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CARDIAC MUSCLE STUDIES WITH RAT VENTRICULAR STRIPS

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INTRODUCTION

Several classical experiments have been used in the undergraduate phsyiology laboratory for many years to demonstrate and compare physiological properties of skeletal, smooth and cardiac muscle. These experiments commonly use frog gastrocnemius skeletal muscle, rat intestinal or uterine smooth muscle, and frog or turtle heart. Details of these experiments are included in many physiology laboratory manuals (1-3).

Mechanical properties are readily studied and compared in the skeletal and smooth muscle preparations. In our experience, however, the turtle heart preparation serves a useful purpose in demonstrating events of the cardiac cycle but has not been suitable for studying cardiac muscle mechanics. It has also given variable results with topical application of pharmacologic agents. We have therefore developed a right ventricular strip preparation from the rat which we feel better demonstrates several important mechanical and pharmacologic properties of cardiac muscle.

The objectives of experiments with this preparation are:

1. to obtain a length-tension curve for cardiac muscle and determine the optimal length at which maximal tension is developed (P_o);
2. to demonstrate the important role of Ca^{++} in excitation – contraction coupling;
3. to show the inotropic effects of several cardioactive drugs.

We have successfully used this preparation in an undergraduate physiology course to compare and contrast physiological properties of cardiac muscle with those of skeletal and smooth muscle.

MATERIALS

Buffer:

Krebs – Henseleit I

NaCl	6.9 grams/liter
KCl	0.35 grams/liter
$NaHCO_3$	1.0 grams/liter
$MgSO_4.7H_2O$	0.293 grams/liter
KH_2PO_4	0.162 grams/liter
$CaCl_2$	0.28 grams/liter
Glucose	1.8 grams/liter

Drugs:

Epinephrine
Norepinephrine
Acetylcholine
Lidocaine

NOTE: Calcium is added after the other salts have been dissolved and the buffer made up nearly to volume. This is to prevent precipitation of calcium phosphate. The solution is made to volume and gassed with 95% O_2/5% CO_2, pH is adjusted to 7.4.

EQUIPMENT

Isometric force transducer – Harvard model 373 or equivalent.
Metric micrometer – Measurement range should be 20 mm in 0.25 mm increments.
Muscle chamber – This can be readily made from plexiglass.
Water bath – Water bath with 37° C temperature control.
Gas tank with 95% O_2 – 5% CO_2 and aeration system.
Physiological stimulator – Harvard model 344, 345, or equivalent.
Recording system – Harvard model 350 recording channel with chart mover; Harvard Biograph with input coupler and 2150 recording channel; or equivalent physiological recording system.

The components mentioned above assembled into a functional system may be obtained from Harvard Apparatus Co., 150 Dover Road, Millis, Mass. 02054.

CARDIAC MUSCLE PREPARATION

Cat papillary muscle is the most commonly used preparation for *in vitro* research studies of myocardial mechanics. It has a linear arrangement of muscle fibers and a cylindrical shape which simplifies the geometry and allows for more accurate measurement of shortening (isotonic) or tension development (isometric) than would be possible using ventricular wall fibers with irregular geometry (4). This preparation is not suitable for the undergraduate physiology laboratory due to economical and technical considerations.

Another *in vitro* preparation using rabbit or rat atrial strips has been used extensively to study the effects of various pharmacologic agents on myocardial mechanics (5). This system has two major disadvantages: 1. rabbits, and facilities to house and care for them, are often not available in the undergraduate physiology laboratory; 2. rat atrial preparations, because of their small size, are difficult to work with and do not develop enough tension to be readily measured with an isometric transducer. (Isometric transducers with enough sensitivity are available but excessive baseline noise from vibration and other factors makes their use in a teaching laboratory difficult.)

Rat right ventricular strips show the same qualitative response when compared with rabbit or rat atrial strips and have the advantages of being economically feasible and technically easy to work with. They have the additional advantage of developing tensions which can be easily measured with a minimum effect from transducer noise.

PREPARATION OF RIGHT VENTRICULAR STRIPS

The preparation we have employed is similar to the myocardial strip preparation used many years ago by Lundin and described in Rushmer's *Cardiovascular Dynamics* (6).

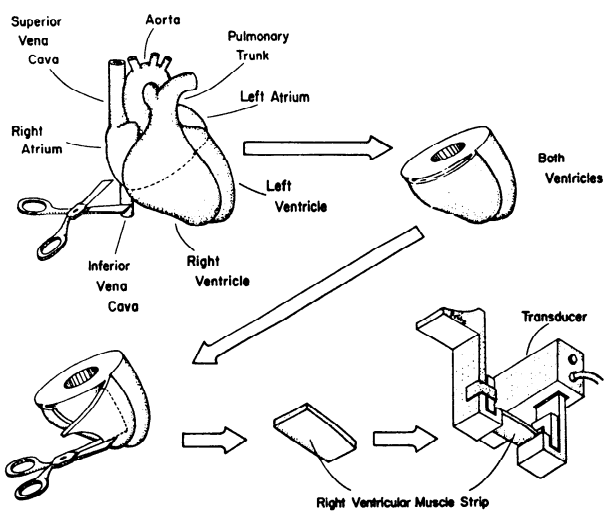

Fig. 1. Method of right ventricular strip dissection.

Laboratory white rats weighing at least 200 grams are sacrificed by decapitation and the heart quickly removed and placed in a petri dish or finger bowl containing oxygenated buffer (see materials section for buffer recipe). The atria are separated from the ventricles by cutting along the atrioventricular septem (Fig. 1). A strip of muscle is cut from the free wall of the right ventricle about 10-15 mm long and 2-3 mm wide. The ends of this strip are squared and placed in the clamps as shown in Figure 1. The strip is now fixed between a clip attached to the arm of an isometric transducer and a second clip which is attached to the moveable barrel of a metric micrometer (Fig. 2). The preparation is then placed in 100 ml of buffer through which a mixture of 95% O_2/5% CO_2 is continuously bubbled. Buffer temperature is maintained at 37°C with a surrounding water bath through heat exchange.

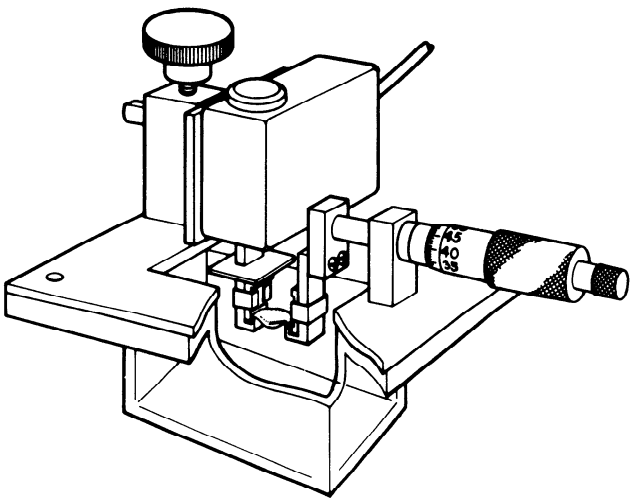

Fig. 2. Transducer assembly – transducer beam is modified with a clamp to hold one end of muscle strip. The other end of muscle strip is held by a clamp which is attached to the barrel of a metric micrometer.

ISOMETRIC RECORDING SYSTEM

Stimulating electrodes connected to either a Harvard model 345 or Grass model S5 stimulator are placed on either side of the muscle strip. The muscle is stimulated through the use of "field stimulation" techniques (5). Initially, a stimulus strong enough to invoke a contractile response is found for a fixed pulse duration and frequency. In our experiments, these were set at 10 msec and 1 per second, respectively. Stimulus intensity is decreased until no response is observed and then increased in small increments to find threshold. Threshold voltages were between 10 and 30 volts. All experiments were run at a stimulus intensity 20% greater than threshold. Electrode type, placement and stimulus parameters greatly influence tissue response; Levy (5) gives an excellent, detailed discussion of these effects.

Force is measured using a Harvard model 373 isometric force transducer which was modified by attaching a muscle clip to the transducer beam (Fig. 2). This is a differential capacitance transducer with a 0-100 gram sensitivity range. The output of the transducer is fed directly into a Harvard model 350 pen amplifier and the signal written out on an oscillographic recorder. Output from this transducer can easily be coupled to most recording systems found in physiology teaching laboratories (i.e., Harvard Biograph, Narco Physiograph, Beckman Dynograph, Grass Polygraph, etc.). Force output can be accurately and easily calibrated using a set of analytical weights. In our experiments, the Harvard model 350 pen amplifier was set at a sensitivity of 100 mv/2cm. Force calibration of the model 373 isometric transducer with attached muscle clip was equal to one gram per centimeter of

pen deflection and was linear over the range of 0.1-1.5 grams.

PHYSIOLOGICAL MEASUREMENTS

The preparation was first used to demonstrate the Frank-Starling, length-tension relationship. The optimal length at which maximum force was developed (P_o) was then used for studies demonstrating the importance of Ca^{++} for force development and for showing the positive and negative inotropic effects of several pharmacologic agents.

Length-tension relationship – The muscle is stimulated with a voltage 20 percent greater than threshold at a frequency of 1/sec. The minimum length at which tension is first developed is determined for the muscle strip. This is defined as resting length. The force of contraction is recorded in grams and the resting length of the muscle measured in millimeters and recorded. The muscle is then stretched a known distance by moving the right hand muscle clip away from the muscle clip which is attached to the transducer arm (Fig. 2). This is accomplished by turning a metric micrometer which is attached to the right hand clip. The muscle is allowed to stabilize for 1 minute. The baseline is adjusted by using the offset control on the transducer. Force in grams is again measured and recorded. The procedure is repeated using 0.25 mm increments until peak force has been reached and several points on the downward side of the length-tension curve have been established. Data are recorded and a plot of length vs. tension made (Fig. 3).

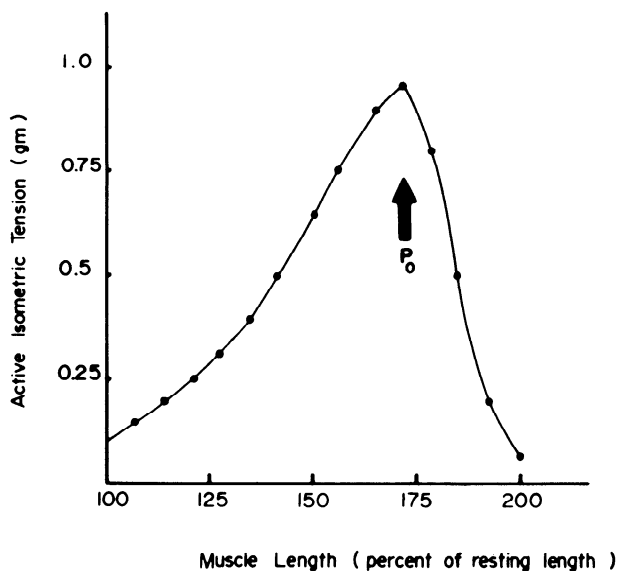

Fig. 3. Length-tension curve for a right ventricular strip. Length at which maximal tension was developed (P_o) was 171% resting length.

Role of Ca^{++} – The muscle is stretched to the length at which maximal force (P_o) was developed (See length-tension diagram, Fig. 3). The muscle is again stimulated with a voltage 20 percent greater then threshold at a rate of 1/sec. Force of contraction is recorded in grams. The normal buffer is replaced with a pre-warmed, Ca^{++} free buffer. The response to a Ca^{++} free buffer is followed for two minutes and force is recorded. The Ca^{++} free buffer is then siphoned out of the chamber and fresh, pre-warmed buffer with Ca^{++} added. The response is again followed for two minutes and force recorded (Fig. 4).

Positive inotropic effects – Fresh buffer is placed into the muscle chamber and the preparation is allowed to stabilize for 5 minutes. Stimulus parameters and initial length are the same as those used in studying the role of Ca^{++} on force generation. After 5 minutes, force is measured and epinephrine (0.2 ml of a 1:1000 solution) added to the buffer. Change in force is measured. The buffer is changed, the preparation allowed to stabilize, and norepinephrine (0.5 ml of a 1:1000 solution) added. The force response is again followed. Change of force as a function of epinephrine and norepinephrine is calculated and recorded (Fig. 4).

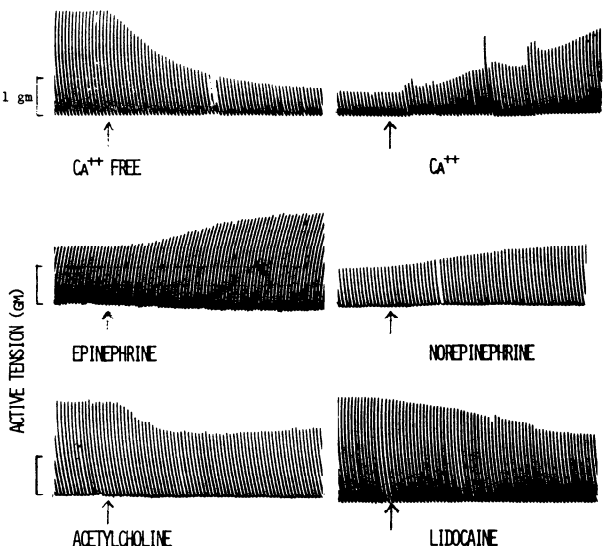

Fig. 4. Influence of Ca^{++} and several inotropic drugs on developed active tension in right ventricular strips. (Strips were stimulated at a frequency of 1/sec.; chart speed was 0.1 cm/sec.; arrows indicate points at which perturbations were made; see text for drug concentrations.

Negative inotropic effects – Fresh buffer is placed into the muscle chamber and the preparation allowed to stabilize for 5 minutes. Stimulus parameters are similar to those described previously. Force is measured and acetylcholine (1 ml – 0.2 mg/ml) added. Change in force is followed. The buffer is changed and the response to a solution of lidocaine (2.5 ml of a 1% solution) is observed. Change in force developed as a function of acetylcholine and lidocaine is also calculated and recorded (Fig. 4).

RESULTS AND DISCUSSION

The experimental preparation and procedures are straightforward and not technically difficult. The most common problems encountered involve maintenance of tissue viability in an oxygenated buffer during dissection, mounting of the right ventricular strip, and electrode choice and placement for good stimulation. Platinum or silver electrodes are best and avoid the problems of electrochemical polarization and corrosion which may accompany the use of ferrous or copper containing electrodes. However, expense is an important consideration with noble metal electrodes and therefore we used stainless steel electrodes for stimulating our preparations. Each electrode should be placed about 1 mm away from the muscle strip and on opposite sides of the muscle strip. Optimal electrode placement will vary depending on type and size of electrode and is best determined by a series of trial placements.

The length-tension curve obtained in our experimental system (Fig. 3) was similar to that obtained by Lundin with frog myocardial strips (6). Maximum contractile tension (P_o) occurred at 171% of resting length with the rat right ventricular strip compared with a P_o of 180% reported for frog ventricular strips by Lundin (6).

The length-tension curve (Fig. 3) for cardiac muscle can be compared with length-tension relationships in skeletal muscle. Myocardial fibers are not restricted by attachment to bone and their resting length is usually less than that required for developing peak tension. This gives the myocardium an inherent reserve capacity so that, when stretched via increased filling during diastole, a greater contractile force can be developed in the following systole (intrinsic compensation). This is in contrast to skeletal muscle which is limited in its length change by anatomical attachments. Under normal resting conditions, skeletal muscle length is close to the length at which peak tension is developed and can only vary from that point by approximately 30%.

Considerable caution must be used when attempting to generalize concepts derived from length-tension relationships in cardiac muscle. Prediction of changes in stroke volume or stroke work from the relationship between resting length and developed isometric tension cannot be made since volume changes require shortening (isotonic contraction) and isometric contraction precludes shortening. This, as Rushmer (6) points out, is the major conceptual problem encountered in attempting to apply the length-tension relationship to cardiac hemodynamics (6). A complex set of relationships between length, force, velocity and time must be invoked to explain the role of myocardial contractility in cardiac hemodynamics. An excellent set of teaching tapes on heart mechanics is available (7) for the advanced undergraduate or graduate student who is interested in pursuing this subject in more detail.

The important role of Ca^{++} ions in mediating excitation-contraction coupling can be observed by first removing Ca^{++} and then adding Ca^{++} to the buffer medium (Fig. 4). The time and magnitude of response (force developed) in cardiac muscle can be compared with similar responses observed with skeletal muscle. These comparisons are valuable in pointing out the rapid equilibration of "contractile Ca^{++}" between medium buffer and tissue compartments in cardiac muscle with respect to similar processes in skeletal muscle (8). The effect of removal of Ca^{++} on force generation in cardiac muscle is immediate and dramatic relative to its effect on skeletal muscle. Students who are interested in a more detailed description of the role of calcium in excitation-contraction coupling may be interested in the recently published papers from the Circulation Group Symposium on excitation-contraction coupling in cardiac and vascular smooth muscle (9).

The positive and negative inotropic effects of several common cardioactive drugs can also be readily demonstrated with this preparation. These effects have been demonstrated at P_o (Fig. 4). A 2.5 x greater dose of norepinephrine was required to get approximately the same magnitude of inotropic response compared to that obtained with epinephrine. This is consistent with the known dose-response characteristics for these two catecholamines on cardiac Beta receptors (10). In addition, a comparison of the effects of epinephrine and acetylcholine on cardiac muscle with the effects of these drugs on intestinal smooth muscle preparations clearly demonstrates the importance of organ specificity in autonomic response.

Students in our undergraduate physiology laboratory have had good success with this experiment and have enjoyed the challenge it presents. We hope that students in other physiology laboratories will enjoy a similar experience.

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PHYSICAL EXERCISE AS A LABORATORY TOOL

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INTRODUCTION

The "felt need" provides a stimulus for learning and needs that have obvious survival value tend to provide the most potent force. They provide a goal to serve as a skeleton to hang facts upon. The current American coronary heart disease epidemic can by utilized to focus the student's attention on cardio-respiratory physiology. It can be pointed out that although once thought of as a disease of aging, cardiovascular disease is now the major cause of death in the 35-44 year old age group and accounts for 13% of all deaths in 25-34 year old age group.[1] Since the majority of heart disease related deaths occur outside of the hospital, it is evident that preventive medicine provides the most logical approach for arriving at a solution to the problem.[2]

Various lines of evidence have indicated that physical activity may serve as a deterent to cardiovascular disease.[3,4] Although the study of the disruption of biological homeostasis brought about by imposed physical exercise has long been of interest to the scientific research community, there has been a general failure to make use of the information gathered from this research in the human biology or physiology course. This neglect has extended to the medical school physiology course as well.[5] This is unfortunate since although exercise conducted properly might benefit man, unaccustomed exercise can produce untoward effects. Shephard and Kavanagh[6] have reported that 30% of the patients in their cardiac rehabilitation program were involved in exercise at the time of the initial episode.

Exercise should not be overlooked as a tool to provide a variety of interesting and informative labs. Labs can be designed which require a minimum of equipment. Since the students serve as subjects, the acquired data take on a special significance.

The laboratory and discussion examples provided in this report will relate to the cardiorespiratory response to exercise. What follows is meant for the unitiated and will offer nothing new to those presently involved in exercise physiology. The instructor making use of these laboratory experiences will find an exercise physiology text such as de Vries[7] or Astrand and Rodahl[8] most helpful.

BACKGROUND

Exercise is classed in two general ways. First, it may be spoken of as being dynamic or static. Dynamic exercise would include the various continuous rhythmic activities such as walking, jogging, dancing, swimming, and cycling. Static or isometric exercise would include such activities as sustained contraction, water skiing, etc. A second classification relates to the relative metabolic quality of a task. If the exercise is of the nature that the performer can meet the oxygen demand of the tissue, it is said to be aerobic. If the oxygen requirement exceeds the performer's supply ability, it is then classed as an anaerobic task.

Immediately upon beginning an exercise there is a certain oxygen requirement imposed by the task. If a subject simply changes from a recumbent to a standing posture there is an increase in the total metabolic activity of the body which is reflected in an elevated oxygen consumption. During such mild exercise the oxygen stores bound to myoglobin in the muscle tissue, along with the oxygen delivered by the cardiorespiratory system normally cover the increased requirement. The determination of the oxygen cost of the task for free ambulation such as walking or running can be caluclated through derived formulas.[9,10] If the task is carried out on a machine, it is easier to standardize the work and calculate its cost. For instance, if a 50 kg subject steps on a 0.5 meter bench at the rate of 30 steps per minute for five minutes the total work would amount to 3,750 kgm X the oxygen equivalent (1 L O_2 = 2153 kgm) which yields an oxygen requirement of 1.74 liters. If the work was done on a treadmill at a +4% vertical grade then the subject's body weight is considered to have been raised four meters for each 100 meters of belt displacement. We could once again work out the actual cost. In our previous example, the oxygen cost of the work amounted to 348 ml per minute. Since the average resting oxygen consumption amounts to about 300 ml per minute we can see that there will be a disparity between the oxygen requirement and the oxygen available until the subject makes the necessary adaptations. During this time local ATP stores are replenished by creatine phosphate and the anaerobic glycolytic route. If the exercise is continued for an adequate period of time (usually 4-5 minutes) the necessary adaptations take place and the oxygen extraction rises to meet the demand as long as the work task is within the maximum oxygen uptake capacity of the subject. The subject is then said to be in "steady state" or on a "pay-as-you-go" basis. Since the blood is virtually saturated as it passes through the lungs, the adaptations that occur during this adjustment are generally considered to be cardiovascular in nature. These would involve an increase in cardiac output which occurs primarily by way of an elevated heart rate, an increased perfusion of the active tissue mediated through the release of local vasodilatory substances and a movement of the O_2 dissociation curve down and to the right as it is influenced by the increased P_{CO_2} (Bohr effect), decreased pH and increased temperature. As the work ends, the oxygen cost immediately reverts to the cost of the resting position. However, the subject's oxygen consumption remains elevated for some minutes. This increased post exercise oxygen consumption is known as the O_2 debt repayment. This debt is characterized by two phases. The first portion of excess oxygen extraction is not accompanied by elevated blood lactate and is known as the alactic portion. The alactic portion is related to the replenishment of oxygen stores in the muscles as well as the replacement of ATP and CP. The remainder of the O_2 debt is associated with the removal of lactic acid.

Although the most predictable effect of an adequate training program on the cardiovascular system is the resultant

bradycardia exhibited in the resting rate, this value as well as any other resting value will not allow us to predict how a subject will tolerate exercise. Instead, a "road test" is required and this usually takes the form of a standardized graded work test. As the subject is exposed to varying work loads the heart rate rises progressively. This rise is paralleled by a rise in oxygen extraction up to a point where the maximum oxygen extraction capability of the individual is reached. Heart rate continues to rise, however; and results in a disparity between the two variables. For these reasons, various strategies have been developed which make use of the linear submaximal work relationship to predict the maximum values. The examples of laboratory experiences which follow may be used to illustrate some of these principles.

QUIET LAB

The purpose of this lab is to demonstrate the heart rate response to posture change and mild activity. It is suggested that the instructor have a stopwatch available to direct the timing of pulse counts. The students are seated in lab and instructed in the method of counting the pulse from the carotid artery. This is best accomplished by demonstration. The instructor turns his head to one side to demonstrate the anterior border of the sternocleidomastoid. The fingers are placed firmly along this border and the head is returned to the neutral position. A pulse should now be palpated. As the students find the pulse, instruct them that each throb is to be counted from the time the instructor says, "begin" until the time they are instructed to "stop". This is important since many students confuse the information about the "lub dub" of a heart sound with what they are about to do. When all of the students can consistently remove the hand and replace it to obtain a count, the instructor then has the class take a count in unison. The seated count is repeated 2-3 times so students can recognize this as their base value. Counts are converted to minute values, averaged, and recorded.

Next the students are instructed to get ready to assume a standing position. They will stand on command and the command to begin counting will be given as soon as everyone is standing. They must have their hand in a position ready to count and should not move too rapidly or too slowly to the standing position. The immediate standing condition is followed by a count taken after one minute of standing at a rigid attention and after a very slow one minute walk. A brief recovery period in the seated position is interspersed between conditions. The students should be instructed not to try and cover ground but rather to try and relax as much as possible.

A class statistician may record the data after each condition and compute the mean and standard deviation. If the precautions suggested are taken, it will be consistently noted that the act of standing results in a dramatic rise in the pulse count which can be explained by describing the baroreceptor reflex response. The post walking pulse count will normally be lower than the prolonged standing count. This can be attributed to the effect of the "peripheral pump" mechanism. The mechanism can be quickly demonstrated by the method of William Harvey. A prominent vein on the back of the hand is occluded with one finger and blood is milked toward the heart and beyond a valve. This same effect results from muscle contractions which increase venous return to the heart.

EXERCISE

To conduct a meaningful lab on the pulse rate response to exercise there must be a means of standardizing the work task. A long bench can be constructed inexpensively out of two by fours and plywood. The benches should be 33 cm high for females and 40 cm for males. If the benches are 6-8 feet long, several students can step on them at once.

A progressive pulse test has been developed by Waxman.[11] In this test, students record their pulse rate adaptation to work intensities which are varied from mild to intense. The only materials required to conduct this test is a bench and a stopwatch. A metronome, if available, is useful for setting the cadence for stepping.

To administer this test, it is best to have students pair off. One student will count the carotid pulse while the partner takes the test. First, a resting count is obtained. This is usually accomplished by allowing the subjects to sit on the bench for five minutes. Several 30 second carotid pulse counts are made until two identical counts are recorded. If a student's count remains erratic. an average may be used.

A demonstration of the stepping procedure is then performed. Since stepping is a four count activity, a metronome set at 48 counts per minute would direct the appropriate rate for 12 steps per minute. The count is then, (1) step, (2) up, (3) step, (4) down. It should be emphasized that one foot is used to lead the activity and that the knees are to be in full extension on the bench. The students then perform the activity for one minute. The performer sits on the bench immediately at the

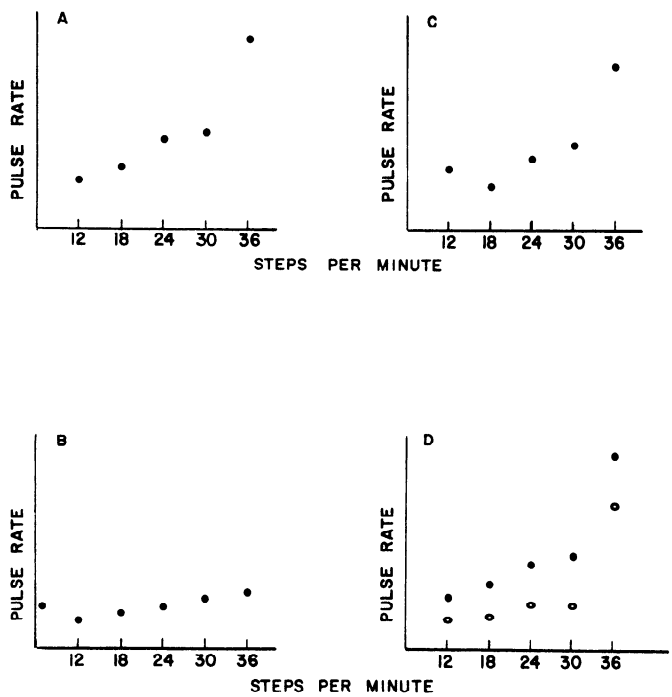

Fig. 1 • Before training. ◦ Post training. A. Non-trained subject. B. Subject with high degree of cardio-respiratory fitness. C. Subject with inflated initial pulse. D. Effect of endurance training.

Table 1

Classification	Total 2' Pulse Count After 12 Steps/Min.	Total 2' Pulse Count After 18 Steps/Min.	Total 2' Pulse Count After 24 Steps/Min.	Total 2' Pulse Count After 30 Steps/Min.	Total 2' Pulse Count After 36 Steps/Min.	Centile
	98	113	125	130	148	99
	104	119	131	137	155	
Excellent	110	125	137	144	162	
	116	131	143	151	169	95
	122	137	149	158	176	
	128	143	155	165	183	
	134	149	161	172	190	90
Very Good	140	155	167	179	197	
	146	161	173	186	204	80
	152	167	179	193	211	70
	158	173	185	200	218	60
	164	179	191	207	225	
Average	170	185	197	214	232	50
	176	191	203	221	239	
	182	197	209	228	246	40
	188	203	215	235	253	30
	194	209	223	242	260	20
Below Average	200	215	229	249	267	
	206	221	235	256	274	10
	212	227	241	263	281	
	218	233	247	270	288	
	224	239	253	277	295	5
Poor	230	245	259	284	302	
	236	251	269	291	309	
	242	257	271	298	316	1
Mean	170.4	184.9	196.8	213.6	232.0	
Sigma	31.2	30.3	31.4	34.4	34.4	
Number	135	135	136	139	132	
Range	99-237	120-258	125-260	132-311	147-320	

H.A. deVries unpublished data. This table from Laboratory Experiments in Physiology of Exercise by H.A. deVries, copyright 1971 has been used with the permission of Wm. C. Brown Publishers.

end of the minute and the counter quickly finds the carotid pulse. At exactly 10 seconds after the termination of stepping the instructor gives the command to begin a pulse count. This post exercise count continues for two minutes and is recorded on a data sheet. The counter and performer then exchange roles and repeat the procedure. Next, the original steppers have their resting pulse counts checked until they return to within 10 beats of the original value. The procedure is then repeated at the rates of 18, 24, 30, 36 steps per minute.

The data obtained in this simple test provide the opportunity for the instructor to introduce a number of interesting concepts. The results can be compared with normal values in Table 1. Unfortunately, these values have been obtained from college age males. However, instructors could retain the values recorded in class and develop a set of norms for their specific populations. It is interesting to have the students graph their individual data. Typical graphs are displayed in Figure 1. Graph A demonstrates the typical response of a non-trained subject. Note the linear increase in the pulse counts at the slower rates and the sharp break at the last rate. Graph B illustrates the performance of an individual with a high degree of cardio-respiratory fitness. We note in this case that all stepping rates are performed at pulse counts which are lower than those in the non-trained state. The most predictable effect of training of an endurance nature is the reduction in resting[12] and submaximal[13] exercise pulse counts. Since each person has a maximal pulse rate which does not seem to be trainable,[13] the graphic relationship between resting, submaximal and maximal pulse counts (the latter is estimated by the formula 220-age) would demonstrate that the unfit organism always lives closer to its ultimate adaptation or closer to death. That is, the unfit have a smaller cardiac reserve.

Graph C demonstrates test results in which a decrease in the pulse count was noted between 12 and 18 steps per minute. The inflated initial pulse count may have occurred as a result of a psychological influence due to some apprehension on the part of the subject. It may also reflect a failure to obtain a true resting pulse count.

Finally, graph D demonstrates the effect of endurance training on this test. The subject has a lower working pulse count at all submaximal work loads and the curve is moved down to the right.

ESTIMATION OF MAXIMAL O_2 UPTAKE

A form of the bench step may be used to estimate the student's maximal ability to extract O_2. The ability is influenced by the physical fitness of the subject. Rowell[14] has recently provided an excellent review on this topic. He concludes that VO_2 max. is not limited by pulmonary factors. Neither is it limited by muscle metabolism since it can be shown that the VO_2 max. obtained from a large working muscle mass is not increased by the imposition of additional working muscles. Instead, Rowell views VO_2 max. as a limitation set by the cardiovascular system's inability to meet the summated perfusion and metabolism demands of the large working muscle mass.

To actually measure VO_2 max. a substantial amount of equipment is required. For instance, it requires the measurement of the amount of air moved and the collection of volumes for analysis of CO_2 and O_2 concentration. However, the parameter may be estimated rather accurately (S. E. 6.7 to 10.4%)[15] at submaximal work loads from the nomogram developed by Astrand and Rhyming (Figure 2). To derive a VO_2 max. estimate, a six minute work task is administered. This usually allows ample time for the subject to make the necessary cardiovascular adjustment to the work. The work

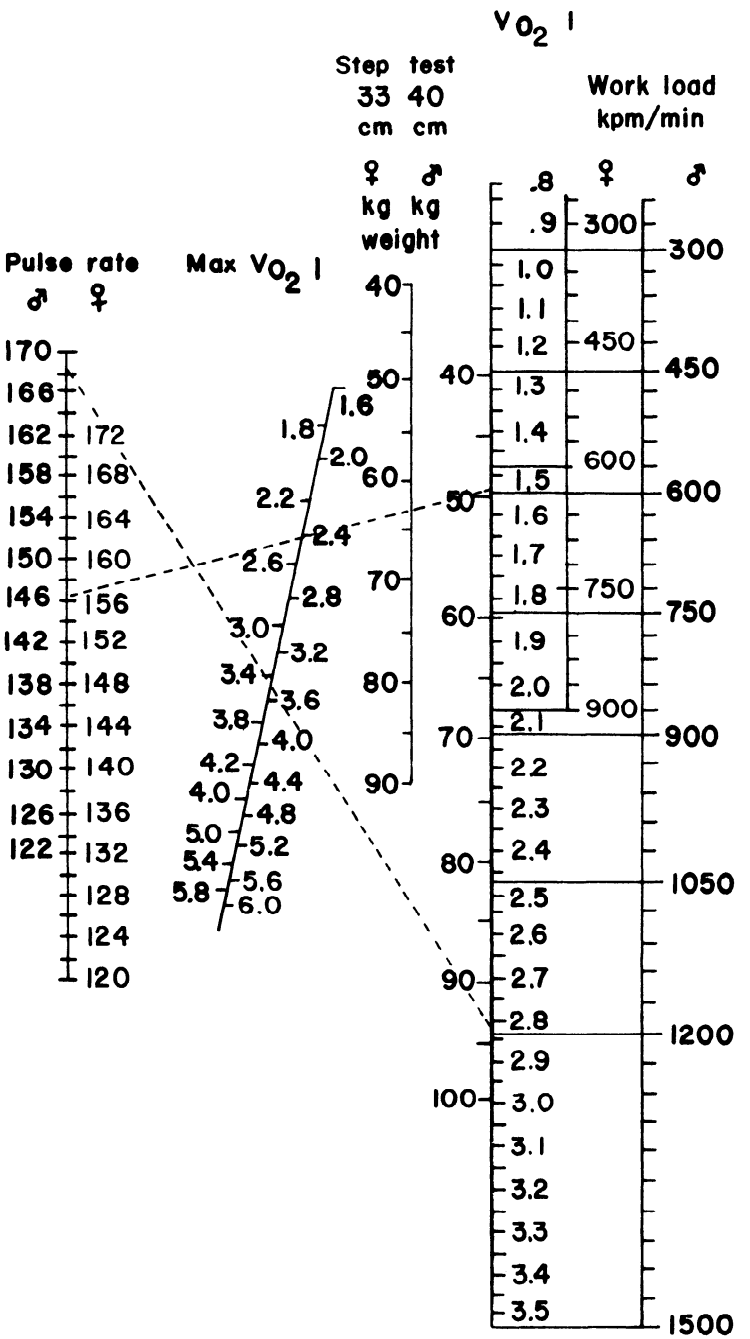

Fig. 2 From I. Astrand, Acta Physiological Scandinavica, 49 (suppl. 169) 1960.

may be performed on the step test or the work may be accomplished on a leg or arm ergometer. The advantage of the ergometer is that it allows a variety of work loads to be set in standard measurement units and it allows measurements of heart rate and blood pressure to be taken during the work. Figures 3A and 3B provide examples of ergometers that may be constructed from old bicycle parts. Further information on the construction and use of ergometers is available in the literature.[16, 17, 18]

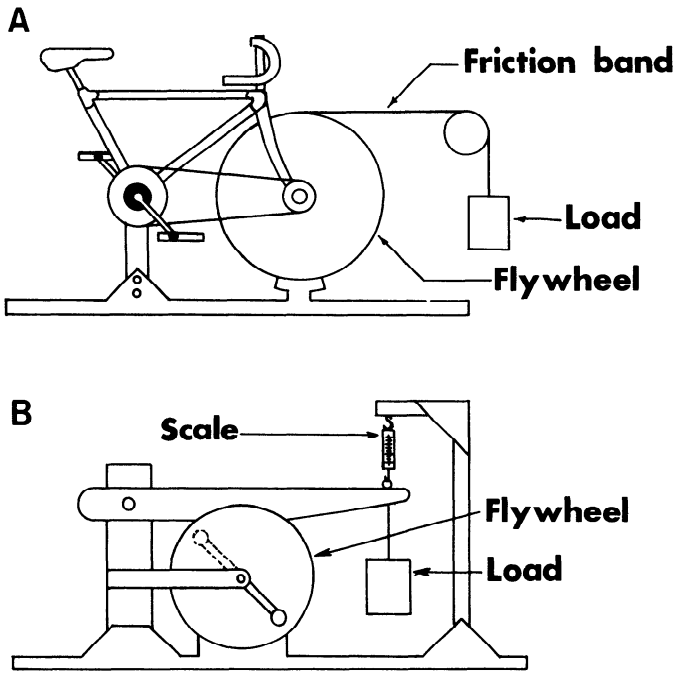

Fig. 3 Examples of ergometers constructed from old bicycle parts.

THE WORK TEST

The subjects position themselves and adjust the ergometer so they can work comfortably. Next, a cadence is set at 100 beats per minute either by a metronome or by counting. This will move the fly wheel 50 times per minute. The subject practices this cadence with no load set. As the cadence is maintained a load is added. The load selected should be sufficient to bring the heart rate to between 130-150 beats per minute. This will usually require a load of 300-600 kgm/min. (2170-4339 ft. lbs.) for females and 600-900 kgm/min (4339-6509 ft. lbs.) for males. Pulse rates should be obtained from a carotid artery during the last 15 seconds of each minute of work. If, at the end of six minutes the heart rate has not reached the 130-150 beats per minute criterian, the work load is increased by 300 kgm/min and continued for another six minutes. To estimate VO_2 max. average the pulse count for the final two minutes of work and enter the nomogram of Astrand which is displayed in Figure 2. In the example, we see that a female subject weighing 51 Kg has achieved a pulse rate of 156 on the step test. When these two points are connected by a straight edge we find the estimated VO_2 max. to be 2.4 liters. To make comparisons between people, it is necessary to divide this value by the body weight. The normal values for teenagers are found in Table 2.[19]

Table 2

(ml/kg/min)

	LOW	AVERAGE	HIGH
Female	35	40	45
Male	39	44	49

It should be emphasized that the value obtained represents an estimate of the maximum ability to extract O_2 from the atmosphere and not simply the amount of air moved. In fact, about 20 volumes of air must be moved to extract 1 L of O_2.[20] It should also be pointed out that this ability to extract O_2 is generally accepted as the best indicator of cardio-respiratory fitness.

The (20:1) relationship between air moved and oxygen extracted is known as the oxygen utilization equivalent. If a lab can afford the expenditure (about $300-$400) for the necessary equipment to measure the air flow during work this equivalent can be used to estimate the oxygen extraction minute by minute during the work and the subsequent recovery phase. These data then provide a means of demonstrating the O_2 debt payback. The necessary equipment would include a low resistance valve, a length of low resistance tubing and a low resistance respiratory gas meter.

Thousands of suspected cardiovascular disease patients as well as post myocardial patients have been subjected to the types of stress imposed by the procedures discussed.[21] Certain precautions should be taken even with normal young adults. The subject should have had the usual mandatory physical exam and be cleared for physical activity. The activity should be stopped if any of the following develop:

dyspnea
ataxia
mental confusion or dizziness
chest pain or pressure
systolic pressure greater than 240
diastolic pressure greater than 125
failure to keep systolic pressure above the work heart rate

If an EKG is taken:

T wave depression
ST segment depression or elevation

The data on working oxygen consumption derived from these labs may be coordinated with measurements on work heart rates and blood pressures which allow some rough estimates of the total peripheral resistance to be made. For instance, if it is assumed that the diastolic pressure is a result of the unstretched volume of the artery and the systolic pressure results in the stretched volume then the pulse pressure may be taken as an estimate of the stroke volume. The formula for the total peripheral resistance estimate would then become:

$$TPR_{est.} = \frac{\text{mean arterial pressure}}{\text{Cardiac Output}} = \frac{(\text{Systolic} + 2\,\text{Diastolic})/3}{\text{Pulse pressure} \times \text{heart rate}}$$

We will find that comparisons of the TPR estimate before and during or immediately after exercise demonstrate a fall in the TPR estimate which may be explained by the potent vasodilatory effect of exercise. To continue the use of these estimates we can remind the student that, at rest, blood

containing about 15 gm Hb per 100 ml will combine with 1.30 ml O_2 per gm to yield 19.5 ml O_2 per 100 ml or 20 volume percent. Since blood leaves the lungs about 98% saturated and returns about 60% saturated, 38% of the oxygen is extracted. That would account for 7.410 ml oxygen per 100 ml of blood. Then, a resting cardiac output of about 5 liters of blood will deliver 370.5 ml of oxygen to the tissue each minute. Finally, volumes of oxygen are converted to calories per minute by multiplying by 4.825 (caloric equivalent of 1 L O_2, assuming a mixed diet). Working backward from estimates of maximum oxygen extraction and recorded working pulse rates and blood pressures allow some assumptions to be made about changes in the A-V oxygen difference which results from exercise stress.

In summary, the lab work outlined in this paper has been well received by students. The data is meaningful since it is derived from themselves rather than a laboratory creature. Not only has the information gained from the labs served to stimulate discussions which draw together the cardiovascular and respiratory units but it has also stimulated many students to alter their sedentary life styles. This latter fact may serve to improve their quality of life if not their longevity and that, after all, is at least part of what education is about.

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EVALUATION OF PHYSIOLOGY COURSE OBJECTIVES BY A MEDICAL SCHOOL FACULTY

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University of Health Sciences/The Chicago Medical School, Chicago, Illinois 60612

For many years educators (Randall, 1967 and others) have noted that physiology in medical school is usually taught by faculty who for various reasons may have limited opportunities to assess the applicability and significance of this discipline to medicine. In recent years, various attempts have been made to remedy this situation through symposia conducted by physicians to inform physiologists as to the clinical application of their discipline. In the United States, the American Physiological Society has offered Refresher Courses which present recent advances in physiology emphasizing the clinical relevance of these developments. Blank (1975) and Forsling (1976) reported on an "Orientation Course in Medicine for non-medically qualified physiologists who teach medical students" sponsored by the Physiological Society of Great Britain. Blank (1975) considered that the "greatest value of this course was to acquaint the physiologist with the clinical aspects of medical training and help him to see the curriculum as a whole."

Both types of programs have been beneficial for the participants. However, a limited number of persons have been involved; and this information has not been applied directly to a specific school curriculum.

The Educational Affairs Committee of the Chicago Medical School agreed that the goal of our school was (a) to give students a firm foundation in the medical sciences and (b) to train them to make their clinical decisions based on the scientific interpretation of the data obtained from the patient. Consequently, in the course of evaluating the curriculum at the Chicago Medical School, one aspect of concern to the Educational Affairs Committee[1] and our faculty was the relation of the course content in physiology (as well as in the other basic science courses) to the problem-solving needs of the physician. Prior feed-back from some students and clinicians indicated that the physiology course was oriented towards training of research physiologists. Other students and clinicians have stated that the course did not include principles and concepts that were relevant to the problem-solving needs of the physician.

To resolve this question, the Educational Affairs Committee requested the faculty of the Department of Physiology and Biophysics to prepare the instructional objectives for medical physiology in a format suggested by Gronlund (1970).[2] This method has been suggested for the preparation of objectives by the Education Office of the American Physiological Society (1973). The objectives were reviewed by a Task Force composed of members of other Basic Science Departments, Clinical Science Departments and senior students to determine their centrality and clarity. Centrality was classified as (a) essential or core knowledge for all physicians and/or necessary for licensing examinations; or (b) only necessary for research activity or for certain specialists. Clarity was defined as "clear communication to the reader as to the behavior displayed by the student in achieving the objective." Objectives were also evaluated as to whether or not there were duplications (repetition and/or reinforcement) in relation to objectives of other courses, since this is an indication of the degree of inter-departmental communication essential for effective presentation of scientific information. If duplications in objectives were noted, the reviewers were asked to indicate if this duplication was repetitious, i.e., repeated in the same way by each department without further development, or reinforcement, i.e., a concept developed in a novel manner or in greater depth to gain new insight. Task Force members were also requested to make recommendations regarding opportunities for interdepartmental teaching as well as identifying omissions in the curriculum.

After reviewing the objectives, the Task Force generally agreed that the objectives were essential or core knowledge for all physicians and that they represented necessary background for making clinical decisions. The Task Force also approved the faculty's addition to the curriculum of objectives in areas of developing knowledge because of their potential value to the physician as well as to encourage the development of an attitude of inquiry and questioning in the student. In addition to indicating a need to improve clarity in the statement of some objectives, the Task Force recommended that the course include objectives in the physiology of birth. An expansion of interdepartmental teaching with the clinical and other basic science departments was also suggested.

While the faculty initially viewed the Task Force process with reservation, their response to the report has been favorable and constructive. Objectives which were considered unclear by the Task Force, have been rewritten. The department has added lectures and objectives on the physiology of birth. Lectures and conferences on pathophysiology have been expanded to acquaint students with syndromes in which physiological concepts are utilized for making clinical decisions.

The peer review of instructional objectives in medical physiology to determine essential objectives in a course designed for training of physicians has been found to be a practical and positive procedure for encouraging interdepartmental dialogue and familiarizing the faculty with the curriculum. The faculty members of the Department of Physiology and Biophysics who served as Task Force members to review other basic science courses became more knowledgeable regarding the background of information the students brought to their course as well as the prerequisites for other courses and thus could be more selective in presenting new material.

In view of the success of the Task Force review process in acquainting members of the faculty with the curriculum and

1. The senior author was Chairman of the Educational Affairs Committee during evaluation of the curriculum.
2. A similar plan for writing and evaluation of instructional objectives was initiated simultaneously for the other basic science courses. These were used for obtaining an overview of the curriculum as well as an evaluation in the same manner as described for Physiology of the course presented by each department.

the needs of the medical student, a similar procedure is being followed for the clinical departments. The clinical departments are now preparing their instructional objectives for review by basic science and clinical faculty and students. The same criteria as specified above will be used for their evaluation. This plan should further acquaint faculty with the curriculum of the school and clarify the knowledge and skills needed by the physician. As a result of this procedure we expect that there will be a better organized educational plan to meet the requirements for scientific knowledge and experience in problem-solving situations, and thus the medical student will become an effective physician.

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HISTORY AT THE FEDERATION MEETINGS

The Committee on History of Nutrition of the American Institute of Nutrition has arranged as an "open meeting" a Session on "Special Topics in the History of Biological Science," to be held during the meetings of the Federation of American Societies for Experimental Biology, April 1-8, 1977, in Chicago, Illinois.

This "open meeting" will be in the Waldorf Room, Third Floor, Conrad Hilton Hotel, on Tuesday evening, April 5, from 7:45 to 9:15 P.M. All interested persons are invited to attend.

The Program, presided over by Dr. E. Neige Todhunter, Archivist of the American Institute of Nutrition, and a Member of the Committee, is as follows:

1. The Value of Studies of the History of Biological Science, E.N. Todhunter (15 minutes)
2. With Professor A.B. Luckhardt, on the Trail of Dr. William Beaumont, F.C. Bing (20 minutes)
3. Dr. James J. Moorhead, Chicago Surgeon, and his Unique Contributions to Physiological Research, Carl A. Dragstedt (15 minutes)
4. The History of Nutrition – A Tour of the Literature, William K. Beatty (20 minutes)
5. The Use of Antibiotics in the Production of Farm Animals, including Poultry (an example of living history), Thomas H. Jukes (20 minutes)

Dr. Todhunter is Visiting Professor of Nutrition at Vanderbilt University. Dr. Bing, a consultant on foods and drugs, is Chairman of the Committee. Dr. Dragstedt is Emeritus Professor of Pharmacology, Northwestern University. Mr. Beatty is Professor of Medical Bibliography at Northwestern University School of Medicine, and is the author of numerous articles and books on medical historical topics. Dr. Jukes is Professor in Residence, Space Sciences Laboratory, University of California, Berkeley, California.

Registrants at the Federation Meetings will also be able to see a display of materials pertaining to the life and career of Dr. William Beaumont (1785-1853), pioneer American physiologist. This exhibit has been designed to show the kind of "little things" that amateur historians can readily acquire, and use to advantage in teaching. The display will be in the Foyer of the Bel Air Room, Third Floor of the Conrad Hilton Hotel, manned by Members of the Committee from 9:30 A.M. to 1:30 P.M., Tuesday through Thursday, April 5 to 7, inclusive.

The Labor Department has released its 1976-77 edition of Occupational Outlook Handbook. Between 1974 and 1985, growth in professional and technical jobs is expected to continue to outpace the rate for all occupations combined, with strong demand in the health field, engineering, personnel and labor relations work, social work and systems analysis. In the sciences, demand is expected to be high for geophysicists with good prospects in store for geologists, chemists, physicists, biochemists, food and life scientists and meteorologists. Prospects are poor and will get worse for lawyers and teachers.

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THE PHYSIOLOGY TEACHER, presently in its sixth volume, is published under the supervision of the Education Committee of the American Physiological Society. Substantive papers, including laboratory experiment descriptions are now refereed by members of the Educational Materials Review Board (constituted of slightly over 100 members distributed throughout the specialities of physiology). The Education Committee has decided to eliminate its inventory of back issues of Volumes I through V by producing a limited number of complete collections bound in spiral binder for convenient use in the laboratory. This 285 page volume is offered at the extremely low price of $10.00 on a first come first served basis as long as the limited supply lasts. Our more recent subscribers may be especially interested in obtaining this collection of back issues. Please use the order form below to obtain this volume.

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BOOK REVIEWS

Electron Microscopy and Cell Structure (Book 2, Basic Biology Course, Unit 1 – Microscopy and its Application to Biology) by Michael A. Tribe, Michael R. Eraut and Roger K. Snook, Cambridge University Press, New York and London, pp. 117, 1975.

"The main aim of this book has been to get you to look critically at the fine structure of plant and animal cells, as seen by the electron microscope." This book is part of a Basic Biology Course for undergraduates written by the Inter University Biology Teaching Project Team at the University of Sussex, England. In 117 pages, the authors succeed admirably in carrying out their aim. The book essentially covers only the fine structure of cells. Functions of cell structures are dealt with briefly, but are covered in more detail in subsequent books in the series.

The book presents many excellent electron micrographs of plant and animal cells. Each micrograph is followed by a series of questions which the student answers in a "response booklet". The correct answer is given in the book after each question, but the format is such that these answers can be covered by a "masking card". The idea is to get the student to write down an answer and then to *check* whether the written answer substantially agrees with the answer given in the book. If any answer is incorrect, the student is to retrace the previous steps to determine why. Some parts of the book require a tape recorder and a slide viewer or projector. For example, a tape and slide sequence on preparing a specimen for the electron microscope is provided. A question and answer section as above for these tape/slide sequences is also given in the book.

The book is divided into four parts. The first part presents a brief history of microscopy and the cell concept. The second part demonstrates the difference in resolution and magnification obtained by the light versus the electron microscope and shows how specimens are prepared for electron microscopy. The third and longest part of the book covers the internal structure of cells. Especially useful are the sections which show how to develop three-dimensional representations of subcellular particles and membranes from two-dimensional electron micrographs. Included also are techniques for fractionating cells: homogenization, differential centrifugation, and density gradients. Clear explanations of electron microscopy techniques and the advantages of each are provided: negative staining, heavy metal shadowing, freeze etching and freeze fracturing, and scanning electron microscopy. The fourth part is a self-assessment examination designed to test the student's understanding of the concepts presented in the book.

By the end of the book the student should have a good grasp of the function of the electron microscope, the likely side-effects of preparing specimens for electron microscopy, the fine structure and relative sizes of cells and cell organelles, and methods for isolating cell organelles. The Basic Biology Course, of which this book is a part, is an excellent example of the usefulness of the audio-tutorial and self-teaching methods of instruction.

D.E. Buetow, Ph.D.

Dynamic Aspects of Cells (Book 3, Basic Biology Course, Unit 1 – Microscopy and its Application to Biology) by Michael A. Tribe, Irwin Tallan, Michael R. Eraut and Roger K. Snook, Cambridge University Press, New York and London, pp. 119, 1976.

This book is part of the Basic Biology Course for undergraduates written by the Inter University Biology Teaching Team at the University of Sussex, England. The aim of the book is to give the student "an insight into some of the dynamic activities going on inside cells by observing a number of different cells in culture" and "an appreciation of the great activity shown by the major cell organelles in the metabolic, genetic and locomotory behaviour of cells". The authors succeed in carrying out this aim.

This book, as are others in this series, is a programmed text. It is designed to be used with time-lapse films of live cells as viewed with phase-contrast microscopy. Locomotion and contact inhibition, mitosis, the cell cycle, fertilization, and meiosis and its genetic consequences are well-covered. In addition, appendices present experiments for the students to do on determining the normal human karyotype, tetrad analysis with fungal ascospores, and genetics and chromosome squashes with the fruit fly. Throughout the book, many questions, practical as well as thought-provoking, are asked. By the end of the book, the student should be able to describe cell locomotion and to understand the significance of contact inhibition in the early development of an organism, explain how chromosomes and cytoplasmic inclusions are distributed during cell division, interpret evidence that DNA replicates during interphase, describe gametogenesis and fertilization, contrast mitosis and meiosis and know the consequences of each, understand the significance of synapsis of chromosomes, relate the transmission of genes to meiotic events, and know the difference between a "cell strain" and a "cell line". The book ends with a self-assessment examination designed to test the student's understanding of these concepts.

By the end of the book the student should have dispelled any idea that cells are inert and static. The Basic Biology Course, of which this book is a part, is an excellent example of the usefulness of the audio-tutorial and self-teaching methods of instruction.

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