Studies in Human Chronobiology

Sheridan V. Merritt

THE FIELD OF CHRONOBIOLOGY has grown remarkably during the past twenty years, and the ubiquity of periodic patterns exhibited by physiological and behavioral processes is now generally acknowledged.

Information about circadian and other rhythms is gradually being integrated into college and high school science programs. Ahlgren and Nelson (1979) in this journal assessed the quality of coverage in a variety of high school biology texts. Chronobiologist Lawrence Scheving has called for wider support of autorhythmometry programs in the nation's high schools to develop a broad base of reference data that might be valuable in maintaining health and detecting conditions such as hypertension (Scheving 1979). In addition, such programs would improve our understanding of normal fluctuations in various body processes that might influence subtle changes in mood, anxiety, and feelings of well-being.

To provide students with "hands-on" experience in designing and executing chronobiology experiments, a wider sharing of techniques and procedures among biologists is needed.

During the past two years, I have offered a college-level course, Biological Rhythms. Because, to my knowledge, no comprehensive lab manual exists, I have designed and tested a number of chronometric procedures for use with various organisms, including humans.

This article describes one set of procedures that has been used in my class. I will present and discuss some of the data obtained and relate them to similar studies from the literature. These procedures have been reported widely enough in published research (see Halberg, *et al.* 1972) that a large body of data exists for comparison of results. I have selected procedures that are related to humans and that require minimal equipment.

Data Recording

All data were recorded, collated, and the averages and moving averages were graphed and examined for evidence of daily periodicity. All modalities were compared to determine whether any correlations could be discovered among them.

Assessing Some Human Circadian Rhythms

Oral Temperature. To determine the pattern of daily temperature rhythms exhibited by a population of students monitored over a one- or two-week period of time, students were asked to monitor their oral temperature at one- and two-hour intervals during waking hours for a period of approximately one to two weeks. Temperature readings were taken using an oral thermometer placed under the right side of the tongue.

Prior to recording any readings, the students were instructed to determine the minimum time required for their particular thermometers to reach equilibrium. This was done by checking the thermometer at 10-second intervals for two to three minutes or until the mercury column ceased to rise. All temperature readings were taken in a seated, relaxed posture; and readings were postponed for 10 minutes if the subject had been breathing hard, drinking, or eating.

Students were cautioned about the toxic effects of mercury, and thermometer carrying cases were designed from empty ballpoint pen cartridges by tucking a small wad of cotton in each end. These cartridges facilitated carrying the thermometers into a variety of situations in which the students would be taking their temperatures.

The pattern of daily fluctuation in oral temperature exhibited by 14 subjects follows closely the patterns re-

Sheridan Merritt is professor of zoology and chairman of the biology department, University of La Verne, 1950 Third Street, La Verne, California 91750. He received his B.S. and M.S. degrees from Oregon State University in 1961 and 1963 respectively, and his Ph.D. degree from the University of Wisconsin in 1974. He taught zoology at the University of Wisconsin from 1964 to 1966, and joined the faculty of the University of La Verne in 1969. Courses he has taught include developmental and general biology, as well as aquatic biology and invertebrate zoology. He has also designed and taught courses on the historical growth of scientific thought and the social implications of recent scientific and technological developments. Merritt has published articles in several journals, including *ABT*, and he enjoys writing poetry. He holds memberships in NABT, AIBS, and the Union of Concerned Scientists, and he served as president of the local chapter of the American Association of University Professors. His hobbies include canoeing, kayaking, and tidepooling.

ported in the literature (fig. 1). The temperature is at its lowest in the morning, and it gradually rises throughout the day to a peak in the late afternoon or early evening; temperature then declines during the evening hours.

When the temperature data for individual subjects were examined, however, consistent patterns of temperature fluctuations unique to that particular individual were found.

The comparison of the patterns exhibited by the pooled *vs.* the individual temperature data provides an excellent opportunity to discuss with students the conditions under which small sample size ($n = 1$) and pooled data should and should not be used. Large sample size and pooled data are statistically more satisfying but valuable insights into the correlative physiological and psychomotor rhythms unique to the individual may be lost or ignored through these procedures.

In addition to recording oral temperature, the parameters listed below were monitored.

Pulse Rate. Hourly pulse rates were taken after a minimum of 15 minutes in a seated posture.

Hand-eye Coordination. The number of seconds required to scratch out fifty of the letter "e" on a printed page of a magazine or book is an accepted procedure for measuring changes in hand-eye coordination and was monitored by several students for rhythmicity.

Arithmetical Computation Skills. Each student was given a packet containing several pages of simple addition problems that had been generated from a set of random numbers by computer. Two sets of 10 problems each were worked every two hours and the average number of seconds required to work each set was determined. Ten seconds were added for each incorrect answer.

Time Estimation. Each hour the subject attempted to estimate the passage of one minute. The number of seconds that had actually passed was recorded, and the difference between estimated time and actual time was displayed graphically.

Correlation of Oral Temperature with Other Rhythms

Correlations (phase relationships) between oral temperature rhythms and other physiological and psychomotor rhythms have been recognized for many years, though the question of a causal relationship remains unanswered at this time. For example, in the 1930s Kleitman identified several perceptual motor skills that paralleled daily temperature oscillations, and he proposed a causal relationship (Blake 1971). Colquhoun (1971) recognizes the positive correlation but questions the assumption of causality. He also provides evidence that the presence of "arousing" stimuli in the environment could lead to a negative correlation between temperature and performance levels during the later hours of the day by inducing a state of hyper-arousal in some of the subjects. Examples of arousing stimuli might include informing the subject of his/her level of performance on each test, or it might involve the tasks being carried out in the presence of ambient noise (Blake 1971).

More recently, Folkard (in press) has suggested that a more consistent correlation exists between long-term or delayed memory rhythm and arousal-level rhythm than between that of long-term memory and body temperature. He further emphasizes the need to characterize carefully the nature of the performance tasks being monitored, particularly with regard to the complexity of information processing required for the task. Thus, the

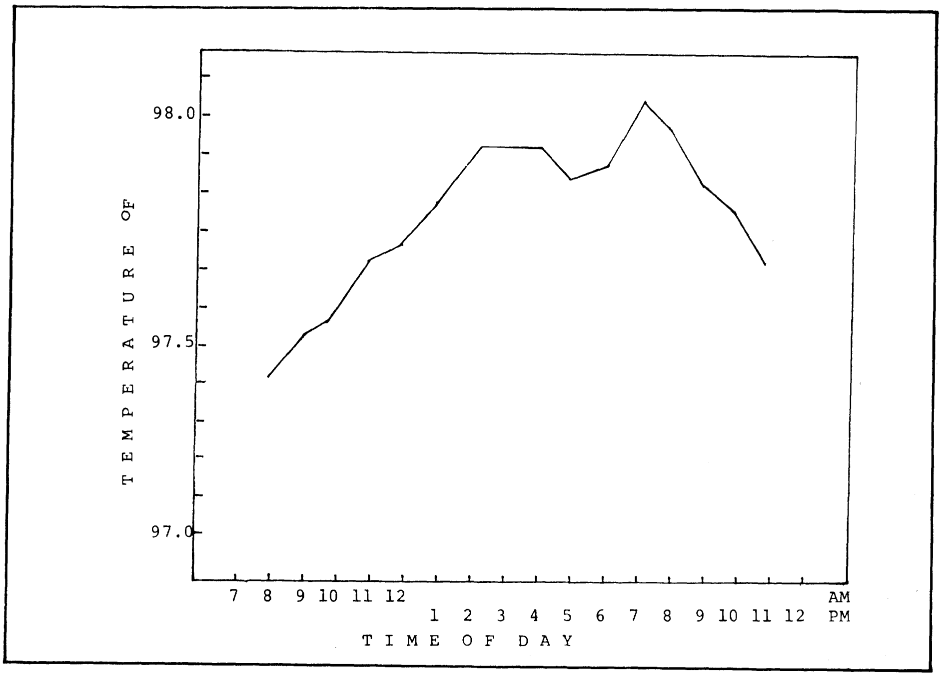

FIGURE 1. The average daily rhythm in oral temperature of 14 students. Temperatures were recorded at hourly intervals during waking hours. The curve was smoothed by plotting two-hour moving averages.

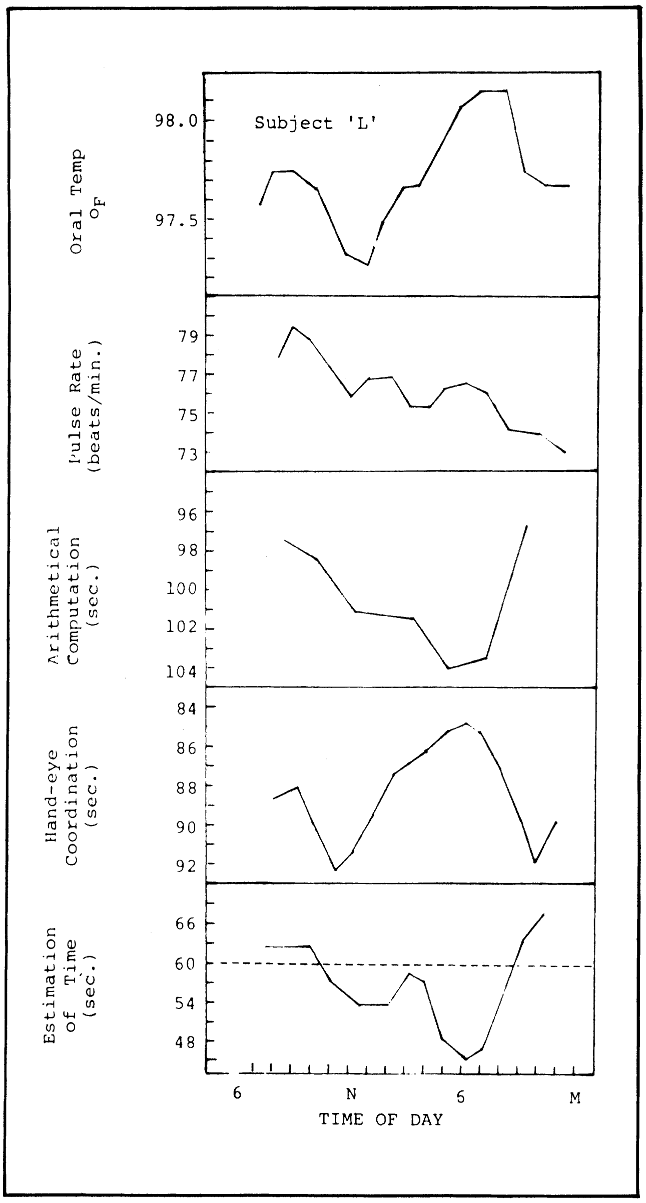

FIGURE 2. Rhythmic variation in five variables measured in single subject. Temperature was observed for ten days; pulse rate for eight days; "e" scratching (hand, eye coordination) for ten days. Two hour moving averages were plotted.

assumption of the universality of a single circadian rhythm for performance efficiency, body temperature, and other physiological variables is no longer as widely held as it once was.

Figures 2 and 3 present comparisons of several variables as measured by two subjects, one of whom exhibited a bimodal and the other a unimodal oral temperature rhythm. Regarding the data for subject L (female, 19 years old) several observations can be made. The pulse rate begins at a high level in the morning and declines through the day. No consistent correlation with body temperature is evident.

Arithmetical computation efficiency is clearly unimodal and is inversely correlated with the major peak in body temperature and in hand-eye coordination ("e" scratching). It is possible that a bimodal rhythm for arithmetical computation with an early morning peak would have emerged had data been collected prior to 8 A.M.

According to Palmer (1976) people attempting to estimate the passage of time tend to overestimate in the morning and evening and to underestimate during the day. Subject L in Figure 2 follows this pattern surprisingly well. The horizontal broken line indicates the 60-second level.

The subject portrayed in Figure 3 (femai , 19 years old) displayed a unimodal curve for oral temperature with rather striking positive correlations with the other three variables measured.

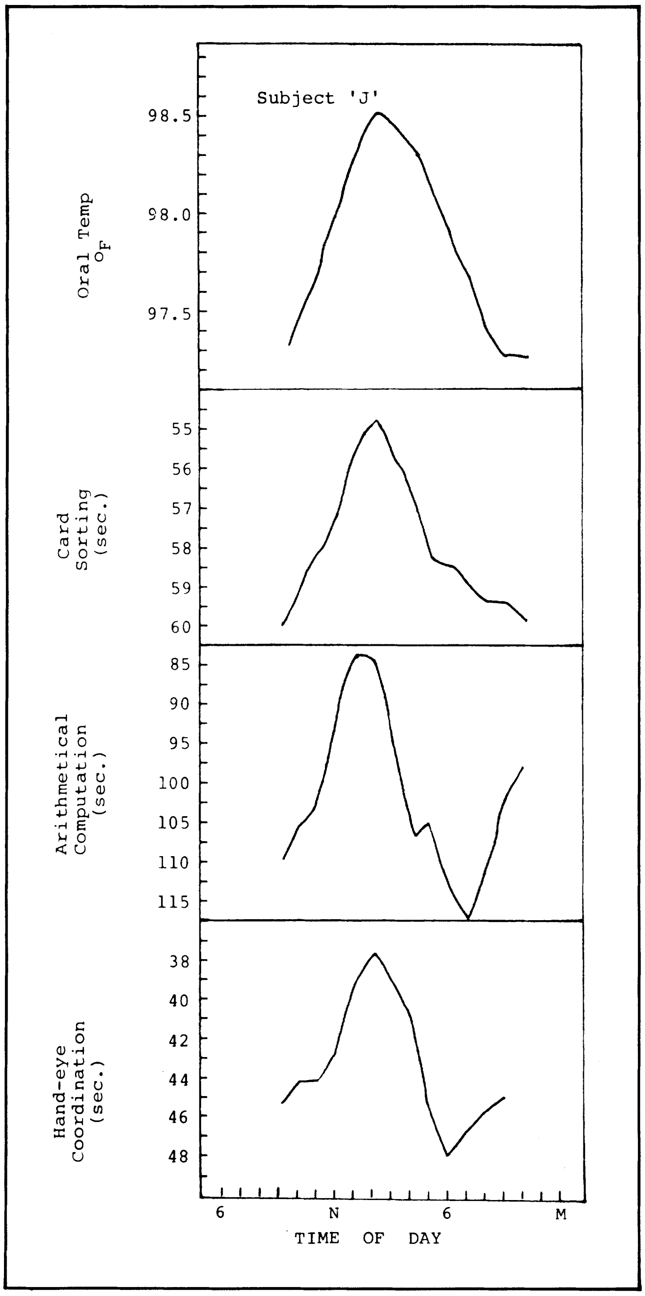

FIGURE 3. Rhythmic variation in four variables measured in a single subject. Temperature observed for fourteen days; card sorting for eight days; arithmetical computation for two days; and "e" scratching (hand, eye coordination) for five days. Two hour moving averages were plotted.

Other Rhythm Studies

Oral Temperature During Ovulation. An excellent opportunity to illustrate the occurrence of a change in amplitude of the temperature rhythm is provided when a subject monitors oral temperature on the days before, during, and after the ovulatory phase of the menstrual cycle (fig. 4).

Monitoring oral temperature hourly during a brief illness would also provide students with an opportunity to observe the effect of temporary changes in amplitude of body temperature.

Periodic Symptoms. It has been demonstrated that symptoms of various clinical and subclinical conditions exhibit rhythmic fluctuations (Luce 1970; Reiman 1963). An awareness of these daily fluctuations in intensity of chronic symptoms might enable the afflicted person to understand better the vicissitudes of his/her condition. This understanding might then be used to enhance the efficacy of medication and perhaps to deal with stress-related symptoms through autonomic self-control techniques (coping strategies, biofeedback, progressive relaxation, etc.). Students should be encouraged to monitor carefully any recurring symptoms such as bronchitis, sinusitus, headaches, aching joints, lethargy, and dizziness. Once evidence of periodicity is established, hourly monitoring can begin and should be continued for a week or more. Although the assessment of the intensity of symptoms is necessarily subjective, the results may still provide valuable insights into the nature of the condition being investigated.

Histamine Levels and Rhythmicity. An examination of published literature on rhythmicity of histamine levels in humans reveals a distinct daily pattern. The response to subdermal injection of histamine, a histamine liberator, and household dust extract (as measured by diameter of inflamed area around injection site) was observed by Reinberg (Scheving, *et al.* 1974) and others to exhibit distinct maxima at night and minima during the day. It was further noted by Reinberg and Sidi (Scheving, *et al.* 1974) that antihistamines were effective for greater numbers of hours when present in the body at the time of day when sensitivity to histamine was least.

The intensity of symptoms associated with a chronic, nonspecific allergy (sinusitis) was monitored by one of my students for eight days. Medication was not used for the duration of the study. Symptoms were rated subjectively on a scale from 0 to 3, with zero representing no symp-

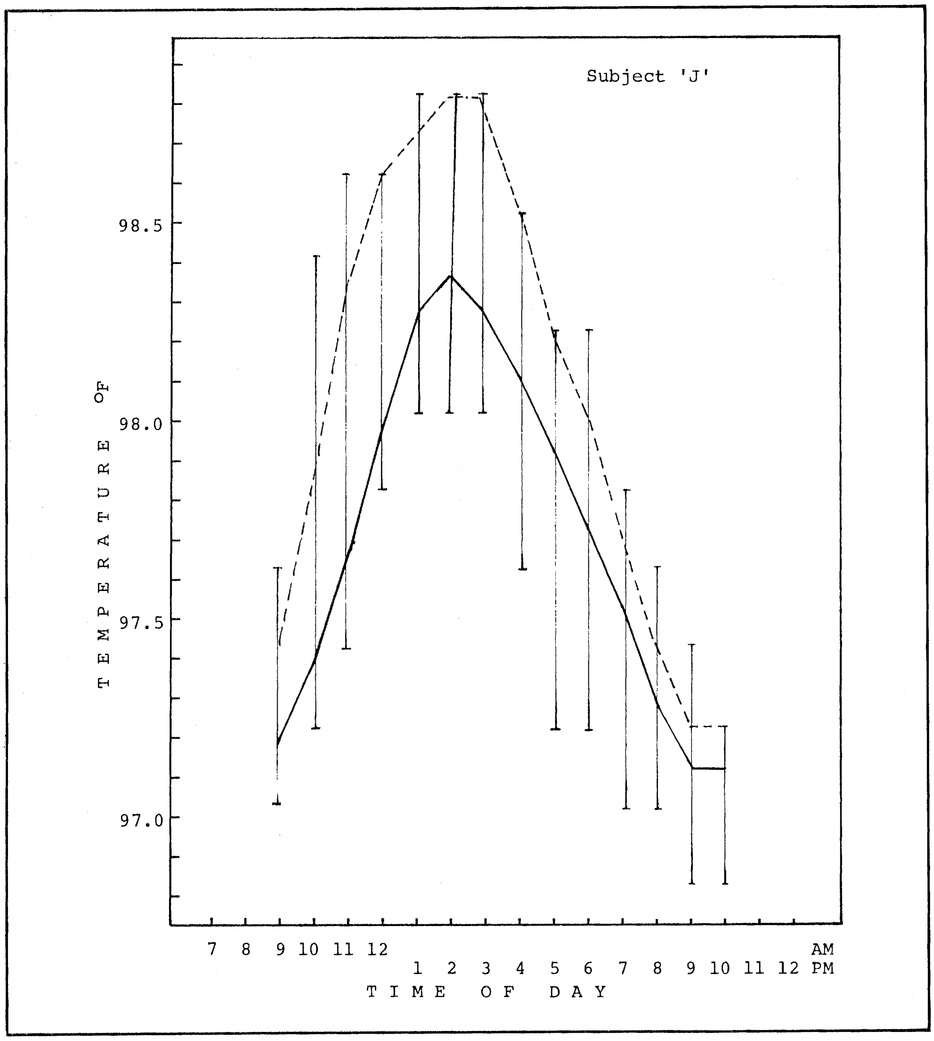

FIGURE 4. Comparison of oral temperature rhythm on the day of ovulation (broken line), with the average rhythm seen on the other thirteen days in this subject. The vertical bars indicate the range of temperature readings for each day.

toms and 3 representing the highest level of intensity. The data revealed a clear rhythm showing maxima in the morning and evening hours with the greatest relief coming in mid-afternoon. A smaller peak was shown at 1300.

This type of information, combined with a knowledge of the pattern of symptom fluctuation and of environmental and emotional factors that exacerbate the condition, should enable a person to deal more creatively with such chronic maladies.

Shift Work and Temperature Rhythm. The response of body temperature and other rhythms to conditions imposed by night shift work schedules has been investigated by a number of chronobiologists and this work has been summarized recently by Folkard (in press). Two principal effects of night shift work on temperature rhythms noted are a flattening of the temperature curve and a gradual phase shift (Coloquhoun 1971).

Prior to the start of my Biological Rhythms class one of the students (male, 21 years old) had terminated a job on which he had worked the night shift (9:00 P.M. to 6:00 A.M.) five days per week for several months. He monitored his oral temperature during the second week after his return to a "normal" day-night wake-sleep cycle, and observed a complete reversal in the pattern (fig. 5).

A variety of other parameters could be monitored in shift workers once a willing subject and employer are identified. A reversal in the wake-sleep cycle is bound to bring about a variety of subtle changes in physiological and psychological rhythms, and information about these

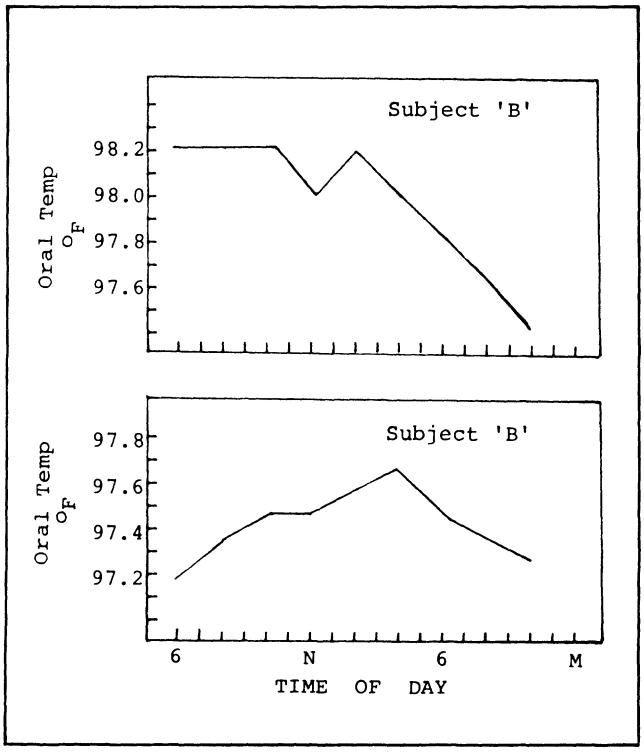

FIGURE 5. Influence of shift work on oral temperature rhythm. Upper graph shows rhythm of subject during second week after ceasing night shift work. Lower graph shows pattern observed during the ninth week after cessation of night work. Note the phase shift in rhythm.

changes could be useful in adjusting work schedules to accommodate individual differences and to determine the times during which different types of tasks would be performed most efficiently.

Further Studies

Many other kinds of chronobiological studies could be designed. Once students become aware that this relatively new field is replete with unanswered questions accessible to the novice, without the need for elaborate or expensive equipment, their interest increases accordingly. They also tend to be motivated by the opportunity to learn more about themselves.

Some examples of further studies might include: a comparison of temperature rhythms among family members, between identical twins, or between grandparents and young children; rhythms in the occurrence of headaches and other symptoms; rhythms in the swelling of joints; rhythms in drowsiness and alertness; rhythm in the growth rate of hair or beard; jet lag syndrome among travelers; possible occurrence of menstrual cycle synchrony among roommates in dormitories. If the equipment is available, one could enter into an assessment of rhythmic changes in K^+, Na^+, and other metabolites of saliva or urine. Other ideas can be gleaned from the various sources cited.

The field of human chronobiology promises to provide us with significant insights into the various internal patterns of recurring change by which we have come to anticipate and flow with the rhythms of nature. We may also begin to recognize patterns in some of our chronic disfunctions and in the process learn to deal with them more effectively.

Acknowledgment—Much of the incentive for writing this article grew out of my participation in the NSF Chautauque Short Course, "Chronobiology: A new dimension in biology and medicine" (1979-80), which provided an excellent context within which to discuss some of the ideas presented here. Dr. Lawrence Scheving, as instructor, shared his considerable knowledge of the field freely and enthusiastically and encouraged all participants to take an active part in developing and disseminating new information in the field.

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Extended Discretion Labs

. . . from p. 256

- Controlled discretionary demand throughout the school year: a gradual increase in time between reviews with gradually increased student responsibility up to or beyond his/her measured maximum.

By having experiences in increased responsibility for the learning process, the student will also experience increased uncertainty. One goal is to correspondingly increase the student's ability to exercise discretion when dealing with uncertainty. I invite you to generate and conduct your own Extended Discretion laboratory activity and to communicate to me your observations of differences in student responses.

The exercise of discretion is so important in one's success outside of school that training in discretion, if possible, certainly should be explored. The biology laboratory seems an excellent opportunity for students to develop to their fullest discretionary abilities. The biology teacher can make an important long-range contribution to the student by providing the student frequent opportunities in the laboratory to deal with uncertainty through the exercise of discretion.

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Debating Creationists

. . . from p. 245

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