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MEMORIES OF FAMOUS NEUROPSYCHOLOGISTS

The Discovery of REM Sleep*

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ABSTRACT

The impetus to pursue the study of ocular motility in sleeping adults was derived from a previous study conducted by the author on infants. He noted through visual observation alone that there was an approximate twenty minute interlude of complete ocular quiescence during each hour of sleep. This period of quiescence was termed 'No Eye Movement Period' or 'N.E.M. Period', and it was the intent of the author to ascertain what effect age would have on the distribution of N.E.M. periods during sleep. In the latter part of 1951, the first continuous all-night recording of ocular motility in sleep using a combined EEG and EOG technique was conducted on the author's eight year old son. Instead of N.E.M. Periods, what he found were approximately twenty minute periods of vigorous ocular activity including saccadic-like eye movements. Although he ultimately termed these epochs as 'REM Periods', his initial intent was to name them 'Jerky Eye Movement Periods' or 'JEM Periods'. Ironically, some three decades later he found that a mathematical measure of jerkiness was a better discriminator than velocity in distinguishing REMs from waking saccades. Kleitman, who was the thesis advisor, played the role of skeptic during the REM discovery and demanded unassailable proof of the existence of REM. His feelings had to be ambivalent inasmuch as the REM state, with its concurrent activated cerebral cortex, negated his own theory that sleep was a completely passive phenomenon.

Keywords: Sleep, dreaming, REM, consciousness, EEG, eye movements.

The door opened slightly. A man with a grey head, a grey complexion and a grey smock peered through the crack and enquired abruptly, 'Yes?'. I responded rather tremulously, 'My name is Aserinsky. I am a graduate student and I wonder if I may speak to you about the possibility of your being my advisor.' This was my first personal contact with Nathaniel Kleitman and the beginning of a series of episodes that led to the discovery of 'rapid eye movements' and REM sleep.

There was no joy in this initial encounter for either of us. For my part, I recognized Kleitman as the most distinguished sleep researcher in the world. Unfortunately, sleep was perhaps the least desirable of the scientific areas I wished to

pursue. My interest was in organ physiology but essentially almost all the faculty was engaged in cellular physiology, leaving Kleitman by default as my choice for a sponsor. For his part, Kleitman could not have been elated with the prospect of my apprenticeship, particularly after scanning my biography which revealed a motley background. First, I was a social science major, then a Spanish language major, a pre-medical student and ultimately a dental student. Worse yet, my work experience for the six years prior to arriving at the University of Chicago was totally irrelevant, including a stint in the army as a high explosives handler followed by civilian jobs as a social worker and as a supervisor in the Department of Employment Security.

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Of course, neither Kleitman nor I could operate independently of the labor market. Whereas I was not exhilarated to enter a field which was dominated by such soft-science types as psychologists, neither was there a line-up of physiology students clamoring to engage in sleep studies. As I learned later in my career when I was in the position of acquiring graduate students, a major criterion for the selection was that the candidate have a heartbeat. Apparently, I had passed the crucial test with Kleitman for in short order we were discussing my future project.

After satisfying himself that my mind was a clean slate devoid of any self-generated ideas, Kleitman related a story. He had read in Nature an article by a physicist named Lawson (1950) who claimed that while riding in a railroad compartment he was able to distinguish sleep onset through observing the blinking rates of fellow passengers. What disturbed Kleitman was the allegation by Lawson that the blinking stopped abruptly with sleep onset rather than stopping gradually. With my nonscientific mentality, I was more perplexed that a highly regarded publication would allow such a casual observation to see the light of day. My assignment, nevertheless, was to use all my ingenuity to test the Lawson hypothesis. If Lawson could achieve recognition by simply glancing at two people, I envisioned immediate success and maybe even a paper in Nature. My sanguine hope for a hasty termination of this project was only slightly diminished when I was forewarned by Kleitman to bury myself into all the literature on blinking thereby becoming the premiere savant in that narrow field.

Kleitman's small office had an entrance to the hallway but there was another door which led into a medium-sized room which had as a principal feature a large, comfortable chair. This room, loosely called a laboratory, was ultimately where I was to monitor the sleep polygraph. The door between this room and Kleitman's office engraved a permanent image upon my mind because it was opened only on relatively rare occasions and represented a sort of Berlin Wall separating two worlds. On occasion, when it was absolutely essential to communicate with Kleitman, I would knock on the door and wait for a

slightly irritated, 'Yes?'. Only then would I enter, and even though years would elapse, the atmosphere was always formal and no warmer than our first meeting. There was no timetable, no progress reports and therefore no reason for me to knock on the door. Thus, it was my perception (or misjudgement) that contacts with Kleitman would be, for the most part, simply indicative of my inadequacy in coping with the simplest of research projects. I kept these meetings, therefore, to an absolute minimum.

For a number of weeks I constructed numerous mechanical contrivances to record lid movements on the smoked drum of a kymograph that had seen better days. None of this was fruitful, thereby leading to an early confession of failure. Kleitman then suggested that I might resort to observing infants who were subjects of a motility cycle study which was his own undertaking at that time. These babies slept in cribs in their respective homes while their body movements were automatically recorded by a device attached to the crib. The same subjects were available to me with the proviso that I limit the recording exclusively to observation – à la Lawson.

Despite a notational scheme to classify each twitter of the eyelids, and after an enormously long period devoted to this effort, I was finally forced to a painful conclusion. It was necessary for me to knock on the dreaded door again. The problem was that the conventional definition of blinking would not apply to much of the infant's ocular motility. If a blink is characterized by a rapid closure and opening of the eyes, can the movement of the lids be termed a true blink if the lids quiver while the eyes remain closed? Furthermore, since rate is an important element in any reflex, how was this to be ascertained through simple eyeballing procedures? Before embarrassing myself with Kleitman, I decided that I would propose a new research project as an alternative to the blinking problem.

As I explained the unfeasibility of continuing with the study of blinking in infants, Kleitman's visage, which was always serious, now seemed gloomier. There was neither reprimand nor criticism, but I knew that silence was not an accolade. Then I sprang my suggestion. Why limit

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the observations to reflex lid movements? Why not consider the absence or presence of any kind of lid movement, even one caused passively through eyeball motion? No restrictive operational definitions for blinking would be required, and all that was necessary was to note whether or not lid movements were present. Kleitman's response was affirmative and I escaped from the office relatively unscathed even though, in one swoop, I managed to abandon completely Kleitman's suggestion to test Lawson's hypothesis. However, I was now faced with a project that had a less clearly defined objective and which seemed about as exciting as warm milk.

I plodded along for months attempting to draw blood from this research turnip but, as I explained elsewhere (Aserinsky, 1977), painstaking, diligent exploration of minutiae will frequently lead to the 'golden manure' phenomenon whereby there is a rewarding result. At any rate, what I found was that in each hourly motility cycle of the infant there was an approximate period of twenty minutes of complete ocular quiescence, which I termed 'No Eye Movement Period' (Aserinsky, 1953a; Aserinsky & Kleitman, 1955b). This helped to confuse me later on as I tried to relate the No Eye Movement period in infants with the REM periods of adults, which have a similar duration and are also associated with relatively low muscle tone. Of more immediate relevance, based on the constancy of the length of the No Eye Movement period, I was able to predict to the mother of the infant almost the exact moment the baby would awaken - and perhaps more importantly, when I would be leaving the household. The mothers were invariably amazed at the accuracy of my prediction and equally pleased by my impending departure.

Contrary to many assertions (Birnholz, 1981), REM was not discovered in infants (Aserinsky, 1982). Inasmuch as REM was unknown to me at the time of the infant study, I had assumed that the lid motions following lid closure were an admixture of typical slow eye movements along with modified waking eye movements. Despite subsequent research by a host of investigators who claim that babies of all ages exhibit REMs, my original doubts may still have some validity

for very young infants. Just a few years ago, while at Marshall University (Figure 1), Joan Lynch and I (1986) reported specifically on the nature of eye movements in infants under the age of three months and found that motor characteristics of so-called 'REMs' were indistinguishable from those of waking saccades. This was in sharp contrast to the results obtained on adults wherein by using the same method of analysis, REMs were indeed different from waking eye movements (Aserinsky et al, 1985).

Following the termination of the lengthy baby project, Kleitman suggested that I embark on a doctoral program, bypassing the Master's degree thesis. When the doctoral committee comprising all the departmental faculty noted that I had no degree whatsoever they were non-plussed as, one member put it sarcastically, I was petitioning to leap directly from high school to the Ph.D. degree. But I knew that, despite the absence of a degree, I had amassed sufficient college credits to challenge a Guinness world record and that by bypassing the Bachelor's and Master's degrees I was actually placing myself in a perilous position. An unrewarding research program would continue to leave me without any degree, and I would be a perennial (and senescent) student. What lay ahead was a gamble - the odds being that, since no one had really carefully examined the eyes of an adult throughout a full night's sleep, I would find something. Of course, the importance of that find would determine whether or not I would win the gamble.

Well, what was I looking for in the upcoming research on adults? Specifically, my intention was to scrutinize the eye movements for amplitude, frequency and consistency in pattern relative to the then-accepted EEG classification of sleep stages. I had good reason to hope, if not expect, that an examination of eye movements would yield some unrevealed aspect of brain function, simply by virtue of the inordinately large representation of the eye and of the extraocular muscles in the brain cortex. Strangely enough, because of my prior study of infant sleep, I had intended to search for distinctly unique 20-minute periods of sleep and to associate them with other physiological variables.

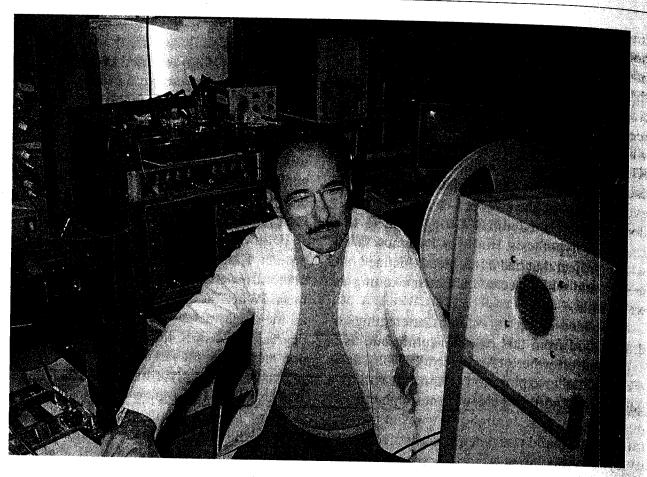


Fig. 1. Eugene Aserinsky.

These epochs, I thought, would be the adult equivalent of the 20-minute periods of ocular quiescence (No Eye Movement periods) I had seen in infants.

I worked under conditions of total independence in which I could pursue whatever direction I pleased with whatever equipment I could scrounge. This 'sink or swim' atmosphere led me to a pragmatic approach towards research, whereby the ultimate objective was being defined and redefined in accordance with the experimental tools which became available. It was an example of the inversion of an adage: 'Invention (tool) is the mother of necessity.' There were no grants to fund this activity, but I ultimately prevailed upon Kleitman to locate some electronic gear to replace the strings and smoked paper. He informed me of the existence of an old Offner Dynograph stored in the bowels of Abbott Hall (in which the Department of Physiology was located), and I was now in business.

I had read the few papers dealing with the corneo-retinal potential and had decided that an adaptation of the procedure showed promise for sleep recording. Developing the technique for applying the electrodes for long-term recording and for calibrating eye movements in darkness and in light was time consuming but not particularly challenging. But analysis of the eye channel tracings was another matter; in fact, at one point I was preparing to abandon the entire project along with any prospect for an academic career.

The tribulations of eye movement recording were exacerbated by the unreliability of the Offner dynograph which spontaneously spewed forth pen movements even when no subject was attached to the instrument. Funds for repairs were not available but Kleitman put an academic gloss to this matter by subscribing to the philosophy that an understanding of the inner mechanism of any tool used by the researcher should be part of his intellectual repertoire. It was thus

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incumbent upon me to repair the infernal instrument. Fortunately, I knew Shirley Bryant (then a fellow graduate student and currently Professor of Pharmacology at the University of Cincinnati), who was an electronic whiz, and he promised to assist me, provided I obtained a schematic for the polygraph. Since Offner, the designer of the instrument, was in Chicago, I phoned him directly regarding the schematic. After describing the instrument to him, he was thoroughly puzzled, particularly since I could find no serial number. Then in utter amazement he recalled that this particular machine was the prototype he had built by hand years previously before he went into the manufacture of the polygraphs bearing his name. He asserted that finding a schematic for that contraption was impossible, and that it was miraculous that the machine was still in existence. Nevertheless, I implored Bryant to use his skills anyway.

The result was that in the calibration mode, at least, there were no longer wild fluctuations although the base line occasionally wavered. The true test came shortly afterwards when I hooked up my eight year old son to the apparatus for a night's sleep session. As I perused the record later, I noticed to my chagrin that the machine was acting up again with some obvious artifacts and also with some pen deflections that looked suspiciously like the saccades I had observed when my son moved his eyes voluntarily during the calibration prior to sleep. I repeated this experiment and obtained similar results. It was now evident that aside from the probability of an erratically functioning polygraph, there was no certitude that a pen deflection necessarily represented an eye movement. Pen deflections could signify physiological artifacts such as EEG, skin potentials or head movements as well as monocular or disjunctive eye movements. Without being able to identify the presence or absence of an eye movement under shut lids, the research project was blowing up before me. Suffice it to say that I discussed this problem with some very bright people, but they provided no solution. Then I decided I would turn for advice to perhaps the most distinguished electroencephalographer in the country, Frederic Gibbs.

Gibbs' counsel was straightforward and simple. The problem of recognizing artifacts was endogenous to EEG and EOG recording, he said, and the best solution for me was to abandon the EOG in favor of mechanical recording. This was virtually a death sentence to the project because, first of all, I had invested an enormous amount of time developing the EOG technique and, secondly, I did not have the heart to fiddle with strain gauges attached to the lids with all the attendant problems bound to arise during sleep recordings.

Weeks passed as I alternated between despondency and panic, when suddenly I had an inspiration. By comparing the phase and amplitude relations of two channels simultaneously I would surely eliminate certain artifacts. Comparing the left and right eye channels should identify the horizontal component of binocular movements, while a comparison of the frontal EEG with the vertical component of the EOG on the same side would identify a vertical movement. Of course, it was idiotically simple, and when I rushed to seek Shirley Bryant's opinion he not only agreed the plan was reasonable, but indicated that it was an ancient method well known in engineering circles.

I tested the eye movement identification schema in an awake subject and then proceeded once more to obtain a night's sleep run. The record was quite similar to the one I had previously run on my son except now I was virtually certain that saccadic-like movements were occurring even though the subject was overtly asleep. There were a limited number of possibilities for the cause of these eye movements. Under consideration was that of awakening with the eyes remaining shut, nystagmoid activity somehow related to spontaneous inner ear activation, and, of course, the unlikelihood that the hoary anecdotal reports tying eye movements to dreaming might indeed be true.

The prospect that these eye movements might be associated with dreaming did not arise as a lightning stroke of insight. First of all, I was specifically aware of Max (1935) who, although he had not seen the eye movements of dreaming, was quite sure that normal persons who have visual dreams would at the same time have

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recordable extra-ocular potentials. Secondly, and more important, is the fact that an association of the eyes with dreaming is deeply ingrained in the unscientific literature and can be categorized as common knowledge. It was Edgar Allen Poe who anthropomorphized the raven, 'and his eyes have all the seeming of a demon's that is dreaming...'

In one of the earliest sleep sessions, I went into the sleep chamber and directly observed the eyes through the lids at the time that the sporadic eye movement deflections appeared on the polygraph record. The eyes were moving vigorously, but the subject did not respond to my vocalization. There was no doubt whatsoever that the subject was asleep despite the EEG suggesting a waking state. At this juncture I advised Kleitman of these events and he prudently suggested that I replicate these trials before further speculation. Considering all the problems that had arisen until now, there was a strong likelihood indeed that there was a prosaic explanation for these apparently haphazardly occurring eye movements.

With repetitive sessions the eye movements were confirmed, but now their periodic appearance as well-ordered epochs was becoming evident. Although I interrogated each subject upon awakening with two brief questions: 'Did you dream?' and 'What did you see?', I was not especially interested in the psychological connotations of the eye movements. Instead I focussed on the concomitant physiological factors which together with the eye movements suggested a new cohesive stage of sleep which I termed the 'Rapid Eye Movement Period'. In my mind the emphasis was on the 'Period' as I was still trying to ascertain if it were purely coincidence that the REM period had a duration remarkably similar to the infants' 'No Eye Movement' periods. Since I had not uncovered any relationship, I did not publish anything about this matter. On the other hand, I did report that the 'No Eye Movement' periods, which so neatly correlated with each hourly sleep cycle in the infant, could be seen residually in a child and perhaps only once a night in the adults (Aserinsky, 1953a; Aserinsky & Kleitman, 1955b). Many years later, in a dogged pursuit of the significance of 20-minute

sleep periods, I did ascertain that the duration of a REM period was indeed an integral multiple of epochs lasting about 20 minutes, so that a 40-minute REM period really consisted of two merged 20-minute REM periods, whereas the relatively infrequent 60-minute REM periods contained three basic REM units (Aserinsky, 1971). The relationship between the REM period and the No Eye Movement period remains chimeric.

In my earliest reports on sleep I had an aversion to the use of acronyms in publications; consequently, I always employed the full terms, 'Rapid Eye Movement' and 'No Eye Movement' (Aserinsky, 1953a; Aserinsky & Kleitman, 1953c, 1955a). The exceptions were at the first oral presentation to the public when, because of space limitations, I was forced to display the term 'REM' on a slide, and then again on some of the laboratory protocols which were private notes (Aserinsky & Kleitman, 1953b). Actually I was not entirely sure whether to continue to employ the term 'Rapid Eye Movement' in subsequent papers. I had been contemplating the use of 'Jerky Eye Movement' instead, because my principal impression on viewing those movements was their jerkiness. And, when I measured the movements from their polygraphic tracings, it seemed they were a tad slower than waking movements of comparable size. While 'rapid' eye movements were clearly rapid in comparison to the other eye movements prevalent in sleep, they were surely not more rapid than waking eye movements. Only the anticipated taunts relative to the popular slang meaning of 'jerk' were inhibiting me. Had I been more courageous we might be referring today to 'JEM Sleep.' Ironically, almost forty years later I became interested in the mathematics of the third derivative of motion and discovered that it is technically termed 'jerk' by verbally less sensitive engineers. I then formulated a modification of the third derivative so it would be independent of velocity, termed this 'proportional jerk', and applied this measure to eye movements. The results showed that, yes, REMS were indeed jerkier than comparable sized waking saccades (Aserinsky, 1986).

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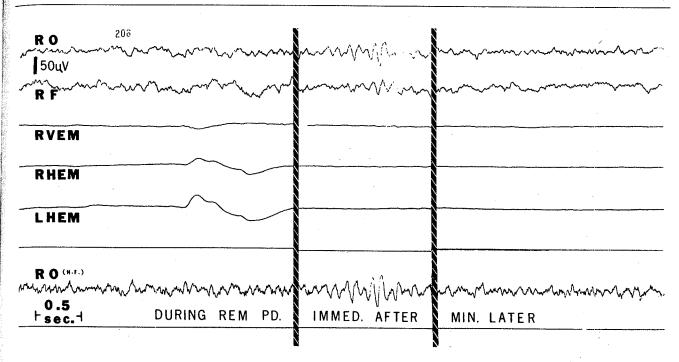


Fig. 2. A sample of the first REM sleep recording. This polygraphic tracing was presented during a slide session at the 1953 FASEB meeting in Chicago. This was the first public disclosure of the occurrence of REM sleep and the first use of the acronym REM. Aserinsky's son, Armond, was the subject who served uncomplainingly in the preliminary studies leading to the discovery of REM sleep. This record shows, from the top, two EEG channels: RO for right occipital and RF for right frontal. Three electrooculographic (EOG) recordings are illustrated: RVEM for right vertical eye movements, RHEM for right horizontal eye movements, and LHEM for left horizontal eye movements. The bottom trace is an occipital EEG recording showing higher frequencies. In the left portion of the figure the upward deflection on the horizontal eye movement traces reflect the rapid eye movement (during REM period). The middle section shows the recordings immediately after (immed. after) REM sleep, and the right portion of the figure shows the recordings one minute after REM sleep (min. later). The time calibration is shown at the lower left. (Reproduced from: Lydic, R. State-dependent aspects of regulatory physiology. FASEB J. (1987) 1:6–15.)

In retrospect, my antipathy to the use of acronyms was (and is) justified. 'Rapid Eye Movements' can be easily translated into virtually all principal languages. But the acronym, REM, had the unfortunate effect of exacerbating national antagonisms which are particularly sensitive to linguistics. 'REM' is a convenient and even rational shorthand for the longer term used in English but it fails on both counts in other languages. The comparable acronym in Spanish becomes 'MRO', whereas in transliterated Russian it is 'BVG', neither term being pronounceable.

National – or at least linguistic – pride would require a different acronym for each tongue. One maneuver has been to abandon 'rapid eye movement' sleep entirely for the term 'paradoxical' sleep which, of course, eliminates the acro-

nym. However, one can debate that the term 'paradoxical' is even more flawed than 'rapid eye movement', although fortunately it is not transmutable to a slick acronym (Aserinsky, 1967).

After the recognition that REMs were definitely not an artifact of instrumentation, their association with dreaming was very high on the agenda for further exploration. This notion was strongly reinforced by the occurrence of one pilot sleep session described in my thesis (Aserinsky, 1953a) but not published elsewhere. In this case I encountered a subject undergoing a nightmare during the course of a REM hurricane, which almost unhinged the pens on the eye movement channels of the polygraph. On direct observation of this subject, I not only saw the violent eye movements under the shut lids but

heard his vocalizations which were slurred but occasionally intelligible. Upon awakening him and hearing his dream report, it seemed to me that his sleep vocalizations and his waking report were definitely related. Despite the apparent association of the REM state with dreaming, I still did not harbor any strong feeling vis-à-vis the possible connection between an individual eye movement and a specific movement to fixate an image. I did make one aborted attempt to study such a relationship.

To determine if there is a connection between REMs and visual imagery in blind persons I managed to convince a blind undergraduate student to sleep in my laboratory. On the appointed night I ushered the young man and his seeingeye dog through my recording room into a small sleeping chamber. Following the same protocol as for all the other sleep experiments, I applied electrodes and other gear to his body, shut the door to the sleeping room, and took my position at the polygraph console in the adjacent room. I monitored the eye movement tracings very carefully, noting that they were quite erratic and basically undecipherable by my accepted criteria. Nevertheless, I knew through visual observation of the subject's eyes that they were capable of limited motion. For the most part, the base line showed possible wavering of the eyes or twitching of the lids, but nothing resembling a normal REM. As hours passed, I noticed at one point that the eye channels were a little more active than previously and that conceivably he was in a REM state. Since my usual criteria for recognizing REM no longer held, it was imperative that I examine his eyes directly while he slept. Very carefully I opened the door to the darkened sleeping chamber so as not to awaken the subject. Suddenly, there was a low menacing growl from near the bed followed by a general commotion which instantaneously reminded me that I had completely forgotten about the dog. By this time the animal took on the proportions of a wolf, and I immediately terminated the session, foreclosing any further exploration along this avenue.

My measurements of respiratory patterns during REM sleep were more successful than my brief encounter with visual imagery in the blind,

but even here I was less than satisfied that there was any relationship between breathing and dream content. Stressing respiratory rate because it seemed to be so relatively easy to measure, I concluded that the rate was significantly higher in REM sleep than in other states of sleep. But I was wary of this result even as I was publishing it because I knew that I had measured only those segments of records that were measureable, omitting sections displaying apnea or hypopnea. After all, I rationalized, I was merely randomly selecting measureable respiratory traces. Why would I select traces that I couldn't measure? This sophistry was perpetuated for about a decade before other investigators reported that it was the irregularity that characterized respiration of REM sleep (Snyder et al, 1964). To psychologists who zealously nurtured the notion that breathing in REM sleep somehow reflected the content of dreams, it was just as easy to reconcile the irregularity of breathing to dreams as it was to connect increased rate with dreams.

In the ten years following my initial work on REM sleep, I divorced myself almost completely from sleep research. However, about three years before Snyder's report, I happened to notice that my 100 kilogram St. Bernard dog was beginning to go into a REM period, and that his muscular twitchings seemed to follow a pattern suggestive of a Jacksonian epileptic march. This stereotypical pattern repeated itself on later occasions and therefore if the notion tying muscular activity and dream content were true, my poor dog, Bruno, was having the same dream again and again. I thereupon gingerly returned to the sleep laboratory to reinvestigate the relationship of respiration to REMs in human subjects. The new results indicated that an astonishing characteristic of respiration in REM sleep was its regularity (Aserinsky, 1965). It would seem that, regardless of the subject, the beginning of a flurry of REMs coincided with some degree of apnea and was then followed, naturally, by a period of hyperpnea. Such regularity of respiratory pattern does not support the contention that different dreams should have different respiratory patterns. One of Kleitman's favorite aphorisms was that no matter how a bologna is sliced

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it is still bologna. With respect to respiration and sleep, the end result depends on how the respiration is viewed. If the predominant or hyperpneic portion of the respiratory record is examined, the respiratory rate will appear high. If one focusses on apneic periods, the REM state can be uniquely associated with respiratory depression and, if one takes an overview as did Snyder, then assuredly the combinations of apnea and hyperpnea of irregular duration signify respiratory irregularity. If one notes, as I did, that each epoch of respiratory depression initially coincided with a burst of REM activity and was afterwards followed by hyperpnea and an irregular eruption of REM activity, then the respiratory pattern has a semblance of regularity. I am not so sure that the bologna aphorism applies here.

Continuing with the historical background of REM – Back at the University of Chicago, after I had ultimately verified that the polygraphic recordings were reliable, I began running night experiment after night experiment by myself. This was a tiring routine but I was highly motivated to complete the project without delay. With the accumulated data showing considerable consistency and with Kleitman beginning to exhibit real interest, I began to explore the possibility that perhaps the end of the project was in sight. Kleitman, on the other hand, felt that the infant and adult work on eye movements was too paltry to merit a doctorate, and he suggested that I plan on an extension, such as a study of the developmental changes of eye movements through the progressive stages of childhood. Meanwhile, since Kleitman had not actually seen the rapid eye movements, he provided me with a small home movie camera so that I could film the REMs. Since the film was insensitive, it was necessary to illuminate the eyes with the bright lights of several photoflood bulbs. Fearful of awakening the subject, I arranged to increase the intensity of light gradually through a rheostat. However, the camera which was quite close to the subject's head made a fairly loud whirring noise and I was sure that the subject would awaken. As another surprise in the evolving story of REM, I was learning that, despite the blinding lights and the disturbing noise, the subject's threshold to external stimulation was remarkably high. I had viewed the REM state as a variant of the waking state with low sensory thresholds, but this situation suggested otherwise.

After the movie was made I showed it to Dr. Nathaniel Apter, who was the Head of the Psychiatry Department at Chicago. He expressed interest, as much as a clinician could at that time, on seeing the eyes wiggling in sleep. A few words passed between us regarding the possibility of the movements reflecting dreaming when I asked him if he thought that infants dream. His reply was in the affirmative and predicated entirely on Freudian concepts. As an experimentalist, I considered his reliance on Freud as a sort of religious faith, and therefore his answer was of no value in helping me understand why I had apparently not seen REM in infants.

Having seen the movie of REMs, Kleitman should have been thoroughly convinced that they did indeed exist. Of course, Kleitman's personal experience as one of my early sleep subjects did not instill him with confidence. As luck would have it, he exhibited no REM in one sleep session. In a subsequent session he had three REM periods. On being awakened from these REM periods, he reported having dreamt following one awakening, of possibly dreaming following another awakening, and of being awake instead of asleep after the third awakening. This was hardly a demonstration to convince Kleitman that my discovery was valid.

Kleitman did suggest that I prepare an abstract and present an oral report at the upcoming FASEB meeting to be held, conveniently, in Chicago. But Kleitman was an extremely cautious scientist. When he published anything one could be absolutely certain that the facts he presented were irrefutable. Even though he was on the periphery of this particular study as an advisor, the work, after all, could still reflect on his reputation. Consequently, it was no surprise that Kleitman asked me to arrange a typical sleep session for his benefit prior to the meeting. As he indicated to me, he wanted to see the experimental procedures first hand so that he could respond to any queries directed to him at the meeting. I was elated at the prospect of finally

showing him the fruits of my labor, and I suggested to him that I already had a subject readily available for such a session. Surprisingly, he responded that I should not call any subject since one of his daughters was available. Why he would subject his daughter to an experience that was less than pleasant I could not fathom at that time.

I did understand this choice many years later, when I was on the faculty of Jefferson Medical College. I was approached by the TV producer of a program entitled 'Concept' to conduct a televised sleep session in which the public could view the highly publicized occurrence of REMs during dreaming. The polygraph, TV recording paraphernalia, and the fairly large TV crew were ensconced in the surgical operating theater of the Eastern Pennsylvania Psychiatric Institute, while a bed was set up in the glass-walled observation room overlooking the operating room. My son, by this time a college student and sleeper par excellence, was the subject for this performance and was hooked up by cable to the polygraph. It was understood that I would monitor the polygraph and that, when the magic moment of REM sleep appeared, I would signal the camera crew to enter the sleeping chamber to begin their recording of the subject in bed.

Hours passed with nary a sign of REM. I began to worry. This was an on-location program already listed in the newspapers, a veritable crowd of TV people, nurses and other on-lookers were milling about in the confined quarters, and the production costs already were in the thousands of dollars. The unthinkable then occurred to me; perhaps, I should surreptitiously advise my son to move his eyes voluntarily to simulate REM. After all, this was not science, this was merely entertainment. Just about that moment I overheard one of the TV crew comment to the Program Director, 'Say, how will we know that the fellow upstairs (the sleep subject) isn't deliberately moving his eyes?' The Director responded, 'That's impossible, Mac. You can't move your eyes when your eyes are closed.' The cameraman shut his eyes and after a few moments of facial contortions answered, 'You're right'. Of course, I knew the cameraman was wrong and that his initial suspicion was

justified. And just then came the realization as to what might have motivated Kleitman to use his own daughter as a subject years back. Naturally, I do not know if it were his purpose to eliminate even the remotest possibility that there might have been collusion between myself and the subjects to fabricate waking-type eye movements in sleep which electroencephalographically was not distinguishable from waking. I am not sure whether I prefer Kleitman's image to be that of the exacting, meticulous scientist, or the less careful but trusting scholar.

Although Kleitman had a tangential role in my REM project, he was far from being disinterested as the implications of the results began to be appreciated. In fact, the results were in direct conflict with his theory of sleep, which was a major basis for his international renown. While his theory held that sleep was a passive process brought about through the reduction of impulses to a waking center in the brain, my data suggested quite the contrary - that sleep could occur with tremendous activation of the brain. Proof of the existence of an activated sleep (REM) state would be a powerful blow to his theory, and therefore it must have been with ambivalent feelings that Kleitman was forced to accept the reality of the REM discovery. To make matters worse, I recall showing Kleitman a paper I had uncovered in which an obscure Russian investigator had promulgated important elements of Kleitman's theory several years prior to Kleitman. (According to Edmund Jacobson in a personal communication to me, it is a dark characteristic of researchers to undermine their colleagues by alleging that a purported work had been done eons before.) In any case, Kleitman's theory was moribund by now anyway, and he was probably ready to accept a new set of facts. This was poignantly manifested by two episodes that occurred at the time that I was preparing the abstract which publicly announced for the first time the discovery of REM.

First, the matter of authorship. I had misgivings about giving Kleitman any authorship at all in view of his minimal role in the study, and I did not anticipate that Kleitman would request any authorship. Nevertheless, as a matter of courtesy, I broached the subject with him as I

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all l I est of timorously opened the door to his office. When I approached Kleitman for his thoughts on the matter he responded evasively by enumerating the four possible permutations available to me. I could be the sole or the senior author, or he could be the sole or the senior author. It was my choice. This was clearly a cat and mouse dance. From the tone of his voice and from his body language, I surmised that he was not apathetic regarding authorship. Since in this pas de deux I was the mouse, a mouse without even a baccalaureate, I decided that prudence would dictate a joint authorship with him as the second or junior author. Kleitman seemed satisfied with the second-place authorship, especially since that signified senior authorship in a number of countries outside the United States. Shortly afterward, he exploited this development in a manner that was unconscionable.

Kleitman informed me that he was going to explain the abstract and discuss publicity with a representative from the University Public Relations Department, but I was not to participate in this meeting. Instead, I was to monitor the conversation from behind his office door, which on this rare occasion was to be kept slightly ajar. I was instructed to listen for any statement made by Kleitman which I deemed incorrect and to inform him afterwards. As the senior author of the abstract, who had initially explained its contents to Kleitman, I was puzzled as to why I had become incompetent to partake in this meeting. This was a bizarre turn of events and I was more than ever determined to complete my dissertation as quickly as possible.

Kleitman was adamant in that the research required a major expansion before the granting of the degree would be approved by him. Months later, I appealed to the Departmental Head to intercede with Kleitman on my behalf. John Hutchens, the chairman, had high regard for me because of a record-breaking grade I attained on a doctoral preliminary examination, but this was probably moderated by my having burned his sofa with a cigarette during a Christmas party at his home. He read a draft of my thesis and then assured me that what counted after all was the potential shown by the thesis, not its content. With that comment he then pro-

ceeded to make an arrangement with Kleitman to grant the degree with the proviso that if I did not have a job awaiting me outside the University I would continue (sans degree) with the REM study. When I apprised Kleitman of my economic difficulties and the absolute necessity for me to obtain employment he sympathetically offered me two hundred dollars (which I subsequently repaid) plus some unforgettable paternal advice on how to economize by eating chicken necks, which were not only economic but very tasty too.

Despite these blandishments, I was still determined to leave. It was during the final throes of the research project that Kleitman introduced William Dement to me, with instructions that Dement would be my assistant and I would indoctrinate him with respect to my methodology. Although the amount of time that Dement could devote to the project was limited because he was a medical student, I was pleased with at least some help in racing through the routine sleep runs. My only misgiving was that Dement seemed to be tinged with a psychiatric interest, and it bothered me that his thought processes might not be attuned to what I considered nononsense research. Two years previously, Kleitman foisted upon me for several weeks a student who was engaged in some Freudian falderal about snoring protecting sleep.

Some time elapsed before I would trust Dement to conduct a sleep run by himself so that I could at last obtain a decent night's sleep at home. On that fateful night, I awakened at about three in the morning with a premonition that I should return to the laboratory. With foreboding, I opened the recording room door and there in semi-darkness was Dement asleep in a chair next to the polygraph while a heap of recording paper was piling up on the floor and pens were moving violently and spewing ink. On a mantel nearby was a gargoyle-like lamp with a demoniacal visage which was connected to the subject so that the latter, in case of emergency, could signal to the investigator to come immediately into the sleeping room. The eyes of the demon lamp were aglow, indicating that the subject had turned the lamp on some time ago. Sure enough, when I opened the door to the sleeping room the subject was wide awake. This was truly 'paradoxical sleep' – with the subject awake and the observer asleep. It was inevitable that many years later, Dement (1972) would title a book, 'Some Must Watch While Some Must Sleep'.

When Dement entered my laboratory in December, 1952, a year had elapsed since I had seen that first REM disgorged by the erratic Offner polygraph. The problems of identifying and recording the REMs had been solved and I had already embarked on running the sleep sessions in a stereotyped manner. I was quite pleased to have some help in accelerating my departure from the Department, and Kleitman, I am sure, had to be elated that he had someone to repeat my experiments. Indeed, this repetition was reported on in 1955 by Dement who, using the original techniques, and using schizophrenic as well as normal subjects, found that there were virtually no differences between the two groups of subjects. No matter, though, because a real purpose of that investigation was to validate the original work.

Fifty-one reportable sleep sessions were run from October, 1952 through May, 1953. Under my supervision, Dement ran five of these sessions starting January 15, 1953, and I conducted all the others. Since I could only run one subject per night and had to do all the analyses by myself in the daytime, it is clear that I was working at a fast pace. The motivation was simple. First, I was not overly fond of chicken necks. Secondly, in the same month that Dement appeared, Kleitman dashed off a letter to the National Institute of Mental Health stating, 'He (Aserinsky) ... discovered a distinct type of eye activity which is found only in sleep and may be associated with dreaming.' This was in support of a renewal of my Fellowship, which was due to expire June, 1953. Thus Kleitman was expecting me to remain another year. I figured that, if I could complete the experimental work before June, 1953, the fellowship renewal would not be necessary. I won the race and left Chicago that summer, receiving my degree in absentia.

There have been a number of narrations of what supposedly transpired during the course of the REM discovery. Some statements including that by Dement (1972) were completely off-tar-

get. For example, the notion that Kleitman was interested in slow, rolling eye movements and that, as a consequence, he assigned me to observe babies is an incorrect speculation. Kleitman, as I indicated earlier, was interested in blinking, which is a waking state phenomenon having nothing to do with the slow eye movements of sleep. More important though was the implication (Dement, 1972) that the REM discovery was a 'team' effort. If anything is characteristic about the REM discovery, it was that there was no teamwork at all. In the first place, Kleitman was reserved, almost reclusive, and had little contact with me. Secondly, I myself am extremely stubborn and have never taken kindly to working with others. This negative virtue carried on throughout my career as evidenced by my resumé, which reveals that I was either the sole or senior author in my first thirty publications, encompassing a period of twentyfive years. In all of these endeavours, with the exception of some technical assistance, I performed most of the laboratory work and all of the analyses myself. Dement, of course, had nothing to do with the REM discovery in my laboratory, although he subsequently became prominent on his own in clinically oriented studies.

My fears about unforeseen occurrences in the sleep laboratory were not unfounded. Some time before Dement arrived, I had recruited as a subject a fellow graduate physiology student who had a reputation for being eccentric. After much cajoling, I enticed him into the sleeping room and began to apply the electrodes to his scalp and face with continual assurance that there was absolutely no danger involved. He spied an awe-some-looking electric rectal thermometer hanging over his bed and was about to flee the room, but I finally convinced him that it was a nonfunctional relic remaining from Kleitman's previous research.

Ultimately, I escaped to the quiet of the recording room, but in a minute or so the Gargoyle's eyes lit up and simultaneously there was a shout from the subject, 'Gene, I feel electricity!' I responded just as vigorously, 'Don't be an idiot! How could I conceivably record an EEG if I am applying an extraneous current to your

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head?' There were several more nervous calls during the night until, at one juncture, I plucked several electrodes off his face, washed them, and plunged them into my mouth. 'If there were electricity coursing through these wires, would I be fool enough to do this?' Placated, he finally fell asleep. Suddenly, there were screams emanating from the room, 'You're electrocuting me! You're electrocuting me! There he was in bed sitting bolt upright clutching a knot of electrodes he had ripped off his head.

Following that debacle, I called in Shirley Bryant, the electronics expert, to recheck every piece of equipment for proper grounding. As I expected, everything was in excellent order. The subject's reputation for idiosyncratic behavior was apparently well deserved. Still, before leaving the lab I determined to apply the acid test to this matter. I applied the electrodes to myself, lay down on the bed and stared up at the ceiling. Absolutely no sensation of electricity. With my hand dangling over the bed I managed unconsciously to work my hand under the mattress — and then I touched the bedspring! The problem was solved. The bedspring wasn't grounded.

It is difficult to conceive today, when clinical sleep centers have mushroomed over the world, and 'Sleep' is a recognized medical subspecialty, that, in the early '50s, sleep was on the fringe of respectable science. Aside from the few scientists of the calibre of Kleitman, most researchers were dabbling in behavioral studies. There were probably more articles on sleep in popular magazines than in scientific journals, and the existence of a sleep laboratory in a physiology laboratory was in itself an anomaly. Except for a mixture of amusement and condescension, there was no emotion generated by the Physiology Department as I presented my work to them. I had invited the noted experimentalist, Heinrich Klüver, to my doctoral defense, but he declined without explanation. Very possibly he thought that he could provide no expertise to the event. Yet his presence would have been more appropriate than that of the cellular physiologists in the Department.

Still later, while in Seattle at the School of Fisheries, I wrote the first full paper describing

REM sleep, and submitted it to 'EEG and Clinical Neurophysiology.' The editor, Herbert Jasper, rejected the paper politely on the grounds that other papers had already filled all the slots. This rejection was only slightly less polite than the apocryphal story of the Chinese publisher who rejected a manuscript because it was of such extreme merit that to accept it would preclude publication of anything else, since nothing could ever approach such a high standard. Of course, sleep as a topic for psychology or psychiatry was acceptable, but its entree into the presumably more rigorous non-mental sciences was still met with skepticism. Thus, when I ultimately applied for a position in the Department of Physiology at the Jefferson Medical College, I had to assert that I was a bona fide neurophysiologist interested in electrophysiology and that CNS research was my forte, sleep studies having been a deviant, unfortunate interlude. I did get the job.

Despite the notion that serendipity was the true progenitor of the REM discovery in 1952, the fact is that the element of chance was not the sole factor. The pursuit to quantify eye movements in sleep was not carried out in a scientific vacuum. Neurophysiological and psychological data relative to oculomotor activity in sleep had already been noted in the literature, but nobody had actually recorded *continuously* the eye movements throughout the course of an entire night's sleep.

The correlation between body movements and dreaming had been made right across the hall from my laboratory at the University of Chicago by Arno Luckhardt (1916), who had reported that he had seen sleeping dogs suddenly engage in various bodily activities. He '... assumed that the dog was experiencing ... a form of cerebral excitation akin to or identical with the dreaming state in man.' Of course, Lucretius (c. 98–c.55 B.C.) made the identical observation – only more poetically - two thousand years earlier. And, a couple of hundred years earlier still, Aristotle stated that 'when sleep takes place, such motions (as occur in the waking state) continue, or are even more apparent.' None of these individuals mentioned eye movements in particular, but there has been no dearth of attempts to dig out reports to show that REM had been observed prior to 1952.

The most advertised claim to the REM discovery has been made on behalf of Ladd (1892). In their zeal, Kramer et al (1966) even asserted that Ladd had associated 'conjugate rapid eye movements' with dreaming, even though Ladd never mentioned the equivalent of conjugate rapid eye movements in his article. A more careful reading of Ladd's paper indicates quite clearly that he was speculating on the possibility of slow eye movements, not rapid eye movements, being associated with dreaming. Specifically, Ladd stated, 'But I am inclined to believe that in somewhat vivid visual dreams the eyeballs move gently in their sockets...' 'Gentle' movements are undeniably the slow eye movements alluded to as far back as ancient Chinese history and are observed in non-REM sleep as well as REM sleep. Indeed, Fuchs and Wu (1948) recalled the legend of General Chang Fei, who lived in the third century A.D. and, because of physiologic lagophthalmos, slept with his eyes open. On a fateful night assassins stealthily approached the general as he lay in bed. But they noticed his eyes were rolling, so they assumed he was awake, and made a hasty retreat. But then, on hearing snoring and finding the general unresponsive to noise, they realized that he was actually asleep, and so they returned to complete their murderous mission.

As for Ladd's speculation regarding the connection of eye motion with dreaming, a similar guess was made some twenty-four years earlier by Griesinger (1868) who stated, 'How the eyeballs behave at pictures or images during a dream, cannot be observed on oneself. But I like to believe that because of a certain liveliness of images a movement of the eyes occurs, to the extent that there is soon an awakening.' Griesinger had made no observations of REM but was perpetuating the notion that motor activity would accompany a dream. Even as late as 1938 there was an assertion by Edmund Jacobson (1938), the father of 'progressive relaxation', that the eyes under the lids move during dreaming. But again, as with his predecessors, Jacobson was not referring to what we recognize as REM. This can be adduced from

his comment, 'Sometimes, already dreaming at the instant of going to sleep...' Since REM does not ordinarily appear at sleep onset, Jacobson must have been associating slow eye movements with some type of mentation. At any rate, Jacobson subscribed to Kleitman's passive model of sleep, in which the reduction or elimination of proprioceptive impulses leads to a unimodal type of sleep, without regard to the existence of REMs or the REM state. Dreaming, in his view, would not occur except when one is tense, or as he stated, '... placidity of the eyes, it seems likely, is carried over into the night by the more relaxed person, so that he sees less in imagination when he sleeps; in other words, his mind is more quiet and he dreams less.' Jacobson's focus was on the relaxation of the extra-ocular muscles and the subsequent decline in slow eye movement leading to restful sleep.

As already indicated, a number of individuals had intimated that there is, or should be, a connection between eye movements and dreaming. It was precisely for that reason that I considered such a relationship on first encountering REMs. What was entirely unanticipated by myself and all my predecessors in sleep research was that there exists a unique stage of sleep which reappears periodically in a near cyclic fashion, and has attributes different from either waking or traditional sleep. How or whether it is related to dreaming is almost incidental with respect to its import in understanding brain function. The mystery remains as to why the REM period had never been reported prior to 1952 inasmuch as no equipment whatsoever was needed to examine the lids of a sleeper. The obvious answer must lie in human behavior. Since the first REM period is not obvious during the first couple of hours of sleep, and cyclicity would require a still longer period of observation, the discovery of REM would have required an obsessive, highly motivated individual to peer continually for hours at a sleeper's eyes. This would explain the failure of the layman to discover REM, but what about scientists who are infamous for both obsessiveness and motivation, and thus should have looked for the eye movements? My guess is that no one was sufficiently driven to expend an inordinate amount of time to fill in the gaps

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of sleep studies in which the position of the eyes was noted by occasional lifting of the sleeper's eyes.

The trigger for the discovery of REM

The trigger for the discovery of REM occurred when I decided to record the eye movements continuously on polygraph paper throughout a whole night's sleep (consuming up to a half-mile length of paper per sleep session). This decision almost guaranteed the discovery of the periodically recurring REM state, and practically made the denuding of the world's timberlands inevitable.

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