APPENDIX 4

The Physiology Medical Course

A. Laboratory Manual for Medical Physiology

B. Examination of advantages and disadvantages of Problem-Based Learning

C. Evolution of the Human Function Course, 1998-2007

D. Lecture outlines for Human Function, 1998 and 2019

E. Lecture outline for current Medical Physiology Course (PSIO820)

L. Sherwood

WEST VIRGINIA UNIVERSITY

LABORATORY MANUAL

for

MEDICAL PHYSIOLOGY

DEPARTMENT OF PHYSIOLOGY & BIOPHYSICS

WEST VIRGINIA UNIVERSITY MEDICAL CENTER

GUIDING PRINCIPLES IN THE CARE AND USE OF ANIMALS

(APPROVED BY THE COUNCIL OF THE AMERICAN PHYSIOLOGICAL SOCIETY)

Only animals that are lawfully acquired shall be used in this laboratory, and their retention and use shall be in every case in strict compliance with state and local laws and regulations.

Animals in the laboratory must receive every consideration for their bodily comfort; they must be kindly treated, properly fed, and their surroundings kept in a sanitary condition.

Appropriate anesthetics must be used to eliminate sensibility to pain during operative procedures. Where recovery from anesthesia is necessary during the study, acceptable technic to minimize pain must be followed. Curarizing agents are not anesthetics. Where the study does not require recovery from anesthesia, the animal must be killed in a humane manner at the conclusion of the observations.

The postoperative care of animals shall be such as to minimize discomfort and pain, and in any case shall be equivalent to accepted practices in schools of Veterinary Medicine.

When animals are used by students for their education or the advancement of science such work shall be under the direct supervision of an experienced teacher or investigator. The rules for the care of such animals must be the same as for animals used for research.

Physiology 245
Medical Physiology

INDEX OF LABORATORY EXERCISES

DEPARTMENT OF PHYSIOLOGY AND BIOPHYSICS
LABORATORY MANUAL

INTRODUCTION

The experiments included in the present outline will allow students to obtain first-hand knowledge of certain fundamental principles of physiology, opportunity being given to repeat many of the classical experiments upon which the subject is based: i.e., Harvey's observations on the heart, Hales' on blood pressure, and many others. It is hoped that every student will cultivate the habit of accepting no fact, the proof of which he has not himself examined, and of holding no doctrine as immutably established. The critical attitude thus engendered will be of inestimable value in the future, particularly to those who take up Medicine, for there is no realm of human endeavor where evidence must be sifted with greater care, and no discipline where more rigorous logical analysis must be employed if success is to be attained.

Many have pointed out that a close correlation exists between manual dexterity and mental capacity. Indeed the phylogeny of the brain suggests that the principal factor underlying its recent development has been the acquisition of a greater variety of skilled movements. At present, however, few human beings tax the resources of their cerebral hemispheres to capacity, and those who fail to cultivate their hands in dextrous performance rob themselves of a potent factor in intellectual development. Few physicians have succeeded without arduous training of their manual skills, and certainly no surgeon without this has ever succeeded. It is for reasons such as these that the "practical" exercises in the preclinical subjects are looked upon as a most important element in the training of medical students, outweighing very considerably the didactic lectures. The value of an experiment, however, varies directly with the amount an individual puts into it. If, with each exercise, the student considers the aim, the sources of error and the inference to be drawn, he will earn the reputation of being logically minded. If he preserves tracings and other objective evidence, and in addition, makes a careful verbal record of the experiment, couched in the King's English, he thereby builds up a background of first-hand knowledge to which he can refer, and which he is not likely soon to forget. If, further, he reads appropriately in textbooks and recent journals in an effort to elucidate his experiment, he will derive much greater benefit than by attending a lecture in which the experiment is described. Finally, if he makes an effort to discover by whom and in what circumstances the experiment was first performed he will find himself led into the profitably byways of physiological history, and he will thus gain some insight into the rich cultural background of medicine and science.

GENERAL INSTRUCTIONS FOR MAMMALIAN EXPERIMENTS

All the apparatus necessary for the experiment is laid out for you. Put all extraneous objects (books, brief cases, etc.) where they will not be in your way. Members of the team may wear lab coats or anatomy dissecting room gowns.

The operating table is connected with a 110 volt A.C. supply. The lamps, clippers, electronic stimulators, recorder, etc. are operated by plugging into outlets on the table. The animal may be warmed by means of the electric desk light.

When you enter the laboratory the animal will be on the table and the data concerning anesthesia will be posted on the front blackboard. Inspect the animal and make sure its airways are clear and that its respiration is even and regular. If a tracheal cannula is being used, clear it occasionally with a gauze stick. Check the body temperature; if necessary make appropriate changes in the lamp position. Unless the instructor has introductory comments to make, proceed with the experiment promptly.

Division of labor. Your group of four or five should be organized into a team with each member assigned specific duties. The following assignments are suggested: 1. surgeon, 2. assistant surgeon, 3. engineer, and 4. potboy and 5. recorder. The surgeon and assistant surgeon are responsible for the dissection and must come to the laboratory with a clear idea of the details of the dissection. The engineer's job is to prepare, assemble and test all recording equipment and to be sure that it is all in operating condition by the time the dissection is completed. The potboy is responsible for running errands, giving assistance where needed, watching the animal's condition, making cotton patties for the surgeon's use, etc. The recorder notes all the pertinent details of the experiment such as anesthesia, paper speeds, stimulus parameters, etc. Although it is desirable that all members of the team share the labor of preparing records, the recorder is held responsible for this task. The above duties will be rotated among the members of the group from experiment to experiment.

Instruments. Special operating instruments such as rongeurs are provided on the front table. When you finish with them return them immediately so that others may use them. Sharp scalpels, a few fine scissors, and daggar-tip forceps are also available for students not having their own instruments. These are signed for by the surgeon and he must return them, washed and dried, at the end of the laboratory period; they must be used only on soft tissues, not on bone, hair or thread.

Position of animal and retraction. A right-handed person usually operates with his left side toward the head of the animal. It is important to have the animal in a convenient position for operating; if the preparation is decerebrate, do not lower the head to the operating table or obstruct the airways. Lead clip weights may be used to retract incised skin edges.

Planning the dissection. As a rule, all exposures and preparations needed throughout the experiment are made before arterial cannulation is performed. The simple routines are best done before the difficult phases of the dissection are undertaken. Surgeons find it helpful to come prepared with

an outline of the dissection required. Time does not permit reading the manuals during the laboratory session, nor do the verbal instructions at the beginning of the experiment take the place of study of the directions in the manual. Previous preparation aids the surgeon in keeping command of the situation.

Surgical maneuvers. These experiments constitute your first, and almost your last, opportunity as a student to acquire surgical technique first-hand. Certain slipshod methods sometimes used in "acute" experiments and certain practices appropriate to the dissecting room should be avoided. By using them you are simply acquiring bad habits that must be unlearned when you begin human surgery. The first step is to identify by palpation the bony landmarks, and to plan the incision. A surgical incision of the skin implies a slow, continuous stroke with the curve or belly (never the point) of a scalpel. The pressure is lightened or increased to give the desired results. Hold the knife like a violin bow or paintbrush, not like a pencil. Never cut skin with scissors. Soft tissues are best handled by blunt dissection, with the handle of the scalpel for example, rather than by cutting. Scissors are often effective for blunt dissection. For example, the closed point of blunt scissors may be inserted between the carotid artery and the vagus nerve, and the blades opened and withdrawn. By such blunt dissection, anatomic planes are followed, and the vessels or nerves are revealed before they are damaged. Try to avoid the finicky niggling and teasing technique of the dissection room. Acquire the habit of not hunching over the table; standing straight prevents fatigue in long operations.

Cleanliness and order. "Keeping a clean table" has a distinct psychological effect upon the operative team. All bits of hair, muscles or chips of bone and especially blood-stained "patties" must be picked up. Keep your instruments in order. Instruments and the surgeon's hands should be kept free from blood. Failure in these respects often means that the dissection, or your team, is getting away from you.

Artificial respiration. In some experiments, it is necessary to open the thoracic cage or to use drugs which interfere with or stop spontaneous respiration. Before any such maneuver is carried out, artificial respiration must be supplied. Each station in the laboratory has a solenoid on-off valve for artificial ventilation and is equipped with a rubber tube for connection to the T-shaped tracheal cannula. Carefully adjust the flow of air from the air outlet to produce a moderate lung inflation. To institute artificial respiration simply attach the rubber tube to the tracheal cannula and adjust the valve. The solenoid and air supply will generate rhythmically recurring pulses of air which inflate the lungs; expiration occurs through the side arm of the cannula during the diastole of the pump, the elasticity of the lungs and chest providing the force for expelling the air. The amount of inflation may be regulated by varying the aperture of the outlet from the side arm; this is accomplished with a screw clamp on the short piece of rubber tubing which is attached to the side arm of the cannula. Adjust the clamp until the excursions of the chest wall are about equivalent to those of normal quiet spontaneous respiration. The novice usually over-ventilates the animal, so it is a good procedure to ask the advice of the instructor until you have learned an appropriate setting. Above all, remember that the pump supplies only positive pressures and that the only path for expiration is through the

side arm. Therefore, never close the side arm completely, otherwise the lungs are gradually but inevitably blown up to the bursting point.

If the valve should fail, be prepared to supply emergency artificial respiration using an anesthesia bag or manual interruption of the air supply.

It is best to postpone beginning artificial respiration until it is absolutely needed; the rate of spontaneous respiration may be different from and out of phase with that of the pump so that the animal "fights" the pump. At all times take care not to obstruct the trachea, or the airline, by kinking the tube of by stepping on it.

Recording of observations. Obtaining good records is the culmination of the extensive dissections and preparations. A schedule of observations to be made, prepared ahead of time, will be of help. Develop a formula for smooth teamwork and work quickly.

With the team at their stations the surgeon calls for "record." After an inch or so of normal record is obtained, he calls for "stimulation" and, after an appropriate interval, "stimulation off." Do not stop the paper until the response being observed stabilizes. The paper drive is then turned off, and the person assigned as recorder writes the pertinent data on the record. Stimulation should be continued until the maximal effect is approached, but usually not longer than 10 or 15 seconds. It is always wise to make observations more than once to bring out the typical features, and to repeat observations using different strengths of stimulation. Write details of a stimulation (nerve, central or distal end, left or right, paper speed, stimulus parameters) in abbreviated form directly on the record. This is preferable to keeping notes on a piece of paper which may easily be lost, of incorrectly keyed to the records. "LVD (2V, 50/sec.)" is sufficient to state that the distal end of the left vagus nerve was stimulated repetitively at 50 shocks per second, each shock being 2 volts.

Termination of experiment. In a very short time at the end of the experiment you may be able to repeat unsuccessful observations from an earlier experiment. Before leaving, tidy the table, wind up clip weights, remove and wash tracheal and carotid cannulae after tying off the carotid artery to prevent bleeding. Remove the ink from the pens of the recorder and turn off all electronic equipment. Place the dead animal in one of the bags provided.

Discussion of results. Whenever possible, your results will be discussed before you leave the lab. Emphasis will be placed on elucidating the physiological mechanisms which are believed responsible for the phenomena observed. Carefully distinguish between restating the contents of the data and interpreting, a habit which will prove valuable in making pathological discriptions, or in writing case histories.

GRASS POLYGRAPH EXPERIMENT

The material in this experiment is intended to be used as a reference by the student throughout the semester as an aid in operating the Grass Polygraph in addition to providing practice in its operation. When setting up the machine to measure biological parameters in later experiments, the summary page at the end of the experiment will be helpful to refresh your memory on the principles learned in this experiment.

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INTRODUCTION TO THE GRASS POLYGRAPH

The Grass model 5 polygraph used in Physiology seems at first glance to be a confusing array of knobs, dials, and buttons which to the student who has had no previous electronic exposure, can be a frightening experience. Therefore, the purpose of this laboratory session is to enable the student to become familiar with the polygraph itself and to think of its operation in functional terms without the additional concern of biological preparations.

The laboratory is divided into three parts:

1. General observation of the polygraph with location and explanation of controls.
2. Experimentation with external voltage source as polygraph input.
3. Exploration of characteristics of pressure and force transducers used in physiology.

In part one, the controls should be identified on the machine by the student as they are explained. The records produced in parts 2 and 3, and their associated calculations, will be discussed in the record review session.

PART ONE

The Grass polygraph is otherwise known as an ink-writing strip chart recorder. This means that it accepts an input in the form of a voltage and writes out a tracing of the variations of the voltage in ink on a moving strip of paper. The input is passed through a series of electronic circuits, mostly amplifiers, which are controlled by the knobs on the front panel of the instrument. In order to write out a signal in proper form, the knobs must be correctly set for the particular input to be displayed.

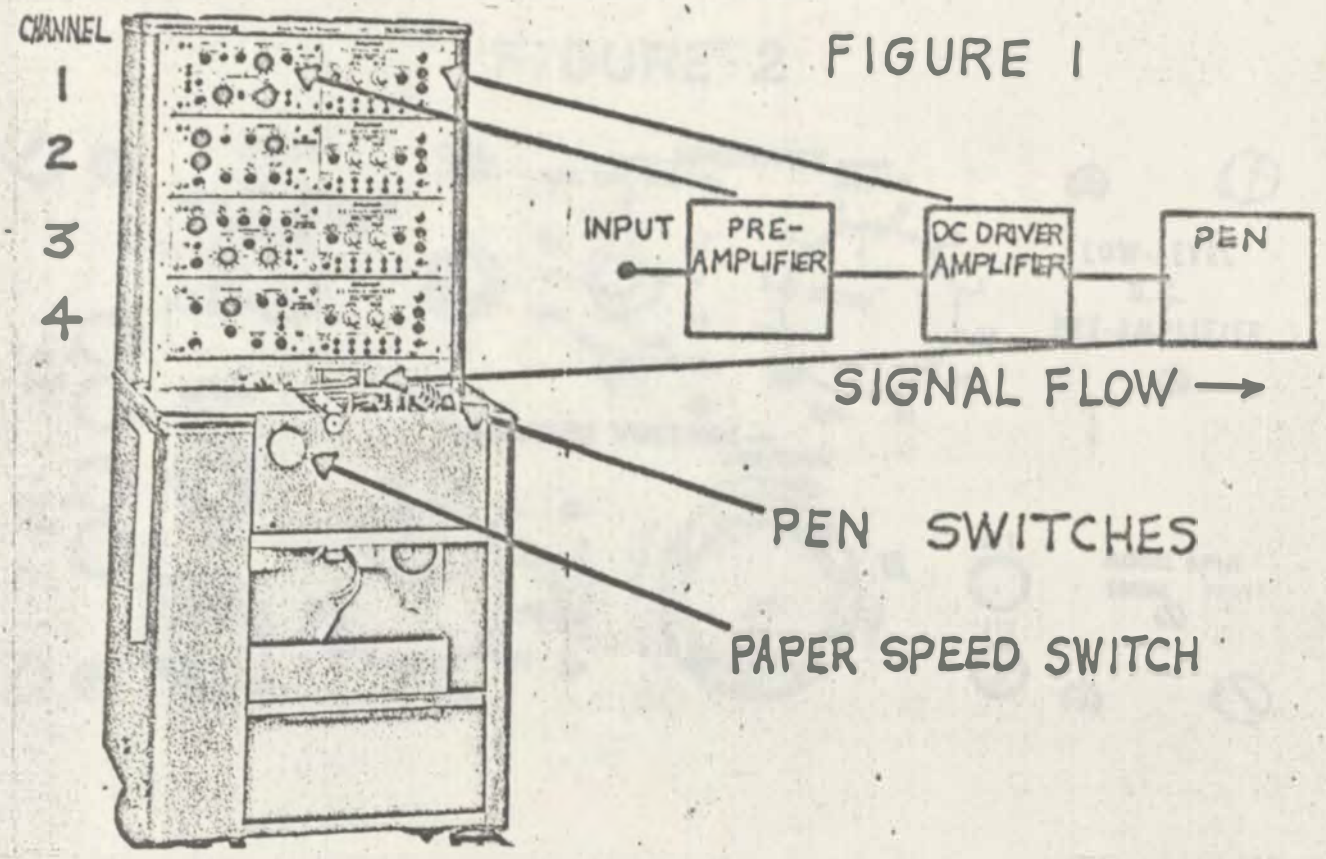


FIGURE 1

Figure 1 shows that the polygraph is divided into four separate channels consisting of three functional blocks each. The two amplifiers in each channel are necessary to raise the input signal to a level sufficient to drive the pens across the paper and to provide controls so that a large range of signals may be recorded.

A logical way to understand the polygraph is to start at the input and follow the signal flow through the machine. The signal enters at one of the four input PRE-AMPLIFIERS on the left of the console through a cable plugged into the input connector. These amplifiers operate independently of each other, feeding their respective DRIVER AMPLIFIERS to the immediate right, and provide for the display of four different input signals simultaneously. (Since these amplifiers are first in the signal flow, they are called pre-amplifiers, or preamps). There are two types of preamps used in the laboratory, the type 5P1 used for direct current (DC) and alternating (AC) current signals, and the 5P4 used for EKG and other alternating current (AC) signals. These preamps are held into the panel by four screws and are removable so their vertical positioning may be changed as desired.

FIGURE 2

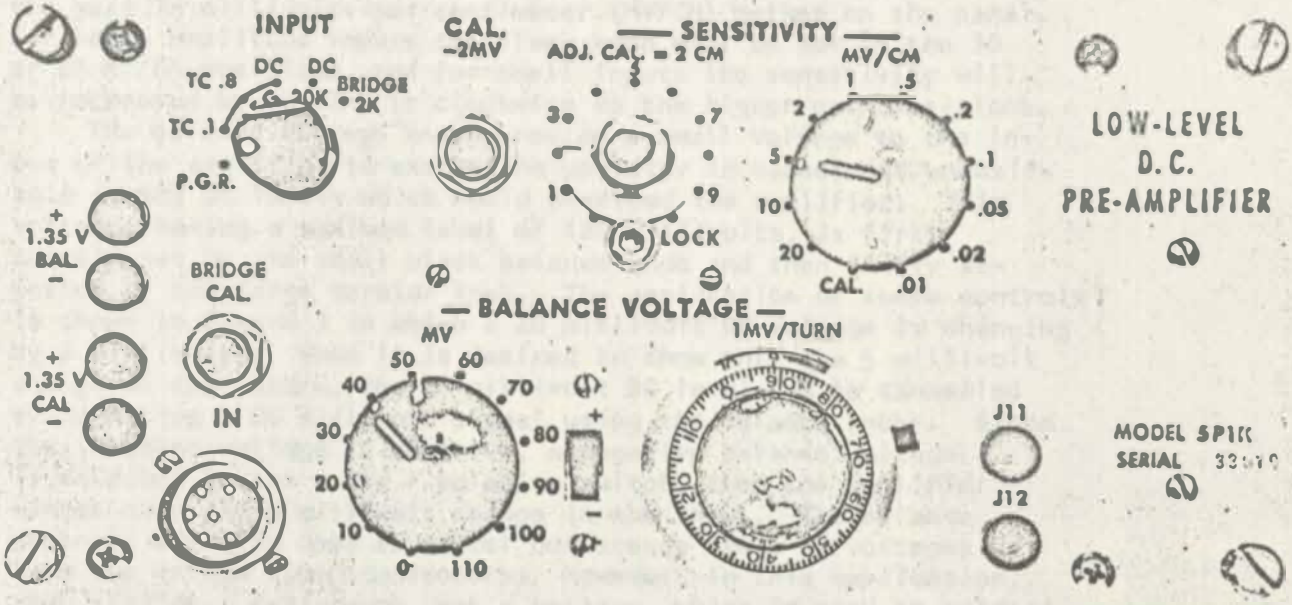


Figure 2 shows the 5P1 PRE-AMPLIFIER. The characteristics of the amplifier input circuitry are selected by use of the input switch-knob. The proper setting of this switch is the first step in preparing the polygraph for the particular signal to be recorded. The positions of the switch are as follows:

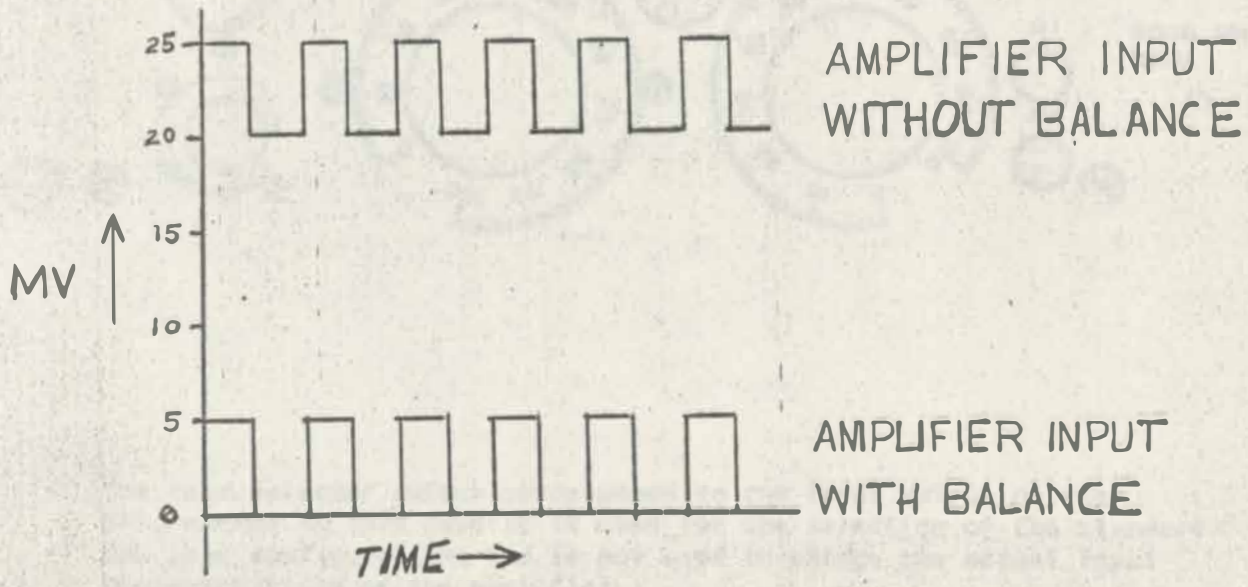
P.G.R.	Used for psychogalvanic reflex (skin electrical resistance) measurement.
T.C. .1	An AC voltage input position with a time constant of .1 second.
T.C. .8	An AC voltage input position with a time constant of .8 second.
D.C.	A DC voltage input position with an input impedance of 1 megohm.
D.C. 20K	A DC voltage input impedance of 20,000 ohms.
Bridge	A DC voltage input for recording from a Wheatstone bridge transducer, such as the pressure and force transducers used in this lab.

This selection of input characteristics makes the amplifier a versatile unit capable of handling a large variety of physiological signals.

The two sensitivity knobs change the gain, or amplification factor of the amplifier. The large black knob is a coarse switch, while the small chrome knob is a fine adjustment control used to calibrate exactly the settings of the black knob so they provide the gain in millivolts per centimeter (MV/CM) marked on the panel. For large amplitude inputs the black knob will be set in the 10 or 20 MV/CM positions, and for small inputs the sensitivity will be increased by turning it clockwise to the higher gain positions.

The balance voltage knobs provide a small voltage to the input of the amplifier to enable the operator to cancel out undesirable steady DC levels which would overload the amplifier. This voltage, having a maximum level of 120 millivolts, is first coarsly set by the small black balance knob and then finely adjusted by the large vernier knob. The application of these controls is shown in figure 3 in which a 20 millivolt DC voltage is changing by 5 millivolts. When it is desired to show only the 5 millivolt change on the record, the 20 millivolt DC level can be cancelled by injecting a 20 millivolt signal using the balance knobs. Since the incoming voltage is positive, a negative balance voltage is selected by the + and - polarity switch, then the amplifier senses only the 5 millivolt change in the input. The balance controls are also used to cancel out steady state DC voltages from the bridge type transducers. However, in this application, they provide a resistance, not a voltage, which is used to balance the bridge, so the polarity slide switch does not function.

FIGURE 3

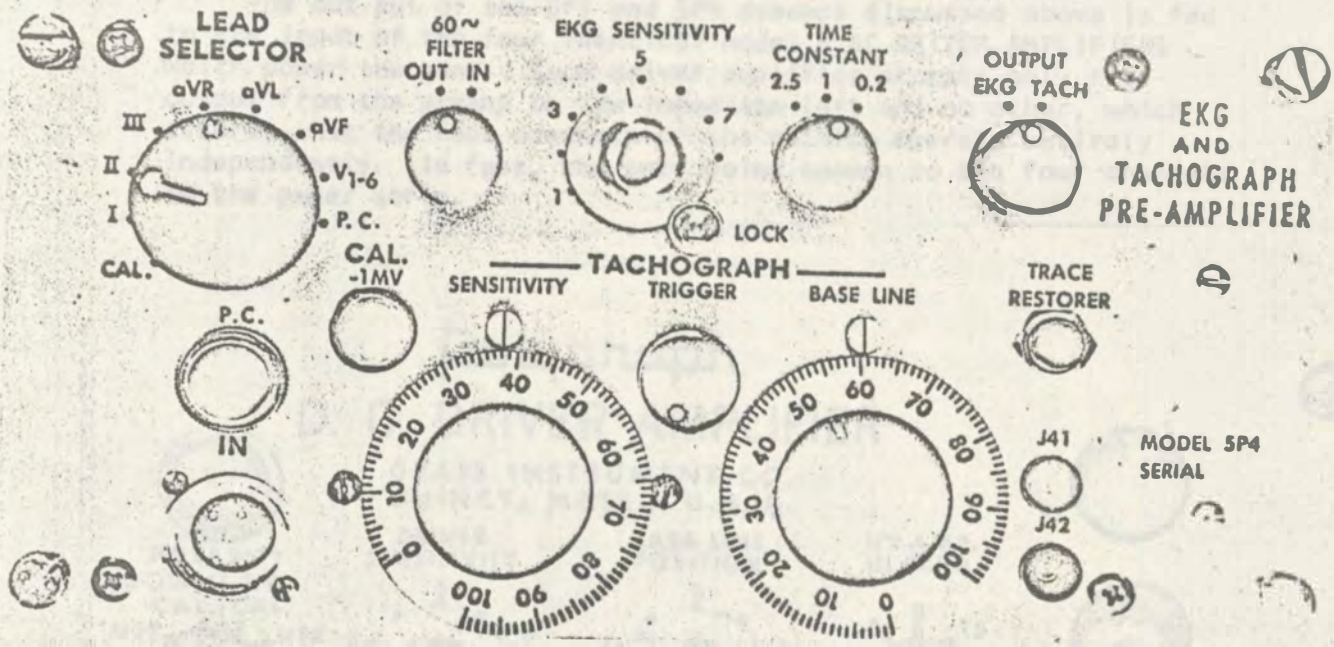


The six pin jacks on the panel are test points and are not used in the laboratory.

The remaining controls on the preamp are the two red calibration buttons, which are used as standardization sources for the DC and bridge inputs. Their use will be explained later.

The 5P4 EKG preamp is a high sensitivity AC amplifier used to record EKG and heart rates. This amplifier is not as versatile as the 5P1 because it will not amplify a DC signal, and for that reason is used only for fast-changing signals such as the EKG. Figure 4 shows the panel of the 5P4.

FIGURE 4



The lead selector switch corresponds to the input switch on the 5P1, except in this case it is used for the selection of the standard EKG lead configurations and is not used to change the actual input characteristics of the amplifier.

The knob to the right of the lead selector is the 60 cycle filter switch. Since 60 cycle interference from electrical equipment is often a problem in EKG recording, this filter is provided to

attenuate the undesired signal.

The sensitivity and time constant controls vary the gain and frequency response of the preamp. In standard EKG recording, the constant is set at 2.5 seconds, which displays faithfully the low and high frequency components of the EKG. When only the high frequency parts are of interest, the switch is placed in .2 second position.

The 5P4 also has a tachograph section which measures the heart rate from the EKG signal. This section is not used in the laboratory, so the three tachograph controls may be ignored.

The trace restorer switch is used to put the pen back to baseline, or zero, when a large random signal causes it to go off scale. This is accomplished by the switch shorting out the amplifier briefly, which bleeds off the excess voltage produced by the random signal. The button should be pressed for only a fraction of a second and then released.

The out put of the 5P1 and 5P4 preamps discussed above is fed to the input of the four identical model 5 DC DRIVER AMPLIFIERS which power the pens. Each driver amplifier accepts only the output from the preamp to the immediate left and no other, which assures that the four channels of the machine operate entirely independently. In fact, the only point common to the four channels is the paper strip.

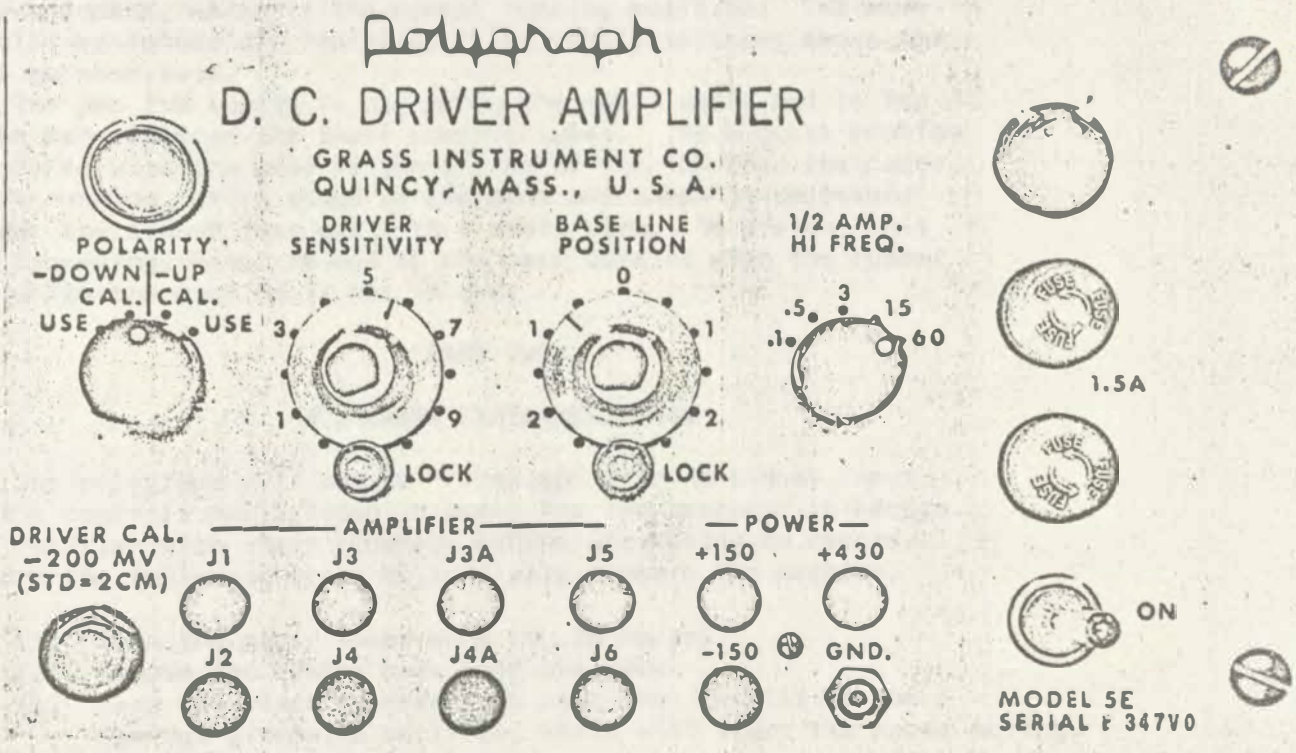


FIGURE 5

Figure 5 shows the DC DRIVER AMPLIFIER controls. The operation of this amplifier is very simple, as there is no input switch or balance control. The polarity switch changes the direction of pen deflection without affecting the amplifier gain. It provides a position for normal recording (USE), and a position (CAL) for calibration purposes which removes the amplifier input from the preamp output. The sensitivity control changes the gain of the amplifier, and the base line control is used to set the pen zero position to a desired location. The high frequency control knob provides high frequency attenuation and integration of the signal. This is used to eliminate 60 cycle interference and for averaging pulse signals (such as blood pressure).

The driver calibrate button injects a 200 millivolt callibrating signal into the amplifier input and will be explained in detail later. The two rows of pin jacks are used for test purposes and are of no concern. The toggle switch labeled ON is the power switch for the driver amplifier and its associated preamp.

Refer again to figure 1 which illustrates the important controls on the front horizontal paper drive section. The large chrome knob on the extreme front is used to set the paper speed and is calibrated in millimeters per second, which corresponds to the millimeter divisions on the paper itself. This paper speed control can be set to a position between any too speeds in order to stop the paper flow and to leave all other sections of the of the machine running. The black pointer-knob has three positions: the first turns off both paper and pens, the second turns on the paper but not the pens, and the third turns on both paper and pens, which is the normal running position. The pens can also be turned off individually by toggle switches above the black pointer-knob.

The pen ink supply is stored in the small wells and is fed to the pens through the small plastic tubes. The biggest problem associated with the pens is the drying of the ink when the paper is not running, which stops up the pens and makes it necessary to ream the end of them out with a small wire. To prevent this from happening, keep the end of the pens covered with the rubber caps while the machine is not in use.

PART TWO

POLYGRAPH EXPERIMENTATION

The polygraph will now be "fired up" with no signal input and the controls manipulated in order for the operator to become more familiar with their function before attempting to record. Perform the following steps to initially prepare the machine.

(1) Turn the paper speed knob to .25 mm/sec.
(2) Remove the rubber caps from the pens.
(3) Turn the black pointer-knob near the inkwells to the maximum clockwise position, which will start the paper moving.

(4) Flip the four pen toggle switches to the right.
(5) Turn the four preamp small sensitivity knobs to the extreme counterclockwise position (including the EKG preamp), and set the 5P1 MV/CM controls to 20.
(6) Set the 5P1 balance controls to zero.
(7) Remove all input cables from the preamps.
(8) Set all DC driver amplifier sensitivity and base line controls to zero.

Now stop and review what you have done in performing the above steps. The paper is running, and the amplifiers are set to their lowest possible sensitivity. This is a good starting point, as no damage can be done to the machine in this insensitive state by accidential signal mishandling. The preamps are now ready to be turned on.

Throw all DC driver amp toggle switches to ON. As the amps warm up the pens will move slightly and settle to new positions in about 30 seconds. Since this part of the experiment is performed using only the top channel, turn the lower three toggle switches back to OFF.

Turn the top DC driver amp high frequency control to 60 cps and move the base line control while observing the top pen. Move the control rapidly back and forth about 3 times per second so that the pen sweeps out large sine waves on the paper. Set the paper speed to 5mm/sec., record about 10 cm of sine waves and then move the high frequency control to .5 cps while continuing to move the knob. Notice that the amplitude of the sine waves is greatly decreased with the high frequency control in this position. Reduce the frequency of your knob turning to restore the sine waves to their original amplitude. Return the paper speed to .25 mm/sec. and label your data for later identification. The effect of the high frequency control on the amplitude of high frequency signals can be very easily seen from the above results. The control must be set for a higher frequency than the actual frequency of the input signal if a true picture of the input voltage waveform is to be obtained. Of course, if an average of the input signal is desired, the control can provide this be setting it to a frequency much lower than the input signal.

Now place the polarity switch in the - down CAL position and push the red calibrate button. The pen should move very slightly. Increase its movement to 2 cm by increasing the driver amp sensitivity setting. As the sensitivity is changed, the base line knob will have to be reset to keep the pen on scale, as the sensitivity changes affect the base line. However, the base line control does not alter the sensitivity. After the correct sensitivity has been established to produce a 2 cm deflection, change the paper speed to 1 mm/sec., switch the high frequency control to .1 cps, and push the calibration button, holding it until the pen comes to rest. Notice that the pen moves the same 2 cm as before, but travels very slowly. Experiment with the other high

frequency control settings and their effect on the calibrating signal. Return the paper speed to .25 cps, the high frequency control to 60 cps, and label your data.

The characteristics of the 5P1 PRE-AMPLIFIER will now be investigated, so establish the following settings on its controls.

(1) Place the input switch in the DC 1 megohm position.
(2) Turn the small sensitivity control to zero.
(3) Set the MV/CM control to CAL (calibrate).
(4) Rotate the balance controls to zero.

Turn the DC driver amp polarity control to - down use. Adjust the 5P1 small sensitivity knob so that the pen deflects 2 cm when the 5P1 - 2mv red calibration button is pushed. This procedure calibrates the preamp so that the amplification is exactly as marked on the MV/CM control. The DC driver amplifier was calibrated in the preceding section of the experiment, so now the response of the pen in centimeters for a given millivolt input will be exactly as marked. For example, if the 5P1 input switch is placed in the 10 MV/CM position and 20 millivolts are fed into the amplifier, the pen will deflect 2 cm.

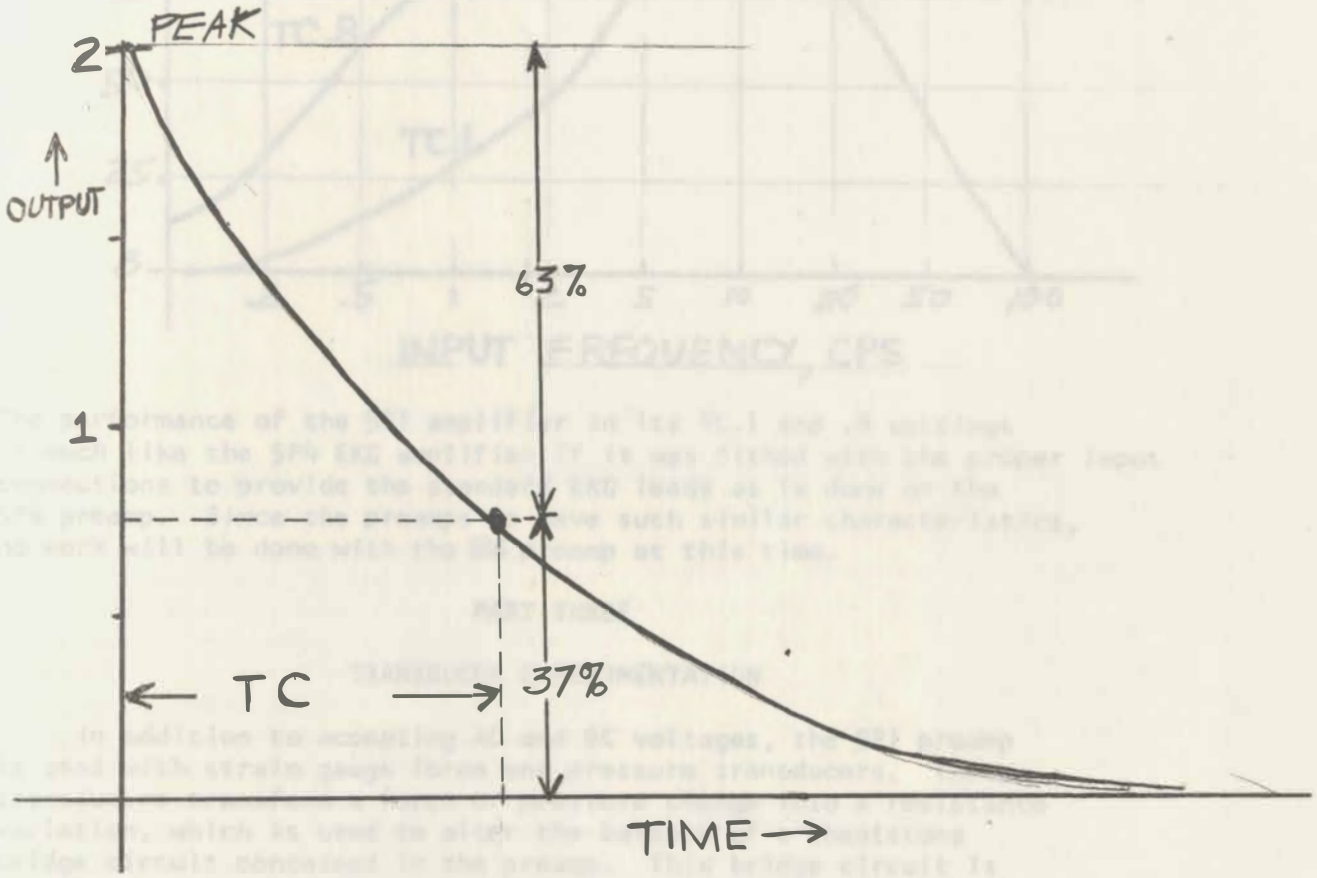
A 15 millivolt DC source will now be used to furnish an external signal to the polygraph. Plug the 5P1 three lead terminal box into the 5P1 input connector. Make sure that the black and blue terminals of the box are shorted. Plug the yellow terminal into the + terminal of the 15 mv source and the black terminal into the - terminal of the source. Move the MV/CM control to 10 and push the source ON button. The pen should deflect approximately 1.5 centimeters. Label your data.

The above 15 mv signal from the source will now be cancelled out with an opposite polarity voltage from the balance controls. Since a negative polarity signal is needed for cancelling the positive source signal, place the ± slide switch in the negative position and the black MV knob on TO. Push the source ON button and rotate the balance control until the pen returns to baseline. Note the vernier reading. It should be approximately 5 mv, which is added to the 10 mv on the black knob, giving 15 mv for the balance voltage, which is the same as the input voltage, but of opposite polarity. This illustrates how the balance control is used to cancel out low DC levels at the input. Make a notation on your record for identification of this cancelling action.

Return the balance controls to zero and again use the 15 mv voltage source to obtain a 1.5 cm pen displacement. Turn the 5P1 input switch to the TC .8 position, which is an AC voltage input. Push the 15 mv source on and off repeatedly and note the pen behavior. How does it differ from the previous deflection using the DC input? Turn the input switch to the TC .1 position and again push the source button on and off. Set the paper speed to 2.5 mm/sec. so that the time relationship of these two AC switch positions (TC.1 and TC .8) can be observed while pushing the source

button on and off at a frequency of 1 cycle per second. Take about 10 cm of record in each position and return the paper speed to .25 mm/sec. The TC stands for time constant, which is the time required for the pen to travel 63% of the way to its final value: The values of .1 and .8 seconds marked on the amplifier panel are wrong, due to internal changes by the manufacturer, and have been replaced by the new values of approximately .4 and 2.5 seconds. This must be kept in mind when comparing your record with figure 6.

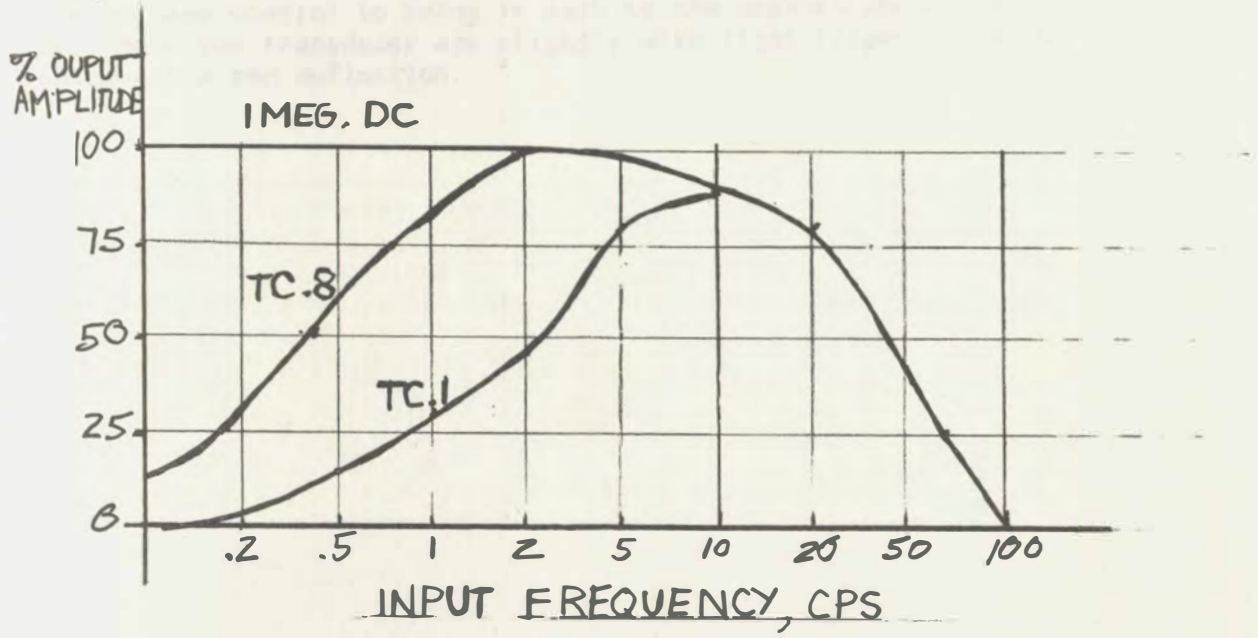
FIGURE 6



TIME CONSTANT = .4 OR 2.5 SECONDS

The time constant is a very important factor in all electronic equipment and circuits, as it determines the low frequency response. The longer the time constant, the longer it takes the signal to decay, which makes possible the amplification of low frequency signals. This is shown in figure 7, which is a graph of the frequency response of the 5P1 amplifier for both time constant settings.

FIGURE 7



The performance of the 5P1 amplifier in its TC.1 and .8 settings is much like the 5P4 EKG amplifier if it was fitted with the proper input connections to provide the standard EKG leads as is done on the 5P4 preamp. Since the preamps do have such similar characteristics, no work will be done with the EKG preamp at this time.

PART THREE

TRANSDUCER EXPERIMENTATION

In addition to accepting AC and DC voltages, the 5P1 preamp is used with strain gauge force and pressure transducers. These transducers transform a force or pressure change into a resistance variation, which is used to alter the balance of a Wheatstone bridge circuit contained in the preamp. This bridge circuit is switched into action when the preamp input switch is placed in the BRIDGE position. The use of these transducers will now be investigated.

Force Transducer

Set the preamp MV/CM switch to CAL. Remove the terminal box cable from the input connector and plug in the Grass FT-03 force transducer cable. Turn the input switch to the Bridge position.

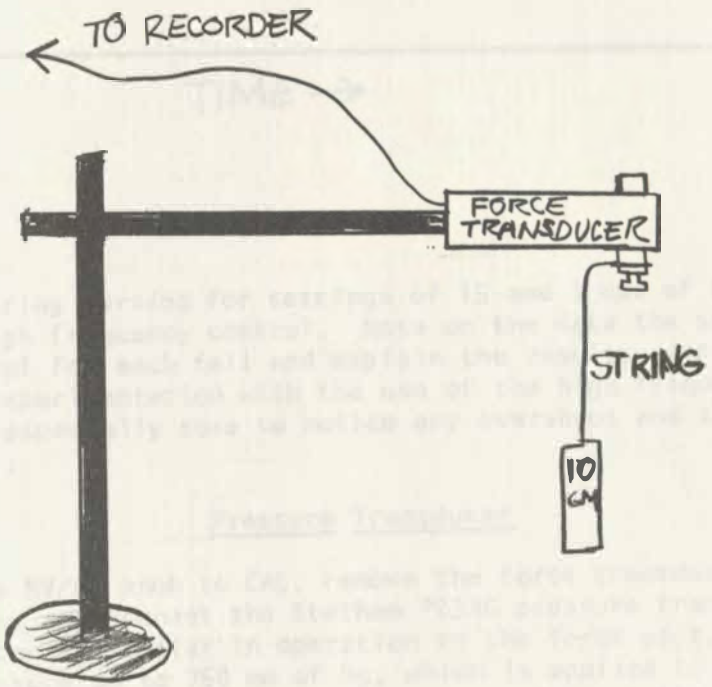
The sensitivity is presently set too high for this application, so reduce it by turning the small sensitivity knob back to 5. Turn the MV/CM knob to 20, and if the pen goes off scale, use the MV balance voltage control to bring it back to the approximate chart center. Move the transducer arm slightly with light finger pressure and observe the pen deflection.

BALANCING THE BRIDGE CIRCUIT

Turn the MV/CM knob back and forth from 10 to 20 several times and note that the pen moves from its base line position. This indicates that the bridge circuit used for the pressure and force transducers is not properly balanced, since under balance conditions sensitivity changes do not affect the base line. Set the MV/CM control on 20 and run off 2 centimeters of paper to establish a balancing base line. Move the MV/CM control to 10 and bring the pen back to the base line with the 1 MV TURN vernier balance control. If this control will not bring the pen back to the base line, set it to zero and rotate the MV balance control to its left until the pen is as close as possible to the base line. Then use the 1 MV turn control to put the pen exactly on the base line. The bridge is now approaching balance, but must also be adjusted for the higher sensitivity positions. Move the MV/CM control to 5 and again bring the pen to base line with the vernier balance knob. Repeat for the 2,1, and .5 MV/CM positions. Then move the control to the 20 MV/CM position and if the base line has changed, repeat the process using the new baseline. The second try should establish a balance sufficient to allow the MV/CM control to be turned from 20 to .5 without changing the base line.

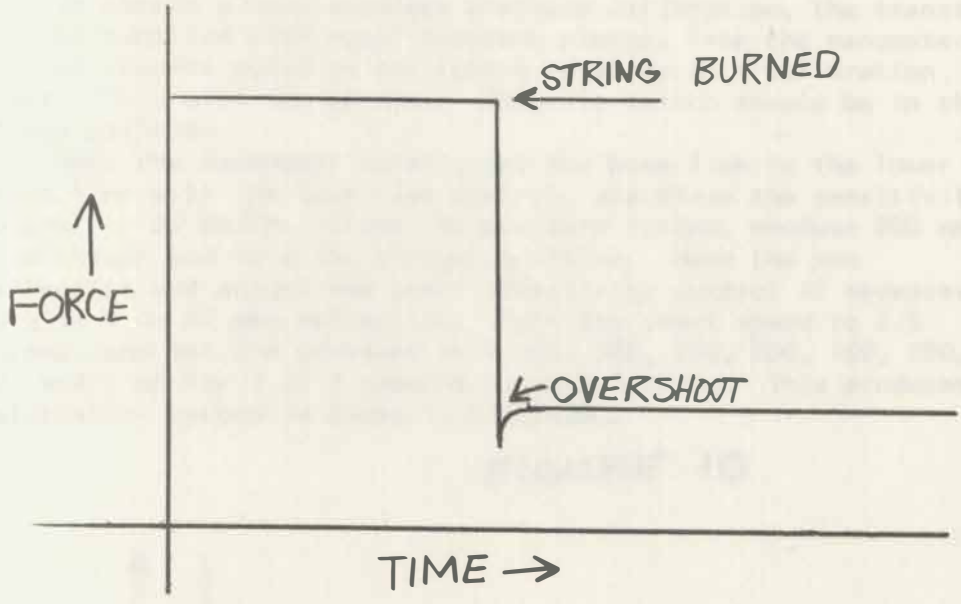
The force transducer will now be calibrated using a known weight. Turn the MV/CM knob to CAL and set up the transducer on a ring stand as shown in figure 8. Use the DC DRIVER AMPLIFIER base line position control to set the base line 2 centimeters below the center of the chart. Support the weight in your hand and turn the MV/CM control to 20 and again set the base line as above, if necessary. Allow the weight to hang from the transducer and note the upward deflection of the pen. Adjust the MV/CM and the ADJ. CAL. sensitivity knobs until a deflection of 1 centimeter from base line is obtained. Again support the weight by hand and notice that the pen returns to base line. Since we are using a 10 gram weight and the deflection is 1 cm, the calibration is now 10 grams per centimeter, or 10 gm/cm. This sensitivity can be doubled by turning the MV/CM knob to the next higher setting, which will make the calibration 5 gm/cm.

FIGURE 8



The response of the transducer to sudden changes in force will now be shown after rapidly removing the weight by burning the string. Adjust the sensitivity controls on the preamplifier so that the pen deflects 3 centimeters from the base line, which may be moved to the bottom of the chart with the base line control. Set the paper speed control on 5 mm/sec., allow the base line to stabilize and burn the string, causing the weight to fall. This instantaneous removal of the weight should produce a record as shown in figure 9.

FIGURE 9



Repeat the string burning for settings of 15 and 3 cps of the DC driver amp high frequency control. Note on the data the setting of this control for each fall and explain the results with respect to previous experimentation with the use of the high frequency control. Be especially sure to notice any overshoot and the effect of the control on it.

Pressure Transducer

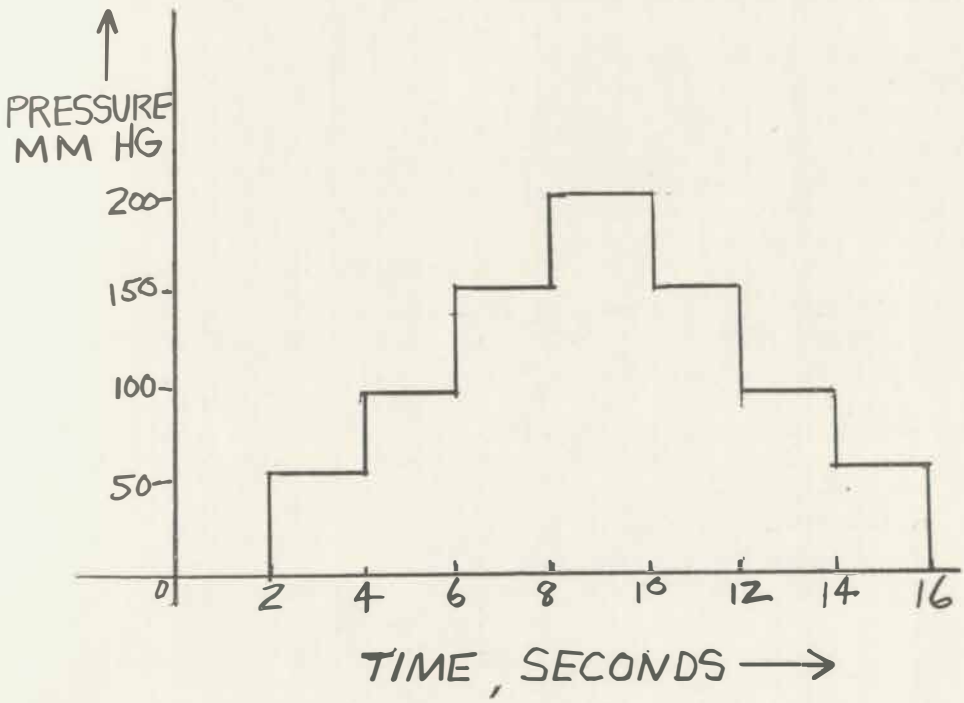
Turn the MV/CM knob to CAL, remove the force transducer from the input plug and connect the Statham P23AC pressure transducer. This transducer is similar in operation to the force unit, but measures pressure up to 750 mm of Hg, which is applied to the connection at the center of the plastic cap. Connect the plastic tube to one outlet of the mercury manometer and open the other outlet of the manometer to air. BALANCE the circuit by use of the MV/CM control and the balance controls as was done for the force transducer. Set the MV/CM control to 20 and adjust the small sensitivity knob so that 1 centimeter of pen deflection is produced when the red bridge calibration button of the 5P1 is pushed. This button produces an electrical calibrating signal which is equal to 100 mm Hg, so the system is now roughly calibrated. Connect the syringe to the other manometer outlet. Push the plunger in to produce 1 cm of pen deflection, hold the plunger position and read the actual pressure from the manometer. The electrically calibrated and actual pressures

should agree fairly closely, but this calibrated pressure cannot be regarded as correct for accurate work due to differences in individual pressure transducers.

To obtain a very accurate pressure calibration, the transducer must be supplied with equal pressure changes from the manometer, and the results noted on the record to serve as a calibration chart. This will now be done. Polarity switch should be in the - UP use position.

Open the manometer to air, set the base line to the lower chart line with the base line control, and place the sensitivity control to 20 MV/CM. Close the pressure system, produce 200 mm of pressure and hold the plunger position. Note the pen deflection and adjust the small sensitivity control if necessary to give 4 cm of pen deflection. Turn the chart speed to 2.5 mm/sec. and set the pressure at 0, 50, 100, 150, 200, 150, 100, 50, and 0 mm for 2 or 3 seconds on each setting. This produces a pressure calibration record as shown in figure 10.

FIGURE 10



Record the pressures at their corresponding pen deflections on the chart. It may be noticed that the step from 0 to 50 mm is not the same size as the last three. This is due to a nonlinearity in the pressure gauge near zero pressure, and shows that the gauge should not be used to record small pressures.

Turn all switches to OFF and replace the rubber caps on the pens. Remove your record from the machine and review it to be sure that all sections of the experiment are properly identified and labeled with regard to what was being performed.

SUMMARY

PARAMETER TO BE MEASURED	IMPORTANT FACTORS
AC or DC voltage	Calibrate DC driver amp first for 2 cm deflection on CAL, then switch to USE. Calibrate preamp by setting MV/CM knob to CAL, pushing -2 mv button, and adjusting small sensitivity knob for 2 cm deflection of pen. Set input switch for type of voltage to be measured.
EKG	Calibrate DC driver amp as above. Place EKG preamp output switch on EKG. Set time constant switch to 2.5. Switch in 60 cycle filter. Set lead selector switch to CAL, push CAL -1mv button and adjust EKG sensitivity to give about 1 cm pen deflection. Switch lead selector switch to lead desired.
Pressure Using P23AC transducer	Calibrate DC driver amp as above. Turn 5P1 input knob to BRIDGE. Set small sensitivity knob to 5. Balance the bridge. Set MV/CM knob to 20, push BRIDGE CAL button and adjust small sensitivity knob for 1 cm pen deflection. Calibration is now 100 mmHg/cm.
Pressure Using P23 BC Transducer	As above P23 AC procedure, except BRIDGE CAL button signal produces calibration of 20 mmHg/cm
Force Using FT-03 Transducer	Calibrate DC driver amp as above. Set 5P1 input knob to BRIDGE. Set small sensitivity knob to 5. Balance the bridge. Hang weight on transducer and adjust both sensitivity knobs for desired calibration.

IMPORTANT POINTS

If the pen deflection is in the wrong direction, it may be reversed by changing the setting of the DC driver polarity switch USE positions.

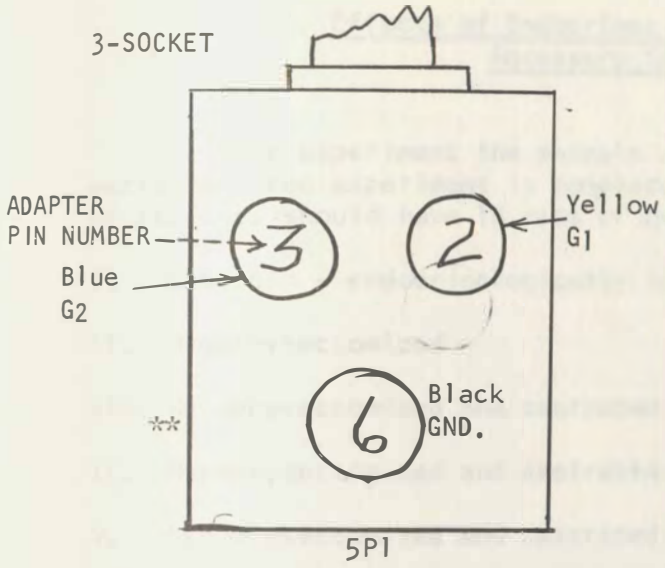
The DC driver amp. base line control does not affect sensitivity or balance so it may be used at any time a base line move is necessary.

If sensitivity changes on the preamp affect the base line, the bridge is not properly balanced.

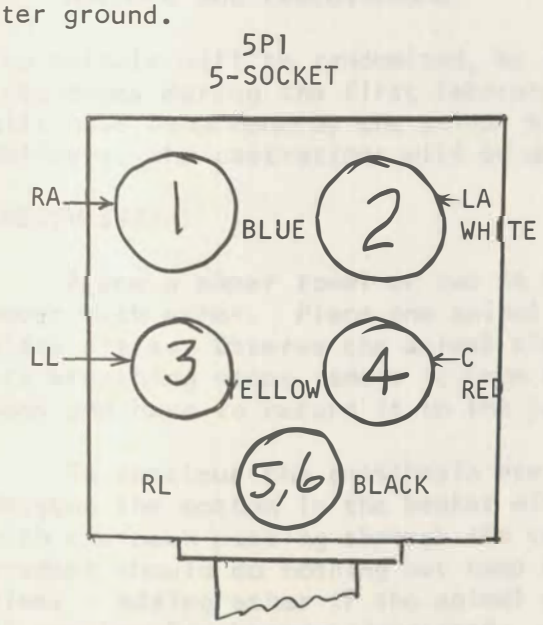
The preamp bridge cal button is used with the pressure (only) transducers, the cal -2mv button is used to calibrate the voltage inputs. Pressure is calibrated with the MV/CM switch on 20, for voltage calibration it is turned to CAL.

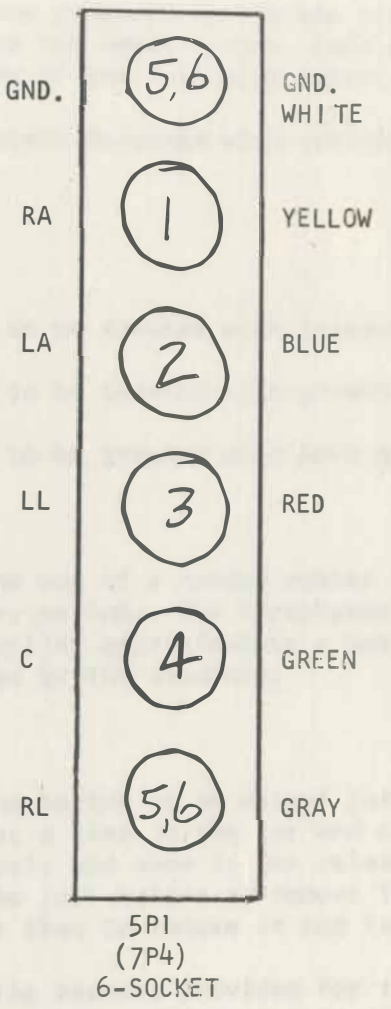
The plus-minus switch between the balance knobs on the preamp can be in either position when balancing the bridge and using pressure or force transducers.

POLYGRAPH CONNECTORS



** Outside of 5P1 case is connected to cable ground, but it is not connected to adapter ground.





Effects of Endocrines on Body Weight and Accessary Sex Glands

In this experiment the animals are prepared during one class period and the experiment is completed two weeks later. Each team of students should have 10 rats of one of the following types:

I. Controls - endocrinologically intact injected with vehicle.

II. Hypophysectomized

III. Hypophysectomized and castrated

IV. Hypophysectomized and castrated to be treated with testosterone.

V. Hypophysectomized and castrated to be treated with growth hormone.

VI. Hypophysectomized and castrated to be treated with both growth hormone and testosterone.

The animals will be randomized, by the use of a random number table, into cages during the first laboratory period. The hypophysectomies will have been done by the animal supplier approximately a week before delivery; the castrations will be done by the students.

ANESTHESIA:

Place a paper towel or two in the bottom of an animal jar; moisten the paper with ether. Place one animal at a time in the jar and cover it with a glass plate. Observe the animal closely and when it has relaxed but before its breathing stops remove it from the jar; better to remove the animal too soon and have to return it to the jar than to remove it too late.

To continue the anesthesia use the beakers provided for this purpose. Moisten the cotton in the beaker with ether and invert over the animal's head with the neck passing through the cut-out in the side of the beaker. One student should do nothing but keep his eye on the anesthetized rat at all times - adding ether if the animal struggles and removing the source of ether if respiration becomes depressed. If the animal stops breathing squeeze the chest repeatedly at a rapid rate.

CASTRATION:

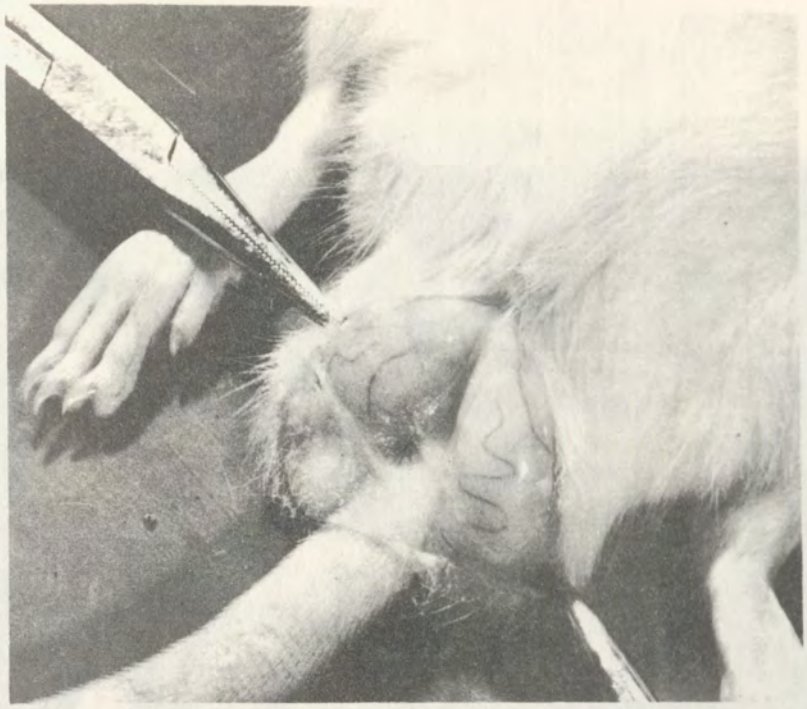
A mid-line incision is made through the skin of the scrotum. The testes may need to be squeezed out of the abdominal cavity through the inguinal canal. (See illustrations next page.)

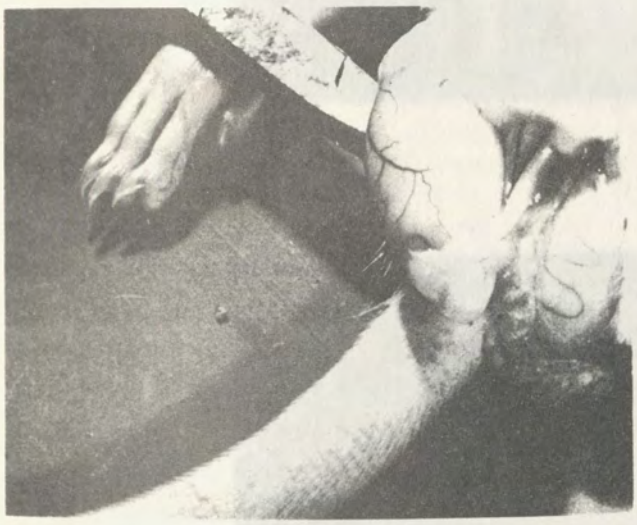
The testes are freely movable within the scrotum; squeeze one against the tunica in the region exposed by the incision through the skin. Slit the tunica, draw out the testis, ligate the spermatic cord and cut it distal to the ligature.

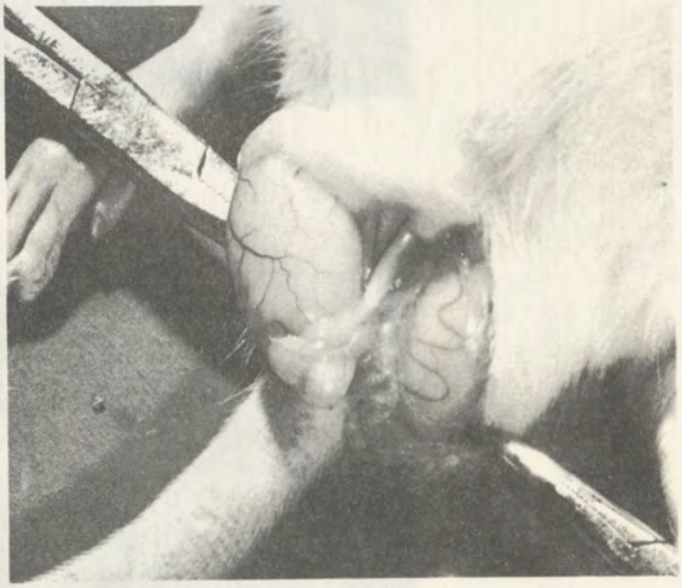
CARE OF ANIMALS:

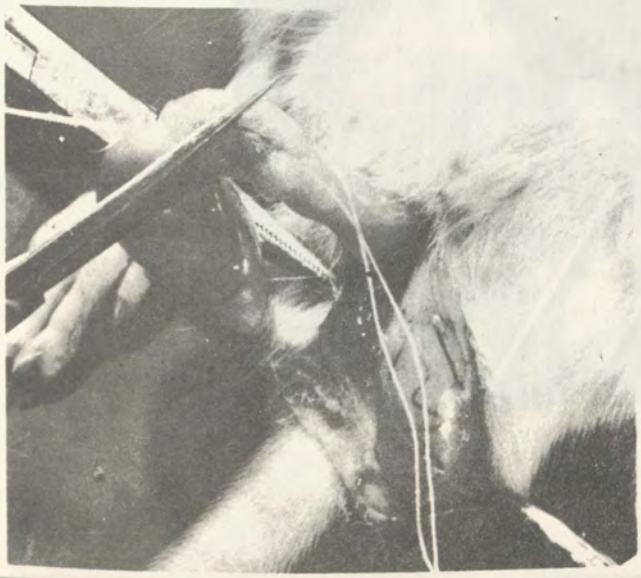
The hypophysectomized animals are extremely susceptible to infection and therefore must be given special diet and handled cautiously during injections. Bedding in the form of shredded paper must be provided and the regular diet of laboratory chow should be supplemented with canned dog food and slices of fresh carrots and oranges. Before injection the site must be carefully prepared as follows: First, clip the skin of the back as closely as possible with animal clippers. Then cleanse the clipped area first with chloroform then tincture of iodine and finally with alcohol. Before removing solution from the vial, cleanse the rubber stopper, through which the needle is inserted, with alcohol. Testosterone will be given at the rate of 0.1 mg/100 gm body weight per day and the growth hormone at the rate of 0.5 mg/100 mg per day; each of these standard doses will be found in 0.5 ml of solution provided for injection. The animals must be injected daily and their weight must be recorded three times weekly on days to be announced in the first laboratory period.

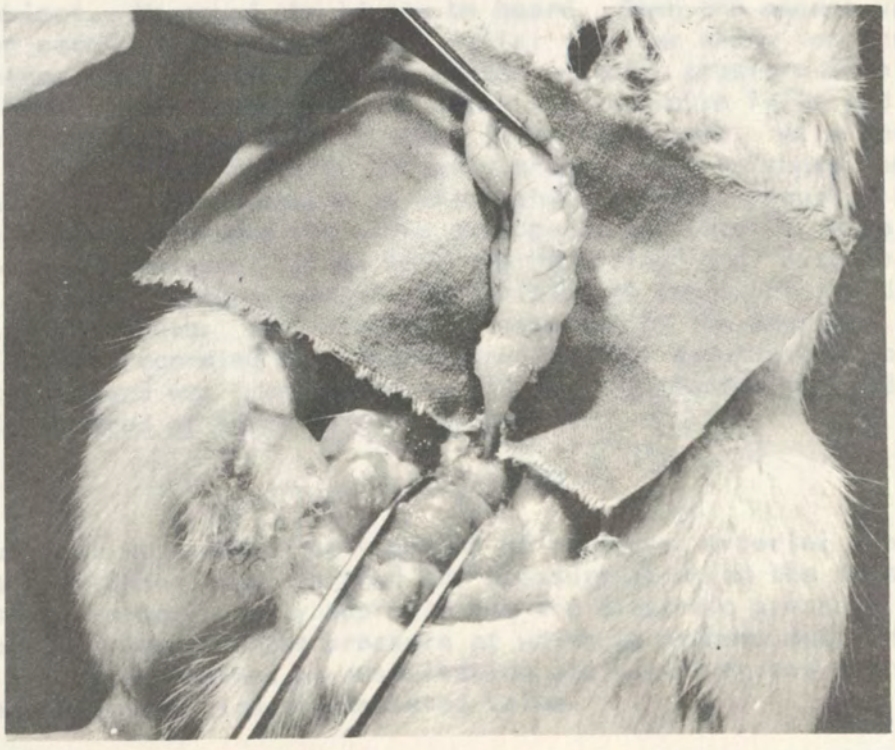
On the last day of the experiment weigh the animals and kill them with ether. Make a long mid-line incision through the abdominal wall. Lying on either side of the urinary bladder will be found a frond-like structure which consists of the seminal vesicle and coagulatory gland; to familiarize yourself with what you are looking for, identify these two structures first in your control animals. (See illustrations) Pull out both structures together and have the two sets of organs from one animal weighed together. Calculate the ratio: combined organ weight in milligrams/100 gm body weight; enter this on your data sheet. Retain all data for later analysis in your Statistics course.











Blood Pressure and ECG

This lab consists of two parts; half the class will be recording ECG's while the others are measuring blood pressures. Mid way through the afternoon the groups will inter-change.

I ARTERIAL PRESSURE IN MAN

A. Technique for determination of pressure by the indirect method.

The apparatus for the measurement of arterial pressure in man by the indirect method (the "sphygmomanometer") consists of an inelastic cuff which encircles the upper arm (or other region). This contains a rubber bag which can be inflated with air by means of a hand pressure bulb. An escape valve controlled by a knurled screw permits slow leakage of air whereby the pressure in the system may be allowed to fall gradually. The rubber bag is also connected to a mercury or anaeroid manometer by which the pressure exerted on the skin surface may be determined.

Wrap the cuff about the bare arm just above the elbow beginning with the larger end in contact with the skin. The cuff must be free of folds. Secure the smaller end in place by tucking it under the part already in place, or by means of the metal clips on the cuff.

1. Auscultatory method: This depends on the principle that, when the flow through the brachial artery is intermittent, a characteristic sound (Korotkow sound) can be heard in the cubital fossa. Place the bell of a stethoscope over the brachial artery in the cubital fossa and raise the pressure in the system to a level well above the expected systolic pressure of the subject. No sound should now be heard. Open the escape valve slightly and listen carefully as the pressure falls. A clear sharp tapping sound (the Korotkow sound) will be heard at the systolic pressure level. Record this pressure. This sound grows louder as the pressure falls and may acquire the character of a murmur, which later disappears. At a certain pressure level the sound fairly abruptly changes from a "sharp tap" to a "dull thud." Note the pressure at which this "muffing" occurs. At a few millimeters lower pressure the sound disappears completely. Note this "disappearance" pressure. Since both the "muffling" and "disappearance" pressure are considered by various authorities to represent the diastolic pressure, record both. The notation recommended by the American Heart Association for recording of arterial pressure for a determination in which the Korotkow sound was first heard at 120 mm. Hg, became muffled at 88 mm. Hg and disappeared at 80 mm. Hg, is as follows:

120/88-80

Throughout your work employ this method of recording arterial pressures. The present evidence suggests that the pressure at which the Korotkow sound disappears more nearly approximates the diastolic pressure (as measured directly) than does the pressure at which it becomes muffled. The systolic pressure obtained by auscultation ordinarily agrees within a few millimeters with the directly measured value.

2. Palpatory method: Locate the radial pulse and then raise the pressure in the cuff until the pulse is no longer felt. Then allow the pressure to fall slowly. The level at which the pulse again becomes palpable is taken as a measure of systolic pressure. Compare this measure of systolic pressure with that obtained by the auscultatory method. It is ordinarily about 10 mm. below the latter.

Procedure

(1) First practice measurement of arterial pressure in the left arm of your partner until you have some confidence in your results.

(2) Arterial pressure under standard conditions: Arterial pressure determinations are most frequently made to enable comparison of the subject's pressure with standard values obtained on groups of "normal" subjects. For this, standard conditions are essential. They are: (I) sitting position; (II) complete rest for at least five minutes (or longer after heavy exercise), (III) no heavy meal less than two hours previously: (IV) comfortable temperature; and (V) absence of disturbing environmental factors.

Obtain a series of at least ten measurements of systolic and diastolic pressure on each member of your group under the above conditions, also obtain the heart rate with each reading, and average all the readings.

(3) Effect of arm position: Measure the arterial pressure in the arm of a lying subject when the arm is (a) held vertically upward, (b) when it is horizontal and the level of the heart, and (c) when it hangs vertically downward. Measure the vertical distance of the center of the cuff in (a) and (c) from that in (b). Divide those distances by 13.6 (sp. gr. of mercury) to give the expected differences (in mm. Hg) in arterial pressure from hydrostatic considerations, and add or subtact these values to or from the values obtained in (b) and compare them with the values obtained in (a) and (c). Account for any discrepancies.

(4) Effect of manometer position (mercury only): With the arm at the level of the heart, place the manometer (a) as high above the arm as possible and (b) as low as possible. Measure arterial pressure in both positions. Account for the results.

(5) Arterial pressure in the thigh: Apply the cuff to the thigh and place the stethoscope bell in the popliteal fossa. Attempt to measure press pressure in the femoral artery. Values considerably above those obtained for brachial artery pressure are usually found, in part because the standard cuff width is inadequate to transmit to the artery in the larger tissue mass the full pressure recorded by the manometer.

(6) Discussion of results: Retain all your results for later detailed Statistical analysis. In the meantime, compare your data to the following results analyzed statistically by Masters et al. (JAMA 1950, 143:1464) obtained on 74,000 employees in industrial plants in the United States. Some of the data for young adults are as follows:

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AGE RANGES	ARTERIAL PRESSURES (mm. Hg)					
	Systolic			Diastolic		
MALES	Mean	S.D.	C.V.%	Mean	S.D.	C.V.%
20 - 24	122.9	13.74	11.18	76.0	9.93	13.07
25 - 29	125.1	12.58	10.06	77.8	8.98	11.54
FEMALES						
20 - 24	115.7	11.83	10.22	71.7	9.68	13.21
25 - 29	116.8	11.43	9.79	73.7	9.05	12.28

The same data can be presented in another form: the normal range is arbitrarily defined as including 80% of the cases; borderline hyper- and hypotension, 5% of the cases each; and hyper- and hypotension, the extreme ranges with 5% of the cases each. The boundaries of the ranges so defined are:

SYSTOLIC

	Upper Limit of hypotension	Lower limit of "normal"	Mean	Upper limit of "normal"	Lower limit of hypertension
Males: 20 - 24 Yrs.	98	105	123	140	150
25 - 29 Yrs.	100	108	125	140	150
Females: 20 -24 Yrs.	95	100	116	130	140
25 - 29 Yrs.	98	102	117	130	140

DIASTOLIC

Males: 20 - 24 Yrs.	56	62	76	88	95
25 - 29 Yrs.	60	65	78	90	96
Females: 20 - 24 Yrs.	55	60	72	85	90
25 - 29 Yrs.	55	60	74	86	92

The following questions will be discussed:

(1) What exactly is meant by "normal arterial pressure?" What procedures are involved in arriving at a figure or figures for "normal arterial pressure?"

(2) What effect, if any, does age have on the arterial pressure levels? What physical changes in the circulatory system are responsible for such effects, if any?

(3) What statistical associations, if any, exist between the arterial pressure levels and life expectancy? What can be said in explanation of such associations?

B. Effects of Posture and Exercise

In this section, the changes in the circulation produced in man by changes in posture and by exercise will be studied. One member of each group will serve as subject, the other as observer. To the extent that time permits, the procedures should be repeated, the students reversing their roles.

The data to be obtained for each procedure are the systolic and diastolic pressures, and the heart rate. From these data certain quantitative estimates of other aspects of the circulation can be made, although only very approximately:

(a-1) Cardiac Output: Since the pulse pressure in light and moderate exercise is approximately proportional to the stroke volume of the heart, the pulse product (pulse pressure multiplied by the heart rate) is approximately proportional to the cardiac output (stroke volume multiplied by the heart rate). Thus: pulse product = pulse pressure x heart rate = k x cardiac output. (In this equation, k is a constant, characteristic of the individual). It may be roughly estimated for each individual from his resting pulse pressure and heart rate, with the assumption that his cardiac output is 3 l. per square m. body surface per min.

(a-2) Since stroke volume is nearly constant in some circumstances estimate cardiac output by assuming that it is simply proportional to heart rate. How does the result compare with (a-1) above? Actually, stroke volume increases during light exercise, remaining constant only during moderate and heavy exercise.

(b) Peripheral Resistance: This is estimated by calculating the pressure generated in the arteries by unit quantity of blood ejected by the heart, i.e. by the mean arterial pressure divided by the cardiac output. Approximately:

$$\text{estimated peripheral resistance} = \frac{\text{mean arterial pressure.}}{\text{pulse product}}$$

Mean arterial pressure has been defined in two ways:

(1) $\frac{D.P. + S.P.}{2}$ (2) $\frac{2\ D.P. + S.P.}{3}$

Use both to calculate resistance.

(1) Effect of posture - Maintaining standard conditions except for posture, obtain pressures and heart rate while your subject is (a) lying horizontally, (b) sitting and (c) standing quietly. In each case be sure that the arm cuff is at the level of the heart. In each posture continue to make observations until the pressures and heart rates have become steady and show no tendency to rise or fall. For each posture calculate the pulse product, mean arterial pressure and estimated peripheral resistance. Tabulate for each posture all observed and calculated values.

(2) Effect of exercise - Each subject will perform one of the following types of exercise:

(a) Master's "two-step" test - walking up and down two 9 inch steps 25 times in 1 1/2 minutes;

(b) standing running as vigorously as possible for 3 minutes;

(c) cycling on a bicycle ergometer at 100 watts, 100 rpm, for 3 minutes;

(d) running up one flight of stairs, down two and up one to the laboratory.

After the exercise he will return to his place in the laboratory and stand quietly while the observer records alternately and as frequently as possible (15 second periods) his heart rate and arterial pressure levels, continuing until stable values are reached as recovery is completed. Each reading should be recorded with a record of time (seconds after completion of exercise), and a chart made on coordinate paper of systolic and diastolic pressures, and heart rate plotted against time. Draw a smooth curve through each set of points, and from these obtain at one minute intervals interpolated values for these three measures. From them calculate the pulse pressures, pulse products, mean pressures and estimated peripheral resistances for each minute. Add these to the chart.

The results obtained in this period will be discussed with special reference to the physiological mechanisms involved in producing the circulatory changes observed.

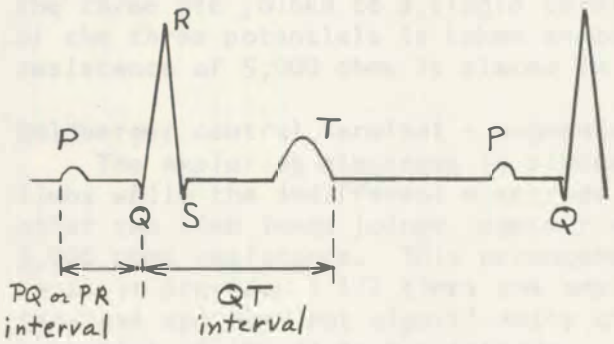
II PRINCIPLES OF ELECTROCARDIOGRAPHY

A. General Principles

Contractions of heart muscle are normally associated with flow of electrical current and changes in electrical potentials occurring in a predictable pattern. The ECG is a method of measuring the direction and magnitude of these electrical events as they exist in the body. The body tissues serve as conductors to the surface, where electrodes may be placed to measure the potentials generated by cardiac depolarization and repolarization.

The electrical forces are directed in three dimensions in the body. In order to record these forces, in taking an ECG, electrodes are paired to form leads and placed to coincide with different planes of the body. The electrical forces are then measured as they are projected onto each of these leads and planes.

The components of the typical ECG recording can be related to cardiac phenomena.



P wave = atrial depolarization
QRS wave = ventricular depolarization
T wave = ventricular repolarization

(atrial repolarization wave buried in QRS complex)

PR interval = atrial depolarization time + conduction time through A.V. node and Purkinje system.
QT interval = duration of electrical events related to mechanical systole.

Types of leads:

(1) Bipolar: Two electrodes, each with its own potential, are used. The tracing records the <u>difference</u> between the potential of the two electrodes. One electrode is designated as <u>positive</u> and by convention, when this electrode remains positive relative to its mate, the reflection in the ECG occurs <u>above</u> the <u>base</u> line and vice versa.

(2) Unipolar: Two electrodes are used. However, one electrode is at zero potential and is called the <u>distant</u> electrode. The other electrode is called the <u>exploring</u> electrode and actually measures the potential directly underneath it without being influenced by potential of its mate. There are two types of distant electrode (also known as <u>central terminal</u>).

(a.) Wilson: (central terminal) or (V lead).
Electrodes are placed on each of RA, LA, LL and the three are joined to a single terminal. The mean of the three potentials is taken as zero. A resistance of 5,000 ohms is placed in each lead.

(b) Goldberger central terminal - augmented V lead (aV).
The exploring electrode is placed on one of the limbs while the indifferent electrode consists of the other two limb leads joined together without the 5,000 ohms resistance. This arrangement is used because it provides 1 1/2 times the amplitude of Wilson terminal and does not significantly change the zero potential of the distant electrode.

B. <u>Placement of Electrodes</u>

By convention, the following leads are used in recording the ECG. The corresponding planes are given as well as the conventional polarity of the electrodes.

(1.) Frontal plane

<u>Standard Limb Leads</u>			(Bipolar)
I	RA	(-) to LA	(+)
II	RA	(-) to LL	(+)
III	LA	(-) to LL	(+)

<u>Augmented Unipolar Limb Leads</u>			
aV_r	Central Term.	(0)	to RA (+)
aV_l	"		to LA (+)
aV_f	"		to LL (+)

(2) Horizontal or transverse plane

Unipolar Precordial Leads

V_1	Central terminal	(0)	to V_1 (+) (4 ics at RSB)
V_2	"		to V_2 (+) (4 ics at LSB)
V_3	"		to V_3 (+) (Bet. V_2 & V_4)
V_4	"		to V_4 (+) (5 ics at LMCL)
V_5	"		to V_5 (+) (LAAL level " V_4)
V_6	"		to V_6 (+) (LMAAL " " ")

(3) Sagittal Plane — Unipolar Esophageal Leads — Not often used but good for recording atrial potentials

C. Methods of Measuring and Recording:
The Difference in Potential between Electrodes

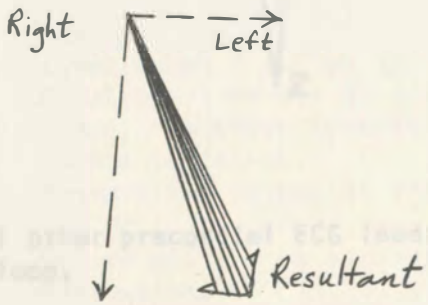
(1) String galvanometer. This is infrequently used now. A gold plated quartz string was connected to two electrodes and suspended between the poles of an electromagnet. The movement of the string was magnified by lenses and projected on to moving photographic paper.

(2) Electronic recorder (direct writer). The potential difference between the two electrodes is amplified by vacuum tubes and directed to a coil suspended between poles of an electromagnet. As current flows through the coil, it rotates, moving an attached pen or mirror, and the movement is recorded on paper (direct writer or photographic).

Types of Pen:
(1) Pen with heated tip
(2) Pen with electric current flowing from tip
(3) Pen with ink at tip
(4) Pen with fine capillary spray at tip

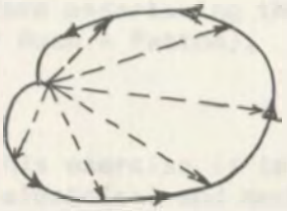
Recording Paper: For 1 & 2 is usually black and coated with white oxide. Heat of stylus or pen volatilizes oxide and leaves black line. For 3 & 4 cheaper paper may be usable.

D. The instantaneous electrical forces of the heart can be viewed as a resultant vector emanating from a single point and having 3 dimensional direction and magnitude.

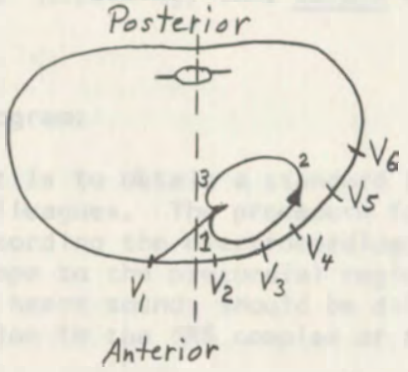


Resultant vector proceeding anteriorly, inferiorly and to the left.

If we combine the resultant instantaneous vectors of cardiac ventricular depolarization, we get a vector loop with direction and magnitude.

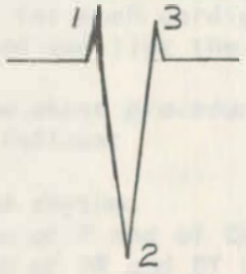


Viewing this loop in the body's horizontal plane,



we can relate it to the ECG, e.g., lead V_1, by drawing a line between V_1 and the E or isoelectric point of the vector loop. Then draw a perpendicular to this line. Forces anterior to this perpendicular will be in the positive sphere.

In the above example, ventricular depolarization viewed from V_1 will look like this



All other precordial ECG leads can likewise be related to the vector loop.

E. Relationship of ECG, Pressure Phenomena Flow and Heart Sounds

Almost all texbooks of physiology contain diagrams showing the precise time relations between these events. Such a figure should be studied carefully before undertaking the following exercise (see for example Chapter 29 of Ruch - Patton).

F. Laboratory Exercise

The purpose of this exercise is to acquire knowledge concerning the relationship between electrical and mechanical events of the cardiac cycle. The anatomic position of the heart in relation to cardiac auscultation will be demonstrated. The cardiac sounds will then be studied and correlated with the apex beat of the heart, the radial pulse and the carotid pulse. These auscultatory and palpatory phenomena will then be correlated with the electrocardiogram. Read the section on the origin of heart sounds in your physiology text before this lab period.

Procedure:

I. The electrocardiogram:

1. Each student is to obtain a standard 12 lead electrocardiogram on one of his colleagues. The procedure for this is to be found below. While recording the electrocardiogram, the student should apply a stethoscope to the precordial region of the subject. The first and second heart sounds should be differentiated. What is their time relation to the QRS complex of the electrocardiogram?

Next, feel the apex beat. This is located around the 5th intercostal space in the midclavicular line. What is the time relation between the apex beat and the QRS complex of the electrocardiogram?

Palpate the carotid and radial arterial pulsations. Determine the temporal relationships of the apex beat, arterial pulsations and the QRS complex of the ECG. Are you able to hear more than two heart sounds for each cardiac cycle? Describe the heart sounds that might be heard and list the dynamic phenomena related to these sounds.

When the above procedures have been accomplished, analyze the 12 lead ECG as follows:

1. Rate and rhythm.
2. Duration of P and of QRS in standard leads V_1 and V_5.
3. Duration of PR and QT intervals in lead 2 and at least 4 other leads. Do these intervals vary? Give a possible reason for such a variation.
4. Measure the height of the R waves and depth of the S waves in V_1 and V_5.
5. Record all of the above figures and retain the ECG for further discussion.

Procedure for obtaining the electrocardiogram:

1. Plug machine to wall socket. Ground unless automatic. Warm up 3-4 minutes.
2. Attach electrodes to extremities. Note proper preparation of skin and strapping. Note proper location of electrodes.
3. Check wires which should be straight but not too close together (if possible) and not in contact with wet floor.
4. Check stylus heat. Dull red glow and base line 1 mm. wide is proper. (This does not apply to Grass polygraph.)
5. Check paper speed. It should be 25 mm. per sec.
6. Standardize (sensitivity). Explain paper ruling (1 mm. squares).
7. Adjust zero or base line with centering device.

VII. Factors Which May Cause Quantitative Errors in ECG.

1. Faulty electrode placement
   (a) Reversal of limb leads.
   (b) Wrong chest lead placement.
   (c) Electrode jelly extending between and connecting chest lead positions.
2. High skin resistance (produces low voltage or inaccurate voltage).
   (a) Inadequate rubbing of skin with jelly. (Rubbing increases blood supply to skin and removes horny layers).
   (b) Insufficient electrode jelly.
   (c) Electrodes too tight. (This causes obstruction of blood flow and also muscle tremors).
3. Faulty standardization (producing falsely high or low voltage).
4. Patient eating or drinking (cold water).
5. Variation in patient position.
6. Marked respiratory variation.
7. Poor frequency-linearity of machine.
8. Wrong resonance of pen.
9. Undervoltage of main power lines.
10. Inaccurate time marking in ECG.
11. Amplifier tubes failing (wavering of base line).

VIII. Factors Which May Cause Poor Quality Tracings and Artifacts.

1. Electrical interference

(a) A.C. 60 cps vibrations are of regular amplitude and frequency. They may be picked up either by the connecting wires, or by the patient, and thus transferred to record. To avoid:

(1) Patient is grounded via right leg to wall plug. (If latter is not available, ground to cold water tap or water pipe).

(2) Patient not to touch metal springs, etc.

(3) Patient not to touch other people.

(4) Disconnect patient cable from machine. If A.C. still present, it does not come from patient.

(5) Keep wires off damp floors.

(6) Keep power cords away from patient, from patient's cable, from other wires, and from other instruments.

(7) Keep patient's cable and leads straight.

(8) Ground patient's bed, if necessary.

(b) Skin current (D.C.), due to glandular activity of skin. (This is not transmitted through amplifier or direct writer but only by string galvanometer).

(c) Somatic tremor vibrations are irregular in amplitude and frequency, usually 2 mm. tall, due to muscle current and electrode movement. To avoid:

(1) Have patient warm and calm.

(2) Avoid excessively tight electrodes.

(d) Magnetic field (like A.C.), caused by electric currents set up by adjacent electrical instruments. To avoid:

(1) Keep ECG wires away from others.
(2) Avoid simultaneous operation of offending appliances, etc.
(3) Ground patient's bed or room.

(e) Polarization of electrodes, causing small vibrations or wandering base line. To avoid:

(1) No metal particles on skin or electrodes.
(2) Keep electrodes clean.

2. Motion of patient. To avoid:

(a) Reassure patient.
(b) Hold extremities using rubber gloves, if possible (why rubber?)

3. Motion of ECG machine.

4. Broken lead connections. One or more leads will not record or will show vibrations.

5. Improper stylus temperature.

6. Faulty paper motion including jerky movements.

7. Fuse blown.

CLINICAL ELECTROCARDIOGRAM LABORATORY

During the first part of the period there will be a demonstration of vectorcardiography. Following this, the class will be divided into smaller groups to discuss applications of electrocardiography in clinical medicine with a number of cardiologists.

TEACHING ANALOG - An ECG teaching analog which illustrates the concept of the heart as a dipole placed in a volume conductor will be available in the teaching laboratory. With a little study and manipulation of this self-teaching device you should be able to learn about the principle of the Einthoven triangle and gain some understanding of the relationships between the potentials (or current) recorded from different sites of the body surface. On the board the volume conductor is simulated by conductive carbon paper. the dipole, which represents the electrical activity of the heart, is a battery with brush contacts. The electrocardiographic indicator consists of a voltmeter with electrical connections to the standard clinical limb-lead positions.

INTERPRETATION

A set of abnormal tracings, in which most of the deviations from normality are arrhythmias or conduction disturbances, will be available.

It is recommended that each student review--prior to this laboratory--reference material which pertains to arrhythmias, conduction disturbances and electrocardiographic interpretation.

PURPOSES

During this session you will have the opportunity to study and interpret clinical electrocardiograms, selected from the heart station, in order to:

(1) Correlate them with the previously learned basic information pertaining to the electrical activity of excitable tissue, and to

(2) Demonstrate the principles involved in detecting changes in rate, rhythm and the sequence of cardiac excitation.

TYPES OF INFORMATION

The clinical electrocardiogram is a graphical presentation of the electrical activity of the heart in which the vertical coordinate represents voltage and the horizontal coordinate is time. It is an inscription of the sequential activation of groups of myocardial cells viewed from the surface of a volume conducting medium. Therefore, the clinical electrocardiographer should have some understanding of:

(1) myocardial transmembrane potentials

(2) volume conductor theory, and the

(3) pathways of excitation through the heart

NOMENCLATURE "Ground Rules"

The following is a partial list of the terminology used in the interpretation of the sequence of cardiac excitation from clinical electrocardiograms.

I Normal Rhythms

1. Normal Sinus Rhythm (NSR). The impulse is regularly initiated in the SA Node, at a frequency between 60 and 100 beats per minute, and propagated through the conduction tissue of the heart in a normal manner.

2. Sinus Arrythmia: The frequency varies, usually with respiration, the faster rate occurring near the end of inspiration and the slower rate at the termination of expiration.

3. Sinus Bradycardia: A cardiac mechanism in which impulses originate in the SA Node at a rate of less than 60 beats per minute.

4. Sinus tachycardia: A cardiac mechanism in which impulses are liberated from the SA Node at a rate greater than 100 beats per minute.

II Abnormal Rhythms

1. Premature Beats (ectopic beats; extrasystoles). An impulse generated in a region of the myocardium other than the "head" of the SA Node, which may or may not be premature in time. There are three main types:

   a. Atrial (APB). The P wave is always present though its shape is usually changed. The P-R interval is characteristically shorter than with the basic rhythm yet longer than 0.12 seconds. The QRS complex generally is not affected. The compensatory pause is incomplete.

   b. Nodal or junction (NPR). The P-R interval is shorter than 0.12 second. Otherwise similar to APB.

   c. Ventricular (VPB) The QRS complex is distinctly abnormal, being wide, slurred and notched. The compensatory pause is complete.

2. Paroxysmal Tachycardia. A cardiac mechanism intiated by an ectopic focus with a rapid and sustained succession of regularly occurring impulses at rates usually between 140 and 240 beats per minute. The three types (atrial, nodal, ventricular) are named for the location of the irritable focus. The arbitrary distinction of duration between paroxysmal tachycardia and premature contractions indicates a close functional interrelation.

3. Atrial Flutter. A rapid and regular sequence of atrial depolarizations at rates between 200 and 380 beats per minute usually with a slower ventricular response due to an incomplete AV block. The flutter (f waves), or P waves, are best seen in leads II and III.

4. Atrial Fibrillation. A cardiac mechanism produced by a rapid irregular depolarization of the atria with a slower irregular response of the ventricles. Though an undulating base line may be detected, definite P waves are absent.

5. Ventricular Fibrillation. The electrocardiogram appears chaotic with the QRS complexes exhibiting irregular, high and wide deflections. This pattern is usually not seen except as a terminal event or during open-heart surgery, with the patient's circulation supported by an extracorporeal cardio-pulmonary bypass (heart-lung machine), when ventricular fibrillation sometimes may be therapeutically produced.

III Atrioventricular Conduction Disturbances

1. Incomplete Atrioventricular Block. The partial block (inhibition of conduction), due to functional or organic cause, may be in the atrial muscle, junctional tissue or AV Node.

   a. 1st Degree AV Block In its mildest form the P-R interval is greater than 0.20 second without "dropped" ventricular complexes.

   b. 2nd Degree AV Block In its more severe form there is, in addition to the prolonged P-R interval, periodic dropping of the ventricular complex, which produces variations in the ratios of P waves to QRS complexes.

2. Complete Atrioventricular Block. (3rd Degree AV Block)
Usually due to organic discontinuity of the conduction tissue in the AV Node or bundle of His, producing a dissociation of atrial and ventricular activity. The atrial rate is generally about twice the ventricular rate and the P-R intervals have a variable and unpredictable duration.

IV Bundle Branch Block (BBB)

The conduction disturbance may occur in the branches of the bundle of His, along the arborization network of Purkinje or within the ventricular muscle.

1. Complete Bundle Branch Block (left or right). Diagnostic criteria include an abnormally slurred or notched QRS complex greater than 0.12 second, and a left (LBBB) or right(RBBB) shift of the mean electric axis. This is present whenever the impulse migrating down from the AV node through the bundle of His is completely obstructed by a lesion in the left or right bundle, so that its passage directly to the Purkinje system is prevented.

2. Incomplete Bundle Branch Block (left or right). Diagnostic criteria include an abnormally slurred or notched QRS complex greater than 0.10 but less than 0.12 second. If the mean QRS electric axis is normal the tracing is interpreted as indicating defective intraventricular myocardial conduction. An axis shift is considered to mean disturbances in conduction but not complete blocking of impulses in the main bundle branches.

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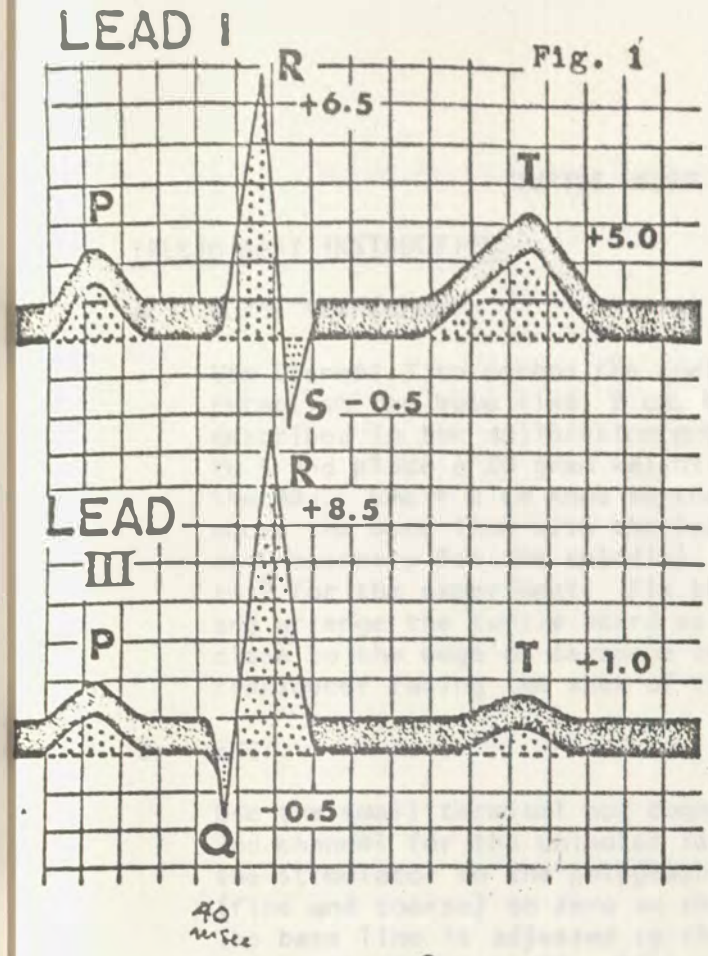


Fig. 1

Current flows in the direction indicated by the vector & always travels from negative to positive.

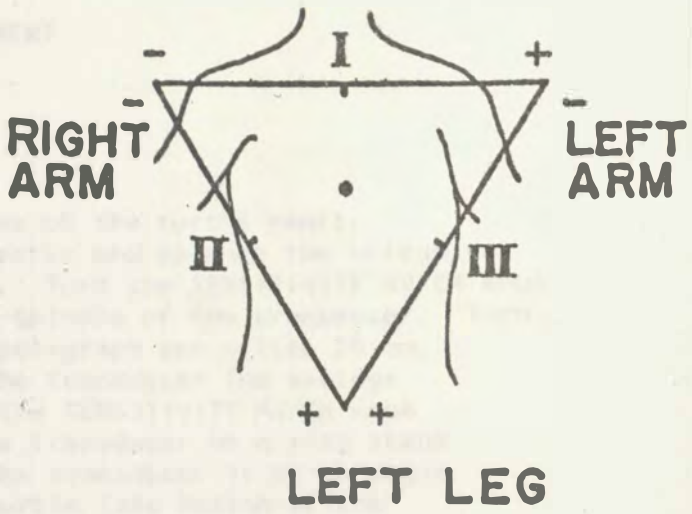


Fig. 2

Polarity of bipolar limb leads in relation to frontal plane & Einthoven's equilateral triangle.

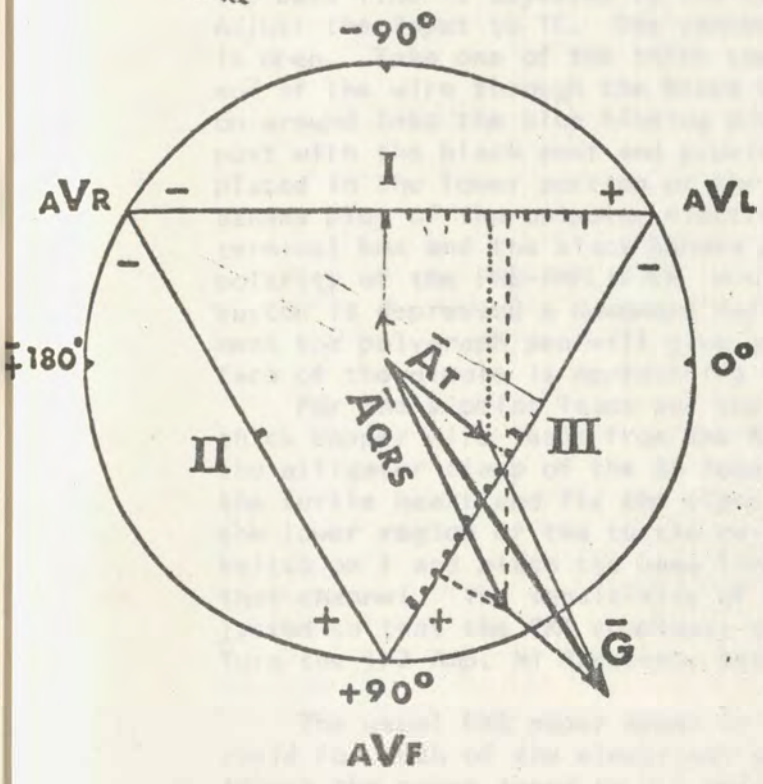


Fig. 3

Einthoven's triangle arranged for analysis of electric axes.

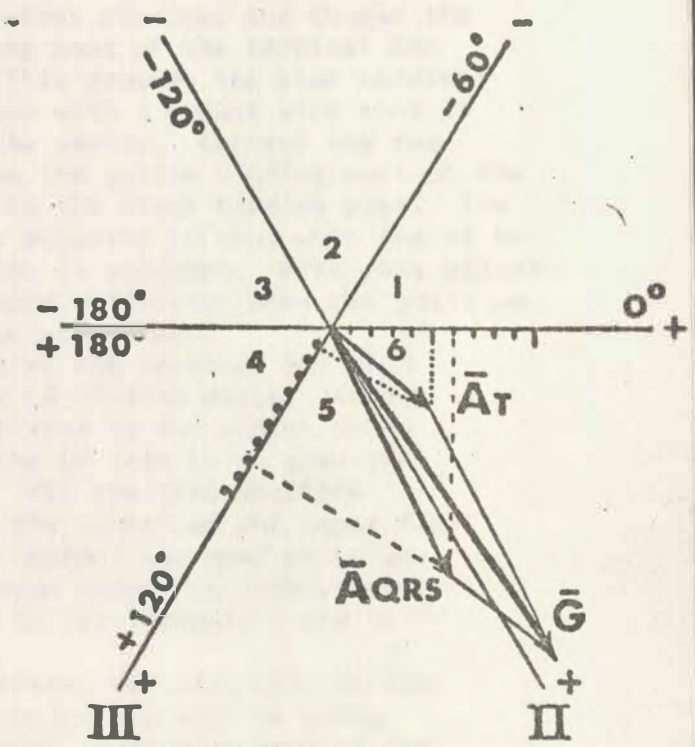


Fig. 4

Triaxial reference system with QRS, T and ventricular gradient vectors drawn from figure one.

TURTLE HEART EXPERIMENT

PRELIMINARY INSTRUCTIONS:

A. Force Transducer:

Use Channel 3 to record the contractions of the turtle heart. Establish the base line, 2 cm. below center and balance the bridge as described in the calibration procedure. Turn the SENSITIVITY MV/CM knob to 5 and place a 20 gram weight on the spindle of the transducer. Turn the ADJ. CAL = 2 CM knob so that the polygraph pen writes 20 mm. above the base line with the load on the transducer (no springs are necessary for the spindle). Turn the SENSITIVITY MV/CM knob to 2 for the experiment. Fix the force transducer on a ring stand and arrange the turtle board so that the transducer is at an angle close to the edge of carapace of the turtle (the bottom of the transducer facing the apex of the heart).

B. EKG:

Use the small terminal box connected to the PRE-AMPLIFIER of the 2nd channel for the unipolar lead. Connect a ground wire from the stimulator to the polygraph. Put the balance voltage knobs (fine and coarse) on zero so the base line does not shift. The base line is adjusted to the center of the paper for that channel. Adjust the input to TC. One cannot balance this circuit, because it is open. Take one of the thick copper wires provided and thread the end of the wire through the black binding post of the terminal box on around into the blue binding post. This grounds the blue terminal post with the black post and provides you with a ground wire that is placed in the lower portion or the turtle cavity. Connect the red banana plug of the unipolar electrode to the yellow binding post of the terminal box and the black banana plug to the black binding post. The polarity of the PRE-AMPLIFIER would be adjusted so that when the -2 MV button is depressed a downward deflection is produced. With this adjustment the polygraph pen will give an upward deflection when the positive face of the dipole is approaching the unipolar lead.

For the bipolar leads use the regular EKG terminal box with thick copper wire leads from the RA and LA binding posts. Attach the alligator clamp of the RA lead to tissue in the region above the turtle heart and fix the clamp of the LA lead to an area in the lower region of the turtle cavity. Put the LEAD SELECTOR switch on I and place the base line in the center of the paper for that channel. The sensitivity of this channel may need to be adjusted so that the EKG complexes are large enough to interpret. Turn the 1/2 Amp. Hi Frequency knob to 15 for channels 2 and 4.

The usual EKG paper speed is 25 mm/sec, but this will be too rapid for much of the electrical exploration you will be doing. Adjust the paper speed to 2.5 mm/sec while performing most of the experiment.

C. Turtle Heart Preparation:

Remove the plastron from the turtle and cut through the tough connective tissue overlying the heart. At the apex note the well-developed frenum. Tie one end of a ligature about the frenum and cut the frenum distal to the ligature. Tie the other end of the ligature to the spindle of the force transducer. The transducer should be situated at an angle close to the edge of the carapace so that the heart will not be pulled out of the cavity with amphibian Ringer's solution and adjust the tension on the heart so that a good record is obtained.

EXPERIMENT:

Relate the activity recorded by the exploring unipolar electrode to the complexes of the bipolar leads. Change position of the unipolar electrode using the various adjustments available to you (the different clamp arrangements and the ring stand adjustment). Note that the positive exploring electrode records a negative deflection when the electrical activity is toward it. Relate the electrical activity of the unipolar and bipolar leads to the mechanical activity of the heart. Keep in mind that you are recording a change in tension from base to apex of the ventricle with each contraction, not a change in intraventricular pressure.

Using the above relationships determine the location of the sinus venosus with the exploring electrode.

ADDITIONAL EXPERIMENTS:

A. Vagal Stimulation:

Repeat the following procedures with the unipolar lead first on the atria and then on the ventricle. Connect the stimulating electrodes to the transformer which acts as an isolation unit and then connect the small transformer to the output of the stimulator.

Make a midline incision the length of the neck and gently retract the skin and tissues immediately underlying the skin. On either side of the trachea expose the large blood vessels (artery and vein) lying between muscle sheaths. Two nerves will be found with these vessels, the vagus and sympathetic nerves. The vagus is larger and lies more dorsal. It should be isolated very gently without pinching or pulling. Tie a ligature about the nerve very loosely so that the nerve can be carefully raised and stimulated with the hand electrodes. During the isolation procedures the nerve that you suspect to be the vagus should be stimulated with multiple stimuli. The heart will slow with vagal stimulation.

Stimulate with multiple stimuli, first the right and then the left vagus, with a weak, medium, and strong voltage. Is there any difference in threshold response between right and left vagal stimulation?

Stimulate the right vagus with a strong tetanic current. Stroke a small portion of the ventricle with a wooden stick after the heart has stopped.

First record the electrical activity with the unipolar lead next to the stimulated area and then move the unipolar lead to the opposite side of the ventricle and record from that position.

What areas of the heart are innervated by the right and left vagi? Is there any change in contractile strength of the ventricle as a result of vagal stimulation?

B. Effects of Epinephrine: (fix the unipolar electrode at one position on the ventricle)

Drip epinephrine (1:1,000 dilution) very slowly on the ventricle. Note the effect on the mechanical and the electrical activity. What influence does epinephrine have on the P-R interval? Are any extrasystoles produced? Identify the location of the extrasystole using the information obtained from the unipolar and bipolar leads.

C. Temperature Effects: (fix unipolar lead on the ventricle)

Place a thermometer in the body cavity of the turtle. Using warmed amphibian Ringer's solution irrigate the cavity until the temperature of the heart is increased 10° C. Determine the heart rate at the elevated temperature and compare it with the rate at the lower temperature. Calculate the Q_{10} for the turtle heart. Were any extrasystoles recorded during the warming process?

D. Effect of Stretching the Heart: (fix unipolar lead on the ventricle)

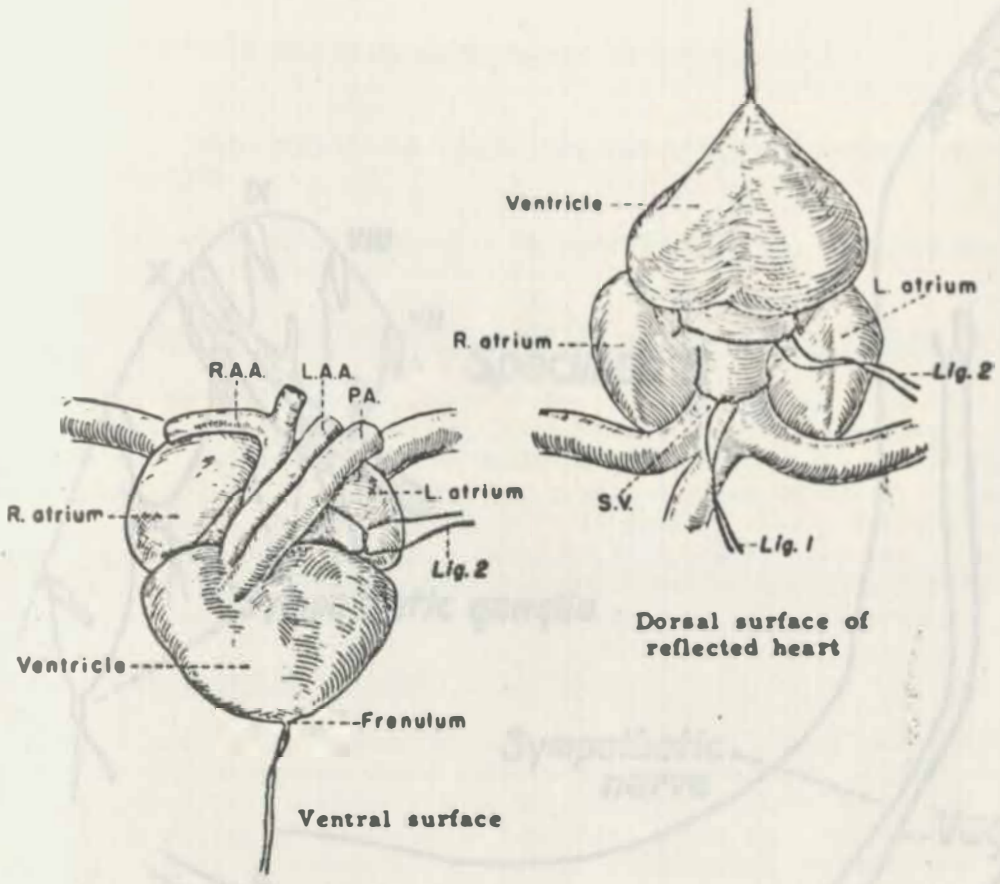
Increase the tension exerted by the transducer on the frenum sufficiently to change the diastolic tension. What influence does this have on the strength of contraction? What are the implications of this procedure concerning diastolic filling pressures?

E. Heart Block: (fix unipolar lead on the ventricle)

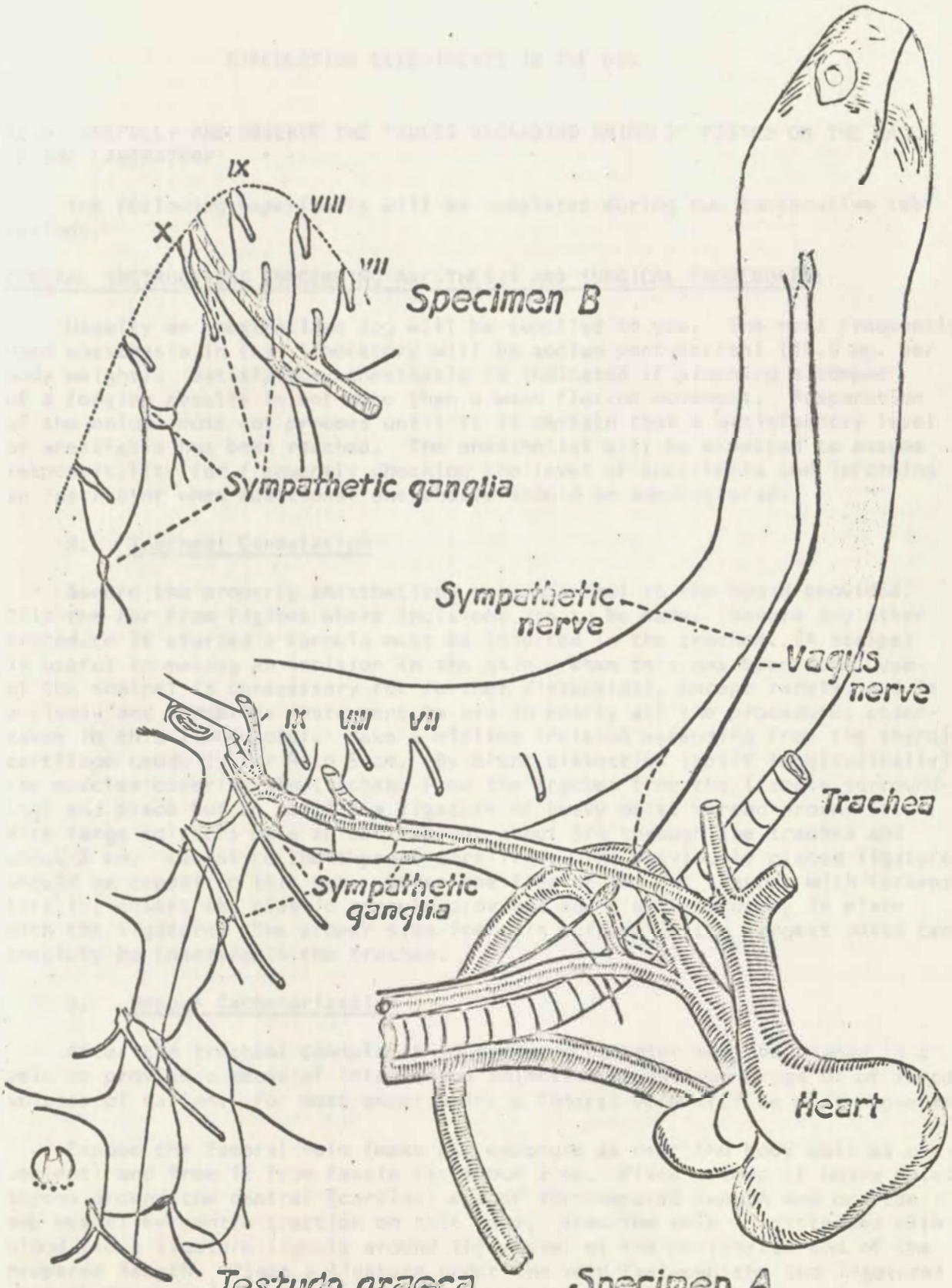
Detach the thread from the force transducer and place a Gaskell clamp around the heart at the atrioventricular groove. Adjust the Gaskell clamp in the correct position and hold it by means of a right angle clamp. Connect the heart to the transducer once more. Screw the clamp very carefully so that first a partial heart block is obtained and finally a complete block. Use extreme care! Do not clamp so tightly as to injure the heart. Gradually release the clamp and restore the proper rhythm of the heart.

F. Injury:

Fix the unipolar lead on one side of the ventricle and pinch the other side of the ventricle. Compare the electrical and mechanical activity of the damaged heart with the normal one.



Turtle heart, showing Stannius ligatures. R.A.A. right aortic arch; L.A.A. left aortic arch; S.V. sinus venosus.


IX
VIII
X
VII
Specimen B
Sympathetic ganglia
Sympathetic nerve
Vagus nerve
IX
VIII
VII
Trachea
Sympathetic ganglia
Heart
Testudo graeca
Specimen A

CIRCULATION EXPERIMENTS IN THE DOG

READ CAREFULLY AND OBSERVE THE "RULES REGARDING ANIMALS" POSTED ON THE WALL OF THE LABORATORY

The following experiments will be completed during two consecutive lab periods.

GENERAL INSTRUCTIONS CONCERNING ANESTHESIA AND SURGICAL PROCEDURES:

Usually an anesthetized dog will be supplied to you. The most frequently used anesthesia in this laboratory will be sodium pentobarital (32.5 mg. per body weight). Satisfactory anesthesia is indicated if pinching a toepad of a foreleg results in not more than a weak flexion movement. Preparation of the animal must not proceed until it is certain that a satisfactory level or anesthesia has been reached. The anesthetist will be expected to assume responsibility for frequently checking the level of anesthesia and informing an instructor when additional anesthetic should be administered.

A. Tracheal Cannulation

Secure the properly anesthetized supine animal to the board provided. Clip the fur from regions where incisions are to be made. Before any other procedure is started a cannula must be inserted in the trachea..(A scalpel is useful in making an incision in the skin. When this has been done, use of the scalpel is unnecessary for further dissection), except rarely, and is a clumsy and dangerous instrument to use in nearly all the procedures undertaken in this laboratory). Make a midline incision extending from the thyroid cartilage caudally for 4 to 5 cm. By blunt dissection (split longitudinally) the muscles covering the trachea. Free the trachea from the (fascia surrounding) and place but do not tie a ligature of heavy moist thread around it. With large scissors make an oblique cut about 3/4 through the trachea and about 2 cm. caudal to the thyroid cartilage; the previously placed ligature should be caudal to this cut. Grasp the flap of the cut trachea with forceps, lift it, insert the plastic cannula provided and tie it securely in place with the ligature. The proper size for this purpose is the largest which can possibly be inserted in the trachea.

B. Venous Catheterization

After the tracheal cannula is in place, a catheter must be placed in a vein to provide a means of intravenous injection of various drugs or of large volumes of saline. For most experiments a femoral vein will be most convenient.

Expose the femoral vein (make the exposure as near the body wall as convenient) and free it from fascia for about 2 cm. Place a loop of heavy moist thread around the central (cardiac) end of the prepared length and occlude the vessel by gentle traction on this loop. When the vein is distended with blood tie a ligature tightly around the vessel at the peripheral end of the prepared length. Place a ligature under the vein (between the two ligatures already in place) to tie in the catheter later. Before insertion of the catheter it should be attached to the rubber tubing and burette provided, the system filled with saline and the screw clamp on the tubing adjusted so that a very slow flow of saline from the burette is maintained.

Grasp the wall of the distended vein with fine-pointed forceps and make an oblique cut in the wall just under the forceps point about 1/2 way through the vein. Lift the flap of vessel wall thus formed, insert the catheter, loosen the traction loop and continue to insert the femoral catheter deep into the vessel. Secure the catheter in place with the ligature. Allow 5-10 ml. of saline to flow into the vein and then reducing the flow to a very slow rate. If this slow flow of saline is not maintained, the catheter and vein will quickly become obstructed with clotted blood. Intravenous injections are made by injecting the substance into the interior of the rubber tubing near the catheter and washing it into the vein with a small amount of saline. A control record preceding each injection should be made to show the effect of 5 ml of saline alone.

C. Catheterization of the Carotid Artery and Isolation of the Vagi.

Using blunt dissection expose the common carotid artery and vagus (both vessel and nerve lie within the carotid sheath). Carefully separate the nerve and artery (do not grasp either of these with forceps) and remove the surrounding fascia from the artery for about 3 cm. of its length. Place 2 wet ligatures around the artery: one should be tied tightly to occlude the artery at the cephalic end of the exposed segment, a second, untied, should be placed in the middle of the segment. Occlude the artery at the caudal end of the segment with a bulldog clamp and with fine-pointed scissors make an oblique cut about 1/2 through the artery about 1 cm. caudal to the cephalic ligature.

While the surgeon is occupied with the above isolation procedures the records man should be preparing the pressure transducer and attached polyethylene tubing for the blood pressure recording. The head of the transducer marked 0-75 cm. and a length of polyethylene tubing is filled with chlorobutanol. This is accomplished by attaching a small polyethylene tube to the needle of a syringe and threading the smaller tubing into the larger tubing leading from the transducer. The smaller tubing is pushed down into the head of the transducer and, asthe head and tubing are filled with the chlorobutanol from the syringe, the smaller tubing is withdrawn so that no air bubbles are obtained. In the last 15 or 20 cm. of large tubing a solution of heparinis substituted for the chlorobutanol so that the end of the tubing will remain free of blood clots. Connect the transducer to the polygraph and prepare the machine for recording blood pressure (see polygraph instructions).

Now that the artery has been isolated and the polyethylene catheter filled with heparin solution the artery can be intubated. Lift the flap that has been made in the carotid artery with the fine-pointed forceps and insert the tubing. Secure it in the artery by the previously placed ligature. When you are sure that the catheter is securely in place release the bulldog clamp that occluded the artery.

The vagus nerve on the side of the intubated carotic artery has already been isolated. Place a previously moistened ligature around the nerve and tie a very loose knot in the ligature so that no pressure is on the nerve. Later in the experiment when you are asked to sever the vagus nerve two ligatures should be tied securely on the nerve and the cut made between them.

In this way the peripheral (cardiac side) and central ends of the vagus can be stimulated separately. Isolate the vagus nerve on the other side of the neck in the same manner and place a loose ligature about it also.

D. Sacrifice of the Animal at End of Experiment.

The animal must be killed while under anesthesia at the end of the experiment. In the first set of procedures an arterial catheter will be placed in the femoral artery (in the same manner as the carotid catheter) and the animal will be bled to death. The students will observe the effect of hemorrhage on arterial pressure. Another method of sacrificing the amimal is to produce asphyxia by blocking the tracheal cannula. Regardless of method of sacrifice, when it appears that the animal is dead, open the chest and examine the heart. Whether any cardiac activity is apparent of not, the heart should be opened by a large incision. No group will be permitted to leave the laboratory until it is certain that their animal is dead. Notify the technician when you are ready to dispose of the animal after you have removed all cannulae, clamps, etc.

INSTRUCTIONS FOR USE OF THE GRASS POLYGRAPH

A. General Directions.

1. Remove the metal guard from under the pens.
2. Plug the main power cable into an outlet on the desk.
3. Turn on the D.C. Driver Amplifier switches that are to be used.
4. Turn on all pen switches that are to be used except No. 4. This switch will be turned on after the EKG instructions are carried out.
5. Set the chart speed at .25 mm. per second.
6. Move the Driver Control Switch (below or to the right of the pen switches) until it points toward the red signal button or to the "Chart and Pens" position.
7. Allow 10 minutes for warm-up.

B. Recording Blood Pressure.

1. Use the top channel to record blood pressure.
2. Fill the transducer marked 0-75 cm. (and its attached tubing) with preservative and anticoagulant by means of a syringe, hypodermic needle and small tubing as described in C of the SURGICAL PROCEDURES.
3. Balance the bridge and calibrate the channel as in Experiment 1.
4. Establish the base line of the pen 2 cm. below center of the polygraph paper for the top channel. Keep the tip of the catheter even with the metal diaphragm of the transducer when establishing the base line and after the artery has been intubated.
5. Set the SENSITIVITY MV/CM knob of the Pre-amplifier at 10 or or 20 (at a setting of 10: one cm.=50 mm Hg; at a setting of 20: one cm.=100 mm Hg). Write on the record which setting is is in use.

THE ABOVE PROCEDURES ARE CARRIED OUT PRIOR TO CATHETER PLACEMENT

6. Insert the catheter in the artery (see SURGICAL PROCEDURES).
7. Set the 1/2 AMP HI FREQ knob of the D.C. Driver Amplifier at 0.1 to record mean blood pressure or 60 to record systolic

and diastolic pressures. Frequently the student will want to duplicate the experimental procedures, first recording mean systolic and diastolic pressure and then recording mean pressure. However, mean pressure can be estimated from pulse pressure accurately enough for our purposes. Heart rate can be determined by counting the R waves of the EKG.

C. Recording EKG.

1. Preparations for recording
   (a) Attach electrode box to bottom channel
   (b) Insert 4 electrode wires into the outlets marked RL, LL, RA, and LA.
   (c) Insert the needles of the electrodes subcutaneously in the animal in the following positions: RL - right leg; LL - left leg; RA - right side of chest; LA - left side of chest.
   (d) Set LEAD SELECTOR knob at II

2. For Recording EKG
   (a) Set OUTPUT knob at EKG
   (b) Set chart speed at 25 mm/sec.
   (c) Turn on pen switch No. 4.
   (d) Move Driver Control Switch (below or to right of pen switches) until it points toward red signal button or "chart and pens".
   (e) Adjust EKG SENSITIVITY to give suitable pen deflection.
   (f) If EKG recording goes off bottom of chart at any time, press TRACE RESTORER.

D. Rules for Selecting Chart Speeds.

1. When using EKG with intent to study the various electrical complexes set the chart speed according to directions given above.
2. If using the EKG for heart rate a slower speed will be adequate (10 mm/sec.) down to 2.5 mm/sec).

E. Signal Marker.

The center pen makes a deflection every second. It may also be used as a signal marker by pressing the red signal button below or to the left of the pen switches.

F. At the End of the Experiment.

1. Turn off all switches on polygraph.
2. Remove paper by tearing along perforated line.
3. Remove polyethylene cannula from carotid artery.
4. Remove electrodes from animal.
5. Disconnect electrodes from electrode box and place electrodes in the bottom of the polygraph.

CIRCULATION EXPERIMENTS

A. Epinephrine Effects.

1. Inject intravenously 0.01 mg. epinephrine per kg. Observe the effects on mean pressure as well as systolic and diastoloc pressures. Are there any changes in the EKG?

2. Repeat the above procedures using 1/10 and 1/100 of the first dose of 0.01 mg. epiniphrine per kg. A reversed effect on the blood pressure should occur with one of the smaller doses.

3. Inject Neostigmine 0.03 mg per kg. (an anticholinesterase). Repeat the injection of 0.01 mg. epinephrine per kg.

B. Effect of Gravity.

Rotate the dog board so that only the forward end rests on the operating table (be careful to keep the carotid and femoral cannulae in place). The carotid cannula should remain at the same height at all times.

1. Quickly lower the hindquarters of the dog. After the blood pressure has stabilized bring the animal back to the horizontal position.

2. Elevate the hindquarters of the dog. Allow pressure to stabilize and then return dog to horizontal position.

C. Effect of Vagal Stimulation.

Make certain that the small transformer (which acts as an isolation unit) is connected between the stimulating electrodes and the stimulator. The isolation unit will allow the student to record the EKG while using the stimulator.

1. Ligate and section the right vagus. Stimulate the central end of the cut nerve with a tetanic current and observe the pupil of the ipsilateral eye.
2. Ligate and section the left vagus. Is there any change in heart rate?
3. Stimulate the peripheral ends of first the right and then the left vagus with a weak, moderate and strong tetanic current. Note differences in EKG complexes with right and left vagus stimulation.
4. Now that the vagi are cut again inject 0.01 mg. epinephrine per kg.
5. Inject Atropine 0.5 mg. per kg. Stimulate either the right or left vagus with a strong tetanic current.

D. Effect of Amyl Nitrite.

1. Crush an ampule of amyl nitrite at the end of the tracheal cannula.

E. Effect of Hemorrhage and Transfusion.

Insert a catheter into one femoral artery as close to the body wall as possible. The catheter should have as large a tip as possible to prevent too rapid plugging of the lumen with clotted blood.

1. While recording blood pressure continuously collect a blood volume in a beaker sufficient to cause a marked and sustained reduction in blood pressure (about a one-third to one-half decrease in original pressure for 10 minutes of more). Defibrinate the blood with a wire whip while collecting it. Strain the blood with cheese cloth to remove clots and determine its volume.

2. Reinfuse the defibrinated blood slowly back into the animal and note the return to normal blood pressure.

3. Again hemorrhage the animal, removing the same volume of blood as in (1). This time inject an equivalent volume of saline warmed to 40°C in an effort to replace the missing blood volume. Compare these results with the blood reinfusion.

4. Now hemorrhage the animal to death and note the changes in blood pressure and respiration.

5. Remove the heart and dissect it.

ADDITIONAL EXPERIMENTS TO BE PERFORMED ON ANOTHER DOG

A. Effect of Stimulation of the Carotid Sinus.

Expose the carotid sinus on the side opposite to that which is catheterized. Exposure is best accomplished by blunt dissection following the carotid artery in a cephalic direction until the bifurcation is seen. It will usually be necessary to extend the skin incision cephalad to facilitate this dissection. Stimulate the carotid sinus (by touching the electrodes to the arterial wall of the bifurcation) with weak, moderate and strong repetitive shocks for at least 10 to 15 seconds. Be careful to prevent the electrodes from touching surrounding muscle and nerve; with the strong stimulus there may be sufficient spread of the current so that some skeletal muscle stimulation occurs even though the electrodes are on the arterial wall.

Note the effect of occlusion of the common carotid just below the bifurcation (be extremely careful not to pull on the vessel while occluding it). Try occluding the external and internal carotids above the sinus. (Be careful to apply the occluding ligatures far enough from the sinus so that there will not be mechanical stimulation of the latter).

Repeat the stimulation and occlusion of the carotid sinus and common carotid artery after cutting first one then the other vagus nerve. What difference would vagotomy be expected to produce?

B. Splanchnic Nerve Stimulation.

Make an incision on the left side of the abdomen parallel to the rib border and from 2.5 to 7 cm. below, depending on the size of dog. The incision itself will be from 10 to 15 cm. long. Two fairly large arteries will be encountered; these may be simply clamped or ligated. A midline incision may also be used. It is less convenient, but entails less hemorrhage.

An assistant should retract the viscera, using gauze pads or towels. Locate the left kidney and adrenal gland for landmarks. The splanchnic nerve will be found under the parietal peritoneum cephaled to these structures. Dissect the peritoneum away from the nerve with a blunt probe, freeing the nerve for a distance of 3 to 4 cm. The area should be well packed with gauze so that it will not be necessary to manipulate the viscera when applying the electrodes.

Stimulate the nerve and note the effect on systolic and diastolic pressure.

Remove the adrenal gland (carefully isolate it with ligatures prior to removal) and again stimulate the nerve.

SUGGESTED TREATMENT OF RESULTS

A. Relate Each Experimental Manipulation to Pressoreceptor Feedback Activity.

B. Hemodynamic Data

1. Plot the hemodynamic data using magnitude of response on the ordinate and time (or intensity) on the abscissa.

2. Assume Stroke Volume to be constant at 1 cc. per kg. of body weight and calculate Cardiac Output and Peripheral Resistance.

C. EKG Data

1. Note P-R interval changes in epinephrine injection and vagal stimulation.

2. Note changes in configuration of the QRS complex with the development of each ectopic focus.

RESPIRATION IN MAN: DEMONSTRATIONS

1. Hpyoxia. A human subject will rebreathe air from a metabolism apparatus, during which time the arterial oxygen saturation (Sa_{O_2}) will be read with an ear oximeter. As the oxygen is consumed by the subject from the bellows of the metabolism apparatus the inspired P_{O_2} will decline, thus producing anoxic hypoxia and simulating ascent to altitude. No increase in CO_2 will occur, since the expired CO2 will be absorbed by the soda lime within the apparatus. The depth and rate of the respiration will be recorded throughout the experiment.

SUGGESTED VARIABLES AT HIGH ALTITUDE

Sa_{O_2}	Pa_{O_2}	PI_{O_2}	Alt., ft.	P_B
97 %	100 mm Hg	150 mm Hg	1166	733 mm Hg
95 %	79	127	4×10^3	656
90 %	60	102	10×10^3	523
85 %	51	92	12×10^3	483
80 %	45	85	14×10^3	446
75 %	40	79	15×10^3	429
70 %	35	73	17×10^3	395
65 %	32	66	19×10^3	364
60 %	29	60	21×10^3	335
55 %	26	56	22×10^3	321
50 %	23	51	24×10^3	294
40 %	19	48	30×10^3	229

2. Hypercapnia The same subject will then breathe from the same apparatus from which the soda lime has been removed and the bellows filled with 100% oxygen. There will be no hypoxia, but expired CO_2 will accumulate. The oximeter will demonstrate the Sa_{O_2}, and the character of the respiration will be recorded as before. Compare the onset and quality of respiratory stimulation here with that during hypoxia.

3. The subject, after a few minute's rest, is connected to a recording spirometer with carbon dioxide absorbent (soda lime) and his resting oxygen consumption is measured, expressed in liters per minute, STPD.

Calculate the subject's metabolic rate in Calories per minute, Calories per hour, Calories per day, and Calories per square meter per hour. We can assume a resting RQ of 0.85, at which value the Caloric equivalent of oxygen is 4.86 Calories per liter.

The subject is then equipped with a Douglas bag with valve for collecting the expired air. He should then walk in the hall at a rate of about 3 miles per hour for a period of six minutes, collecting his expired air for the final four minutes of the period.

Repeat the exercise by pedalling on a bicycle ergometer at 100 rpm, generating 50 watts of power.

Calculate:

Ventilation rate, liters per minute BTPD.
Oxygen consumption, liters per minute STPD.
Carbon dioxide production, liters per minute STPD. Assume 0.03% CO_2 and 20.96% oxygen in the inspired air.
Respiratory quotient during exercise.
Exercise metabolism, Calories per minute, per hour, and per day.
Excess of exercise metabolism over resting metabolism in Calories per day.
How much fat would be needed per hour and per eight hour day to provide the energy for this kind of exercise.

PULMONARY FUNCTION TESTS AND BLOOD GASES

1. Lung volumes and MVV.

A. By means of a recording spirometer, with a capacity of at least 6 liters, obtain records of the normal resting tidal volume (TV), the expiratory reserve volume (ERV), and the inspiratory reserve volume (IRV). Convert all volumes from ATPS to BTPS. Assuming residual volume (RV) is 1.2L BTPS, what are the subject's vital capacity (VC), total lung capacity (TLC), functional residual capacity (FRC), and inspiratory capacity (IC)? Consult Comroe (Chapter 2) for normal values and significance of changes. Note: Since the subject rebreathes from this spirometer, periodically raise and lower the can to recharge it with fresh air.

B. The maximum voluntary ventilation is the maximum volume of gas that can be breathed per minute by voluntary effort under test conditions. The subject is instructed to breathe into a large spirometer or Douglas bag, or into a smaller integrating spirometer, as deeply and rapidly as he can for 15 sec. He must be urged continuously and emphatically during the test to breathe as hard and fast as possible, but he should be permitted to choose his own rate and depth. The tidal volumes will be considerably less than the total VC because extreme inspiratory and expiratory excursions waste time and energy. The average subject generally chooses a rate between 40-70/min. and a TV of about 50% VC. Normal values are greater than about 120 L/min. See Comroe for significance of changes.

2. Forced expiratory volume (capacity) and MEF.

A. Timed vital capacities give an indication of the flow rate possible from the lungs. Operation of the Gaensler-Collins "Timed" Vitalometer should be studied before measurements are made. Empty the spirometer and set the two dials fully clockwise, but do not bend them. Set the electric timer to the desired value (0.5, 1.0, or 2.0 sec). When the subject exhales, the black dial is released after the preset interval and the red dial continues to read the whole vital capacity. Thus, the first dial indicates the volume of air expelled in say, 1.0 sec. The subject is instructed to exhale from his full inspiratory position to full expiratory position as rapidly as possible. Encouragement and a little excitement can increase FEV's by 50%. Normal values are: $FEV_{0.5}$ = 0.68 VC, and $FEV_{1.0}$ = 0.84 VC, and $FEV_{2.0}$ = 0.94 VC. These percentages are considerably reduced in patients with obstructive puimonary disease, but not in those with restrictive disease.

B. The Wright Peak flow Meter is used to measure the maximum flow rate attained during a forced expiration from full inspiratory capacity. Again, some exhortation from the experimenter improves the subject's effort. The MEF in healthy young men is generally about 400 L/min., but may be reduced to 20 L/min. in severe emphysema or asthma.

3. Lung and chest static compliance (the relaxation curve).

Restrictive respiratory diseases are those in which the compliance of either the lung or chest is diminished, e. g. fibrosis, respiratory distress syndrome, kyphoscoliosis, carcinomatosis, etc. To assist in determining the nature and extent of such disorders, one may measure the pressure - volume characteristics of the lung - chest system, or of the lung and chest separately. Pressure-volume curves appear to be the best means of describing the elastic properties of the lungs and thoracic cage.

The lung-chest p-v curve, or relaxation curve, is obtained as follows: the subject inspires his full vital capacity with a nose clip in place, then places a tube leading to a water manometer into his mouth and relaxes. The manometer reading (cm H_2O) represents the pressure needed to expand the whole chest to that particular volume. The volume is measured by having the subject immediately exhale completely into a spirometer. This first volume measurement is 100% VC. Plot "Percent VC" on the vertical axis versus "Distending pressure" on the abscissa. Repeat the measurement at several other volumes, right down to RV. The pressures will become negative below FRC. (Why?)

Note: It is of the utmost importance that the subject relaxes his chest muscles completely and keeps his glottis open for the pressure measurement. Otherwise, the scatter in the data points will be distressing and furthermore meaningless.

4. Measurement of blood P_{O_2}, P_{CO_2}, pH.

Arterial blood gas measurement is becoming an important and occasionally life-saving tool in diagnosing and monitoring respiratory and acid-base disorders. Additional sampling of mixed venous blood provides an estimate of circulatory adequacy. Development of electrodes (See App.) which permit rapid determination of P_{O_2}, P_{CO_2}, and pH on small volumes of blood has provided the impetus to this type of patient evaluation. The following experiment will serve as introduction to the potential usefulness of such techniques.

Following sterile cleansing of the area and local instillation of a small quantity of local anesthetic (1% Procaine or Xylocaine), puncture of the radial or branchial arteries is performed with a small gauge needle (#23 or 25). 3 ml. samples of blood are collected anerobically in a 5 ml. syringe in which the dead space has been filled with heparin. Samples are introduced into electrodes for determination of P_{O_2}, P_{CO_2}, and pH. Samples will be obtained (1) while the subject is breathing normally, (2) after 3 to 5 minutes of hyperventilation, and (3) after 5 minutes of oxygen breathing. Results will be analyzed in regard to adequacy of alveolar ventilation, acid-base status, and amount of anatomical shunt while on oxygen.

1. Alveolar ventilation and physiologic dead space.

(a) If a sample of mixed expired gas is collected in a 50 ml. syringe and analyzed for $P_{E_{CO_2}}$, the ratio of physiologic dead space to tidal volume can be calculated from the Bohr Equation:

$$F_{A_{CO_2}} V_A + F_{I_{CO_2}} V_D = F_{E_{CO_2}} V_T$$

Since $F_{I_{CO_2}} = 0$ and $V_A = V_T - V_D$

$$F_{A_{CO_2}} (V_T - V_D) = F_{E_{CO_2}} V_T$$

and

$$\frac{V_D}{V_T} \quad \frac{F_{A_{CO_2}} - F_{E_{CO_2}}}{F_{A_{CO_2}}}$$

(b) From V_T of your spirometer tracing calculate V_D.

(c) Calculate alveolar ventilation, $\dot{V}_A$, from:

$\dot{V}_A = f(V_T - V_D)$ where f = respiratory rate

(d) CO_2 production: $\dot{V}_{CO_2} = F_{A_{CO_2}} \dot{V}_A = F_{E_{CO_2}} \dot{V}_E$

Calculate $\dot{V}_{CO_2}$ and convert to standard conditions.

2. Acid-base status.

Plot pH_a and $P_{a_{CO_2}}$ for the resting and hyperventilated states on the Davenport diagram.

(a) What is the in vivo buffer slope obtained from these two points?

(b) How does it differ from the buffer slope on the diagram?

(c) Classify the acid-base abnormality as to respiratory and metabolic components.

(d) If the calculated buffer slope is not normal, what might explain the difference?

3. Shunt.

With the subject breathing oxygen, true right-to-left shunt may be calculated. The shunt equation may be derived from the knowledge that the quantity of oxygen in arterial blood equals that in the shunt blood plus that in non-shunted blood, and that total flow (cardiac output) equals shunt flow plus non-shunt flow:

$$\dot{Q}_T = \dot{Q}_S + \dot{Q}_{NS} \quad \text{or} \quad \dot{Q}_{NS} = \dot{Q}_T - \dot{Q}_S$$

and $$C_{a_{O_2}} \dot{Q}_T = C_{\bar{v}_{O_2}} \dot{Q}_S + C_{c_{O_2}} \dot{Q}_{NS}$$

$$C_{a_{O_2}} \dot{Q}_T = C_{\bar{v}_{O_2}} \dot{Q}_S + C_{c_{O_2}} (\dot{Q}_T - \dot{Q}_S)$$

$$C_{c_{O_2}} \dot{Q}_S - C_{\bar{v}_{O_2}} \dot{Q}_S = C_{c_{O_2}} \dot{Q}_T - C_{a_{O_2}} \dot{Q}_T$$

$$\dot{Q}_S (C_{c_{O_2}} - C_{\bar{v}_{O_2}}) = \dot{Q}_T (C_{c_{O_2}} - C_{a_{O_2}})$$

$$\frac{\dot{Q}_S}{\dot{Q}_T} = \frac{C_{c_{O_2}} - C_{a_{O_2}}}{C_{c_{O_2}} - C_{\bar{v}_{O_2}}}$$

where $C_{a_{O_2}}$, $C_{\bar{v}_{O_2}}$, $C_{c_{O_2}}$ are, respectively, concentration of oxygen in arterial, mixed venous, and pulmonary capillary blood. The $P_{c_{O_2}}$ is assumed to be in equilibrium with $P_{A_{O_2}}$ which equals $P_B - P_{H_2O} - P_{CO_2}$ when denitrogenation is complete. These concentrations include dissolved oxygen (0.3 ml. O_2 /100 mm Hg P_{O_2} /100 ml. blood at 37°C) and oxyhemoglobin as determined from a dissociation curve at appropriate pH and temperature.

C_{O_2} (vol. %) = S (% saturation) x Hgb. conc. (gm %) x 1.34 ml. O_2 /gm Hgb.

(a) Calculate $\dot{Q}_S / \dot{Q}_T$ from the arterial blood gas while breathing oxygen, using the following assumptions:

1. Hemoglobin conc. = 15.0 gm%
2. $C_{a_{O_2}} - C_{\bar{v}_{O_2}} = 6$ vol.%
3. $pH_{\bar{v}} = pH_a - 0.05$
4. T = 37°C

(b) Using the shunt equation calculate "venous admixture" from the air-breathing samples, using the same assumptions. $P_{A_{O_2}}$ may be estimated as equal to $P_B - (P_{H_2O} + P_{CO_2} + P_{N_2})$ if one assumes P_{N_2} is the same as that in wet inspired air (i.e.,that R = 1).

(c) What is the $AaDO_2$?

(d) What factors besides pure right-to-left shunt might contribute to the venous admixture ($AaDO_2$) when breathing air instead of oxygen?

1. Oxygen electrode. The Beckman dissolved O_2 sensor is basically a polarographic O_2 electrode. The sensor contains a silver anode and a gold or platinum cathode, both protected from the sample being measured by a thin membrane, e,g, Teflon, polyethylene, polypropylene. A cellulose-base KCl gel is held in place by the membrane and serves as an electrolytic agent. Since the membrane is premeable to gases, oxygen can diffuse to the cathode and take part in the following oxidation-reduction reaction:

Cathode reaction: $O_2 + 2H_2O + 4e^- \rightarrow 4OH^-$

Anode reaction: $4Ag + 4Cl^- \longrightarrow 4\,AgCl + 4e^-$

With a potential of 0.4-0.8 volts applied across the electrodes, oxygen in the sample reaching the cathode will be consumed causing a small current to flow. The magnitude of this current is proportional to the amount of O_2 present in the sample. The current produced may then be amplified and recorded.

Oxygen electrodes have been miniaturized to the point where they may be placed directly in medium-sized blood vessels. Response times down to 1 sec. have been attained.

2. Glass pH electrode. The glass electrode has become the most useful means of determining the pH of a solution. It requires very little attention and is widely used in industry, chemistry, and biology.

It consists of a reversible electrode, such as Ag-AgCl, in a solution of constant pH inside a thin membrane of a special glass. The thin glass bulb is immersed in the solution to be studied along with a reference calomel electrode. Hydrogen ions diffuse across the glass which acts as a membrane, and set up a Nernst potential of 59mV per pH unit at 25°C. This potential is amplified by a very high input impedance amplifier and displayed on a meter or recorded.

3. CO_2 electrode (Severinghaus 1958). A small amount of dilute $NaHCO_3$ is separated from the solution to be measured by a thin membrane permeable to CO_2. The pH of the $NaHCO_3$ solution is related to the P_{CO_2} by the Henderson-Hasselbalch equation. Hence by measuring its pH with a glass electrode one can indirectly determine the P_{CO_2} of the external solution.

The response time is limited by the rate at which the CO_2 - bicarbonate equilibrium is reached. The response is 99% complete in one to two minutes.

MAMMALIAN RESPIRATORY REFLEXES

Obtain an anesthetized dog. Tracheotomize. Arrange to record mean blood pressure from a carotid artery as in Experiment on Circulation. Prepare to record EKG as in the same experiment.

RECORDING RESPIRATION WITH THE GRASS POLYGRAPH

I. Arrange a pneumograph on the dog's thorax.

II. Be certain that the transducer marked 0-5 cm is attached to the second channel from the top.

III. Attach the top outlet of the transducer to the pneumograph with a piece of rubber tubing.

IV. Be sure the side arm of the transducer is closed off with a cap or a stopcock.

V. Set the SENSITIVITY MV/CM knob at whatever position provides the most suitable excursion of the pen.

EXPERIMENTAL PROCEDURES

1. Take a few inches of normal record.

   A. Submit the dog to marked artificial respiration for about 2 minutes: i.e., induce forced overventilation. Record the entire procedure. What is the effect on the character of respiration? What factors are involved? Discuss.

   B. Expose the sciatic nerve. Stimulate its central end with:
      1. Weak tetanic induction shocks
      2. Medium strength tetanic inductions shocks

   C. 1. While recording, clamp the tracheal cannula tube with a large clamp forceps at <u>exactly</u> the height of inspiration. After a few seconds release and allow normal respiration. Try again if you do not obtain a period of apnea.
      2. Next clamp the trachea exactly at maximum expiration. What happens to the respiratory movements? What is the significance of the results you have obtained in the two instances?
      3. Fully inflate the lungs by using compressed air or oxygen but guard against extremes of intra pulmonic pressure. Clamp the tracheal cannula tubing to maintain this inflation. Note the effects on respiration and blood pressure.

   D. Dissect out one vagus nerve, ligate it loosely, but do not cut it: while a tracing is being taken tighten the ligature, cut the nerve, and stimulate its central end, first, with a very weak tetanizing current and then with a strong one.

   E. While a record is being taken, cut the other vagus and observe the effect.

F. Repeat part C. What differences in respiration do you observe after vagotomy?

G. Make an incision through the abdominal wall in the midline and study the movements of the diaphragm. Find the nerves from which the phrenics take origin in the neck. In the dog they arise from the fifth, sixth, and seventh cervical nerves. Stimulate the phrenic nerve on one side with a tetanic current and observe that the diaphragm on the corresponding side is now contracted.

H. Induce asphyxia in the dog by clamping the tracheal tubing with a large hemostatic clamp. Observe and record respiratory responses and blood pressure. Just prior to the cessation of heartbeat, remove the clamp and revive the animal.

I. Insert a polyethylene tubing for bleeding into a femoral artery. While a record is being made, allow the blood to flow from the artery. Hyperpnea will be seen when the blood pressure has fallen markedly. Continue the tracing until death from hemorrhage occurs, being careful to obtain the record of the final respiratory gasps.

Urine Formation and Renal Clearance

The renal clearance of any substance, S, is defined by the equation

$$C_s = \frac{UV}{P} \quad \text{or} \quad C_s = \frac{(S)u\ \dot{V}u}{(S)_p} = \frac{\dot{Q}su}{(S)_p}, \text{ where}$$

C = the clearance of the substance, in ml/min.,
$\dot{V}u = V$ = the rate of urine formation, in ml/min.,
$(S)u = U$ = the concentration of the substance in the urine, in mg/ml,
$(S)p = P$ = the concentration of the substance in the plasma, in mg/ml, and
$\dot{Q}su = UV$ = the filtered load of the substance, in mg/min.

In the case of certain substances, S*, which are completely filterable at the glomerulus (so that the concentration in the filtrate is the same as that in the plasma), and for which the amount of material filtered is not changed during passage of the filtrate through the tubules, the clearance is equal to the volume of filtrate formed per minute (glomerular filtration rate or $\dot{V}g$ or GFR). Since the substance is not acted upon by the tubules, the amount of the substance appearing in the urine is equal to the amount filtered at the glomerulus, or

$$F \cdot GFR = UV, \text{ or } (S^*)g\ \dot{V}g = \dot{Q}s^*g = (S^*)u\ \dot{V}u = \dot{Q}s^*u$$

where $F = (S^*)g$ the concentration of the substance in the filtrate. Since the substance is completely filtered at the glomerulus,

$F = P$, or $(S^*)g = (S^*)p$, and therefore by substituting in the above equation: $P \cdot GFR = UV$, or $(S^*)p\ \dot{V}g = (S^*)u\ \dot{V}u$, so that $GFR = \frac{UV}{P} = Cs^*$, or

$$\dot{V}g = \frac{(S^*)u\ \dot{V}u}{(S^*)p} = Cs^*$$

Such a substance can therefore be used to measure the GFR, by the clearance technique. For the dog, creatinine can be considered to be treated in this way by the kidney.

Preparations:

Obtain an anesthetized dog, and insert a tracheal cannula. Open the abdomen in the midline with a two-inch incision terminating at the symphysis pubis, and with as little exposure and handling of the viscera as possible, isolate the ureters near the bladder. Insert a small polyethylene tube into each ureter (toward the kidney). Run the other ends of the tubes through a two-hole rubber stopper into a plastic test tube with a hole in the bottom. This hole should be accurately placed above the electrodes of a drop counter.

Inject 200 mg/Kg of creatinine as an 8% solution subcutaneously at two sites, in order to elevate plasma levels for the GFR measurement later.

The input cable of the Grass polygraph having three binding posts on the cable terminal should be attached to the third channel from the top of the polygraph. The electrical output of the drop counter should be attached to G_1 and G_2 binding posts of the cable terminal along with a 0.1 megohm resister shunted across the same binding posts. The INPUT selector knob of Channel 3 should be at PGR. Set the SENSITIVITY MV/CM knob at 5 or at such a setting as gives proper sensitivity (sufficient pen amplitude).

Arrange to record mean blood pressure from a carotid artery.

Insert a cannula connected to a burette into the femoral vein for injections.

Procedures:

1. Take a normal blood pressure tracing and record the rate of flow of urine. Inject through the burette 10 ml/kg. of normal saline warmed to 40°C. Note the effect on blood pressure and urine flow.

2. Inject 10 ml/kg. of 2 1/2% urea in normal saline, warmed to 40°. Note any alterations in blood pressure and urine formation.

3. Glycosuria: Inject about 75 cc. of a warmed 20% solution of glucose. Note the effect on the rate of the flow of urine. Collect the urine in test tubes every 2 minutes and test each portion at once for reducing sugars with Benedict's solution. Determine the interval between injection and the appearance of sugar in the urine.

4. Creatinine clearance. Urine flow should be at least 20 drops per minute. Take a 10 ml. blood sample from a vein and transfer it to a centrifuge tube containing dried oxalate. Mix well. Start collecting urine and continue for 30 minutes. At the end of this time measure the volume of urine collected and take another blood sample, again transferring to an oxalated centrifuge tube. Centrifuge the blood samples.

Transfer 2 ml. of plasma from each sample to 50 ml. stoppered flasks and add first 14 ml. of water and then 2 ml. of 10% sodium tungstate solution. Mix. Then add slowly and with shaking 2 ml. of two-thirds normal sulfuric acid. Stopper, shake well, and filter.

Place 10 ml. of the filtrate from each sample into small flasks and add to each 5 ml. of freshly prepared alkaline picrate solution. Allow to stand for 15 minutes and then read the transmittance in a spectrophotometer set at 520 millimicrons. The spectrophotometer should be set at 100% transmittance with a reagent blank, prepared by mixing 10 ml. of water with 5 ml. of alkaline picrate solution. Determine the creatinine concentration from a previously prepared standardization curve.

The same procedure as used on the plasma protein-free filtrate may be used for the determination of the urine creatinine, except that the urine should be diluted 200 times. Measure 1 ml. of urine into a 200 ml. volumetric flask and add water to the mark. Mix. Take 10 ml. of this dilution and add alkaline picrate as above, and determine the concentration by the same procedure as for plasma creatinine.

Calculation of clearance: $Ccr = \frac{UV}{P} \times \frac{1}{A} = \frac{(Cr)u\ \dot{V}u}{(Cr)p} \times \frac{1}{A}$

$(Cr)u$ = U = urine creatinine, mg/ml

$\dot{V}u$ = V = urine volume, ml/min

$(Cr)p$ = P = plasma creatinine, mg/ml (average of the two determinations)

A = body surface area, square meters

Then C = creatinine clearance, ml/min/M^2. It also equals the glomerular filtration rate in ml/min/M^2.

The body surface area of the dog may be calculated from the approximate formula:

$A = 0.091 \times W^{2/3}$ where W = the weight of the dog in kilograms, and A = surface area in square meters.

5. Effect of changes in blood pressure: Ligate and cut a vagus nerve central to the ligature. Stimulate the peripheral end to produce a prolonged fall in blood pressure. What is the effect on the rate of urine secretion?

   Inject slowly about 1 cc. of 1:10,000 epinephrine through the rubber tube of the femoral cannula, flushing each portion into the circulation with a little saline from the burette. The injection should be arranged to produce a prolonged rise in blood pressure. Is the effect of urine flow due purely to the blood pressure rise, or is the kidney affected directly by the epinephrine?

6. Inject 0.09 gm. of methylene blue in 3% solution. Note how long it takes the dye to appear in the urine.

ACTIVITY OF SMOOTH MUSCLE

Obtain a special plastic L-tube, and mount so as to extend into the special Dewar flask filled with mammalian Ringer's solution warmed to 37°C. Use a measured quantity of Ringer's solution. Connect the horizontal portion of the L-tube to a rubber tube leading to a source of oxygen. Place a screw clamp on the rubber tube, and regulate so that a stream of fine bubbles of oxygen issues through the solution without agitation of the muscle strip. Mount above the flask a light heart lever. Fasten a small section of rabbit small intestine (to be obtained from the instructor) with thread between the heart lever and the L-tube. The gut strip may be arranged to record either longitudinal or circular muscle contractions. The upper end of the thread should not be tied to the lever, but merely pressed into a bit of soft wax on the lever. Recording will be done on smoked drum.

I. Record normal activity. If contractions do not start after a few minutes, increase the inflow of oxygen slightly, and increase the tension upon the muscle by placing a light weight, such as a small ball of wax upon the lever.

II. After a normal record has been obtained, but while still recording, increase the tension still further, by placing a 10 gram weight on the lever. Note the effects on the rate of contraction, the amplitude of contraction, and on resting length. Remove the extra weight and repeat.

III. Add to the Ringer's solution a sufficient amount of 1:10,000 epinephrine to make a final concentration of 1:10,000,000 in the fluid surrounding the muscle. Record the activity during and after the addition.

IV. Now remove the preparation from the Dewar flask and place it in a special tall beaker containing fresh Ringer's solution at 37° C. After a normal period of contraction has been recorded cool the beaker with ice in a surrounding vessel and record the changes. Record the temperature at one minute intervals.

V. When contractions cease, warm slowly and record the recovery of activity, continuing to note the temperature on the record.

VI. Remove the preparation from the Ringer's solution temporarily and record the effect of induction shocks applied directly to the muscle (by means of fine wires), singly and with tetanic current.

VII. Replace the smooth muscle in the Ringer's solution and, after a control tracing is taken, add enough acetyl choline to make a concentration of 1:10,000,000. Note the response and wash out with fresh fluid.

If time permits the student should himself devise and carry out other experiments on the isolated gut, having a bearing on its characteristics and function.

BILE FLOW AND COMPARATIVE STUDIES IN ABSORPTION

Note: abdominal viscera must be handled with great care to avoid shock. They should be kept moist and warm by the liberal use of isotonic saline at body temperature. All solutions used in washing or filling the viscera must be kept at body temperature.

Obtain an anesthetized dog that has fasted for 24 hours. Open the abdomen by a mid-line incision and expose the viscera.

Arrange a drop counter to record on the third channel of a grass polygraph. Locate the common bile duct as it runs from the liver and gallbladder toward the duodenum. Insert one end of a long piece of #200 polyethylene tubing into the common bile duct running it toward the bile duct and liver but not beyond the joining of the cystic with the hepatic ducts. Attach the other end of the polyethylene tubing to a drop counter. If necessary, compress the gallbladder in order to fill the length of polyethylene tubing with bile. Then block any possible flow from the gallbladder by ligating the cyctic duct or clamping with a small hemostat. Record the flow of bile, and when it has become stabilized arrange to make an intravenous injection of Decholin into a femoral vein. The dose is 20 mg per kg or 1/10 ml per kg. Observe any change in rate of bile flow as a result of the injection. Bile flow may be recorded for the remainder of the experiment during which intestinal absorption will be studied.

Make an opening into the wall of the duodenum a few cm distal to the pancreas. Make another opening just proximal to the cecum. Wash out the entire small intestine with isotonic saline. Strip the entire loop of gut between the fingers to assure the recovery of all the fluid used in washing. Doubly ligate the ends of the loop of gut and divide it into two loops of equal length by ligating it doubly at the mid-point. Using a large needle fill the proximal loop of the gut with the solution labeled "A" assigned to your group taking care to avoid over distension. An additional ligature is then put on the gut to isolate the needle puncture from the loop. Record the time of injection and the amount of fluid injected. After waiting a suitable interval, inject into the remaining loop the solution "B" assigned to your group.

Set I.	A.	Hypotonic saline (0.4%).	B.	Isotonic saline (0.9%).
Set II.	A.	Hypertonic saline (2.0%).	B.	Hypotonic $MgSO_4$ (3.0%).
Set III.	A.	Isotonic $MgSO_4$ (6.7%).	B.	Hypertonic $MgSO_4$(12.0%).
Set IV.	A.	Hypotonic Glucose (2.5%)	B.	Hypertonic Glucose (10.0%).
Set V.	A.	Isotonic Glucose (5.4%)	B.	Isotonic Sucrose (10.3%).

At the end of one half hour from the time of injection remove, being careful about hemostasis, each respective loop of gut, and measure its contents. Determine and record the amount of absorption in each case.

The results from all groups are to be tabulated on the blackboard. Each student will be responsible for a copy of the table to be used for review of records.

APPENDIX 4B

PROBLEM-BASED LEARNING VS TRADITIONAL CURRJCULA:

A REVIEW OF THE EVIDENCE IN 1996

By Bob Goodman, Professor of Physiology

Since we began discussing the introduction of problem-based learning (PBL) into our medical curriculum, our discussion has been beset by the question of whether there was evidence that PBL makes a difference in the performance of those who take it. Unfortunately, these discussion have for the most part, been based on anecdote and theoretical considerations. The problem with the former is that it is easy to produce anecdotes supporting any position. The problem with the latter is clear to those of us with even a cursory knowledge of history: many historical tragedies have been based on experiments that sound good in theory. So what is the empirical evidence on PBL? To date the only discussions of this have been at the level of: "There is no evidence" vs "Yes, there is" (I). To clarify this question, I read and critiqued nine articles provided by members of the Educational Goals Task Force. Five of these (4 reviews and a primary article on the performance of students on NBME I, II, and III) were particularly useful and are described in some detail at the end of this summary. Four others were more limited in their scope, and thus less useful; however, none of these provided information that contradicted the conclusions reached on the basis of the original 5 articles. All nine of these articles are listed in the annotated references at the end of this summary.

I wrote this summary primarily to help myself collate and integrate the information provided in these articles. I offer it in hopes of informing some and stimulating others to read these articles and draw their own conclusions; at the very least I hope it will help elevate the discussion to a level where some consensus can be reached. If others have reached substantially different conclusions from this material I would be delighted to have an open discussion of the articles. I approached these articles with a healthy skepticism. I think we at West Virginia University currently do a good job training clinicians, but that there is also a lot of room for improvement and innovation. I also think, based on my experience as a facilitator, that the introduction of PBL into the first year curriculum this year has been a very positive development, but have serious concerns about the cost, in faculty time, if these, and other small groups, come to make up a significant proportion of the curriculum. A few other caveats about the conclusions described below. First, these are based primarily on review articles, so that they are dependent on accurate descriptions of the primary literature. Although there appears to be fairly good agreement on the broad conclusions among these reviews, the summary of the results of primary articles did vary significantly in the case of some specific references. Second, the primary literature is still not particularly extensive so thatdifferent conclusions may be drawn from further studies; nevertheless, it is again worth noting that the primary articles now available are fairly consistent in their conclusions. Third, many of the assessments of overall outcomes are relative crude measurements and the means of evaluation may influence the outcome (e.g., students in the

conventional curriculum tend to do better on multiple choice exams). Fourth, because of the nature of the data, very few studies have randomly assigned students to PBL or conventional curricula; thus differences inherent in the students who prefer either curriculum may influence the outcome. Finally, it is important to note that most of these studies have attempted to compare "pure" PBL with "pure" traditional curricula; any conclusions drawn may not be particularly useful to mixed curricula,such as we are considering.

In this review, I will provide the conclusions I have drawn from this literature to several questions that areasked about PBL and summarize the evidence comparing specific outcomes of PBL and conventional curricula. Rather than describing in detail the supporting evidence for these conclusions and summaries, I will simple cite the articles on which they are based. Those interested in further details are referred to theannotated summaries provided or the original articles (these can be obtained from Dr. Jamie Shumway).

l. Does PBL teach problem-solving skills that are useful to clinicians?

No. Both articles by educational psychologists (5,6) agree that "the notion of a general problem- solving skill that can be taught and learned is not a particularly useful construct" (5, p..558). There is alsosome evidence that the "hypothetico-deductive reasoning" taught in PBL is not the approach expert clinicians use to solve medical problems (2, p. 60-61; 6, p. 580).

2. Do PBL students enjoy their educational experience more than conventional students?

Yes. This is perhaps the most consistent finding of these studies (2, p. 62-63; 3, p. 552 and 554; 5, p. 564; 6, p. 483). On the other hand it is worth noting that a majority of students consistently chose atraditional curricula rather than PBL (2, p. 63-64; 4, p. Table I), even after they have had experience withPBL (2, p. 63). Moreover, attrition rate is either similar between the two curricula (3, p. 556) or higher inPBL (2, p. 64).

3. Does PBL promote self-directed learning skills that carry over into the physician's practice?

Here the picture is less clear. PBL students make more use of the library and there is one report that this difference carries over into Years 3-4 (2, p. 62; 3, p. 557), but in that study "only the PBL students had been formally introduced to the library and search techniques" (6, p. 584). PBL students also spend more hours/day studying, but this probably reflects differences in curricular structure because the time spent in the evening is virtually the same (2, p. 62). The limited evidence available on independent learning in post-graduates suggest that there is little difference in PBL and traditional graduates (6, p. 584)

4. Does PBL provide an adequate range of content?

Although this is a concern that we have identified in our discussions, only one of these papers specifically addresses it and concludes that PBL students identify approximately 62% of

faculty generatedobjectives (2, p. 72) and that the overall coverage is approximately 82% of that of traditional curriculum (2, p. 77). The results of the NBME I exam (see below) may also be relevant to this issue.

5. Do PBL students retain and retrieve more knowledge?

Based on experimental psychology PBL should enhance retention and retrieval of the information learned (5, p. 559-562; 6, p. 580-583). There is general agreement that PBL students study more for "meaning", whereas traditional students' studying is more for memorization (2, p. 61; 3, p. 556;6, p. 580), but the way they are tested may be just as important as they way they are taught (6, p. 580). Whether these differences in approach influence the retention depends on how the latter is assessed. PBLstudents do retain a higher percentage of what they learn (2, p. 71; 5, p 559-560), but they apparently start out with less information initially (see #4) so that the percentage of correct answers converges over time for students in the two curricula (2, p. 71). Whether PBL enhances retrieval is also controversial as direct tests of this have given conflicting results (2, p. 60; 5, p. 561); both studies did note, however, that PBL students did tend to "hypothesize a large number of causal explanations, many of which were incorrect" (5, p. 561). The results ofNBME I, II, and III (see below) may also be relevant to this question.

6. Does PBL increase the interest of students in basic science material?

One argument in favor of PBL is that by coupling basic science information to clinical problemsthe interest of the students in the former will be enhanced; this is referred to as "intrinsic motivation" as opposed to "extrinsic motivation•• such as tests or monetary reward. There was surprisingly little discussion of this question in these articles, perhaps because it seem intuitively obvious or because motivation is difficult to measure (6, p. 583). This question is discussed in the two psychologically oriented articles (5, p. 563; 6, p. 583); there is some evidence that PBL stimulates inherent interest, but no effect could be found on the subsequent performance of the students on a test (5, p.583).

7. What are the relative costs of PBL and the traditional curricula?

Since the issue under consideration is primarily a cost-benefit analysis, I was surprised how little attention in the literature has been paid to the cost side of the equation. There is apparently only one study that directly compared the two curricula in terms of faculty time (cited in both 2, p. 70 and 6, p. 585). This study from New Mexico concluded that the faculty time involved was approximately the same for both curricula. But the faculty commitment to teaching in the traditional curriculum seems grossly inflated (21 faculty worked about 9 hrs/week [each presumably giving lectures] to 53 students [2, p. 70]) and the volunteer time of MD preceptors (for PBL) was not included in the comparison (6, p. 585). Thus there appears to be no adequate assessment of the relative costs in faculty time of the two.

8. Does PBL have an effect on the ultimate product?

In general, four different assessments have been done to address this question.

a. NMBE I: There is general agreement that PBL students do less well on this exam than students in the traditional curriculum (2, p. 57; 3, p. 555-556; 4, p. 619); howevr, reference 3 questioned the significance of this because of heterogeneity in variance in their data. It should be noted that traditional students have more experience with multiple choice tests, which may give them an advantage on this exam (2, p. 59).

b. NMBE II: In general there is no difference in performance of PBL and traditional students onthis exam (2, p. 58; 3, p. 557; 4, p. 619)

c. NMBE III: Only one study has examined this test (4) and it found that PBL students did significantly better than traditional students (p. 619). However, this may be due to self-selection among students choosing these two paths; students who chose PBL, but were randomly placed in the traditional curricula did better (551) than those who chose PBL and were randomly assigned to PBL (521), althoughthis difference wasn't statistically significant.

d. Clinical ratings: PBL students tend to have better ratings by their clinical preceptors in Years3 and 4 and post-graduate Year I; most of the individual reports did not observe significant differences (2, p. 65-66), but a meta-analysis was significant (3, p. 557), with a moderate effect size. Interpretation of these data is complicated by the possibility that better students are attracted to the PBL curriculum (2, p. 64; 4, p. 619)

e. Other: The article by Albanese and Mitchell (2) has some interesting observations on affects of PBL on other professional behavior (e.g., specialty choice, billing and time allocation), but since theseissues were not discussed in any of the other articles, I will simply refer you to the summary or the original of that specific paper.

Overall conclusions and observations:

PBL enhances the quality of the educational experience for students, encourages the students to study for meaning rather than to memorize, and modestly increases their clinical skills (at least early in their career). On the other hand, the traditional curriculum does a better job at giving students a broad knowledge base of the science underlying the practice of medicine and this more structured curriculum may be particularly important for students who enter medical school less prepared (4, p. 622).

These conclusions raise the following interesting question (posed in 6): "Why does the product of a PBLcurriculum seem (largely) indistinguishable from the product of a traditional schooJ'/" As pointed out in the same article: " Many will argue that the available measurement tools are insensitive, incapable of capturing important areas of competence in which problem-based students excel …But in persisting to seek distinctions between the PBL and traditional student, the educational community avoids an obviousand perhaps more important consideration: that the observed similarity is real … (If this is the case), the research question becomes not how

are these two groups different, but why are they the same?" (6, p.584)

A few other random thoughts and observations based on this reading:

1. Our new PBL sessions are specifically designed to help students integrate across disciplines; this use ofPBL has not been described or evaluated in the literature.

2. Another major reason we instituted PBL was to increase students interest in the material presented in the traditional basic sciences courses. There was no information on whether this approach is effective in part because these articles didn't examine mixed curricula.
3. Given the range in preparation of our incoming students, the importance of a structured curriculum forpoorly prepared students should be kept in mind as we revise our curriculum.
4. A comparison of the abstracts and content of these articles suggests that proponents of PBL have a tendency to overstate the benefits of PBL; the opposite may be true of the opponents of PBL, but thesample size (I abstract and 2 papers) was not large enough to observe any trends.
5. It may be that, because medical students are particularly motivated and intelligent, the way we teach maynot be as important as we think. It may therefore be useful to focus our upcoming debate more on the content, than the mode, of instruction. In particular, issues such as what we teach, when (in the four years) we teach it, and who we teach it to (all medical students or only those going into certain subspecialties) have the potential to have a much more profound effect on the overall experience of our students. This is not to imply that innovations in the way we teach are not important, just that so far this issue seems to have dominated the debate to the exclusion of other issues.
6. The way we examine students may be just as important, or more important in determining how they study than the way we teach. I would find it extremely useful if we could develop ways to emphasize concepts and integration, over regurgitation of facts, in our testing.
7. Many of these articles agreed that the usefulness of PBL is greatly enhanced if there is appropriate feedback on content from "expert" facilitators. In light of this consensus, we may want to redesign someaspects of our current PBL course(s).

In conclusion, I would like to end with another quote: "Those who see in this paper a defense of past andongoing resistance to innovation in medical education will have misread the argument of the work. PBL was offered as a solution to widely recognized deficiencies in traditional medical education: content overload, poorly attended lectures, poor retention of basic science into the clinical years, student dissatisfaction with the satus quo. Have the expectations of PBL been mer' No, the expectations were probably unrealistic. But in their commitment to the medical student and their attention to pedagogical principle, the advocates and participants of PBL deserve our respect and emulation." (6, p. 586).

REFERENCES

I. Anyone interested in a more detailed view of this approach to debate are referred to the Monty Pythonskit: "The Argument"

2. Albanese MA, Mitchell S. Problem-based learning: a review of literature on its outcomes and implementation issues. Academic Medicine 68:52-81, 1993

This article does an excellent job describing what PBL is and defining five important questions about PBL. It then goes on to discuss the methodology used with a particular emphasis on the limitations inherent to it. After a summary of the available literature, they had a useful discussion of the "nuts and bolts" of organizing PBL classes.

Summary of Outcomes

A. Performance on basic science examinations: PBL students did less well in 6 of 10 studies, but only 3 of these were statistically significant; in these studies PBL students generally did better than traditional students in behavioral sciences and less well in other areas. In the other 4 studies there was generallyno significant difference between the groups.

B. Performance on clinical science exams; PBL students did better in 5 of 7 studies, but only I of these was statistically significant (and that was an ethics problem solving task). One interesting note was that traditional students did better on multiple choice exams, PBL students tended to do better on essay exams.

C. Thought processes promoted (onlv 3 studies): Two were based on analysis of patient cases and both observed that PBL students provided more erroneous or irrelevant material; there was no difference in information recall between the two groups. One of these studies also noted that PBL students tended to use a reasoning that involved "a search driven process typical of novices", while the traditional students tended to use reasoning "characterized as a schema-driven process used by experts" that was akin to pattern recognition. The third study found no difference between PBL and traditional students but was criticized for a lack of detailed description of methods and results.

D. Studv behaviors promoted; Studies consistently find that PBL students study for meaning, while traditional students study for memorization. PBL students used library material more extensively and one study reported that these difference continued into the clinical years. PBL students study more hours/day but this may have been because they had more free time (study time between 6 p.m. and 6 a.m. was similar in the two groups).

E. Leaming environment: In general students view PBL in a more positive light and, feel that it is less stressful, than the traditional curriculum. PBL students viewed the following as most satisfying: "problem solving, applicability, group discussions, and clinical relevancy" and "competition and essay exams" as least satisfying. Traditional students viewed "balance between individual excellence and group competence" as most satisfying and "memorization of facts, lectures, and

multiple choice tests" as least satisfying. On the other hand, most students chose the traditional curriculum if given an opportunity, even after they have had exposure to PBL and the attrition rate from the traditional curriculum was consistently lower than from the PBL curriculum.

F. Profession outcome:
   1. Graduate perceptions of preparation: Generally PBL graduates perceived themselves to be equal to or better prepared than traditional graduates, particularly in humanistic areas and clinical reasoning; traditional graduates rated their training more positive in clinical medicine and biomedical science.
   2. Ratings in clinical training and residency: Four studies of 3rd and 4th year students reported more favorable ratings for PBL students, but these were generally not significant. Similarly results were reported in four studies of postgraduate year residents and these were generally statistically significant. The only ratings more negative for PBL students were in internal medicine for 4th year students (not significant) and nurse's ratings of residents ($P<0.09$).
   3. Assessment as physicians. Only 3 studies, but generally agreed that PBL graduates spent more time in direct patient care (see 4), saw fewer patients and requested fewer services, but billed more (per patient and per service) and relied more on psychotherapy service. Depending on your bias these data can be interpreted to mean that PBL graduates deal with important psychosocial issues or they have difficulty at arriving at a diagnosis and thus resort to psychotherapy. Evaluation of these results is also limited because all 3 studies used graduates of one program (McMasters).
   4. Specialty choice. Seven of eight studies reported that PBL students were more likely to go into family practice; all the effects were statistically significant, including the one that observed they were less likely. One potential problem is that New Mexico's PBL program (which was examined in 2 of the 7 studies) is specifically designed as a primary care tract; whether this is true elsewhere is not clear.

3. **Vernon OTA, Blake RL. Does problem-based learning work? A meta-analysis of evaluative research. Acad. Med. 68:550-563, 1993**

A meta-analysis reviewing essentially the same material as Albanese and Mitchell, although some of the references were considered "non-evaluative" including modes of reasoning and specialty selection. A total of 22 research reports were evaluated, with no distinction between published and unpublished reports. Individual reports were not evaluated for statistical significance; but the significance of the means of these reports was determined. The results are generally consistent with those of Albanese and Mitchell, but the report is more limited in its scope and the description of data in individual papers.

Summary of Results:

A. Program evaluation: All 12 reports agreed that students viewed PBL more positively than traditional curriculum; "effect size" averaged +0.55.

B. Academic achievement: On NBME I: Effect size showed a trend for traditional students to do better than PBL students (mean of -0.18), but "vote count" of studies was equal. There may also have been an effect of Institution on the outcome. On other academic tests: There was again a non-significant trend for traditional students to do better than PBL students (mean of -0.09).

C. Approach to learning: Two studies report that PBL students place more emphasis on meaning of the material, traditional students on memorization. Four studies agree that PBL students make more use of library materials.

D. Clinical functioning: Based on the results of NBME II and Flex tests, there was a non-significant trend in favor of PBL students (ES= +0.08). However, of 16 studies on clinical performance, 13 found PBL students better; the effect size wasmoderate (+0.28), but significant.

4. Mennin SP, Friedman M, Skipper B, Kalishman S, Snyder J. Performances on NBME I, II, and III **by medical students in problem-based learning and conventional tracts at the University of New Mexico. Acad. Med. 68: 616-624, 1993.**

This was an excellent paper that compared traditional students with PBL students at New Mexico in terms of their performance on NBME I, II, and III. In addition to these overall group comparisons, groups were subdivided based on whether they selected traditional study or PBL; some of the latter were randomly assigned to PBL or traditional groups to provide a controlled experiment. It also included a group of students, identified as at risk when admitted into the program, and assigned to the traditional curricula. There was no significant differences among groups in MCAT scores or undergraduate science GPA, except for those students identified as at risk, for whom both were lower.

Summary of results:

A. NBME I: Traditional students did significantly better than the PBL students (mean scores and % failing on the first attempt). This was also true when the students randomly assigned to the PBL and traditional groups were compared. Mean scores of at risk students (assigned to the traditional curriculum) were not different from other groups, but the % failing was higher than other traditional (not different from PBL) students.

B. NBME II: No differences were observed.

C. NBME III: Overall PBL students did significantly better (mean scores), but this may reflect differences between those who chose PBL and those who preferred the traditional curriculum; students who selected PBL but were randomly placed into the traditional group had a higher score (551) than students who chose PBL and were randomly selected for PBL (521), although these were not significant.

The authors also suggest that the more structured traditional curriculum is important for at risk students.

5. **Norman GR, Schmidt HG. The psychological basis of problem-based learning: a review of the evidence. Acad. Medicine 67: 557-565, 1992.**

6. Berkson L. Problem-based learning: Have the expectations been met? Acad Medicine 68: 579- 588, 1993

I list these two together, because both focus on the evidence from experimental psychology that provides a theoretical basis for PBL. One is written by advocates of PBL (5), the other by a skeptic (6). There is some consideration of the empirical evidence about PBL, but the previous three articles provide a better description of those data than either of these. I found it more difficult to critique these two articles because of my limited understanding of the limitations of the psychology experiments describe. However, I did find that reading both of them provided me with a useful perspective on these issues because one advocates PBL (5), and the other does not (6). If you read one, I would urge to read both. The authors point out that it is now generally agreed that "there is no evidence indicating that one curriculum or another, problem- based or otherwise, is able to enhance students' problem solving skills independent of their acquisition of knowledge. They then critique the evidence that PBL is a better approach because: I) the use of a problem to introduce factual information encourages a "deeper" approach to learning than memorization; 2) learning material in the same "context" in which it will be needed later enhances retrieval of that information when it is needed in the future; 3) the use of clinical problems increases the students' intrinsic interest in the basic science material; and 4) exposure to more clinical problems will enhance the students' ability to use pattern recognition approaches in the future.

The other articles provided to me were all of limited scope:

Kaufman DM, Mann KV. Evaluating Problem-based learning. Acad Medicine 71: S52-S54, 1996.

A survey of two classes at Dalhousie University, one that took the traditional curriculum and one that took PBL. Students who took PBL had more favorable impressions of the curriculum.

Curry RH, Makoul G. An active-learning approach to basic clinical skills. Acad Medicine 71: 41-44, 1996.

Describes use of PBL in teaching basic clinical skills; very little evaluation, but what was presented was positive.

Cooksey JA, Danziger LH, Ervin NE, Groves SL, Tyska C, Kirk G. Problem-based learning in an interdisciplinary community-based primary care course. Teaching and Leaming in Medicine 7: 241-245, 1995.

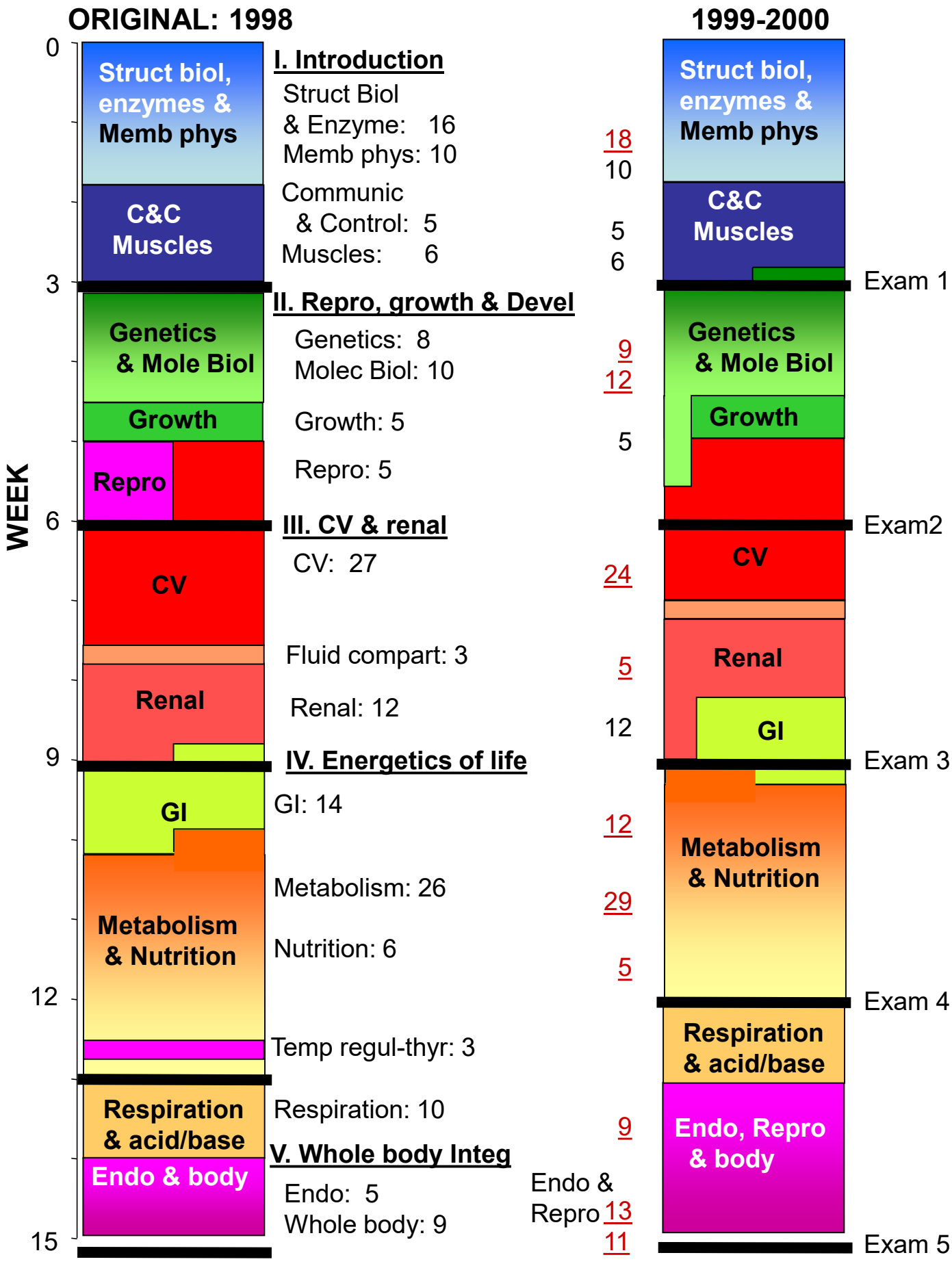
Essentially a description of this course.

APPENDIX 4C

Evolution of the Human Function Course

1988 to 2002

From a 2007 retreat focused on future changes in the course


ORIGINAL: 1998
1999-2000
WEEK
0
3
6
9
12
15
Struct biol, enzymes & Memb phys
C&C Muscles
Genetics & Mole Biol
Growth
Repro
CV
Renal
GI
Metabolism & Nutrition
Respiration & acid/base
Endo & body
I. Introduction
Struct Biol & Enzyme: 16
Memb phys: 10
Communic & Control: 5
Muscles: 6
II. Repro, growth & Devel
Genetics: 8
Molec Biol: 10
Growth: 5
Repro: 5
III. CV & renal
CV: 27
Fluid compart: 3
Renal: 12
IV. Energetics of life
GI: 14
Metabolism: 26
Nutrition: 6
Temp regul-thyr: 3
Respiration: 10
V. Whole body Integ
Endo: 5
Whole body: 9
18
10
5
6
9
12
5
24
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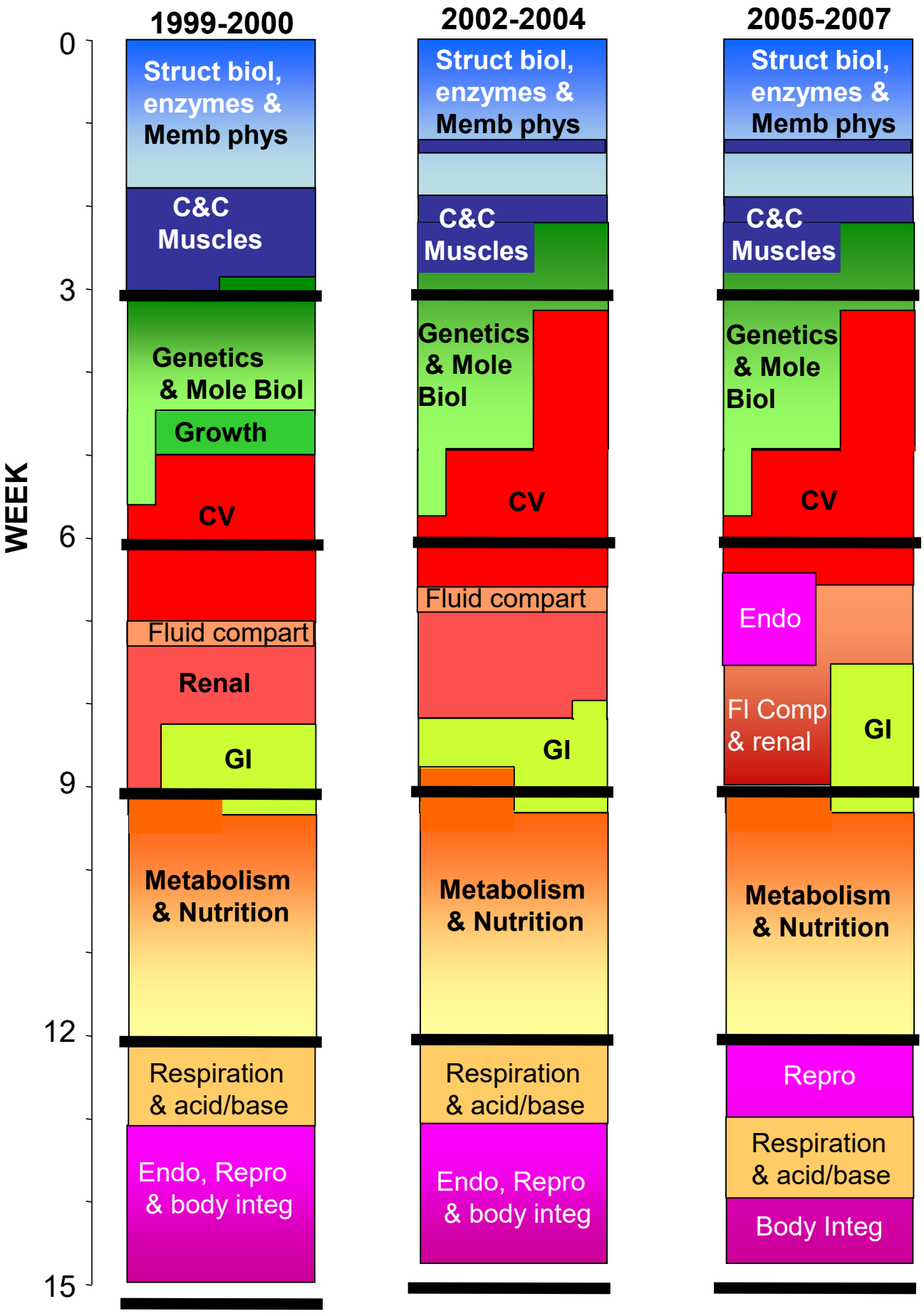
Endo & Repro 13
11
Exam 1
Exam2
Exam 3
Exam 4
Exam 5


1999-2000
2002-2004
2005-2007
WEEK
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Struct biol, enzymes & Memb phys
C&C Muscles
Genetics & Mole Biol
Growth
CV
Fluid compart
Renal
GI
Metabolism & Nutrition
Respiration & acid/base
Endo, Repro & body integ
Struct biol, enzymes & Memb phys
C&C Muscles
Genetics & Mole Biol
CV
Fluid compart
GI
Metabolism & Nutrition
Respiration & acid/base
Endo, Repro & body integ
Struct biol, enzymes & Memb phys
C&C Muscles
Genetics & Mole Biol
CV
Endo
Fl Comp & renal
GI
Metabolism & Nutrition
Repro
Respiration & acid/base
Body Integ

APPENDIX 4D

HUMAN FUNCTION SCHEDULES

FROM 1998 and 2019

HUMAN FUNCTION, 1998 (Physiology Material Highlighted)

Date Day	*Hour*	*#*	*Topic*	*Lecturer*
			Section I: Introduction to Human Function	
			A. Cell and biomolecular structure and function	
8/24 M	8:00	I-1	Overview of module and cell structure	Harris
	9:00	I-2	Water and Physiological pH	Wimmer
	10:00	I-3	Phospholipids and membranes	Harris
	11:00	I-4	Amino acids and the peptide bond	Wimmer
8/25 T	8:00	I-5	Levels of protein structure I	Wimmer
	9:00	I-6	Levels of protein structure II	Wimmer
8/26 W	8:00	I-7	Collagen/ Nucleus	Wimmer/ Harris
	9:00	I-8	Cell Organelles and Cytoplasm	Harris
	10:00	I-9	Diffusion through membranes	Franz
	11:00	SG*	SG:Small group session 1	Bio/Gen
8/27 Th	8:00	I-10	Molecular trafficking and sorting	Harris
	9:00	I-11	Osmosis	Franz
	10:00	I-12	Cytoskeleton	Beattie
	11:00		Computer Training	Russell
8/28 F	8:00	I-13	Extracellular matrix/ cell-cell interactions	Beattie
	9:00	I-14	Oxygen binding proteins: Myoglobin and Hemoglobin	Wimmer
	10:00	I-15	Carrier-mediated transport; active transport	Franz
	11:00	SG	SG session 2	Bio/Gen
8/31 M	8:00	I-16	Transport through channels	Franz
	9:00	I-17	Membrane potentials I	Franz
	10:00	CC*	Marfans *(CC: Clincial Correlation)	
	11:00	I-18	Enzyme catalysis	Wimmer
9/1 T	8:00	I-19	Membrane potentials II	Franz
	9:00	I-20	Epithelial transport	Franz
9/2 W	8:00	I-21	Enzyme kinetics and Inhibition	Wimmer
	9:00	I-22	Action potentials I	Franz
	10:00	I-23	Action potentials II	Franz
	11:00	SG	SG session 3	Physiol.
9/3 Th	8:00	I-24	Action potentials III	Franz
	9:00	I-25	Therapeutic enzyme inhibitors	Wimmer
	10:00	I-26	Enzyme Regulation	Wimmer
	11:00		Problem Based Learning (PBL)	
			B. Introduction to Multicellular Organisms	
9/4 F	8:00	I-27	Introduction to endocrine system	Goodman
	9:00	CC	Peripheral neuropathy (2 hrs)	
	11:00	SG:	SG session 4	Bio/Gen
9/7 M			Labor Day	
9/8 T	8:00	I-28	Introduction to nervous system	Goodman
	1:00	I-29	Neuromuscular junction I	Stauber
	2:00	I-30	Neuromuscular junction II	Stauber

9/9 W	8:00	I-31	Signal transduction I	Beattie
	9:00	I-32	Biochemistry of muscle contraction	Stauber
	10:00	I-33	Electrical-contraction coupling	Stauber
	11:00	SG	SG session 5	Physiol.
9/10 Th	8:00	I-34	Muscle mechanics	Stauber
	9:00	I-35	Smooth/ cardiac muscle	Stauber
	10:00	I-36	Signal transduction II	Beattie
	11:00		PBL	
9/11 F	8:00	I-37	Hypothalamus- pituitary	Goodman
	9:00	CC	Myasthenia gravis (2 hrs)	
	11:00	SG	SG session 6	Physiol.

9/14 M EXAMINATION 1

Section II: Reproduction, Growth and Development

9/15 T	8:00	II-1	Mitosis, meiosis, cell cycle	Wenger
	9:00	II-2	Chromosome structure I	Harris
	2:00	II-3	Modes of Inheritance	Hummel
9/16 W	8:00	II-4	Chromosome structure II	Wenger
	9:00	II-5	DNA replication I	Harris
	10:00	II-6	Population genetics	Hummel
	11:00	SG	SG session 7	Bio/Gen
9/17 Th	8:00	II-7	DNA replication II	Harris
	9:00	II-8	Transcription	Harris
	10:00	II-9	Genetic screening	Hummel
	11:00		PBL	
9/18 F	8:00	II-10	RNA processing	Harris
	9:00	II-11	Genetic code and translation	Harris
	10:00	CC	AIDS; Reverse transcriptase	Pathak
	11:00	SG	SG session 8	Bio/Gen
9/21 M	8:00	II-12	Mechanism of Protein Biosynthesis	Harris
	9:00	II-13	Mutation and DNA repair	Harris
	10:00	CC	Xeroderma pigmentosum; repair defects	Gibson
	11:00	II-14	Human gene therapy	Hummel
9/22 T	8:00	II-15	Regulation of gene expression I	Harris
	9:00	II-16	Regulation of gene expression II	Harris
9/23 W	8:00	II-17	Molecular genetics I	Gibson
	9:00	II-18	Molecular genetics II	Gibson
	10:00	II-19	Growth factors and receptors	Mathers
	11:00	SG	SG session 9	Bio/Gen
9/24 Th	8:00	II-20	Signalling cascades	Mathers
	9:00	II-21	Endocrine control of growth	Goodman
	10:00	II-22	Cancer	Harris
	11:00		PBL	
9/25 F	8:00	II-23	Apoptosis	Beattie
	9:00	CC	Gardners Syndrome	Hummel
	10:00	II-24	Male reproductive system	Goodman
	11:00	SG	SG session 10	Bio/Gen
9/28 M	8:00	II-25	Female reproductive system I	Goodman
	9:00	II-26	Female reproductive system II	Goodman
9/29 T	8:00	CC	Infertility	
9/30 W	8:00	II-27	Initiation of pregnancy	Goodman
	11:00	SG	SG session 11	Bio/Gen
10/1 Th	8:00	II-28	Molecular genetics of development	Mathers
	10:00	CC	Teratogens	Hummel
10/2 F	8:00	II-29	Maintenance of pregnancy, parturition, and lactation	Goodman

Section III: Homeostasis I: Cardiovascular and Renal Function

9/28 M	10:00	III-1	Overview of cardiovascular/renal function	Yokota
			Blood components and the clotting process I	Wimmer
	11:00	III-2	Blood components and the clotting process II	Wimmer
9/29 T	9:00	III-3	Cardiac electrical activity I	Franz
9/30 W	9:00	III-4	Prostanoids	Salati
	10:00	III-5	Cardiac electrical activity II	Franz
10/1 Th	9:00	III-6	Cardiac electrical activity III	Franz
	11:00		PBL	
10/2 F	9:00	III-8	Mechanical events in the heart I	Yokota
	10:00	III-7	Mechanical events in the heart II	Yokota
	11:00	SG	SG session 12	Physiol.
10/5 M	EXAMINATION 2 (Section II only)			
10/6 T	8:00	III-9	Mechanical events in the heart III	Yokota
	9:00	III-10	Mechanical events in the heart IV	Yokota
10/7 W	8:00	III-11	Hemodynamics	Yokota
	9:00	III-12	Vascular mechanics I	Yokota
	10:00	III-13	Cardiac and smooth muscle biochemistry	Boegehold
	11:00	SG	SG session 13	Physiol.
10/8 Th	8:00	III-14	Vascular mechanics II	Yokota
	9:00	CC	ECG	Arbogast
	10:00	CC	Conduction abnormalities	Arbogast
	11:00		PBL	
10/9 F	8:00	III-15	Control of cardiac output and vascular function I	Yokota
	9:00	III-16	Control of cardiac output and vascular function II	Yokota
	10:00	III-17	Control of cardiac output and vascular function IIA	Yokota
	11:00	SG	SG session 14	Physiol.
10/12 M	8:00	III-18	Control of cardiac output and vascular function III	Yokota
	9:00	III-19	Control of cardiac output and vascular function IV	Yokota
	10:00	III-20	Local vascular control and the endothelium I	Boegehold
	11:00	III-21	Local vascular control and the endothelium II	Boegehold
10/13 T	8:00	III-22	Special circulations I (Main auditorium)	Boegehold
10/14 W	8:00	III-23	Special circulations II (Main auditorium)	Boegehold
	9:00	III-24	Transcapillary exchange I (Main auditorium)	Yokota
	10:00	III-25	Fluid compartments I (Main auditorium)	Lee
	11:00	SG	SG session 15	Physiol.
10/15 Th	8:00	III-26	Fluid compartments II	Lee
	9:00	III-27	Fluid compartments III	Lee
	10:00	III-28	Renal anatomy	Baylis
	11:00		PBL	
10/16 F	8:00	CC	Burns	Fogarty
	9:00	III-29	Renal hemodynamics and Glomerular Function I	Baylis
	10:00	III-30	Renal hemodynamics and Glomerular Function II	Baylis
	11:00	SG	SG session 16	Physiol.
10/19 M	8:00	III-31	Renal hemodynamics and Glomerular Function III	Baylis
	9:00	III-32	Renal clearance	Baylis
	10:00	CC	Hypertension and salt	Elnicki

10/20 T	8:00	III-33	Tubular reabsorption and secretion I	Lee
	9:00	III-34	Tubular reabsorption and secretion II	Lee
10/21 W	8:00	III-35	Renal concentrating mechanisms I	Lee
	9:00	III-36	Renal concentrating mechanisms II	Lee
	11:00	SG	SG session 17	Physiol.
10/22 Th	8:00	III-37	Renal mechanisms of salt and water balance I	Baylis
	9:00	III-38	Renal mechanisms of salt and water balance II	Baylis
	10:00	CC	Volume crises	Schmidt
	11:00		PBL	
10/23 F	8:00	III-39	Renal mechanisms of salt and water balance III	Baylis
	11:00	SG	SG session 18	Physiol.

Section IV. Energetics of Life Processes

A. Nutrient Entry Into the Body

10/21 W	10:00	IV-1	Introduction to GI Tract	Connors
10/23 F	9:00	IV-2	Mouth, pharynx, esophagus	Connors
	10:00	IV-3	Stomach- secretion	Connors
10/26 M	EXAMINATION 3 (Section III only)			
10/27 T	8:00	IV-4	Stomach- motility	Connors
	9:00	IV-5	Pancreas- Structure/function	Connors
10/28 W	8:00	IV-6	Pancreas - control of secretion	Connors
	9:00	IV-7	Biliary secretion and excretion	Connors
	10:00	CC	Peptic ulcer	Gaskins
	11:00	SG	SG session 19	Physiol.
10/29 Th	8:00	IV-8	Small intestine - Functional morphology and secretion	Connors
	9:00	IV-9	Carbohydrate and Protein Digestion	Connors
	10:00	IV-10	Transport of glucose/overview of glycolysis	Beattie
	11:00		PBL	
10/30 F	8:00	IV-11	Motility and absorption (Main auditorium)	Connors
	9:00	IV-12	Regulation of Glycolysis (Main auditorium)	Beattie
	10:00	IV-13	Other pathways to pyruvate: Pentose cycle; Fructose;Galactose (Main auditorium)	Beattie
	11:00	SG	SG session 20	Bio/Gen

B. Nutrient Metabolism and its Regulation

11/2 M	8:00	IV-14	Lipid digestion - lymph	Connors
	9:00	IV-15	Water and electrolyte absorption	Connors
	10:00	IV-16	Large intestine	Connors
	11:00	CC	Hirschbrung's Disease	Koch
11/3 T			Election Day No classes	
11/4 W	8:00	IV-17	Regulation of food intake (Main auditorium)	Connors
	9:00	IV-18	Fates of pyruvate (Main auditorium)	Beattie
	10:00	IV-19	Citric acid cycle (Main auditorium)	Beattie
	11:00	SG	SG session 21	Physiol.
11/5 Th	8:00	IV-20	Temperature Regulation	Connors
	9:00	IV-21	Electron transport	Beattie
	10:00	IV-22	Oxidative phosphorylation	Beattie
	11:00		PBL	
11/6 F	8:00	IV-23	Oxygen radicals	Beattie
	9:00	IV-24	Fatty acid mobilization	Salati
	10:00	IV-25	Fatty acid oxidation and ketone body formation	Salati
	11:00	SG	SG session 22	Bio/Gen
11/9 M	8:00	IV-26	Macronutrients I	Hoeldtke
	9:00	CC	Diabetes (2hrs)	Chideckel
	11:00	IV-27	Reactions of amino acids	Salati
11/10 T	8:00	IV-28	Macronutrients II	Hoeldtke
	1:00	IV-29	Gluconeogensis	Beattie

11/11 W	8:00	IV-30	Thermogenesis - BAT, futile cycle	Hoeldtke
	9:00	IV-31	Glycogen synthesis and breakdown	Beattie
	10:00	IV-32	Urea cycle/Fates of carbon skeletons	Salati
	11:00	SG	SG session 23	Bio/Gen
11/12 Th	8:00	IV-33	Obesity	Hoeldtke
	9:00	IV-34	Regulation of glycogen metabolism/pentose pathway	Beattie
	10:00	IV-35	Fatty acid synthesis	Salati
	11:00		PBL	
11/13 F	8:00	IV-36	Micronutrients (Main auditorium)	Hoeldtke
	9:00	IV-37	Triacylglycerol synthesis and storage; Production of VLDL (Main auditorium)	Salati
	10:00	IV-38	Phospholipid/Sphingolipid Synthesis (Main auditorium)	Salati
	11:00	SG	SG session 24	Bio/Gen
11/16 M	8:00	IV-39	Cholesterol metabolism	Salati
	9:00	IV-40	Regulation of cholesterol metabolism	Salati
	10:00	CC	Fever	Khakoo
1/17 T	8:00	IV-41	Alcohol Metabolism	Salati
	9:00	CC	Alcoholism	Elnicki
11/18 W	8:00	IV-42	Lipoprotein metabolism	Salati
	9:00	IV-43	Amino acid synthesis; essential amino acid vs. nonessential	Salati
	10:00	CC	Arteriosclerosis	Ulrich
	11:00	SG	SG session 25	Bio/Gen
11/19 Th	8:00	IV-44	1 - carbon metabolism	Salati
	9:00	IV-45	Purine, pyrimidine metabolism	Harris
	10:00	IV-46	Overview of metabolism	Beattie
	11:00		PBL	
11/20 F	8:00	IV-47	Thyroid I (Main auditorium)	Connors
	9:00	IV-48	Thyroid II (Main auditorium)	Connors
	10:00	IV-49	Nutrition and Disease Prevention (Main auditorium)	Collins
	11:00	SG	SG session 26	Bio/Gen

11/23 M EXAMINATION 4 (GI and Metabolism)

11/24-11/27 THANKSGIVING VACATION

C. Dynamics of Gas Exchange

11/30 M	8:00	IV-50	Introduction to respiration	Miles
	9:00	IV-51	Respiratory mechanics	Miles
	10:00	CC	Thyroid Disfunction	Chideckel
12/1 T	8:00	IV-52	Respiratory mechanics	Miles
	9:00	IV-53	Respiratory mechanics & airway physiology	Miles
12/2 W	8:00	IV-54	Diffusion of gases	Miles
	9:00	IV-55	Pulmonary blood flow/ventilation - perfusion	Miles
	11:00	SG	SG session 27	Physiol.
12/3 Th	8:00	IV-56	Hemoglobin and gas transport in blood I	Wimmer
	9:00	IV-57	Hemoglobin and gas transport in blood II	Wimmer/ Miles
	10:00	CC	Pulmonary Function Tests	Banks
	11:00		PBL	

12/4 F	8:00	IV-58	Regulation of respiration	Miles
	9:00	IV-59	Lung metabolism/non-ventilatory lung function	Miles
	11:00	SG	SG session 28	Bio/Gen/ Physiol

Section V. Homeostasis II: Whole Body Integration

12/2 W	10:00	V-1	Regulation of calcium and phosphate	Goodman
12/4 F	10:00	V-2	Physiology of bone	Goodman
12/7 M	8:00	V-3	Acid-base I (Room 4080)	Baylis
	9:00	V-4	Acid-base II (Room 4080)	Baylis
	10:00	CC	Osteoporosis (Room 4080	Brick
	11:00	V-5	Adrenal cortex I (Room 4080)	Connors
12/8 T	8:00	V-6	Adrenal cortex II (Main auditorium)	Connors
12/9 W	8:00	V-7	Renal failure	Baylis
	9:00	CC	Chronic renal failure	Moss
	10:00	V-8	Adrenal medulla and response to stressors	Goodman
	11:00	SG	SG session 29	Physiol
12/10 Th	8:00	V-9	Exercise I: Energetics	Stauber
	9:00	V-10	Exercise II: Adaptation	Stauber
	10:00	CC	Exercise and health	Reger
	11:00		PBL	
12/11 F	8:00	V-11	Fetal and newborn physiology	J. Graeber
	9:00	V-12	Aging	Briggs
	10:00	V-13	Maternal adaptations to pregnancy	Baylis
	1:00	SG	SG session 30	Physiol.

12/14 M Biochemistry NBME Shelf Exam 9 AM

Physiology NBME Shelf Exam 1 PM

12/16 W EXAMINATION 5 (Respiration and Section V) 1 PM

HUMAN FUNCTION SCHEDULE

FROM 2019

Human Function, 2019

(Physiology material highlighted)

Date	Day	Hour	Lecture Topic	Lecturer
Lectures are presented in Room 1905 of the Learning Center				
8/12	M	8:00	Introduction to Human Function	Shiemke
		9:00	Water, buffers and Physiological pH	Gunther
		10:00	Amino acids and the peptide bond	Shiemke
8/13	T	8:00	Levels of protein structure I	Shiemke
		9:00	Levels of protein structure II	Shiemke
		10:00	Fibrous proteins collagen and elastin	Shiemke
8/14	W	8:00	Glycoproteins, proteoglycans and extracellular matrix	Shiemke
		9:00	Myoglobin, hemoglobin, O2 Transport & blood buffering	Shiemke
		10:00	Marfan Syndrome (CC: Clinical Correlation)	Hummel
		11:00	Problem Based Learning (PBL)	
8/15	Th	8:00	Diffusion and osmosis	Yu
		9:00	Biological membrane structure	Shiemke
		10:00	Introduction to membrane transport	Shiemke
		11:00	Active Learning & Integration	Shiemke
8/16	F	8:00	Applications of Membrane Transport	Shiemke
		9:00	Ionic current & fluxes	Yu
		10:00	Membrane potential and Action Potentials	Yu
		11:00	Active Learning & Integration	Yu/Shiemke
8/19	M	8:00	Enzyme catalysis, kinetics, and mechanisms	Shiemke
		9:00	Cardiac Action Potential and Ion Channels (I)	Yu
		10:00	Cardiac Action Potential and Ion Channels (II)	Yu
8/20	T	8:00	Regulating Enzyme Activity	Shiemke
		9:00	Enzyme inhibition	Gunther
		10:00	Normal ECG	Yu
8/21	W	8:00	Therapeutic enzyme inhibitors I	Gunther
		9:00	Therapeutic enzyme inhibitors II	Gunther
		10:00	AIDS (CC)	Labus
		11:00	PBL	
8/22	Th	8:00	Blood clotting I	Gunther
		9:00	Blood clotting II	Gunther
		10:00	Blood clotting disorders (CC)	STAFF
		11:00	Active Learning & Integration	Gunther/Yu
8/23	F	8:00	Introduction to nervous system	Goodman
		9:00	Neuromuscular junction I	Stauber
		10:00	Neuromuscular junction II	Stauber
		11:00	Active Learning & Integration	Gunther
8/26	M	8:00	Skeletal Muscle I	Stauber
		9:00	Skeletal Muscle II	Stauber
		10:00	Introduction to signal transduction	Goodman
8/27	T	8:00	Cardiac Muscle I	Stauber
		9:00	Cardiac Muscle II/Smooth muscle	Stauber

		10:00	Introduction to the endocrine system	Goodman
8/28	W	8:00	Hypothalamus- pituitary	Goodman
		9:00	Mitosis, meiosis, cell cycle	Sasi
		10:00	Chromosome structure I	Sasi
		11:00	PBL	
8/29	**Th**		**STUDY DAY FOR EXAM 1 - NO CLASS**	
8/30	**F**	**8:30**	**EXAMINATION 1**	
9/2	**M**		**Labor Day Recess (No Class)**	
9/3	T	8:00	DNA replication I	Pugacheva
		9:00	Intro to Cardiovascular Physiology	Paternostro
		10:00	Cardiac Cycle I	Paternostro
9/4	W	8:00	DNA replication II	Pugacheva
		9:00	Cardiac Cycle II	Paternostro
		10:00	Myocardial Mechanics	Paternostro
		11:00	PBL	
9/5	Th	8:00	Mutation and DNA repair	Pugacheva
		9:00	Pressure-Volume relationships	Paternostro
		10:00	Cardiac Work & Metabolism	Paternostro
		11:00	Active Learning & Integration	Pugacheva
9/6	F	8:00	Xeroderma pigmentosum; repair defects (CC)	Hummel
		9:00	Chromosome structure II	Sasi
		10:00	Heart Failure	Paternostro
		11:00	Active Learning & Integration	Paternostro
9/9	M	8:00	Modes of Inheritance I	Hummel
		9:00	Modes of Inheritance II	Hummel
		10:00	Hemodynamics	Paternostro
9/10	T	8:00	ECG I	Rhodes
		9:00	ECG II	Rhodes
		10:00	Transcription	Mathers
		11:00	Biochemistry review session	Shiemke
9/11	W	8:00	Population genetics	Hummel
		9:00	mRNA synthesis and processing	Mathers
		10:00	RNA processing: tRNA and rRNA	Pugacheva
		11:00	PBL	
9/12	Th	8:00	Vascular mechanics I	Paternostro
		9:00	Vascular mechanics II	Paternostro
		10:00	Genetic code and translation	Pugacheva
		11:00	Active Learning & Integration	Paternostro
9/13	F	8:00	Vacular Function Curves	Paternostro
		9:00	Extrinsic Control of Circulation	Paternostro
		10:00	Regulation of gene expression in prokaryotes	Mathers
		11:00	Active Learning & Integration	Mathers/Hummel

		Afternoon	Cardiovascular simulation lab	
9/16	M	8:00	Regulation of gene expression in eukaryotes	Mathers
		9:00	Baroreceptor Reflex	Paternostro
		10:00	Intrinsic Control of Blood Flow	Paternostro
		11:00	Physiology review session	Paternostro
		Afternoon	Cardiovascular simulation lab	
9/17	T	8:00	Capillary exchange	Paternostro
		9:00	Special Circulations	Paternostro
		10:00 CC	Ultrasound Evaluation of Cardiovascular Physiology in the	Minardi
		11:00	Biochemistry review session	Shiemke
9/18	W	8:00	Integrated Cardiovascular Response I	Paternostro
		9:00	Integrated Cardiovascular Response II	Paternostro
		10:00	Genetic screening	Hummel
		11:00	PBL	
9/19	**Th**		**STUDY DAY FOR EXAM 2 - NO CLASS**	
9/20	**F**	**8:30**	**EXAMINATION 2**	
9/23	M	8:00	Mechanism of protein biosynthesis	Pugacheva
		9:00	Protein synthesis; Protein degradation	Pugacheva
		10:00	Fluid Balance	Paternostro
9/24	T	8:00	Molecular genetics I	Mathers
		9:00	Molecular genetics II	Mathers
		10:00	Volume and Osmotic Challenges	Paternostro
9/25	W	8:00	Molecular trafficking and sorting	Pugacheva
		9:00	Cell Volume Challenges and Regulation 1	Paternostro
		10:00	Cell Volume Challenges and Regulation 2	Paternostro
		11:00	PBL	
9/26	Th	8:00	Cell Cycle Control	Pugacheva
		9:00	Renal Structure	Paternostro
		10:00	Regulation of Renal Blood Flow	Paternostro
		11:00	Active Learning & Integration	Pugacheva/Mathers
9/27	F	8:00	Cancer	Pugacheva
		9:00	Glomerular filtration	Paternostro
		10:00	Renal Clearance 1	Paternostro
		11:00	Active Learning & Integration	Paternostro
9/30	M	8:00	Colon cancer (CC)	Hummel
		9:00	Human Genomics: Applications to Medicine (CC)	Hummel
		10:00	Renal Clearance 2	Paternostro
		11:00	Physiology review session	Paternostro
10/1	T	8:00	Tubular Sodium Transport	Paternostro
		9:00	Regulation of Sodium Excretion	Paternostro
		10:00	Introduction to Metabolism; Bioenergetics	Shiemke
		11:00	Biochemistry review session	Shiemke
10/2	W	8:00	Treatment of Genetic Disease I	Narumanchi

		9:00	Treatment of Genetic Disease II	Narumanchi
		10:00	Tubular Potassium Transport	Paternostro
		11:00	PBL	
10/3	Th	8:00	Signal Transduction in Metabolism	Shiemke
		9:00	Glucose uptake and glycolysis	Shiemke
		10:00	Urea and Concentrating Mechanism 1	Paternostro
		11:00	Active Learning & Integration	Paternostro
10/4	F	8:00	Urea and Concentrating Mechanism 2	Paternostro
		9:00	Metabolic Fates of Pyruvate	Shiemke
		10:00	TCA Cycle	Shiemke
		11:00	Active Learning & Integration	Shiemke
10/7	M	8:00	Chronic renal failure /Volume crises (CC)	Schmidt
		9:00	Oxidative Phosphorylation I; Electron transport	Shiemke
		10:00	Oxidative phosphorylation II; ATP Synthesis	Shiemke
		11:00	Physiology review session	Paternostro
10/8	T	8:00	Renal Handling of Hydrogen Ion and Bicarbonate	Paternostro
		9:00	Calcium, phosphate and organic solute handling	Paternostro
		10:00	Oxygen radicals	Shiemke
		11:00	Biochemistry review session	Shiemke
10/9	W	8:00	Mitochondrial Diseases/ Parkinson's Disease	Shiemke
		9:00	Regulation of the Extracellular Fluid	Paternostro
		10:00	Introduction to Gastrointestinal Physiology 1	Connors
		11:00	PBL	
10/10	**Th**		**STUDY DAY FOR EXAM 3 - NO CLASS**	
10/11	**F**	**8:30**	**EXAMINATION 3**	
10/14	M	8:00	Introduction to Gastrointestinal Physiology 2	Connors
		9:00	Introduction to Gastrointestinal Physiology 3	Connors
		10:00	Lipid digestion	Salati
10/15	T	8:00	Introduction to Gastrointestinal Physiology 4	Connors
		9:00	Fatty acid synthesis	Salati
		10:00	TAG synthesis & storage; Production of VLDL	Salati
10/16	W	8:00	Salivation, Mastication, and Swallowing	Connors
		9:00	Pentose-phosphate shunt & Gylcogen synthesis	Hillgartner
		10:00	Glycogen degradation	Hillgartner
		11:00	PBL	
10/17	Th	8:00	Fatty acid mobilization	Salati
		9:00	Fatty acid oxidation and ketone body formation	Salati
		10:00	Gastric secretion and motility 1	Connors
		11:00	Active Learning & Integration	Connors
10/18	F	8:00	Gastric secretion and motility 2	Connors
		9:00	Fructose & Galactose metabolism; Gluconeogenesis I	Hillgartner
		10:00	Gluconeogenesis II	Hillgartner
		11:00	Active Learning & Integration	Hillgartner/Salati
10/21	M	8:00	Biliary secretion and excretion	Connors

		9:00	Phospholipid/Sphingolipid Synthesis	Salati
		10:00	Prostanoids	Salati
		11:00	Physiology review session	Paternostro
10/22	T	8:00	Pancreatic exocrine secretion	Rajendran
		9:00	Nutrient Digestion and Absorption	Rajendran
		10:00	Cholesterol metabolism	Salati
		11:00	Biochemistry review session	Shiemke
10/23	W	8:00	Amino acid metabolism 1	Hillgartner
		9:00	Amino acid metabolism 2	Hillgartner
		10:00	Lipoprotein metabolism I	Salati
		11:00	PBL	
10/24	Th	8:00	Small intestine electrolyte & fluid absorption and secretion	Rajendran
		9:00	Lipoprotein metabolism II	Salati
		10:00	Biochemistry of Type-1 and Type-2 Diabetes	Salati
		11:00	Active Learning & Integration	Salati
10/25	F	8:00	Functions of the large intestine	Rajendran
		9:00	Integration of Metabolism	Hillgartner
		10:00	Molecules derived from amino acids	Hillgartner
		11:00	Active Learning & Integration	Hillgartner/Raj
10/28	M	8:00	Purine metabolism	Hillgartner
		9:00	Pyrimidine Metabolism; Deoxyribonucleotide Synthesis	Hillgartner
		10:00	Alcohol Metabolism I	Salati
		11:00	Physiology review session	Paternostro
10/29	T	8:00	Gout (CC)	Labus
		9:00	Alcohol metabolism II	Salati
		10:00	Whole Body Energy Metabolism	Hillgartner
		11:00	Biochemistry review session	Shiemke
10/30	W	8:00	Obesity	Hillgartner
		9:00	Type-2 Diabetes (CC)	Ponte
		10:00	Atherosclerosis (CC)	Balla
		11:00	PBL	
10/31	**Th**	**STUDY DAY FOR EXAM 4 - NO CLASS**		
11/1	**F**	**8:30**	**EXAMINATION 4**	
11/4	M	8:00	**OPEN**	
		9:00	Macronutrients I	Salati
		10:00	Macronutrients II	Salati
11/5	T	8:00	Micronutrients	Salati
		9:00	Introduction to respiration	Paternostro
		10:00	Respiratory mechanics I	Paternostro
11/6	W	8:00	Review of Endocrine; Endocrine control of growth	Goodman
		9:00	Respiratory mechanics II	Paternostro
		10:00	Oxygen Transport	Paternostro
		11:00	PBL	

11/7	Th	8:00	Thyroid I	Connors
		9:00	Thyroid II	Connors
		10:00	Male Reproduction	Goodman
		11:00	Active Learning & Integration	Paternostro
11/8	F	8:00	Female reproduction I	Goodman
		9:00	Female reproduction II	Goodman
		10:00	CO2 Transport and Respiratory Regulation	Paternostro
		11:00	Active Learning & Integration	Connors/Goodman
		Afternoon	Pulmonary simulation lab	
11/11	M	8:00	**OPEN**	
		9:00	Respiratory mechanics & airway physiology, Part 1	Paternostro
		10:00	Respiratory mechanics & airway physiology, Part 2	Paternostro
		11:00	Physiology review session	Paternostro
		Afternoon	Pulmonary simulation lab	
11/12	T	8:00	Non-ventilatory Lung Functions	Paternostro
		9:00	Pregnancy I	Goodman
		10:00	Pregnancy II	Goodman
		11:00	Biochemistry review session	Shiemke
11/13	W	8:00	Teratogens	Hummel
		9:00	Disorders of the Reproductive Tract (CC)	Meter
		10:00	Introduction to Acid-Base	Paternostro
		11:00	PBL	
11/14	Th	8:00	Adrenal Cortex I	Connors
		9:00	Adrenal Cortex II	Connors
		10:00	Acid-base I	Paternostro
		11:00	Active Learning & Integration	Paternostro
11/15	F	8:00	Temperature regulation I	Connors
		9:00	Temperature regulation II	Connors
		10:00	Fever (CC)	Khakoo
		11:00	Active Learning & Integration	Connors
11/18	M	8:00	**OPEN**	
		9:00	Acid-Base II	Paternostro
		10:00	Physiology of Bone	Goodman
		11:00	Physiology review session	Paternostro
11/19	T	8:00	Pulmonary Function Tests (CC)	Weissman
		9:00	Regulation of calcium and phosphate	Goodman
		10:00	Adrenal Medulla	Goodman
		11:00	Biochemistry review session	Shiemke
11/20	W	8:00	Exercise I: Energetics	Stauber
		9:00	Exercise II: Adaptation	Stauber
		10:00 CC	Assisted Reproduction Technology (CC)	Vernon
		11:00	PBL	
11/21	**Th**		**STUDY DAY FOR EXAM 5 - NO CLASS**	
11/22	**F**	**8:30**	**EXAMINATION 5**	

11/23-12/1 THANKSGIVING RECESS

12/4 W Biochemistry NBME Shelf Exam, 8-11:00

12/10 T Physiology NBME Shelf Exam, 8-11:00

APPENDIX 4E

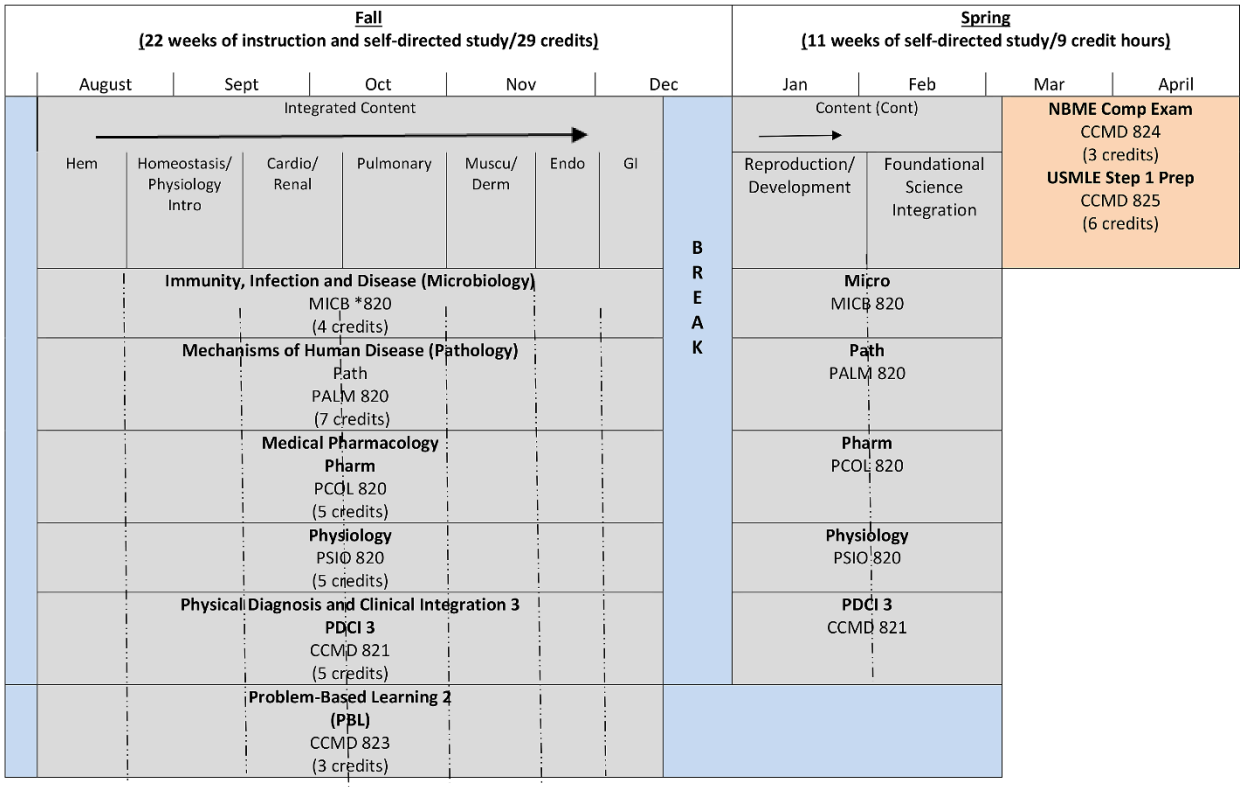
MEDICAL PHYSIOLOGY SCHEDULE

2021-2022

OVERVIEW OF MS2 CURRICULUM

Pre-Clerkship Phase: Academic Year 2 of the Curriculum

33 weeks of instruction, experiential and self-directed study (38 credit hours)



TOPIC COVERAGE IN MS2 CURRICULUM

Block	Month	Week	Subject	Classes
1	Aug	2	Hematology	PCOL 7*, PATH 8*, MICRO 3*, PDCI 4*
1	Aug	3	Hematology	PCOL 4, PATH 4, MICRO 5, PDCI 6
			Exams	
2	Aug	4	CV& Renal (CV)	**PHYS 27**
2	Aug	5	CV& Renal (renal)	**PHYS 14**, PATH 1, MICRO 7
			Exams	
3	Sept	1	CV & Renal (CV)	PCOL 7, PATH 3, PCDI 3
3	Sept	2	CV & Renal	PCOL 9, PATH 3, PDCI 7
3	Sept	3	CV & Renal	PCOL 5, PATH 2, MICRO 4
	Sept	4	CV & Renal	PATH 1, PDCI 7
			Exams	
4	Oct	1	Pulmonary	**PHYS 14**, PATH 1, MICRO 7
4	Oct	2	Pulmonary	PCOL 3, PATH 1, MICRO 9
4	Oct	3	Pulmonary	PCOL 2, PATH 1, MICRO 4, PDCI 7
			Exams	
5	Oct	4	Skeletal muscle & bone	**PHYS 6**, PCOL 4, PATH 6, MICRO 1, PDCI 2
5	Nov	1	Skeletal muscle & bone	PCOL 1, PATH 1, MICRO 4, PDCI 5
			Exams	
6	Nov	2	Endocrinology	**PHYS 8**, PCOL 1, PATH 3, PDCI 1
6	Nov	3	Endocrinology	PCOL 5, PDCI 5
			Exams	
	Nov	4	THANKSGIVING BREAK	
7	Nov	5	Gastrointestinal track	**PHYS 13**, PATH 2, MICRO 3, PDCI 1
7	Dec	1	Gastrointestinal track	PCOL 8, PATH 1, MICRO 7, PDCI 6
7	Dec	2	Gastrointestinal track	PCOL 2, PATH 2, MICRO 1, PDCI 11
			Exams	
			CHRISTMAS BREAK	
8	Jan	1	Reproduction & Development	**PHYS 6**, PCOL 2, PATH 3, MICRO 2, PDCI 3
			Physiology Review	**PHYS 7**
8	Jan	2	Reproduction & Development	PCOL 5, PATH 4, MICRO 1, PDCI 13
8	Jan	3	Reproduction & Development	PATH 1, MICRO 3, PDCI 3
			Exams	
	Jan	4	General reviews	**PHYS 2**, PCOL 5, PATH 1, MICRO 8, PDCI 9
9	Feb	1	Integration & review	**PHYS 4**, PCOL 2, PATH 1, MICRO 2, PDCI 14
9	Feb	2	Study days & exams	**PHYS**, PCOL
9	Feb	3	Study days & exams	PATH, MICRO
9	Feb	4	Study days & exams	PDCI

* Number of contact hours for each class in week

PSIO 820-Medical Physiology
2021-2022

Unless otherwise stated topics will be covered live in class, Room 1909. Attendance is not mandatory but strongly suggested. All live lectures will be recorded and posted on SOLE later that day. **Note:** This is a tentative schedule regarding content title and delivery of material (classroom or video-asynchronous). Please refer to the daily SOLE integrated schedule for the latest version.

Block 1-No Physiology Content			
Block 2 Cardiovascular and Renal Physiology-32 Hours			
Monday Aug 22	9-10 am	Paternostro	Electrical Properties of Cardiac Cells
Monday Aug 22	10-11 am	Paternostro	Cardiac Cycle
Monday Aug 22	11 am-12 pm	Paternostro	Cardiac Cycle
Monday Aug 22	Video 1 hour	Stauber	Cardiac Muscle 1-3
Tuesday Aug 23	9-10 am	Paternostro	Cardiac Output
Tuesday Aug 23	10-11 am	Paternostro	Ventricular Function and Pressure Volume Curves
Tuesday Aug 23	11 am-12 pm	Paternostro	Ventricular Function and Pressure Volume Curves
Tuesday Aug 23	Video 1 hour	Paternostro & Stauber	Cardiac Work and Metabolism Smooth Muscle 1
Wednesday Aug 24	9-10 am	Paternostro	Physiology of Heart Failure
Wednesday Aug 24	10-11 am	Paternostro	Valve Disorders
Wednesday Aug 24	11 am-12 pm	Paternostro	Hemodynamics
Wednesday Aug 24	Video 1 hour	Paternostro	Vascular Mechanics-Arteries and Arterioles Arterial Pulse Amplification and Augmentation
Thursday Aug 25	Video 4 hrs	Paternostro	Venous Return and Vascular Function Curves Extrinsic Control of Circulation Cardiac Reflexes Intrinsic Control of Blood Flow Organ Blood Flow
Friday Aug 26	9 am-10 am	Paternostro	Capillary Exchange
Friday Aug 26	10-11 am	Paternostro	Fluid and Electrolyte Distributions
Friday Aug 26	11 am-12 pm	Paternostro	Volume and Osmotic Challenges
Friday Aug 26	Video 1 hour	Yu	Normal ECG
Monday Aug 29	9-10 am	Rhodes	Basics of Electrocardiography
Monday Aug 29	10-11 am	Paternostro	Cell Volume Regulation and IV Fluids & Renal Intro
Monday Aug 29	11 am-12 pm	Paternostro	Renal Blood Flow and GFR
Monday Aug 29	Video 1 hour	Stauber and Paternostro	Smooth Muscle Bladder Function Filtration Fraction Assessment

Tuesday Aug 30	8-9 am	Paternostro	Renal Clearance Introduction
Tuesday Aug 30	9-10 am	Paternostro	Renal Clearance Measurements and Meaning
Tuesday Aug 30	10-11am	Paternostro	Renal Handling of Na+
Tuesday Aug 30	11 am-12 pm	Paternostro	Renal Handling of Na+ continued
Wednesday Aug 31	8-9 am	Paternostro	Renal Handling of K+
Wednesday Aug 31	9-10 am	Paternostro	Urea Transport & Urine Concentration Mechanisms
Wednesday Aug 31	10 am-11 am	Paternostro	Renal Handling of H+ and Bicarbonate
Wednesday Aug 31	11 am-12 pm	Paternostro	Renal Handling of Calcium, Phosphate and Organics
Thursday Sept 1	8 am-12 pm		Study for Block 2 Exam
Friday Sept 2	8 am-12 pm		Block 2 Exam-96 questions
Block 3 No Physiology Content			
Block 4 Pulmonary Physiology- 10 Hours			
Monday Oct 3	9-10 am	Paternostro	Introduction to Pulmonary Physiology
Monday Oct 3	10-11 am	Paternostro	Static Respiratory Mechanics
Monday Oct 3	11 am-12 pm	Paternostro	Dynamic Respiratory Mechanics
Monday Oct 3	Video 1 hour	Paternostro	Physiology of Obstructive and Restrictive Airway Disease
Tuesday Oct 4	9-10 am	Paternostro	Arterial Oxygen Delivery and Tissue Exchange
Tuesday Oct 4	10-11 am	Paternostro	Arterial Oxygen Delivery and Tissue Exchange
Tuesday Oct 4	11 am-12 pm	Paternostro	Carbon Dioxide Transport and Neural Regulation of Breathing
Tuesday Oct 4	Video 30 mins	Paternostro	Ventilation and Perfusion Matching
Tuesday Oct 4	Video 30 mins	Paternostro	Pulmonary Response to Stress
Wednesday Oct 5	9 am-10 am	Paternostro	Classification and Evaluation of Hypoxemia
Wednesday Oct 5	10 am-11 am	Paternostro	Quantitative Assessment of Acid Base Balance
Wednesday Oct 5	11am-12 pm	Paternostro	Quantitative Assessment of Acid Base Balance
Friday Oct 21	8 am-12 pm		Block 4 Exam-33 questions
Block 5 Skeletal Muscle and Bone Physiology- 6 Hours			
Monday Oct 24	8-9 am	Stauber	NMJ and Skel Muscle I
Monday Oct 24	9-10 am	Stauber	NMJ and Skel Muscle I
Monday Oct 24	10-11:30 am	Goodman	Bone Physiology-Calcium/Phosphate Homeostasis
Monday Oct 24	Video 30 min	Paternostro	PTH and Vitamin D Disorders
Wednesday Oct 26	8-9 am	Stauber	Skeletal Muscle Physiology Energetics
Wednesday Oct 26	9-10 am	Stauber	Skeletal Muscle Senses and Control of Movement

Friday Nov 4	8-12		Block Exam 5-18 questions
Block 6 Endocrine System- 8 Hours			
Monday Nov 7	9-10 am	Goodman	Overview of Endocrine Principles and Systems
Monday Nov 7	10-11 am	Goodman	Growth, GH and GH Disorders
Monday Nov 7	video	Paternostro	ADH and ADH Disorders
Monday Nov 7	video	Paternostro	Thyroid and Thyroid Disorders
Wednesday Nov 9	9-10 am	Paternostro	Physiology of the Pancreas
Wednesday Nov 9	10-11 am	Paternostro	Physiology of Diabetes Mellitus
Wednesday Nov 9	video	Paternostro	Adrenal Cortex
Wednesday Nov 9	video	Paternostro	Adrenal Cortex and Medulla
Friday Nov 18	8 am -12 pm		Block Exam 6-24 questions
Block 7 GI Physiology-12 Hours			
Monday Nov 28	9-10 am	Hardy	Introduction to GI function and control 1
Monday Nov 28	10-11 am	Hardy	Introduction to GI function and control 2
Monday Nov 28	11 am-12 pm	Hardy	The mouth and functions of saliva
Monday Nov 28	Video 1 hour	Hardy	Salivation, mastication, and deglutition
Tuesday Nov 29	9-10 am	Hardy	The stomach and gastric secretion
Tuesday Nov 29	10-11 am	Hardy	Gastric motility and stomach emptying
Tuesday Nov 29	11 am-12 pm	Hardy	Hepatobiliary secretion
Tuesday Nov 29	Video 1 hour	Hardy	The gallbladder and enterohepatic circulation of bile acids
Wednesday Nov 30	9-10 am	Rajendran	Physiology and pathophysiology of pancreatic exocrine secretion
Wednesday Nov 30	10-11 am	Rajendran	Macronutrient digestion and absorption in the small intestine
Wednesday Nov 30	11 am-12 pm	Rajendran	Micronutrient absorption in the small intestine
Wednesday Nov 30	Video 1 hour	Rajendran	Water movement associated electrolyte absorption and secretion in the large intestine
Friday Dec 16	8 am-12 pm		Block Exam 7-36 questions

Block 8 Reproduction/Pregnancy- 6 Hours			
Tuesday Jan 3	9-10 am	Goodman	Male Reproductive Function
Tuesday Jan 3	10-11 am	Goodman	Elements of Female Reproduction
Tuesday Jan 3	11-12 pm	Goodman	Integration of Reproductive Function in Females
Wednesday Jan 4	11-12 pm-video	Bowdridge	Placental Development and Function
Friday Jan 6	8-9 am	Goodman	Initiation of Pregnancy
Friday Jan 6	9-10 am	Goodman	Maintenance of Pregnancy, Delivery, and Lactation
Friday Jan 20	8 am-12 pm		Block Exam 8-18 questions
Block 9 Integration of Systems- 3 hours			
Monday Jan 30	9-10 am	Stauber	Muscle Energetics
Monday Jan 30	10-11 am	Stauber	Muscle Energetics
Monday Jan 30	11am-12 pm	Hardy	Temperature Regulation
Friday Feb 10	8 am-12 pm		Block Exam 9-9 questions
Tuesday Feb 14	8 am-12 pm		NBME Shelf

Block Exam Questions

Block 1- no physiology

Block 2- Cardiovascular Renal: 96 questions

Block 3-no physiology

Block 4-Pulmonary, Acid-Base: 33 questions

Block 5-Skeletal Muscle, Bone: 18 questions

Block 6-Endocrine: 24 questions

Block 7-GI: 36 questions

Block 8-Pregnancy: 18 questions

Block 9- Muscle Energetics, Temp Regulation: 9 questions

Total Questions: 234 questions