained of an unbearable sensation in his calf muscles as he rubbed his legs madly. In the end he managed to fall asleep. All of a sudden, just as I was about to be overcome by Morpheus myself, I heard a strange intermittent noise which after a time I realized was the scratching sound produced by the pens of the polygraph connected to the tibialis muscles. I rushed over to the patient who was sound asleep behind a screen and noted that his leg muscles would suddenly jerk every 15-20 seconds. The next morning, as Elio and I were examining this strange recording enthusiastically, the friar told us that his mother and all his siblings suffered from the same complaint. We managed to make one or more polygraphic recordings from almost every member of his family and the result was identical.

## About Elio Lugaresi...

I have taken the trouble to recall this anecdotal episode because, had the first polygraphic recording made at our laboratory not been as successful, the history of sleep medicine in Bologna would have taken a very different turn. This pioneering finding fired Elio Lugaresi with an enthusiasm which made him almost neglect his main scientific interest, epilepsy. We made polysomnographic recordings whenever we could, but our primary concern, together with RLS, was another newly discovered sleep disorder, obstructive sleep apnea syndrome (OSAS).

This new topic aroused our attention after an EEG ski-meeting (informal annual get-togethers organized by Henri Gastaut at various European ski resorts) where we heard a short report by Dr. Kuhlo from Freiburg on the presence of apneas during sleep in Pickwick syndrome. Straight away, Lugaresi and I in Bologna, Gastaut, Tassinari and Duron in Marseilles set about performing polysomnographic recordings of these patients. We soon reached the conclusion that different types of apnea may arise during sleep but the most common are obstructive.

The time was ripe to exchange our findings with leading sleep experts in Europe, the United States and Japan. Yet again, Elio Lugaresi's friendship with Gastaut proved crucial. During the XIVth European Meeting on Electroencephalography, which as usual took place in Marseilles, Gastaut offered him the chance to

*The pioneering finding of Restless Legs Syndrome fired Elio Lugaresi with an enthusiasm which made him almost neglect his main scientific interest, epilepsy.*

organize the XVth Meeting in Bologna on the topic of "The abnormalities of sleep in man". The Congress was held in 1967 and was a great success because it was attended by all the major sleep experts of the time and links were forged then which still hold. Elio Lugaresi's school went on to gain worldwide recognition. After this meeting, we focused on the study of sleep apnea syndrome also because my wife, an anesthesiologist, joined us for what was the next inevitable step forward in the definition of the syndrome, the study of the hemodynamic and ventilatory effects of obstructive apneas. Our findings obtained by recording arterial and pulmonary pressure and measuring gasanalytic levels together with the outcome of tracheostomy in OSAS patients led Elio Lugaresi to organize another historic meeting, the Rimini Congress held in 1972. On that occasion, all the clinical and pathophysiological features of OSAS were

characterized in full. It was now clear that only by eliminating the upper airway obstruction by tracheostomy could patients be cured. Another decade, however, was to pass before a novel form of treatment, CPAP, was first proposed by Sullivan as an effective alternative to surgery.

*He discovered a hereditary prion disease known as Fatal Familial Insomnia.*

Yet Elio Lugaresi's interests in sleep did not rest here. In the last ten years he has undertaken research in normal and pathological movements during sleep and discovered a hereditary prion disease known as Fatal Familial Insomnia. More will be said of this, I am sure, by the younger members of the Bologna sleep laboratory staff.



by  
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I cannot feel but greatly honored and at the same time flattered to be asked to write a piece on the occasion of Professor Elio Lugaresi's retirement from active teaching from our University. My feelings are made even more poignant considering the fact that he has been my teacher all these years, beginning from my early undergraduate course in Neurology until now as I work with him as an Associate Professor of Neurology in the same Institute. When I look back at all these years of collaborative work that have so fast elapsed, I cannot but feel a sense of awe at Professor Lugaresi's scientific achievements. Mine is therefore a tribute to a man of superior understanding.

It is hard for people living in other countries to realize the degree of stamina and ingenuity needed for an Italian scientist first to get engaged into the field of sleep medicine, still an uncharted territory when Professor Lugaresi began his career, and to persevere in it for more than 30 years in Italy, a country

*A man of superior understanding...*

then and now not very conducive to scientific enterprise and inquiry. One is reminded of the fact that at the beginning he had to acquire EEG machines on the sly, because people thought them useless and remembers still the desultory smiles of clinical colleagues when mentioning one's involvement in sleep research, and the appalling scarcity of money and other resources. And yet, there came from his engagement the first world congress of sleep medicine (Bologna, 1967); the first polysomnographic studies of the then-called nocturnal myoclonus and Restless Legs Syndrome, in my opinion unrivaled until now; the first description of the physiological periodic events of sleep, anticipating what 20 years later we define as the microstructure of sleep; the detailed definition of the cardiorespiratory events underlying what we now know as obstructive sleep apnea syndrome and the definition of its natural history and its relationship to the "trivial" snoring; the description of the nocturnal paroxysmal motor events which are now comprised within the syndrome of Nocturnal Frontal Lobe Epilepsy, the first reporting of the recurring stupor attacks due to increased endozepines; and the thorough clinical, neurophysiological, pathological and genetic characterization of the prion disease he named Fatal Familial Insomnia with the attending innovative considerations on the role of the thalamus in sleep physiology. All this is still new and sometimes controversial, but remains at the very cutting edge of clinically oriented sleep research.

*Elio Lugaresi has an obstinate faith in the power of clinical judgement and logical reasoning.*

And yet sleep medicine was not everything: his was the first description of orthostatic tremor, albeit in Italian, of some paroxysmal events occurring in the course of multiple sclerosis; the first recordings of the respiratory pattern typical of Rett's syndrome; his was the unifying conception of the spinal amyotrophies, controversial at the time but well-established now; and his were the pioneering studies of the natural course of the secondary epilepsies and of scotosensitive epilepsy. When I try and explain to myself the reasons for his striking scientific success—and I owe him several discussions and considerations on the methods of scientific research—I must cite first his obstinate faith in the power of clinical judgement and logical reasoning, his obturate refusal to trivialize even the "simplest" clinical finding and phenomenon, and his resistance to commonplace and standard explicative hypotheses. He has never been afraid of engaging in other fields and scientific methods, as long as he deems they hold the key to some scientific fact of interest; and he has such an obliging way of motivating other people into research because he communicates to them his inner tension, his inner spark. My debts to him are uncalculable: he has taught me to "reason with my own head" and not to accept anything on the principle of authority; to accept

the lesson of facts and dislike idle theories and useless classifications (those "drawers", as he likes to call them, to put to untroubled rest disquieting clinical findings and diagnoses); to feel the beauty of research, the excitement of scientific controversy, and the daring of new hypotheses and methods. These debts of mine to him represent, I believe, a lesson for all of us who have the luck to be involved in clinical research. Let's hope that we can rise to the challenge.



by  
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I am very pleased to join in honoring Elio Lugaresi. He has contributed so much to our field and certainly can rightly be named as one of the fathers of sleep disorders medicine. We first met at the 1st International Congress of Sleep Research that was held in Bruges, Belgium, in 1971, and then later in September when I was spending the first of many happy periods at the Institute of Human Physiology with Pier Luigi Parmeggiani. That was the first time I saw Elio's clinic laboratory and had a chance to discuss some of his interesting cases. His great desire as a clinician to get at the pathophysiological basis of each of the problems facing him and his colleagues was very evident then as it is now.

*Elio Lugaresi can rightly be named as one of the fathers of sleep disorders medicine.*

On many of my yearly visits to Bologna since 1984 I have had the opportunity to continue those discussions. Most memorable was my introduction to Fatal Familial Insomnia in, I think, 1985. Elio invited me to view a video of the first patient who seemed to be exhibiting REM without atonia behaviors much like the cats we had studied. This was before the patient had continued into more advanced stages leading to death. We discussed where the caudal brainstem lesion might be. Being newly excited about our idea that not enough attention was being paid to structures rostral to the pons in REM control, I said, "Don't neglect those areas in the search." Fortunately, his neuropathologist collaborator, Pierluigi Gambetti, working in Cleveland, did not. He eventually found degeneration in the mediodorsal nucleus of the thalamus, as we know. Of course, the disease has now added an interesting new chapter to the prion story.

One cannot end a comment on Elio Lugaresi without mentioning one other important thing—important to both of us I

*One cannot end a comment on Elio Lugaresi without mentioning food...No visit with Elio is complete without a great meal.*

might add—food. No visit with Elio is complete without a great meal. They all have been indescribably good. And eaten in the company of friends from his clinic and the Institute, what could be better?



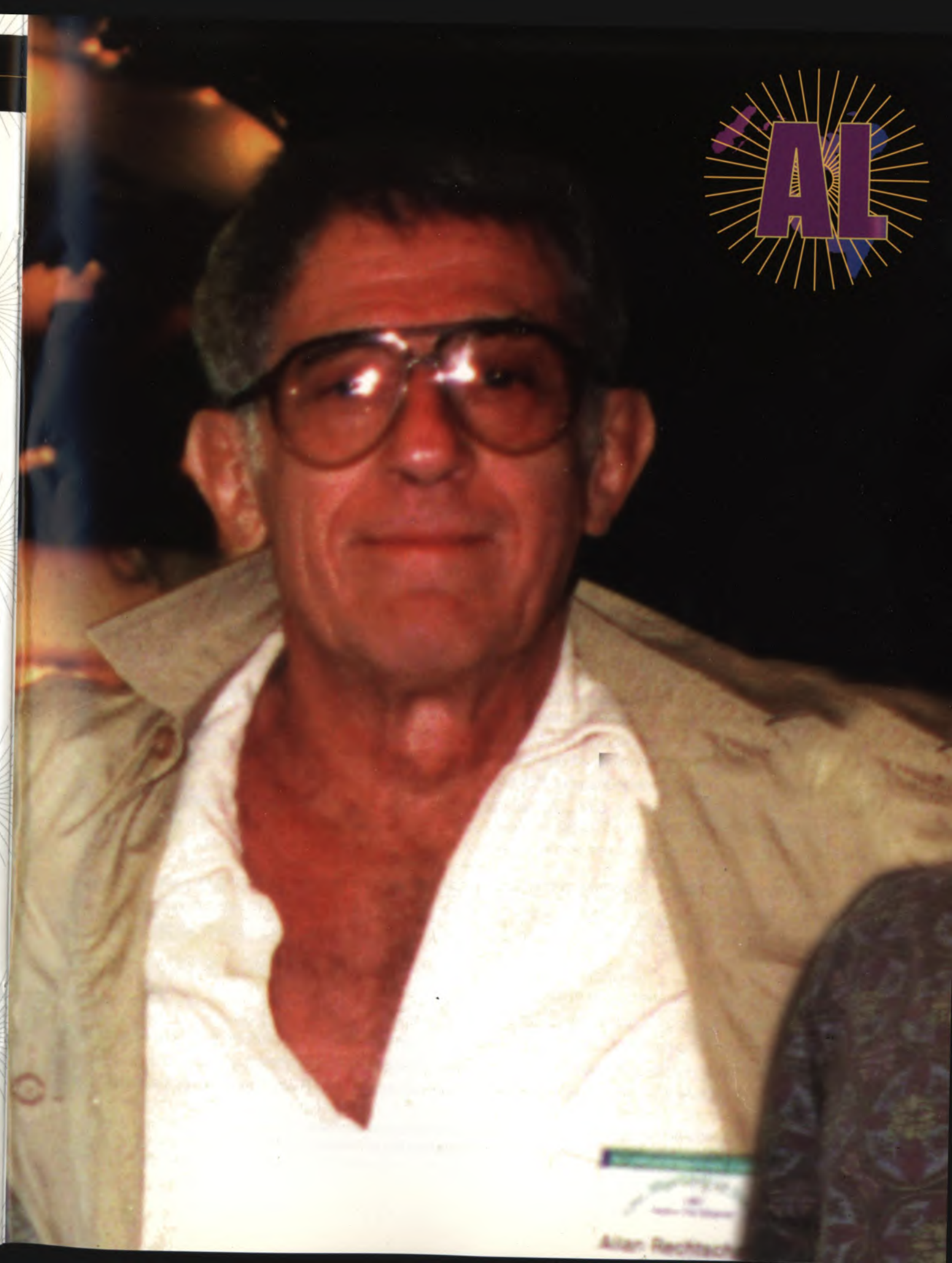
by  
Pier Luigi Parmeggiani, M.D.  
Istituto di Fisiologia Umana  
University of Bologna  
Bologna, Italy

Following Joseph Conrad, we may consider the age of retirement an approaching shadow line. To scientists the crossing of this line may be rich in both satisfaction and regret. Considering with La Rochefoucault that "Le m'Érite des hommes a sa saison aussi bien que les fruits", I recently congratulated Elio Lugaresi on his living this season fully. He admitted this, however, adding that the future span of his research endeavor was getting short. This regret comes naturally to Elio's personality so passionately engaged is he in scientific work.

*I was impressed by Elio's appreciation of physiological paradigms.*

My friendship with Elio dates back to the early sixties when I was carrying out a study on the interaction between sleep and thermoregulation. He invited me to present the results at the international meeting on "Abnormalities of Sleep in Man" he was organizing in Bologna in 1967. On this occasion, Professor Moruzzi was in the audience and heard my story. Much to my surprise, he asked me to send him the manuscript for publication

See About Elio Lugaresi, page 39





## BIOGRAPHY OF AL RECHTSCHAFFEN

**Date of Birth:**  
December 8, 1927

**First University Position and Date:**  
1957-Instructor  
Department of Psychiatry  
University of Chicago  
Chicago, Illinois, U.S.A.

**Most Recent University Position:**  
Professor Emeritus  
Department of Psychiatry  
University of Chicago  
Chicago, Illinois, U.S.A.

### Representative Awards:

- Nathaniel Kleitman Distinguished Service Award from the Association of Sleep Disorders Centers for service to sleep research and sleep disorders medicine (1985)
- Distinguished Scientist Award, Sleep Research Society (1989)

### Service Contributions:

- Co-founded (with William Dement) the Association for Psychophysiological Study of Sleep (now the Sleep Research Society). President of the Society from 1979-82.
- Co-authored (with Anthony Kales) the Manual for Standardized Terminology, Techniques and Scoring System for Sleep Stages of Human Subjects which remains the standard for the field.

### Representative Publications:

- Rechtschaffen, A., Wolpert, E.A., Dement, W.C., Mitchell, S.A. and Fisher C. Nocturnal sleep of narcoleptics. *EEG Clin Neurophysiol* 15:599-609, 1963.
- Rechtschaffen, A. The psychophysiology of mental activity during sleep. In: McGuigan, F.J. and Schoonover, R.A. eds. *The Psychophysiology of Thinking*. Academic Press. New York, 153-205, 1973.
- Rechtschaffen, A. The single-mindedness and isolation of dreams. *Sleep* 1:97-109, 1978.
- Rechtschaffen, A. and Bergmann, B.M. Sleep deprivation in the rat by the disk-over-water method. *Behavioural Brain Research* 65:55-63, 1995.
- Rechtschaffen, A. Current perspectives on the function of sleep. *Perspectives Biology & Medicine*, in press.

### The following reflect either the first finding in the field or a significant pioneering construct or theory:

- ▶ Early laboratory studies of narcolepsy (with W. Dement), insomnia (with L. Monroe), and hypersomnia (with B. Roth).
- ▶ Formulation of narcolepsy symptoms of hypnagogic hallucinations, sleep paralysis, and cataplexy as dissociated REM sleep phenomena.
- ▶ Stimulus determinants (TV films, retinal stimulation) of dream content (with D. Foulkes); patterns of mental activity across the night (with G. Vogel); bizarreness in dreams (with E. and W. Dorus).
- ▶ Search for REM-like physiology in hallucinating schizophrenic patients. (There was none.)
- ▶ First laboratory study of napping (with L. Maron and E. Wolpert); hypothesis of circadian rhythm of REM sleep propensity.
- ▶ Effect of daytime sleep on subsequent nocturnal REM and delta sleep (with W. Whitehead).
- ▶ Studies relating "depth of sleep" to sleep stage (with Peter Hauri); dreaming (with R. Watson), and prior sleep loss (with C. Frederickson).
- ▶ Studies of tonic nuchal and phasic oculomotor muscle activity in cats and humans; relationship to PGO and oculomotor activity in cats; relationship to sleep mentation and psychopathology in humans (with D. Bliwise, J. Metz, F. Michel, T. Pivik, and R. Watson).



## Commemoration of AI Rechtschaffen

### A Tribute to AI Rechtschaffen

by Gerald Vogel, M.D.  
Sleep Research Laboratory  
Emory University School of Medicine  
Atlanta, Georgia, U.S.A.

**H**ow does one pay tribute to AI Rechtschaffen for his contributions to sleep research? He is unique.

The range of his discoveries as well as his methodological precision, his encyclopedic knowledge, his incisive, scholarly reviews, and his organizational direction make him the master of our field. This brief review is an attempt to specify some of these achievements. I begin with remarks made about Dr. Rechtschaffen in 1985.

The occasion was a joint meeting of the Association of Sleep Disorders Clinics and the Sleep Research Society. It was a special occasion. It marked the 10th anniversary of our clinical society and the 25th anniversary of our research society. The clinical society had chosen this special occasion to honor AI Rechtschaffen with the Kleitman award for services to sleep disorders medicine. Note, not for his scientific research, but for

**A**I Rechtschaffen really started sleep disorders medicine.

his services. Why did the clinical society pick that special occasion to honor a man who is a researcher and not a clinician, and who didn't even work in a clinical setting.

In general terms the answer involves AI's contributions to the whole field of sleep—not just basic research, not just clinical research, not just organization and educational activities—but all of these—and all of them done with a classy style that has served as a model for the rest of us. Let me mention specific areas of his contributions.

First, AI Rechtschaffen really started sleep disorders medicine. I mean that he originated the clinical application of laboratory sleep research. AI's sleep laboratory was

the first to compare good and poor sleepers, i.e., to study insomnia. AI's sleep laboratory was the first to study excessive daytime sleepiness in the form of narcolepsy. He discovered the sleep onset REM periods and formulated the idea that the accessory symptoms of narcolepsy were a precocious triggering of the dissociated aspects of REM sleep. AI's laboratory was the first to study naps polysomnographically. AI's laboratory was the first to study a parasomnia or behavior disorders during sleep, viz., bruxism. AI's lab was the first to study the effects of stimulant drugs (in this case amphetamines) on sleep. In short, AI was the first to use the sleep laboratory to study sleep pathologies and several different kinds of them: viz.,

**A**I was the first to use the sleep laboratory to study sleep pathologies.

### First finding in the field or a significant pioneering construct or theory (continued):

- ▶ Early studies on effects of age on sleep and circadian rhythms in rats (with R. Rosenberg and H. Zepelin).
- ▶ Sleep in crocodilia, turtles, tortoises, and iguanas (with W. Flanigan and K. Hartse).
- ▶ Relationships between sleep parameters and constitutional variables (life span, size, metabolic rate, brain weight) in 54 mammalian species (with H. Zepelin).
- ▶ Studies of rat sleep: EEG characteristics; response to sleep deprivation, thyroid hormone, SCN lesions, sensory stimulation, stress, exercise; circadian rhythms (with B. Bergmann, C. Eastman, L. Friedman, R. Mistlberger, R. Rosenberg).
- ▶ Studies of color, brightness, hue, clarity, and figure-ground relationships in visual dream imagery (with C. Buchignani).
- ▶ Effects of sleep deprivation in the rat by the disk-over-water method on survival, organ pathology, brain cells, metabolic rate, heart rate, intermediary metabolism, hormones, brain and body temperature, temperature setpoint, brain neurotransmitter levels and receptors, skin condition, immune function, and rebound patterns (with S. Balzano, R. Benca, B. Bergmann, C. Everson, V. Fang, P.-F. Feng, M. Gilliland, C. Kushida, C. Landis, W. Obermeyer, J. Pilcher, F. Prete, S. Refetoff, D. Schoeller, P. Shaw, L.-L. Tsai, C. Zenko, and others).





insomnias, hypersomnias, and parasomnias. It would not be accurate to say that he deliberately set out to originate the field of sleep disorder medicine. That distinction belongs to others. But it is accurate to say that he was the first to show that there are reliable physiological indicators of subjective sleep disorders. This is the foundation of sleep disorder medicine and this foundation started the field. It encouraged other workers to investigate the physiological foundations of the whole array of disorders that now comprise sleep disorders medicine.

**A**l may be tough, but he is fair... he has made us better investigators and clinicians.

A second reason to give AI Rechtschaffen the Kleitman Award for service was his non-research contributions to the field. As we know, he is the senior author of the manual for standardized scoring of human sleep stages. The work and effort that went into the preparation of that manual were substantial. And the payoff—the service to all of us—has also been substantial. A standard scoring system that is both reliable and sufficiently broad to encompass most of our human polysomnographic data is a necessary condition for the scientific collection and comparison of polysomnographic data about human sleep. Dr. Rechtschaffen also compiled the first categorical bibliography of modern scientific literature on sleep. He then donated his bibliography to the Brain Information Service. We still use a derivative of his categorical bibliography system. It is the foundation of the bibliography published in the journal *Sleep* and in the annual volume of *Sleep Research*.

based on a clear understanding of the scientific issues, not petty personal issues. As a result, he has made us better investigators and clinicians. He has also been a superb teacher. Many of his students now direct clinical sleep disorders centers and sleep research laboratories.

It has been 13 years since the meeting that honored AI for his services to the clinical society. We now pay tribute to his research contributions.

The range of Dr. Rechtschaffen's lasting contributions to our knowledge about sleep is too great for adequate review in this space. As I will specify, he has made significant contributions to our knowledge about dreams, psychophysiological parallels during sleep, relations between sleep and serious mental illness, the phylogeny of sleep, and most recently and importantly, the function of sleep. To the best of my

**H**is lasting contributions to our knowledge about sleep is simply too great for adequate review in this space.

knowledge, no other scientist in our field has such a wide range of contributions. Two additional qualities characterize his contributions. First, his findings are lasting. Over time their reliability has been repeatedly demonstrated. Based on experience, we know when Dr. Rechtschaffen publishes a finding it's real, solid as a rock. Secondly, he has an uncanny ability to ask the basic questions in our field and to ask them in empirically meaningful ways. So his major contributions concern empirical answers to basic questions about sleep and dreams.

Here is a brief review of some of his findings, organized in terms of the basic empirical questions he asked.

**Dream psychology**

What is the basic difference between waking and dream (at least REM) mentation? Dr. Rechtschaffen found that the unique quality of the REM dream is its single-mindedness and its isolation from external and internal stimuli. The significance is that an adequate account of dream psychology and of the physiological difference between waking and REM consciousness must involve and explain these previously unnoticed dream properties.

**Psychophysiology of sleep**

What is the basic difference between REM and nonREM mentation? Along with David Foulkes, Dr. Rechtschaffen found that compared with typical (modal) REM reports, typical nonREM reports were less perceptual, more thought-like, less emotional, less bizarre, and more concerned with contemporary life. The significance is that in the search for mind-brain correlates, this modal REM-nonREM difference identifies predictable, reliable psychological differences that require different physiological correlates. In purely psychological terms, the REM/nonREM differences in mental activity imply different avenues to study the relation between sleep and wake mentation.

**Psychiatry—relation between dreams and madness**

Since the time of the ancient Greek civilization, the similarity of dreams and of symptoms of madness (e.g., hallucinations, delusions, and thought disorders in both) has suggested that madness (today called schizophrenia) is an intrusion of the dream state into wakefulness. More recently, Hughlings Jackson wrote: "Find out about dreams and you will find out about insanity". Thus, the dream-madness hypothesis is a venerable one. Dr. Rechtschaffen realized that the discovery of REM sleep as a reliable physiological indicator of dreams offered an opportunity for an empirical test of the dream-madness hypothesis. He looked for indicators of REM sleep in waking hallucinatory schizophrenic patients.

**H**e has an uncanny ability to ask basic questions in empirically meaningful ways.

There were none. So, after 3000 years, went one version of a venerable hypothesis.

**Sleep and Constitutional Variables**

What is the relationship between sleep variables (total sleep, REM sleep,...) and constitutional variables such as life span, metabolic rate, and brain weight? Some versions of these very old questions had been answered speculatively, but systematic empirical data were lacking. With Harold Zepelin, AI Rechtschaffen studied these relationships across 53 mammalian species. Does sleep promote longevity? Dr. Zepelin and Dr. Rechtschaffen found no correlation between total sleep time—or any other sleep variable—and longevity. Does sleep enforce rest to conserve energy? Dr. Zepelin and Dr. Rechtschaffen found a negative correlation between body size and total sleep time. This empirical finding is consistent with the view that sleep duration is a response to waking energy expenditure. Is brain size related to any sleep variable? Dr. Zepelin and Dr. Rechtschaffen found a strong, positive correlation between sleep cycle duration and brain size. The source of this surprising correlation is unknown, but the correlation emphasizes the unknown significance of the sleep cycle,

**H**e has uncanny abilities to see to the heart of a scientific problem.

including its ontogenic and phylogenic significance.

**Sleep function**

And finally Dr. Rechtschaffen investigated the central question of our field: What is the function of sleep? I believe that this question has preoccupied him from the beginning of his career. For several reasons he concluded that the most efficacious way to answer the question was to determine the effects of sleep deprivation (see his methodology paper). In previous studies, effects of sleep deprivation were confounded by

effects of the stimuli used to produce sleep deprivation. As we all know, Dr. Rechtschaffen then devised the disk-over-water technique for sleep deprivation of rats. This technique effectively eliminated confounds of sleep deprivation. For the first time it became possible to determine the unambiguous effects of prolonged sleep deprivation. They were dramatic. Without sleep, animals die.

Thus, for the first time, we know rather than suspect, that sleep is vital. Furthermore, sleep deprivation produced a reliable syndrome, the salient feature of which was increased energy expenditure. Further, nonREM sleep loss and

**R**echtschaffen's work uncovered the first unequivocally causal evidence about sleep function.

REM sleep loss contributed different components to increased energy expenditure. NonREM sleep loss increased core temperature set point and REM sleep loss increased heat loss - both of which stimulated increased energy expenditure. In a nutshell, Rechtschaffen's work uncovered the first unequivocally causal evidence about sleep function, viz., sleep plays a role in thermoregulation and sleep is necessary for life.

No description of Dr. Rechtschaffen's salient contributions can omit his methodological reviews. Look at his papers on Dream Reports and Dream Experiences; or Psychophysiology of Mental Activity during sleep, or the Function of Sleep: Methodological Issues. They are masterpieces. My own predilections lead me to the conclusion that here is his special genius. I often think that had he chosen, AI could have been an outstanding logician or mathematician. His clear grasp of conceptual issues, his incisive logic and his ability to penetrate to the heart of the issue are without parallels.

Lastly, a tribute to AI's role as a model for many of us who had the privilege of knowing and working with him. This may be his most subtle and intangible

**W**hat is the function of sleep? This question has preoccupied AI from the beginning of this career.

contribution, but it is certainly not the least important. Anyone who has had scientific contact with AI soon recognizes that he has uncanny abilities to see to the heart of a scientific problem. And then he frames the problem in simple empirical terms; he also sees the implications of the various empirical outcomes. Simply put, he is an incredibly clear thinker. More or less, we all envy this ability of his. But more importantly, we also try to emulate it. Having seen such clear thinking about scientific issues, we try just a little harder to achieve that goal. In this way, AI has served the field as a model. Of course, we're all empiricists, but there is something special about AI in this regard. I believe that for AI, more than most of us, the meaning of an idea lies almost exclusively in its empirical referents. He just naturally discards the fringes of easily associated meanings connected with an idea and sees the heart of its empirical foundation. That's a marvelous faculty and I believe that it has helped the whole field.

Let me put it this way. About 125 years ago the English biologist Thomas Huxley wrote—and I quote, "Sit down before facts as a little child. Be prepared to give up every preconceived notion. Follow humbly wherever nature leads or you shall learn nothing." Dr. Rechtschaffen proceeds in that way. In so doing, he nudges our scientific conscience, enlarges both our basic and clinical knowledge, and is a model of empirical integrity for the entire field.

We are proud and fortunate to be working with you, AI.



## About Al Rechtschaffen...



by  
Ruth Benca, M.D.,  
Ph.D.  
Clinical Science Center  
University of Wisconsin-Madison  
Madison, Wisconsin, U.S.A.

Almost exactly fifteen years ago, I met Al for the first time. Daniel X. Freedman, then Chairman of Psychiatry at the University of Chicago, sent me to him. I had been looking for a way to use my immunology training in psychiatric research, and Dr. Freedman thought Al would be "a good person to talk to." I remember sitting in the chair next to Al's desk, drinking the instant coffee he always had handy while discussing science. Al offered me the chance to look at the effects of sleep deprivation on the immune system.

Over the next several years, I finished my residency, had several children and tried to plan my life. Al and I had many more conversations (with bad coffee) by that always-immaculate desk. He was helpful even in areas where I least expected it, such as how to take care of infants, but the focus was on sleep and discovery. As a result of those conversations, Al became my most important mentor and at some point I consciously switched my research focus to sleep. In time, I also found my clinical interests centered on sleep. Al was largely responsible for that as well; his clinical acumen is in no way inferior to his scientific abilities.



They were principles that are central to who Al is, like "The data are the data"...



In some ways, Al is one of the most patient people I have known, although I'm sure most people wouldn't use that word to describe him. He taught me to be patient about science, in particular. There are a number of things he told me repeatedly; I still hear his voice as I now repeat them to my own students. They were principles that are central to who Al is, like "The data are the data," "That which gets in the way of the work is the work" (always attributed to Marcus Aurelius), and "What's your hypothesis?" Then there were the more practical principles, such as, "Nice people are people who do their work," "If you don't sleep, you die," and "Don't trust anyone under 30."

Sometimes I think that Al must have a kinship with Tom Sawyer; science is often difficult, but Al made one covet the chance to do it. Research, though, suits Al the way whitewashing a fence never could suit Tom. Sometimes we used to talk about why one does research. For Al, there was always one simple answer: because he had to.



by  
Mary A. Carskadon, Ph.D.  
Sleep Research Laboratory  
E.P. Bradley Hospital  
Providence, Rhode Island, U.S.A.

I have been an admirer of Professor Rechtschaffen and his research for many years. His meticulous experimental designs, his rigorous reasoning, his methodical search for scientific truth, and his outspoken demand for these qualities in others make him the prototypical scientist for me. When I was new to the field, however, these characteristics struck me otherwise.



Al said, "So, Bill, how long has Mary worked for you?" Bill's response, "Uh, a couple of years, I guess," ...Al's riposte, "Well, you ought to give her a raise!"



I first encountered this scientific giant in 1974 at the annual meeting of the Association for the Psychophysiological Study of Sleep in Jackson Hole, Wyoming. I had been working as a research assistant in Dr. Dement's laboratory for a few years, and this was my first APSS meeting. As I watched the proceedings, Dr. Rechtschaffen made a profound impression on me. Time after time, he pointed out a speaker's logical fallacy or experimental flaw. Each day, his stature grew in my eyes until he assumed a looming aspect rivaling that of the Grand Tetons themselves.

I was in awe—and in fear—of Dr. Rechtschaffen, and I remember hoping that I could forever avoid arousing his scrutiny, as I was sure I would wither to dust if he even so much as looked my way. Alas, on the last day of the conference, Dr. Dement and I were having coffee when Dr. Rechtschaffen entered the room and began talking to Dr. Dement. I shrank back, looked away, and began to tremble, as my ears roared. Then I heard my name as Al said, "So, Bill, how long has Mary worked for you?" Bill's response, "Uh, a couple of years, I guess," was met by Al's riposte, "Well, you ought to give her a raise!" To this day, I am thankful that Dr. Rechtschaffen's first nod my way was not only gentle but also affirmative. It has made me work all the harder to live up to his scientific standards.



by  
Michael H. Chase, Ph.D.  
Department of Physiology  
University of California  
at Los Angeles  
Los Angeles, California, U.S.A.

Some things change, yet forever remain the same. When I think back to my earliest interactions with Al, only one comes strongly to mind. It took place in the corridors of the Town Hall in Bruges, Belgium, in 1971, on the Opening Day of the 1st International Congress of the Association for the Psychophysiological Study of Sleep (now renamed the Sleep Research Society). That day represented for me the culmination of an extraordinary amount of work, coupled with incredible difficulties, for I had just finished organizing the first international meeting of any sleep society. For reasons that 25 years later are clearly unimportant and even forgotten, I was not one of those who was scheduled to meet with the Queen of Belgium at a special reception in her honor. The fact that I was excluded from meeting her somehow affected me much more than it should have; I guess it came to represent all of the difficulties that I had encountered in organizing the Congress. I ran into Al in the corridors when everyone else was inside with the Queen (I now wonder if he didn't actually come looking for me). I frankly don't remember what he said; I wish I did. I think that he talked about the importance of organizing the first international sleep congress, its scientific significance, that she may be the Queen but I was the Congress Chair, what was important and what wasn't—things like that. But what I do recall most clearly (and dearly) is that he somehow took care of me. Little did I know then that this was a pattern that would be repeated many times in the years to come. And as I discovered later, for me and countless others, Al takes care of all of us in the sleep community.



Al adheres to only one precept.  
The precept is honesty.



In writing this piece I thought I would describe how Al functions as a counselor, role model, scientist, friend, etc., but I realized very quickly that he functions in all these areas in exactly the same manner; that he adheres to only one precept and then expresses it in different contexts and fashions. The precept is honesty. Al is an honest individual, easy to say, accurate in its precision, but a feat impossible for anyone else that I know of to accomplish, except for Al. With others, there are degrees of honesty. With Al, it is a singularly defined word; it means to tell the truth.

In the movie *Amadeus*, the King complains that Mozart's music has too many notes. And Mozart replies, something to the effect that there are precisely the correct number of notes, neither



Al inspired all with whom he came in contact to do their scientific best with the highest moral integrity.



one too many nor one too few. When one is vigorously honest and communicates only that which is true and valid, and does not let one's ego rule the day with superfluous or redundant descriptions or with excessive or extraneous statements (as I am now!), then facts can be communicated in a simple honest manner. Unfortunately, too many researchers add to the data their personal evaluation of their findings, or take poetic license when describing simple facts. Al struggles for weeks over manuscripts so that they contain only the requisite number of words that are sufficient to communicate the findings. There are no extraneous descriptions or self-aggrandizement's. Once I tried for hours to reduce the length of an article that he wrote; I was unable to shorten it by even one line. Each sentence was "minimalist" in its construction, fully accurate and complete; none were redundant. To accomplish this feat, one must be rigorously honest with the data and with one's self. In this regard, he is the quintessential purist.

Over the years I can recall every so often the statement that, oh yes, the first laboratory studies of insomnia, Al did that, the discovery of REM sleep onset in narcolepsy, that was Al's, the first studies of the effects of age on sleep and circadian rhythms in animals, that was Al also. (Of course, Al would be the first to say that all of these studies were carried out in collaboration with others.) And yet if one were to ask most research scientists what they felt were Al's most significant contributions, they might list a few of them, but not many. I think that with all of his incredible achievements, any one of which would have been sufficient upon which to build a research career, none have been publicized or advertised in such a way that others would come to honor or "deify" the individual behind the discovery. Rather, for Al, it is first the discovery and the validation of the data that are important. Having made one discovery, he then went on and discovered another truth about sleep, and then another, and then another. There are certainly important lessons to be learned from this behavior, and the honesty of the scientific inquiries, as well.

One of the most telling stories about Al, that has been repeated many times, is the degree to which his search for the truth and his scientific integrity are integral parts of his character. I can recall occasions when Al evaluated grants or papers of mine or those of his other close friends, and the first time that he expressed negative views about a review that I had written. My first reaction was, "I thought he was my friend." It was only later that I came to understand that that's what a true friend does, which is to tell the truth, no matter what, but also in a constructive manner. In the end, my work product was far better than it could ever have been had he simply acted as a "typical" friend and approved it blindly. It did, however, take some time to appreciate that his search for the truth and that his scientific

integrity were also part of a rock-stable foundation that underlies his personal friendships and interactions.

I began my research career with an interest in the vagus nerve; my thesis dealt with an exploration of its functional effects upon behavior and reflex and electroencephalographic activity. The main reason I turned to sleep research was because of AI and the honesty, fairness, rule of law, integrity, and kindness that were literally the hallmarks of the Sleep Research Society (SRS) at that time. In those days, after co-founding the SRS, AI was the principal functioning cohesive force that inspired all with whom he came in contact to do their scientific best with the highest moral integrity.



*AI lives at the top of the moral food chain in our field.*



In a sense, AI lives at the top of the moral food chain in our field. His very being represents the highest scientific virtues which the individuals and groups, ranging from scientific societies, to institutes of health, to colleagues, students, associates and friends strive to achieve. Many of us try to emulate AI, and our success is measured by the degree to which we can be as honest a scientist, as dear a friend, as clear-minded a researcher, as broadly knowledgeable, and on and on. It's the individual that is at the top of the scientific and moral food chain who traditionally does not need the accolades and support of others. I would hope, however, that by these brief paragraphs and those by others in this *Newsletter*, that he will have some awareness of the depth of gratitude owed him by the field of sleep research as a whole and by literally hundreds of individuals.



by  
Charmane Eastman, Ph.D.  
Biological Rhythms Research  
Laboratory  
Rush-Presbyterian-St. Luke's  
Medical Center  
Chicago, Illinois, U.S.A.

### A MEMORY OF AI AND THE SLEEP LAB

I have many fond memories of AI and the Sleep Laboratory from my nine years of "living" there. This one happened when I was a relatively new graduate student. I gave AI an abstract I wrote for the annual APSS meeting, which at that time was still called the Association for the Psychophysiological Study of Sleep. When he returned it to me, the only changes he had made were to add a few commas and to cross his name off. I was shocked. Why didn't he want to be an author? Was it that bad? Was he mad at me? I finally gathered enough courage to ask him about it. He said that he really didn't have enough to do with the work to claim authorship, but that he thought it was good—except of



*What fairness. What honesty. What integrity.*



course for the commas. Whew! What a relief! And what fairness. What honesty. What integrity. Looking back on my Curriculum Vitae, I can count several abstracts from his laboratory without his name on them.

However, this venerated academic custom was not destined to last. Some time later, and I can't remember if it was months or years, AI called a meeting in the laboratory library. His demeanor was a little unusual as he prepared to tell us something grave and important. He seemed apologetic, almost shy. Here was the story. In the last review of the renewal for his Research Career Development Award, he was told that he didn't have enough publications and that he should put his name on all the papers written by his graduate students. This was what all laboratory directors did, and so should he. Or something like that. I don't remember exactly. But I do remember that without hesitation we all chimed in—Of course! It's only right! We all wanted his name on our stuff anyway. We were proud to be associated with him. He seemed so sweet that day.

**Another Fond Memory.** It happened during a Sleep Laboratory X-mas party. We were all in the library when my coat was stolen! It was a brand new purple, long, down coat. Perfect for Chicago. It had been expensive too! My office was in the back of the laboratory by the fire escape. The coat was hanging on a hook in back of the door. We all realized later how easy it must have been to open that door and walk outside with the coat. AI gave me money to buy a new coat. His own personal money! I bought a new coat which actually wasn't as good as the stolen one—I couldn't find the same one again. But somehow the new purple coat meant a lot more to me.

**Does It Sleep?** Don Bliwise and I spotted a huge cockroach in the Sleep Lab. It must have been about 3 inches long. I've heard them called June bugs—but why? This looked exactly like a roach, but bigger. Like two little kids, Don and I captured it and put it in a jar with a screw-on lid. We showed it to AI, who glanced up from his reading ever so briefly and said nonchalantly, "So?..... Why don't you implant it?"



*We spotted a huge cockroach in the sleep Lab, we showed it to AI, who glanced up from his reading ever so briefly and said nonchalantly, "So?..... Why don't you implant it?"*



by  
David Foulkes  
Atlanta, Georgia, U.S.A.

### THE PSYCHOLOGY AND PHYSIOLOGY OF SLEEP: CAREER CONTRIBUTIONS BY ALLAN RECHTSCHAFFEN

Because the discovery of REM sleep was made at the University of Chicago, and because the pioneering follow-up work by Bill Dement and associates was done at this same University, Chicago was the original "capital" of the new sleep-dream research movement. By 1960, however, Eugene Aserinsky, Nathaniel Kleitman, and Bill Dement had all left Chicago. That the University, and the city, retained its pride of place in the world of basic research on sleep and dreams for the next three and a half decades was entirely attributable to one person: Allan Rechtschaffen.



*AI transformed himself into the Renaissance Man of the field.*



Originally trained as a clinical psychologist, AI Rechtschaffen, like many others in the early days of our field, "happened" upon sleep-laboratory research. But what a union this happening soon became! In 1961, he organized the first conference solely devoted to the new sleep research methods, and became the co-founder of, and guiding force behind, the original APSS—the Association for the Psychophysiological Study of Sleep. As APSS meetings began to reveal an explosion of findings by French and Italian investigators on basic sleep mechanisms in experimental animals, AI immersed himself in these findings and mastered the methods that generated them. He transformed himself into *the* Renaissance Man of the field; the neurophysiology and pharmacology of sleep took their places as areas to which AI made contributions equally significant and equally exacting as those he had made, and continued to make, at the level of sleep behavior and dream phenomenology.

A common theme in AI's work in the many diverse areas to which he made significant contributions was his focus on methodological and epistemological issues. In dream psychology, the results are now-classic papers on dream reports vs. dream experiences, and dream consciousness and the mind-body problem. No one else, I think, has ever considered the methodological foundations of research on states of consciousness as thoroughly and clearly as AI did, most notably in a contribution to a regrettably obscure volume published by the

Drug Abuse Council in 1975. As he pointed out, many people profess to want to "learn" about states of consciousness, but few realize how difficult it is to develop the reliable scientific knowledge that constitutes the only genuine learning of them.

In basic sleep research, AI played a major role in developing the standard manual for hand scoring of human sleep stages and in devising computer scoring of sleep stages in animals. The perfect union of AI's rigorous methodological concerns with his far-reaching substantive ones is evident in the elegant methods of his experiments on total sleep deprivation and REM sleep deprivation in the rat. This research brought us as close as nature apparently now is prepared to permit, to answers to the most basic questions of our field: Why is there sleep? and Why is there REM sleep? But AI's other research attacks on questions of sleep function were as methodologically precise as his deprivation studies. His early evaluations of the serotonin and norepinephrine hypotheses of sleep mechanisms are gems of lucid and logical analysis. His original studies and his analyses with Harold Zepelin of the phylogeny of sleep are the standards of the comparative approach to sleep function.

Sleep disorders, and sleep in other disorders, are those greatly oversubscribed entries in the (Rechtschaffen-derived) category system of the Brain Information Service bibliographies. AI was among the first to study narcolepsy, hypersomnia, and somnolence. The work of his doctoral student, Monroe, on subjectively-described good and poor sleep, opened the floodgates to research on insomnia, addressing the question, is the hallucinating schizophrenic a waking (REM) dreamer? In research conducted in Denmark, AI disproved that ancient contention. But AI's interests in sleep disorders and in disordered sleep were always subservient to his more general basic-research interest in sleep mechanisms and functions and he therefore did not succumb to any possible temptation to become a "specialist" in sleep disorders.

Of particular interest to me, of course, is AI's body of research on dreaming (and, unlike just about every other researcher from the early days of APSS, he retained a keen and career-long interest in dreaming). Here, the methodological slant and the crisp and logical analysis that worked so well elsewhere were especially welcome. AI became the spiritual godfather of factor analyses and rating scales and ways of isolation and measuring dimensions in reports of dream experience. He also led and aptly summarized research attempting to correlate dream variables with concurrent physiological events. Although adept at research on experimental manipulations of dream content, he was equally fascinated by simple phenomenological



*AI's rigorous methodological concerns with his far-reaching substantive ones is evident in the elegant methods of his experiments.*





*He is a man of far-ranging interests and great imagination—he focuses on genuinely significant issues and operates almost as a machine of logical analysis.*



descriptions of what dreaming is and of how the dreams of a single night are interrelated. His intricate methodology gave us new vistas on the sensory phenomenology of dreaming: studies, for example, of the eyes-open dreamer and of the photographic properties of dream imagery. And, the *Sleep* paper on the single-mindedness and isolation of dreaming has a magisterial quality unrivaled in the history of dream research.

Well, all and good, this is a little bit of the man's works. But what about the man? What was he like to work with? What kind of guy is he? His works suggest, correctly, that he is a man of far-ranging interests and great imagination that are kept under the discipline of single-minded (!) focus on genuinely significant issues and of a mind that operates almost as a machine of logical analysis. Passionately devoted to science, he is as dispassionate and as cool an observer of research findings and claims (his own and that of others) as ever existed. Not a bit of a purveyor himself, he has the best bullshit detectors in the business.



*He has the best bullshit detectors in the business...To know AI well is an inherently humbling experience.*



As you would imagine, these qualities, exemplary in science, prove a little risky in life for the rest of us, with our own special games to play and our own inadequacies. Thus, for mere mortals, continuing daily encounters with AI could sometimes become intense and prickly. AI is the sort of guy who engenders perpetual, wishful rumors of a "mellowing" process. Yet, everyone I know who passed through AI's laboratory over the years not only respects his work but also reveres him as a person. He is a marvelous teacher, not by blah-blah-blah, but by a living, shining example. He cuts through all of the crap, and gets right to the heart of any issue or concern. He holds you to high standards, but holds himself to the highest. He is passionately rational and reasonable. To know AI well is an inherently humbling experience. Without his constant presence, neither Chicago, nor

the sleep-and-dream field, will ever seem the same.

Nathaniel Kleitman clearly was the major figure in sleep research in the first half of this closing century of the millennium, but the 1963 revision of his classic tome did not show a full understanding of the significance of the discovery of REM sleep made in his own laboratory. However, this did not leave the University of Chicago bereft of claims to further historic significance. By way of training at City College of New York and Northwestern University, and by your own guts and energy and intelligence, you, Allan Rechtschaffen, with your lifetime scientific career as a faculty member at the University of Chicago, became the major presence of late-20th-century, and therefore of our millennial understanding of sleep and dreams. Thanks, AI, we are forever in your debt.



by  
Peter J. Hauri, Ph.D.  
Sleep Disorders Clinic  
Mayo Clinic  
Rochester, Minnesota, U.S.A.

**W**hen I came to the University of Chicago in 1961 as a foreign student, I needed a job. Only two were open: one in opinion research, one in sleep. I barely knew one from the other, but the guy in sleep was called "Rechtschaffen," which in German means "solid, well-built". I hoped that he might be German and that we could speak our native language. Little did I know that he was Jewish and from Brooklyn!



*"Rechtschaffen," in German means "solid, well-built".*



When I went for the interview, AI Rechtschaffen was bent over the old Grass Model 3, resoldering wires. I had recently finished a course in the Swiss Army Signal Corps on equipment maintenance and 10 minutes into the interview, I started helping him with the resoldering job. That convinced him that I should be hired! So you see, I am a sleep clinician because AI Rechtschaffen has a German name and I know how to solder!

In a much larger sense, of course, I remained in the area of sleep because AI was a superb role model for us graduate students, showing us his hard work, devotion, honesty, and excitement for this field. I could not have found a better teacher and friend at the University of Chicago and he was strongly involved in molding my career.



by  
Michel Jouvet, M.D.  
Laboratoire de Médecine  
Expérimentale  
Université Claude Bernard  
Lyon, France

**D**ear Allan,  
Don't be afraid to retire. I did it last year. Since this crossing, I feel younger every month, but for my back pain. This is why I am going to a Spa near Venice (Italy). I spend my mornings in a very hot mud bath, and the afternoon in Venice where I can look at beautiful girls, while drinking white wine.

I am glad to exchange with you some common memories which come to my mind. Possibly, the first one is from Chicago where we first met at the APSS—1961 or 1962—I still remember your very warm reception and the visit to Kleitman's laboratory. Then, of course, there are a lot of memories from your stay in Lyons (1962-1963). Your habit of sleeping at any time (mostly in the afternoon, usually on a table), your love for the mushrooms with cream in the "Vivarais Restaurant" (it still exists but there are no more mushrooms!), your taste for good wines and beautiful girls, and our endless discussions concerning "the function of Paradoxical Sleep".



*Possibly in 200 years, scientists will refer to your lifetime experiments as the XX<sup>th</sup> Century studies on sleep*



If I remember well, we even wrote some grants to the NIH about the Neurochemistry of Sleep (mostly concerning the effects of sodium and potassium!). This is why Seymour Ketty came later to my laboratory to discuss this grant. Finally, of course, I did not get any money...

There are so many memories from so many congresses, in so many cities, that I mix them like in some dreams. But I will always remember your superb work with REM deprivation in the rat. Nobody will ever do it again. It will remain as a classical work. Possibly in 200 years (if there is still research about sleep), scientists will refer to your lifetime experiments as the XX<sup>th</sup> Century experiment on sleep (and as a big mystery).

I am glad to have this opportunity to send you my warmest regards for your retirement and I wish you a pleasant time, surrounded by your lovely wife and children. You should write a book about your life with the rats and with the dreamers.

*Your friend forever, Michel Jouvet*



by  
Gary Richardson, M.D.  
Department of Medicine  
Miriam Hospital  
Providence, Rhode Island, U.S.A.

I first met AI Rechtschaffen at Stanford in 1976. I was an undergraduate research assistant in Bill Dement's laboratory, and AI was a site visitor for a grant application. I do not now recall the focus of this particular grant application (there were so many), nor the names of any of the other site visitors. I remember AI because of the off-stage introduction we were given, "Be careful of AI Rechtschaffen; he's nobody's fool." Aside



*"Be careful of AI Rechtschaffen; he's nobody's fool."*



from the questions this raised about what exactly we were attempting with the grant proposal, the introduction forever defined my view of AI. In the years I have known him, I have come to think of AI as our arbiter, our field's judge and jury, distinguishing with remarkable speed and loud, unambiguous pronouncements, between good science and all the rest. Above and beyond his storied research contributions to so many different aspects of sleep research, AI is most prominently the guidepost we all use to tell if we're on the right track, if we've got a clue. I can recall many meetings in which I have sat in the same audience with AI and listened to good science and bad. Presentation of good science is, of course, its own reward. The other presentations at least have the delicious compensation of watching AI grow restless, then agitated, then angry, then verbal, leaving scores of people staring at their shoes saying to themselves, "I wish I'd said that", but not daring to glance at the pillar of salt behind the lectern. Of course, I for one refuse to present if AI is in the room. Just to be safe.

There is certainly more to AI than the "Grouchy old uncle of sleep" award he graciously accepted at the APSS meeting a few years ago. As a teacher and a mentor, he is without peer in our



*AI is most prominently the guidepost we all use to tell if we're on the right track*



field. Most would probably agree that Al's greatest legacy is the extraordinary list of former students, graduate students, and post-doctoral fellows who have spent time in Al's laboratory and are now making independent scientific contributions to our field. As it is, it now seems like "APSS" and the "Al Rechtschaffen Alumni meeting" are redundant terms, and the number is still growing. But there are just as many who, like me, never spent formal time in his laboratory, yet still consider Al our mentor. Throughout my career, I have availed myself shamelessly of Al's extraordinary generosity with his time and intellect. Whenever I needed advice or had a question, I always found him a patient and knowledgeable teacher. From abnormal eye movements with fluoxetine, to the effects of thyroid hormone on sleep, it was difficult to find a topic Al didn't understand at a basic, core level; he either knew the literature or, more likely, had done the study himself (I found it useful to consult a copy of his Curriculum Vitae before calling to avoid undue embarrassment).

*It is difficult to find a topic Al doesn't understand at a basic, core level*

My favorite story about Al-as-consultant occurred while I was in Boston. I was in a conference room with colleagues when a dispute arose about the results of the Rechtschaffen sleep deprivation studies. Much less sure of the correct answer than I pretended to be, I offered to call Al and find out. After consulting my watch to make sure it wasn't nap time in Chicago, I called and Al answered the phone. I asked the question, got the answer (the one I wanted), and hung up. I looked up to find my colleagues staring at me as if I had returned with the answer on a stone tablet.

The foundation of teaching is learning, and like all great scientists, Al is a living lesson in intellectual curiosity. If there is something he wants to know or doesn't understand, he asks. And his only rule about sources is that they have to know the answer. At the annual meeting of the National Multi-Site Training Program in Basic Sleep Research run by Michael Chase at Lake Arrowhead, I have watched both students and faculty find themselves in the heady position of Al's teacher. In front of a poster, or in a corner after a lecture, Al will start asking questions. Of course, if you don't know the answer, you had better say so right up front. Otherwise, it's not much fun. My own favorite experience as Al's teacher came at the Bahamas meeting of the World Federation of Sleep Research Societies. We were in a

*Al is a living lesson in intellectual curiosity.*

hotel room with a group of people watching a basketball game, when the conversation turned to a particularly mathematical presentation earlier that day on human circadian physiology. Al said, "Now there's something I don't quite understand...", picked up a pad of hotel note paper, pulled up a chair and started asking questions. Some time later we had used up all the paper, I had spilled all I knew, said "I don't know" about three thousand times, and missed the entire game. Those who know Al know that it's not particularly surprising that he would rather talk science than watch basketball, presuming, of course, that the Bulls aren't playing.

Arguably, Al's greatest talent is marrying well. It is impossible to think of Al without also thinking of Karen Rechtschaffen. She's far more interesting than he is (Al knows this and accepts it gracefully), and given a choice between whiling away the hours with mai-tais and Karen on the beach at Maui or the Bahamas, and accompanying Al back to the scientific sessions...well, I missed a lot of science. Al and Karen are a team in the best sense of that word, and it often seems that their goal in life is the care and nurturing of sleep scientists. Many times I have imposed upon their hospitality in Chicago, and now, just when I've finally figured out how to navigate the one way streets of Hyde Park and find their house on the first try, they move to Arizona. Of course, with this defection, Chicago loses its best restaurant and its best Bed & Breakfast.

*Arguably, Al's greatest talent is marrying well—Karen Rechtschaffen is far more interesting than he is (Al knows this and accepts it gracefully)...*

One last story: With the Boston meeting of the APSS, we finally had a chance to repay some of the Rechtschaffen hospitality. We invited Karen and Al over for dinner. In the days leading up to the event, I became increasingly nervous. Not about Al, about Karen. What would we serve the woman who had prepared so many effortlessly fabulous meals? We finally settled on lasagna from a take out deli, surreptitiously transferred to our own baking dishes. (We burned it anyway.) The one deft move was that instead of inviting other sleep people, we asked our neighbors, including a woman who runs a high-school day care project that had caught Karen's attention. They immediately formed a little mutual admiration society, while her husband wanted Al to tell about growing up in "the neighborhood". We talked for hours and sleep never came up. Everyone had a good time, particularly my kids. They have trouble with the name (who doesn't?), but they still talk about the night "your friend the scientist" came to dinner.

That's probably a good place to stop, because I'm not sure I could say it any better. Al Rechtschaffen is my friend, the scientist.



by  
Thomas Roth, Ph.D.  
Sleep Disorders and  
Research Center  
Henry Ford Hospital  
Detroit, Michigan, U.S.A.

My introduction to sleep research and to Al Rechtschaffen both occurred in 1970 at the APSS meeting in Santa Fe, New Mexico. At that meeting, the attendees felt that they should deviate from the planned program and allow "Al" to present some of the new work of his laboratory on PIPs. My next interaction with Al occurred at the Lake Minneswaska meeting when Al came over to one of my fellow graduate students and told him that he had been the reviewer of a paper of his and rejected it. However, he went on, there were some good ideas in the paper and he would be pleased to discuss it over lunch. Al needed to reject the paper because it did not meet the standards, but he also needed to help a fellow sleep scientist. While serving on the program committee, he not only scored abstracts like everyone else, he also rewrote them to make them better. Al Rechtschaffen is an individual whose research can command the attention of an entire field, but who has the time to have lunch with graduate students from other people's laboratories and rewrite abstracts for junior scientists.

*Al's greatest contribution to the sleep field is to keep us focused on the important questions in our field. What is the function of sleep?*

My introductions to the breadth of Al's science came through the literature. As a young researcher, I found that every time I did a literature search on a new topic, there was always a key paper authored by Al. After years of reading his work, I decided to stop reading the reprints and just talk to him directly. Al has, over the years, been the single most important influence on my research. In interacting with Al, one cannot help but be persuaded by the importance of rigorous methodology and clear unbiased thinking. The field of sleep will never again have Al as a scientist who has the breadth and clarity of understanding about sleep physiology. I feel fortunate in that my personal relationship with Al will allow me to take advantage of his intellect and friendship even after his retirement. It is very easy to take advantage of Al because of his incredible generosity.

Aside from his direct scientific contributions, Al has produced more graduate students than any other sleep researcher. His students are EEG researchers, molecular biologists, circadian rhythm researchers, and directors of sleep clinics. What they learned from Al was mental discipline. However, Al's greatest

contribution to the sleep field was to keep us focused on the important questions in our field. What is the function of sleep? What are the basic control mechanisms of REM and NREM sleep? For Al it was never electrophysiology, neurochemistry or

*Al has provided us is a standard by which all future sleep researchers will be measured..*

molecular biology. The issue is the rigor of your research and the question being asked, not the technique being used. His goal was not to be a basic researcher, clinical researcher, or a molecular biologist. It was to discover the function of sleep. As he had only one question, Al had only one grant. It must be recognized that it was successfully renewed, including a Merit Award, across his entire scientific career. By his own evaluation, Al concluded that he has not discovered the primary function of sleep. However, what Al has provided us is a standard by which all future sleep researchers will be measured.

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#### About Elio Lugaresi, cont. from page 26

in the *Archives Italiennes de Biologie*. From that time on, Elio and I were always in touch, and in 1972 he invited me again to attend a now historical symposium he organized on "Hypersomnia with Periodic Breathing" in Rimini. Since then, we have worked together on many occasions and I like to recall the workshop on "Sleep and the Neurovegetative System" at the ESRS Congress held in Montpellier in 1976 and, in particular, the APSS 4th International Congress held in Bologna in 1983.

Early, I was impressed by Elio's appreciation of physiological paradigms and particularly of the integrative views of Walter Rudolf Hess, who had started me on sleep research. This consonance is always a solid foundation for our discussions about the physiopathology of sleep and the underlying mechanisms in autonomic, cardiovascular and breathing functions. Elio is open-minded in accepting suggestions, but firm in defending his views when based on experimental evidence.▶

*Elio is not only a scientist but also a generous man candidly loving all joys of life and friendship.*



The personality of a leader is imprinted in his school. This is another admirable achievement of Elio's since he has raised to international excellence a great number of sleep researchers. Also, the collaboration with my group has had positive results with the organization of several courses on sleep physiology and pathology. The last product of such fruitful collaboration is the volume on *Somatic and Autonomic Regulation in Sleep: Physiological and Clinical Aspects* published by Springer in 1997.

Elio is a straightforward man and, thus, not prone to academic maneuvers. The national and international recognition he has obtained is due only to his merits. His achievements are so well known that a friend feels embarrassed insisting on their importance. I wish, however, to stress that his sharp eye in seeing and his will in pursuing new lines of research make him both a pioneer and a systematic researcher—a combination of perspective and judgment which is only rarely encountered.

I must confess that in writing these lines today I was almost stricken by Dante's sunset melancholy: "Era già l'ora che volge il disio...". But, I have driven it out of my head after raising the horn of the ringing phone and hearing Elio saying "Pier Luigi, I wish to invite you to give a lecture at the course on sleep physiopathology I am organizing this year. Remember that this will also be an occasion to enjoy good food and wine together with our colleagues". This is Elio, not only a scientist but also a generous man candidly loving all joys of life and friendship.



by  
Markku Partinen, M.D., Ph.D.  
Haaga Neurological  
Research Centre  
Helsinki, Finland

## GOOD TIMES IN BOLOGNA

My first visit to Professor Lugaresi's territory was in May 1982, when he organized a Workshop on Epidemiology and the Natural History of Sleep Disorders in Milano Marittima, on the Adriatic coast. I had already been working for some years with him on snoring and other sleep disorders related to cardiovascular diseases as well as with epidemiological issues of sleep research. The meeting in Milano Marittima was a success, as were all the other meetings and congresses that Professor Lugaresi organized.

I have good memories from the Fall of 1987 when I spent some four months at the Clinica Neurologica. I had a room at the Clinica, and the nurses were very helpful. They barely spoke any English but somehow we understood each other very well. I enjoyed the way the staff worked. The clinical meetings were excellent. I then began to understand why Professor Lugaresi has found so many new syndromes. He is really an excellent clinician. But he is also an expert in wines and good food. Dining out with him and his wife was a joy. He never read menus. He always spoke directly with the patron or the chef de cuisine, such as "Patron, what is fresh today—bring us the best that you have".

My best memories are from one weekend that Elio, his wife, Dr. Montagna and I spent at Professor Lugaresi's villa in Milano



Professor Lugaresi is really an excellent clinician. But he is also an expert in wines and good food.



Marittima. After an excellent Saturday night dinner, he asked us (Montagna and me) if we liked biking; we both answered, yes. Early on the following sunny Sunday morning we went out to the garden. He opened the doors to the garage and there we saw many, many bikes. All of the bikes were in excellent condition and shining in the sun. He asked me what bike I would like to take. Because I could not decide he said "why don't you take this old black Bianchi". It was the finest bike I have ever ridden. As we pedaled in the pine forest, I felt as if I was in one of Fellini's movies. At the seaside we stopped and walked to the sand. We sat down and Professor Lugaresi ordered cups of espresso, as we watched the sunset. It was wonderful. Thank you Elio, for all the good memories and for your friendship.



by  
Dr. Antonio Vela Bueno  
Department of Psychiatry  
Universidad Autonoma  
Madrid, Spain

I first met Professor Elio Lugaresi in the early 1970's when, as a young physician, I went to the University of Bologna to continue my postgraduate education. I immediately realized that I had found in him an excellent role model. His work and, as far as I am concerned, his generosity were very clear to me. During the time I worked with Elio I had the opportunity to experience and share the enthusiastic atmosphere surrounding the translation into the scientific realm of the sagacious clinical observations he and his colleagues were making. To emphasize the importance of Lugaresi's many research contributions to the field of sleep disorders medicine seems unnecessary. Everyone acquainted with the scientific literature knows his seminal studies on snoring and sleep apnea, abnormal movements, epilepsy's and Fatal Familial Insomnia, to mention just a few.

I share with Elio Lugaresi some interests other than medicine and science. On a rather "dionysian" side, the good cuisine (especially seafood)—do not forget he is Romagnolo and lives in Bologna. On a more "apollinian" side, we shared the reading of some novelists and thinkers. As one of them, Nietzsche, would put it, Elio Lugaresi is a virtuous man because he has developed his many talents.

Grazie tante professore, for the long lasting beneficial influence you have had on sleep disorders medicine as well as on my career.

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## About Michel Jouvet, cont. from page 16

not sleep, he would get out of bed to work and rework these constructs. He conceived of the receptacles as sequentially receiving and sometimes reciprocally emptying neurotransmitters from and to one another, a schema responsible for turning on and sustaining the progression of stages of sleep and waking that we know so well. Here was the young Jouvet, who with his students had already made stunning and signal discoveries, still obsessed, too excited to sleep, trying through the nights to figure out how the cholinergic and monoaminergic sequences worked, striving to figure out the neurochemical triggering of the sleep states "once and for all". He was, in fact, charting out what was a first "wet (but structure-related) neurophysiology" of sleep. Michel Jouvet never stopped trying to "get it right". He has pioneered and provoked us to where we are now. Thank you Michel for sharing your genius with us.

by  
Markus H. Schmidt, M.D., Ph.D.  
Riverside Methodist Hospital  
Columbus, Ohio, U.S.A.

Michel Jouvet is undoubtedly one of the most remarkable persons that I have ever encountered. When I look back at my four years of research spent in his laboratory, I realize that the scientific knowledge gained working with him is only a portion of my complete learning experience. What Jouvet taught me cannot be reduced simply to didactic teaching, but also involved teaching by his own example, by simply being who he is. Jouvet has a unique balance between his love of science and his love of philosophy and culture. He has a true passion for his work, yet, as with many Frenchmen, he cultivates a passion for food, wine and life in general. I have always been struck by his enthusiasm, subtle humor and charisma. As a perpetual explorer, he never fails to amaze me with his plethora of new ideas and concepts, or his remarkable ability to synthesize vast amounts of information.



...Jouvet has a unique balance between his love of science and his love of philosophy and culture...a passion for food, wine and life in general.



When I first arrived in Jouvet's laboratory in 1991, I was amazed by its sheer size and the number of researchers working on the neurophysiology of sleep. In one long corridor, Jouvet had amassed neuroanatomists, electrophysiologists, neuropharmacologists, microbiologists, biochemists and, the workhorse of the study of sleep, physiologists. He had created one of the only departments of neuroscience dedicated to the study of sleep and

wakefulness. For me, it was a student's dream to have such a wealth of information no more than a few doors away.

Jouvet's ability to unite such a diverse group of people with various ideas, interests and theories is a testament to his extraordinary character. Although some followed closely his interests, many others diversified and developed their own models or paradigms. I believe part of Jouvet's success in maintaining such a laboratory was that he encouraged independent thinking, allowing his researchers to formulate their own ideas. Indeed, one of the greatest concepts he conveyed to me as a student was that one should always challenge current theories and be leery of existing dogma. On several occasions, I remember Jouvet telling me: "Never believe what we have taught you." This is perhaps one of the greatest lessons a mentor can give to a student in the world of scientific research.



by  
Mircea Steriade, M.D., Ph.D.  
Department de Physiologie  
Université Laval  
Québec, Canada

Besides some experiments I performed in Michel's laboratory during a short period of time in the early 1980's, I met him only occasionally, during symposia, conferences, while visiting Japanese shrines in Kyoto, and during memorable blowouts at restaurants close to his *manoir* outside Lyon, accompanied by many bottles of white and red wine (I suspect him of trying to check my resistance to this sport, and I always remained well behind his capacities). More importantly, as I never miss the opportunity to embarrass my colleagues with the passion I nourish for my 8-year old daughter Claude, I shared with him his passion for his boy Frédéric.



...Michel described all key phenomena we are continuously using to distinguish REM sleep.



In addition to these private affairs, I continuously thought of Michel's scientific achievements because, surprisingly, despite his seminal discovery of the REM-sleep oscillator within the brainstem core, and despite the fact that during the late 1950's he described all key phenomena we are continuously using to distinguish this state, and despite the series of hypotheses of monoamine's implication in the wake-sleep cycle that pushed people to work, he was not awarded the prize. He deserved and obtained better: our love and admiration.

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# Photo Gallery



Elio Lugaresi eating crustaceans in Carcassonne, France. (photo and quote from Pier Luigi Parmeggiani)



Henri Gastaut and Elio Lugaresi at the Xth European EEG Meeting in Bologna. Most of Elio's major decisions have been made while sitting around a dining table. (photo and quote from Giorgio Coccagna)

At Rechtschaffen representing the press at a mock sleep trial at the Sleep Training Workshop of the Multi-Site Training Program for Basic Sleep Research. (photo and quote from Michael Chase)



From the left: Shiro Fujita, Markku Partinen, Elio Lugaresi, Colin Sullivan, and Jean Krieger. (photo from Markku Partinen)



Michel Jouvet and his dog, 1995. (photo and quote from Vladimir M. Kovalzon)



Michel Jouvet at the APSS Meeting, Stanford, California, 1978. (photo from Michael Chase)



A barefoot Al Rechtschaffen hard at work on a stone bench outside the Coliseum in Rome, Italy. (photo and quote from Michael Chase)



Michel Jouvet addresses the attendees during the final banquet at the First International Congress of the WFSRS, Cannes, France, 1991. (photo and quote from Michael Chase)



Elio Lugaresi (middle) with Pier Luigi Parmeggiani and Pierluigi Gambetti at the First Fatal Familial Insomnia Symposium held in Bologna, May, 1992. (photo and quote from Elio Lugaresi)



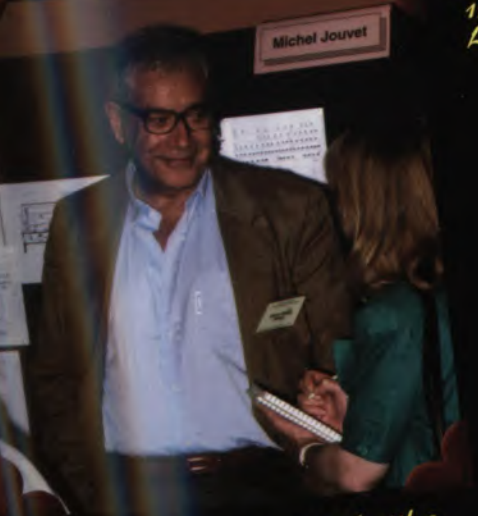
Elio Lugaresi with Giorgio Coccagna at the International Meeting on Sleep Abnormalities in Man held in Bologna, May, 1967. (photo and quote from Elio Lugaresi)



Elio Lugaresi with Henri Gastaut at the International Symposium on Epileptic Syndromes held in Bologna, September, 1983. (photo and quote from Elio Lugaresi)



At Rechtschaffen doing intensive on-the-sleep research with Bill Dement. (photo and quote from Michael Chase)

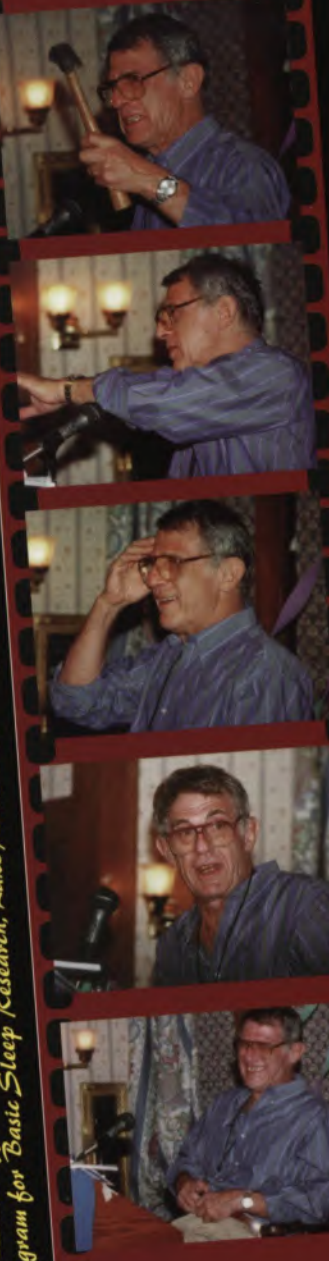


Michel Jouvet discusses his research with a trainee at the WFSRS Meeting on the "Cellular Consequences of Sleep", Maui, Hawaii, 1993. (photo and quote from Michael Chase)



Tom Roth, Michael Chase, Al Rechtschaffen, and Gary Richardson Second International Congress of the World Federation of Sleep Societies in Nassau, September, 1995. (photo from Michael Chase)

Al Rechtschaffen serving as judge of a page of a book at the Second International Congress of The World Federation of Sleep Research Societies in Nassau, September, 1995. (photos and quote from Michael Chase)



Elio Lugaresi at 26 returning from a hunting expedition for wild duck. (photo and quote from Elio Lugaresi)



Elio Lugaresi at 30 in Marseilles while studying with Professor Gastaut. (photo and quote from Elio Lugaresi)



Mature Elio Lugaresi smiling. (photo and quote from Pier Luigi Parmeggiani)



Elio Lugaresi and Adrian Morrison at the Ontra-Science Research Foundation Symposium, Santa Monica, California, 1981. (photo from Adrian Morrison)



1963



1993



Al Rechtschaffen and Joëlle Adrien at the WFSRS meeting on the "Cellular Consequences of Sleep", Maui, Hawaii, 1993. (photo and quote from Michael Chase)



Elio Lugaresi in his younger days working in his laboratory. (photo and quote from Pier Luigi Parmeggiani)



Elio Lugaresi at 26 walking in Bologna. (photo and quote from Elio Lugaresi)



Michel (Jouvet (right) visiting René Drucker-Colin in Mexico, in the 80's. (photo and quote from René Drucker-Colin)



A discussion with Al Rechtschaffen at the WFSRS Meeting on the "Cellular Consequences of Sleep", Maui, Hawaii, 1993. (photo and quote from Michael Chase)



Al Rechtschaffen telling Michael Chase what is what and what is not at the Sleep Training Workshop for the Multi-Site Training Program for Basic Sleep Research, Lake Arrowhead, California, 1988. (photo and quote from Michael Chase)

An active Michel Jouvet arguing a point at The Second International Congress of The World Federation of Sleep Research Societies in Nassau, September, 1995. (photos and quote from Michael Chase)

