

THE DEVELOPMENT OF AN ANATOMY AND  
PHYSIOLOGY TUTOR MANUAL

THE DEVELOPMENT OF A TUTOR MANUAL FOR  
YEAR ONE ANATOMY AND PHYSIOLOGY  
TEACHING ASSISTANTS

By

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## ABSTRACT

A "Tutor Manual" was developed to facilitate the small group learning experience in the laboratory and tutorial component of the introductory Anatomy and Physiology Nursing course at McMaster University. The manual included a comprehensive discussion of the information and important concepts in the laboratory and tutorial sessions, and provided guidelines on how to facilitate the group effectively in its consideration of the topics. Theoretical educational concepts were considered in the development of this manual, including: lifelong learning; principles of adult learning; the use of small-group discussion in teaching and learning; the role of the facilitator; and the use of objectives.

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## INTRODUCTION

The history of higher education has been marked by continual controversy over its function and purpose, the question of the pursuit of knowledge for its own sake versus transmission of an established body of knowledge, and the question of a specialist versus a generalist education. Moreover, the appropriate and most beneficial methods of imparting knowledge to students has been a major issue (Knapper and Cropley, 1985, p. 13). "Despite the special provisions made for educating professionals, both in technical institutions and traditional universities, there is by no means universal agreement about what constitutes appropriate professional education, either in terms of aims, content areas or - especially - instructional methods" (Knapper and Cropley, 1985, p. 36).

The consideration of such topics has been of interest to theorists, politicians, employees, parents, students and university faculty members. In recent years these discussions have taken on an increasingly critical tone and many educational challenges in the realm of higher education have emerged.

Educational theorists have completed extensive research on higher education. Some of the important issues and topics emerging from such work are: the concept of "lifelong learning"; principles of adult learning; the use of small-group discussion as a learning strategy; the role which an effective facilitator plays in small-group discussion; and the use of objectives.

The faculty of Nursing at McMaster University have devoted a considerable amount of time to the development of a learning environment most suited to the learning needs of the students enrolled in the Nursing Program. One of the major innovations emerging from this work has been the implementation of small-group tutorial sessions comprised of students and a faculty member who serves as a "facilitator" for the group. Discussions among the group members are focussed on a "problem" which the students have been given prior to the session. This problem-based, self-directed learning approach has been adopted for a number of the courses in the Nursing curriculum, including the Anatomy and Physiology courses.

The first year "Anatomy and Physiology" course covers many topics including: histology, cell interactions, gross anatomy, the cardio-respiratory system, the renal system, and the digestive system. The material is covered in lectures as well as in small group laboratory and tutorial sessions, as described above. The group facilitators for the laboratory and tutorial sessions are "Medical Science" graduate students, who come from diverse backgrounds within the life sciences.

A number of shortcomings have been identified in the existing system or specifically, the problem-based, small-group learning component of the course. In order to overcome some of these problems, a "Tutor Manual" was developed. In the introduction to the manual, these shortcomings were listed, as well as the means by which the manual could remedy the problems:



1. Since the tutors for this course are Medical Science Graduate students coming from a wide range of backgrounds, they may not be familiar with all the material which is covered in the laboratories and tutorials. The contents of the laboratories and tutorials are outlined in sufficient detail for the tutors to gain a good understanding of the topic, thereby filling in any gaps of knowledge as they arise.
2. The lab/tutorial sessions have the advantage that the students can discuss the problems as small groups, with the tutor serving as a facilitator to the discussion. However, because of this small group structure, inconsistencies may arise among the different groups. The possibility of different material being covered in different groups creates anxiety for the students; they cannot be sure that they have not missed some points which other groups covered. A manual for the tutors will alleviate the problem of inter-group inconsistencies. The manual will not, however, limit the contents covered in the sessions, but rather, will ensure that the key concepts are covered in all groups. The manual will also allow for the lab/tutorial material to be examined, since the examiner can be certain of what was covered in all the groups.
3. Finally, the manual brings out some topics which may otherwise have been overlooked. Of course, other issues may emerge as the session progresses, and the group may decide they would like to investigate such topics further to satisfy their own personal learning needs.

This tutor manual forms the bulk of this project. In addition, the justification of the instructional methods used in the small group sessions is considered using the theoretical work emerging from the educational research in the topics listed above, as well as the role which the tutor manual plays in these topics.

## Chapter 1 - LIFELONG LEARNING

One area in higher education which has received considerable attention recently is the implementation of developing strategies to promote "lifelong learning". Descriptions of the personnel, processes, methods and materials, institutions, administrative and organizational conditions necessary for its facilitation have been provided (Knapper and Cropley, 1985, p. 21). According to Fuare (1972) the approach of lifelong learning should be adopted as the guiding principle for reforming education at all levels and in all countries. In their discussion of the ambiguity surrounding the meaning of lifelong learning, Knapper and Cropley (1985) suggest that:

...one way of looking at lifelong education is to regard it as a rationalisation of a number of existing trends in contemporary theory and practice... When viewed as a unifying principle linking existing trends and tendencies, lifelong education is a useful device for bringing together under a common heading a number of practices which, although possessing an inherent unity, would otherwise have continued to be treated as distinct from each other (pp. 16-17).

The reasons that have lead to the interest in the promotion and the importance of lifelong learning are social, economic and cultural in nature (deSanctis, 1977), as well as the growth in the phenomenon of "change" that is becoming a major element in contemporary life (Cropley, 1977). The relationship between education and change has been described by McClusky (1974) who points out that "continuous change required continuous learning" (p. 101).

One area which is clearly undergoing rapid change is the world of work:

...factors such as technological progress, development of manufacturing techniques, emergence of new products and increases in knowledge are combined to produce a situation in which some jobs are simply ceasing to exist, while others in basic skills are changing so rapidly that it is no longer possible to acquire them once and for all during an initial education and then spend the rest of one's life applying them (Knapper and Cropley, 1985, p. 22).

One example which is pointed out is the profession of medicine where "diagnostic procedures in medicine are rapidly being transformed by technological advances, while chemotherapy is constantly altered by new discoveries" (p. 23).

There are many implications of these changes in the area of education. Three specific implications which will be considered: the use of an integrative approach to a discipline; the implementation of problem-based learning; and the approach of self-directed learning.

It is now realized that since the information which is available to students in any field grows exponentially, "the ability to integrate and maintain an overall perspective becomes critically important - perhaps even more important than mastery of specialized technical expertise" (Knapper and Cropley, 1985, p. 58).

In light of the changing needs of students as dictated by the changes in society, there has been a move away from specialization. This is one of the recommendations emerging from the Leverhulme study program, namely that there is a need to

reduce undue specialization at both the level of secondary school and higher levels of education (Leverhulme, 1983). The advantages of integrated degree courses in which the students can be exposed to the methods and concepts of different disciplines are discussed. Such an approach has practical advantages, since jobs in the future will require individuals who have the broad general aptitudes that an interdisciplinary and integrative method imply (Knapper and Cropley, 1985, p. 59).

In addition to a move toward a more integrative approach to education, other innovations are receiving considerable attention. The traditional combination of teaching and learning in University education is teacher-centred and subject-based. In such an educational setting, the competencies needed by the student include: the ability to listen attentively; the ability to take careful notes; the ability to read rapidly and with good comprehension; and the ability to prepare for exams by predicting exam questions and memorizing facts (Knowles, 1975, p. 23). The predominant format of this teacher-centred subject-based learning is that of large lecture-hall instruction in which students are passive learners, and receive answers to questions they may not have asked (Waterman and Butler, 1985). In this educational process, lectures cannot be delivered at the convenience of the learner, nor can they be given with appropriate emphasis and at a pace to accommodate the needs and desires of each learner (Barrows and Tamblyn, 1980, p. 8). Moreover, a steady decline in concentration after a peak at 10-15 minutes has been observed in

students during lectures of this format (Stuart and Rutherford, 1978).

Recently there has been a trend at various centres of higher education to move away from this traditional format, and adopt innovative teaching and learning strategies. One example is the implementation of problem-based learning. In problem-based learning, subject material is covered as students discuss it in relation to a given problem. Indeed, the need to require students to consider problems is generally accepted, as problem solving forms a large part of the practical work in technological subjects, in both natural and social sciences (Miller, 1987, p. 27). Furthermore, given the rapid rate of change in society, as discussed above, while the acquisition of information is important, the process by which this information is acquired becomes more critical:

The knowledge that a student will receive today will be out of date or modified within a very short time. Education must aim for a more subtle goal: the facilitation of change and learning. The educated man is the man who has learned to adapt to change: the man who has realized that no knowledge is secure, that only the process of seeking knowledge gives a basis for security. In our fast-changing world, reliance on process rather than upon static knowledge is the goal for education that makes sense (Vaines, 1974, p. 162-163).

The application of a problem solving approach to education is by no means new. Indeed, the essence of the Socratic method from ancient Greece is that the teacher suggests a problem which is perceived to be important by a student, and guides students toward a solution of the problem by means of questioning. Dewey

(1916) recommends that the students should be presented with real life situations or problems, and he stressed the "importance of the process of learning, rather than the products that were learned" (Hendley, 1986, p.26).

Within the framework of problem-solving there are two broad approaches which can be taken in higher education.

The traditional approach of universities is to have the students master a certain body of information, as defined by a teacher or textbook, ultimately learn to extract what is relevant, and to apply their knowledge to help solve real-world problems. A contrasting approach is to begin with a problem and have students try to solve it working "backwards" to acquire the necessary information and skills (Knapper and Cropley, 1985, p. 54).

In addition to the use of problem-based learning, the concept of student-centred, self-directed learning is also gaining in popularity. In this format, it is up to the student to pursue the information which is pertinent to his needs. "By providing choices about what is learned and how it is learned, the instructor recognizes not only differences in personal goals, but differences in students' rates of learning, life situations, and learning styles" (Kozma et al., 1978, p. 35). In the discussion of the need for more student-centered learning, the Leverhulme Program of Study into the Future of Higher Education emphasized the concomitant need for flexibility in approaches to teaching (Bligh, 1982). More specifically, there is a need to produce "authoritative uncertainty" in students, and to stress "action-oriented" thinking based upon practical, real world learning experiences, as opposed to passive learning approaches

(Goodlad et al., 1982).

One example of an institution which has adopted a problem-based, self-directed learning approach is the Medical School at McMaster University. The method of learning by problems has been adopted as it "represents an alternative to studying blocks of classified knowledge in a strictly organized sequence" (Neufeld and Barrows, 1974, p. 1042). Problem-based learning can occur both individually and in small group settings. A common approach taken at McMaster's Medical School, is the students are given a description of a patient or other clinical situation, and the tutorial group comes up with a number of questions concerning the situation. The students will then identify and retrieve educational resources which provide information relevant to the learning objectives which were identified, and will synthesize this information into a cogent explanation of the situation. Additional questions, suggestions and hypotheses for further steps in the evaluation of the situation follow.

This kind of learning has many advantages. In the problem-based learning approach, the learner is able to control the time, pace, sequencing of learning, select from a variety of resources, and have some control over the learning environment. (Knowles, 1984, p. 19). "By allowing the students to take some control over the direction, speed and depth of their study, frustration is diminished and the learning environment is more conducive to creativity and enthusiasm" (Waterman and Butler, 1985, p. 17).

Problem-based learning contributes to the students' motivation; it entails intellectual processes at the higher cognitive levels; information is learned in the context of trying to understand a patient problem, facilitating recall and transfer of that information in work with future related problems; information is reinforced through reuse; the information from many disciplines is integrated in the mind of the learner; learning is seen by the student as being relevant; students are actively involved and motivated; and students can be treated as adults responsible for their own learning (Barrows and Tamblyn, 1980, p. 193; Neufeld and Barrows, 1984, p. 212).

Moreover, problem-solving is a legitimate goal in itself. "It is useless to have a stockpile of information without a method of handling it. On the other hand, given a good approach to problem-solving, students will be able to define the information they require to handle encountered problems." (p. 214).

In addition to medicine, this teaching-learning format is both relevant and appropriate for the education of other health professionals. The common element of such disciplines is:

...the need to actively apply knowledge to the assessment and care of patients and the ability to continue to identify areas where further learning would enhance or improve the practice of these skills. As in medicine, problem-based, student-centred learning is the most efficient method of simultaneously developing knowledge, reasoning skills and study skills. Disciplines will differ in the problem situations they select for their students and the goals and expectations for patient assessment and care, but the basic learning method can be the same (Barrows and Tamblyn, 1980, p. xiii).



The tutorials in the Nursing program at McMaster follow a similar format to that of the Medical program, described above. A problem (often a clinical situation) is given to the students and they have about one week to research it. The focus of the problem deals with an applied topic of the material which is being covered in lectures. The students are given guidance into the important aspects of the problem by being given a list of objectives, and a few questions are posed within the problem. In their research of the topic, the students must be self-directed in locating appropriate resources which deal with the topics. The students assemble in their tutorial groups of about eight students, and discuss the problem. The topics covered by the group are recorded, and these "Recorder Sheets" are available for the other groups to read.

Barrows and Tamblyn (1980) have described a method of selecting problems which "is probably the most appropriate and widely applicable to any curriculum or course that needs to select problems for problem-based learning" (p. 159). One characteristic which the problem must have is that it "emphasizes or underlines important concepts in basic sciences, such as anatomy, physiology, biochemistry, pathology, pharmacology, epidemiology, and so forth, necessary to give the student a sound foundation or prepare him for new trends or concepts in medicine" (p. 159). While each Nursing tutorial problem in this course does not necessarily include aspects from all of these disciplines, anatomical and physiological considerations of a

problem are always present, and usually at least one other scientific disciplines is relevant. In addition, considerations of patient care from a Nursing perspective are included in many tutorials. Thus, the students are forced to take a multidisciplinary, integrative approach in dealing with the problems.

While the tutorial sessions take a somewhat more structured approach than in the medical school this is appropriate for a number of reasons. The course curriculum and structure is limited in its requirements by the Nursing Program and the University policies. This has many implications, including: a specified number of hours required for lectures, laboratories and tutorials; examinations and grades are required; and the topics to be covered in the curriculum are pre-determined. While such policies prevent a complete adoption of the problem-based approach, this method of learning can be used in a modified manner. "In the usual subject-based/teacher centred courses, these units (PBL units) could be used easily as problems to amplify learning or to provide the students with experiences in the application of learned material to patient problems." (Barrows and Tamblyn, 1980, p. 183).

Despite some of the differences, the advantages outlined above for the problem-based approach are relevant to the Nursing tutorial problems. The students have flexibility in the resources they use and the time-frame for researching the problem. In their research of the problem they can integrate the

information of many disciplines, and the group discussion approach affords the advantages of a small group outlined above.

## Chapter 2 - PRINCIPLES OF ADULT LEARNING

"It is often assumed that young people will automatically abuse freedom. Given the chance, runs this type of thinking, today's students will always take the easiest way, learn just what he has to, indulge himself...and escape scotfree with a degree he has done nothing to deserve" (Vaines, 1974, p. 161). Such attitudes are less likely to prevail in a program which encourages the responsibility of students, and has an atmosphere which favours learning; then students will assume that responsibility (Vaines, 1974). Moreover, university students are adults, which clearly indicates the need to rely on the responsibility of the students as learners. Thus, instead of considering some of the teaching and learning principles that may apply to young students, a more appropriate goal at a university would be to apply the principles of adult learning.

The issue of adult learning and the characteristics of adult learners has been the subject of lively debate in recent years. While it is clear that there are real differences in performance on learning tasks between adults and children, as well as between older adults and younger adults, these differences should not be seen as the presence or absence of a single, generalized learning ability. Rather, differences among such learners are in areas such as the types of things that are most readily or least readily learned, the circumstances most favourable for promoting learning, and the speed and efficiency with which certain kinds

of learning are carried out (Knapper and Cropley, 1985, p. 49).

Gregor (1981) studied the special characteristics of adult learners and the prevailing teaching practices at Canadian universities. University lecturers were interviewed about their experiences with teaching mature students. They often reported frustrations and problems relating to both the learning difficulties and attitudes of the students. Gregor suggested that many of the attitudes of the adult learners were reasonable, but often provoked a defensive response in the instructors who were attempting to maintain the "adolescent learning" approach to which they were more accustomed. Gregor condemned the "complacent lack of appreciation that there was in fact an issue: that adults do learn differently and should be approached differently" (p. 538).

The Canadian Association for Adult Education (1982) has called for greater attention to be paid to the development of teaching methods which are more appropriate for mature students. They point out that many adult learners are entering an educational institution with previous negative educational experiences. They need special orientation, counselling and tutoring and such services are largely unavailable in traditional universities. Indeed most educational institutions fail to respond to the special needs and problems that adults often bring to the learning situation.

Most of the theories and assumptions made about learning

have been derived from studies in children and animals, and most of what is known about teaching stems from experiences with children in compulsory education (Knowles, 1970, p.37). Concerned about the use of theories and assumptions emerging from pedagogy in the education of adults, Malcolm Knowles developed a comprehensive "andragogical" (literally, "the art and science of helping adults learn") model to aid in the education of adults. The inherent assumptions of this model are contrasted with those of the traditional pedagogical model:

(1) **Regarding the concept of the learner:** Within the framework of the pedagogical model, the teacher has full responsibility for making all decisions about what should be learned, and whether it has been learned. In contrast, within the andragogical model, the self-concept of the learner moves from being a dependent personality toward one of being a self-directing human being. Adults "develop a deep psychological need to be perceived by others, and treated by others, as capable of taking responsibility for ourselves" (Knowles, 1984, p.9). Indeed, adult learners may be faced with an internal conflict that results from a conditioned expectation of school and education which contrasts their deeper psychological need to be self-directing.

(2) **Regarding the role of the learner's experience:** The pedagogical model assumes that learners enter into an educational activity having little personal experience that can be used as a valuable resource for learning. It is the experience of the

teacher, the textbook writer and the audiovisual aids producer that counts, hence the pedagogical methodology is one of transmission techniques. The andragogical model assumes that adults enter into an educational activity with both a greater volume and a different quality of experience than that of a younger student. Thus, adults are themselves a rich source of information. A consequence of this difference in experience is that the teaching techniques employed should utilize this resource, and an emphasis should be placed on such techniques as group discussion, simulation exercises, laboratory experience and problem-solving projects.

(3) **Regarding readiness to learn:** In the pedagogical model, readiness to learn is simply a function of age, and students become ready to learn only what they are told they are ready to learn. In contrast, adults are ready to learn when they experience a need to know, or do something in order to perform more effectively in some aspect of their lives. Such 'needs' do not necessarily develop intuitively but rather may be fostered within the learner by the educator.

(4) **Regarding orientation to learning:** According to the pedagogical model, the orientation into which students enter into an educational activity is subject-centred. Therefore, the curriculum is organized according to content units and is sequenced according to the logic of the subject matter. Given that adults, on the other hand, enter an educational activity with a life-centred, task-centred or problem-centred orientation

to learning, it is important to make clear the relevance of the material, and to organize the learning experiences around life situations rather than according to subject matter units. Moreover, adults usually bring more clearly developed personal goals and better formulated ideas about what constitutes useful information to the learning situation. Knox (1974) has summarized this characteristic of adult learners succinctly when he states that adults are seldom interested in learning answers to which they do not already know the questions!.

(5) **Regarding motivation to learn:** In contrast to the pedagogical model within which students are motivated primarily by external pressures (for example, teachers, parents and grades) the andragogical model predicts that internal motivators (for example, self-esteem, recognition and self-confidence) are more powerful motivators.

Knowles (1984) addresses the question of which model to choose. For centuries, education has only had the pedagogical model, and as a result, educational institutions have based their teaching methods on the principles it has outlined. In some educational institutes, regardless of age, this may be appropriate; "they may be truly dependent on didactic instruction before they can take much initiative in their own learning" (p.13). However, in many more situations, the andragogical assumptions would be more realistic.

Although in promoting andragogy Knowles is attempting to



meet quite a legitimate need - the need to provide a viable alternative to traditional "school-like" education - it seems difficult to devise a workable definition of andragogy. (Cross 1986, p. 225). Furthermore, the question as to the nature of andragogy has arisen. Cross (p. 225) has considered whether andragogy is a learning theory (Knowles, 1978), a philosophical position (McKenzie, 1977), a political reality (Carlsen, 1979) or a set of hypothesis subject to scientific verification (Elias, 1979). "Whether andragogy can serve as the foundation for a unifying theory of adult education remains to be seen. At the very least it identifies some characteristics of adult learners that deserve attention" (Cross, p. 227).

Despite the controversy on the nature of andragogy, Knowles' andragogical model has been widely adopted or adapted in a variety of programs at various levels of education as well as across many institutions, including elementary and secondary education, colleges and universities, business and industry, government agencies and volunteer organizations (Knowles, 1984). The implementation of principles of andragogy are particularly appropriate and important in programs of professional education simply because people preparing for professional careers definitely are adult learners: "they have made one of the most adult decisions possible, choosing a career" (Knowles, 1984 p. 205).

A number of factors which mitigate against the complete adoption of the andragogical concept in nursing education have

been outlined (Mast, and John Van Atta, 1986). One consideration is the lack of awareness of this concept and its desirability on the part of many faculty. Faculty members may be resistant to change their present teaching methods. The structure of the system - schedules, grading, funding are still fixed within the traditional model and a change necessarily involves the expenditure of time and money. Moreover, many of the students must be reconditioned to function as self-directed, involved and active learners and this process also involves added time and energy on the parts of both teachers and students. Despite such barriers to change, they suggest that "a growing interest and concern in better teaching methods is leading educators to search for innovative and flexible methods that will make more effective use of their own time and better prepare their students for nursing's expanding role in health care" (p.36).

The characteristics of adult learners and the significance these have in teaching and learning styles have been applied to the tutorial approach in the Anatomy and Physiology Nursing course. Each of Knowles' assumptions in his model can be considered.

The tutorials are largely students directed; the tutors serve as facilitators of the group process and ensure accuracy and completeness of the topics covered. In their experience with nursing students, Arms and colleagues (1984) suggest that: "Although we are dealing with students in the chronological sense

of the word, they have been socialized through prior learning experiences to be dependent on instruction for direction and guidance. Therefore, they cannot be expected to assume an adult learner role at the outset" (p. 284). Thus, the tutor who facilitates the group can serve to provide a buffer as the students slowly develop the characteristics of adult learners as they proceed through the course. Furthermore, a tutor is able to perceive the individual needs and expectations of the students in the small group setting, and tailor the sessions to better meet these needs.

Although the students do not have complete control over what is to be learned, there is enough flexibility afforded by the tutorial problems that the students can focus on specific aspects of the problem that are of interest. In addition, the students are self-directed in their approach to researching the problem.

With respect to the role of the learners' experience, Knowles (1970) has suggested teaching techniques such as group discussion, the case method, role playing, and laboratory methods. "There is a distinct shift in andragogy away from the transmittal techniques so prevalent in youth education...toward the more participatory experimental techniques" (p. 45). The group discussion format encourages the sharing of knowledge among the group members, with the individuals acting as rich resources of experience for their peers.

The problems have been developed so that they are applicable to the topics covered in lecture, and in this way, the need for

the information is fostered within the student. Moreover, a need for the information is felt since most of the problems are clinically oriented and will be encountered in their practices as nurses. This is in keeping with the "life-centred, task-centred, or problem-centred" orientation to learning, which is the orientation of adult learners.

Finally, the value of the topics and information covered in the laboratory and tutorial sessions is apparent as they will be useful in the future nursing practices of the students. However, the policies of the institution require a grade for the tutorials, so "external pressures" cannot be fully overcome. Presumably, however, the internal rewards of the participation in the group process as well as the acquisition of important and relevant information are also present, so that the students are motivated. Furthermore, the grade assigned to the tutorial is downplayed.

In summary, the facilitated discussion in the tutorial and laboratory sessions incorporate many of the principles of andragogy, thus providing a suitable learning environment for the adult learners in the Nursing program. A detailed consideration of the use of the technique of discussion, as well as the role of the facilitator in this process, follows.

### Chapter 3 - THE USE OF SMALL-GROUP DISCUSSION IN TEACHING AND LEARNING

The use of discussion as a method of teaching has been increasing in popularity in recent years, at all levels of education, particularly higher education.

Educators have long been aware of the beneficial effects which the presence of other individuals exerts on the performance and thinking of a learner (Allport, 1920). It has also been known for a long time that working in a group can facilitate a person's learning experience (Thorndike, 1938). However, a systematic use of the small group as a medium for learning did not stem from such information, but rather from innovations in the field of adult education. Adult educators found that their more conventional techniques were not altogether satisfactory for teaching mature students (Gordon, 1955, p. 16). It was found that such learners exhibited strong resistance to instruction presented as dogma without opportunity for discussion and rebuttal. When provided with the opportunity to participate in the educational process, the motivation of most adult learners was very high (Olmstead, 1974, p. 79).

The recognition of the value of active participation of students led many adult educators to the use of small group discussion as an important vehicle for learning. It was found that "well-conducted discussions of relevant problems and issues satisfy the adults' needs for active learning, and what is more, are better for overcoming resistance to new ideas than are more

dogmatic methods based upon persuasion by an instructor" (Olmstead, p. 80). Moreover, "within educational institutions--as in the workplace and many other aspects of everyday life--colleagues can provide invaluable information and advice, yet learning from peers is often neglected or even discouraged" (Knapper and Cropley, 1985, p. 113).

In the context of education as an educational tool, "discussion" takes on a more precise meaning than it does in general usage. In the educational sense, discussion is a "calculated and systematic attempt to apply knowledge, thought and fact-finding to solution of a problem, or resolution of an issue so that learning may occur". (Olmstead, p. 81). Thus, the kind of discussion around which small group discussion is built in an educational setting has been defined as "'group deliberation', carried on through oral discourse, aiming at the cooperative solution of a problem or resolution of an issue through reflective thinking" (Wagner, 1965, p. 3).

While there have been few studies on the connection between discussion and learning, those that have been conducted confirm that discussion can lead to a number of desirable outcomes, including: increased curiosity about the subject area; more positive perceptions about the value of the subject; higher ratings of the course; increased time spent reading materials related to the subject; and higher attendance at course sessions (Smith, 1980).

In her discussion of the value of 'seminars' (defined as

discussions within a group with an emphasis on subject matter), Abercrombie (1974) points out that:

...the group system of teaching focusses on the interaction between all participants, not on the polarized interaction of a student with a teacher... Exposed to the same display of information, each student has taken in not only different amounts, but different interpretations, and each learns by comparing and contrasting his uptake with that achieved by his peers. There is a network of communication between all members...In the group system, the student discovers his strengths and weaknesses himself as he sees his behaviour in the light of others, and he modifies his attitudes or strategies as he sees that there are as many alternatives to them as there are members of the group. (p. 5).

The importance of discussion as a means of stimulating student learning has been emphasized by Cockburn and Ross (1977). Small group discussion is an excellent medium to fulfill a number of objectives: promotion of the understanding of a body of knowledge and the relational thinking that this needs; elucidation of students' misunderstandings and difficulties; practicing skills (intellectual, verbal, computational, social) and the application of principles to familiar and unfamiliar situations; the exploration of personal and professional attitudes and values; and finally, as a two-way exchange of information on the teaching-learning process (p. 10).

Discussion is also advantageous as it is responsive to the needs of the student (Kozma et al., 1978). A small-group discussion is an ideal setting for a student to compare his or her concept of a topic with that of another student. The student also has the opportunity to respond to other's needs and share

information. "This interaction among students presents the group with a variety of perspectives, opinions and options, a condition which can lead to the students' personal development" (Kozma et al., 1978, p. 234). In addition, skills such as speaking, listening, sharing, and leading can be fostered through discussion.

Discussion seems appropriate for the application of concepts and the acquisition of problem-solving skills. The problem-solving techniques of individual members can be shared, and perhaps used by the other members of the group. Critical thinking skills, or the ability to consider a number of viewpoints in dealing with a topic, can also be developed with this method of learning. The interdisciplinary approach taken to the problems necessitates the consideration of alternative views. Indeed, Smith (1977) found that classes that engaged students in peer-to-peer interactions were consistently related to the acquisition of critical thinking skills.

It is clear that discussion in the small group setting has many benefits, however potential disadvantages and problems also exist. In a workshop focussed on discussion techniques, Rasmussen (1984) has outlined some problems which participants encountered in facilitating discussions. Some of the more frequently mentioned issues were:

1. some group members dominate the discussion and the other more passive members are resentful;



2. the discussion often gets bogged down and does not flow;
3. the leader has difficulty pulling things together as the discussion goes off on tangents;
4. participants seemed bored with the discussion and appear anxious for it to finish.

Kozma and colleagues (1978) point to the additional problem of unreliability with the use of discussion. "Apart from the times it may become aimless or boring, it is usually haphazard, even when done well. That is, because discussion is a less structured activity, not all of the important points may be raised, nor all of the information be accurate, nor all the students' needs met" (p. 235).

Another problem with discussion is that a significant amount of class time is required to maintain the group, particularly in the first few discussions when the students are primarily interested in getting to know each other and group dynamics are developing (Stanford and Roark, 1974).

Many of these problems can be minimized or overcome if the discussion is facilitated in an effective manner. Indeed, a well-prepared and knowledgeable group facilitator can overcome most of the mentioned potential problems. The group facilitator can draw the more passive group members into the discussion, and be more directive to the point that the discussion does not go off on inapplicable tangents, and that irrelevant points are not belaboured. "A frequent problem in discussion is that the

direction will go off topic. When this happens, the instructor may want to see if the group redirects itself; if not she may remind the group of the task or the goal" (Kozma et al., 1978, p. 237). (The role of the facilitator will be discussed in more detail in Chapter 4).

A discussion need not be "boring" if the topic is relevant and applicable to the learner. The tutorial problems upon which the discussions were based were chosen to complement the material which was covered in lectures, and more important, to involve clinical situations which the students would encounter in their practice of nursing. Thus, the information covered in the discussions was undoubtedly relevant. In addition, the tutor manual was fortified with a few pieces of relevant and interesting information in the format of questions, which were related to the problem at hand, but which most students would not have considered in researching the problem. The facilitator could bring this information into the discussion by posing a question, thus making the sessions more interesting and stimulating thinking processes.

Finally, while it has been argued that time spent in discussion may tend to be less productive and a low-task oriented period, it can also be an important process if the goals for the course are the acquisition of interpersonal skills (Kozma et al., 1978, p. 234-235). This is the case in the Nursing program; in addition to the ability to gain knowledge, use knowledge, and problem-solve, another goal of the program is the development of communication and interpersonal skills.

## Chapter 4 - THE ROLE OF THE FACILITATOR

However self-directed the mode of instruction, the role of the instructor remains important. "Self-directed learning does not mean that the individual always learns by himself, but that he is able to seek and to use others to explore, reinforce, and validate learning" (Cooper, 1983, p. 147). Indeed, from the theoretical base of andragogy there emerge characteristics of adult learners which have great significance for educators who see themselves as "resources for self-directed learners" as opposed to "imparters of knowledge" (Knowles, 1970). In accordance with Knowles' andragogical model, the role of the teacher is "redefined as that of a procedural technician, resource person, and co-inquirer; he is more of a catalyst than an instructor, more a guide than a wizard...Andragogy assumes that a teacher can't really 'teach' in the sense of 'make a person learn', but that one person can only help another person learn" (Knowles, 1970, p. 43).

In self-directed learning, the role of the instructor is primarily to give support and guidance, and help provide a framework for discovery. The instructor will initiate and encourage dialogue that will involve all members of the class- as opposed to merely telling the students the correct answer (Knapper and Cropley, 1985, p. 119). In student-centred discussion, the active, participatory role of the instructor diminishes coincidentally with an increase in the time spent by students discussing the issues and problems. Questions and

comments are directed to other students more than to the instructor. The instructor's role is to pose key questions, present dilemmas and paradoxes, and foster insight (Kozma et al., 1978, p. 133). "The responsibility of the discussion is turned over to the learner and, as a result, the students become more directive and play an active role in their own learning" (Kozma et al., 1978, p. 234).

Special skills are required for instructors in the facilitation of small-group discussions.

The effective use of small group discussion techniques requires a great deal of skill and experience on the part of the instructor. Although the ideal situation would require a minimal input from the instructor, the students typically lack skills necessary to conduct a successful discussion. This puts the pressure on the instructor to facilitate discussion by compensating for the lack of student skills, while diverting attention from himself to the students. The technique thus requires the instructor to attend to two things at once - the content of the discussion and the dynamics of the group. (Kozma et al., 1978, p. 237).

Olmstead (1974) has considered the training required for instructors of the "conference method", a specific format of discussion. This format uses a pre-determined agenda and each topic on it is discussed. In this method the discussion may be "free", or unguided, though it is more frequently guided by a leader who makes sure that all the appropriate points are covered.

The conference method has much to recommend it...For example, relatively inexperienced personnel can be trained to lead conferences. Subject-matter experts are not necessary, although such experts are certainly able to improve the quality of the program. Conference leaders' guides can be prepared by experts to provide

complete instruction with regard to steering a discussion. If necessary, a step-by-step outline can be developed to include all points to be covered, the actual words to use in opening and closing each session, and similar materials. The method thus permits conduct of training with whatever personnel may be at hand. (p. 94-95).

Olmstead continues to describe problems which may be encountered when the leader is not a content expert:

...there is much greater risk of superficiality in the discussions. Because of lack of expertise among students, discussions tend to skirt issues unless the conference leader can skillfully probe relevant points and raise questions which will give students insight into underlying problems. In order to accomplish this well, the leader must be sufficiently knowledgeable in content areas to identify both superficial diagnoses and critical issues so that the group can be guided into more meaningful discussion. (p. 95).

Another factor in the success of adopting facilitators for self-directed learning is whether or not the instructors "will be prepared to give up their role as experts and instead become facilitators and mentors, helping students to take a more active role in directing their own learning" (Knapper and Cropley, 1985, p. 72). At the heart of the matter is the question of whether or not the traditional roles of the teacher will change in response to a emerging generation of learners whose needs are not sequential, predictable or orderly as in the manner to which educators are accustomed (Heerman et al., 1980, p. 9).

Given the importance of subject-matter experts for the success of small-group discussions, a comprehensive guide of the subject matter would be beneficial for the Anatomy and Physiology

Nursing course, as was recommended by Olmstead. Since the facilitators of the small group discussion are graduate students from diverse backgrounds within the broad field of "Medical Sciences", it was felt that such a guide was imperative. The material covered in the manual was developed so that it was clear and comprehensive, and covered all the relevant material for which the students were responsible. The format of the content matter was carefully developed in a manner so that the tutor would not be overly directive; much of the information was outlined in a question and answer format. In this way, the tutors could use the questions to stimulate the students' thinking, and guide the students through the discussion in an organized fashion. The answers in the manual dealt with the questions posed in a clear, succinct manner. Thus, the facilitator would be able to ascertain quickly if the students' answers, ideas and concepts pertaining to the topic were appropriate and valid.

The guide also provides a brief summary of the tutors' role in the program. Specifically, they are reminded that their role is one of a facilitator, and not one of a traditional didactic teacher. Because of the tremendous importance of this aspect of their role, this written summary is supplemented by discussions in "pre-laboratory/tutorial meetings" which are headed by the course co-ordinator. In this way, the facilitators are reminded of their role and responsibilities on a regular basis.

## Chapter 5 - THE USE OF OBJECTIVES

Objectives for students are an important part of their learning. "Objectives are derived from what education is, what it will be and what it ought to be. Without objectives, no concentration of resources and effort is possible, no priorities can be allocated - other than the result of fancy or whim... Objectives in other words, can serve as a very useful stimulus to clear thinking, as well as a means of allowing teachers to communicate with each other in relatively precise and unambiguous manner" (Davies, 1976, p.73).

In the 1930s, Ralph Tyler proposed the practice of specifying the content of instruction in terms of observable student change. Debated, refined and promoted, the use of objectives at all levels of education has become widespread.

The provision of objectives to students has a number of uses. They guide the students in their learning, stimulate them, and motivate them. They can be used as a framework within which they can hang present and subsequent knowledge, as well as a series of targets for which to strive. By specifying the outcomes of learning, one of the major difficulties in higher education, namely, student identification of what is important to learn, is overcome. "Although a commonly expressed goal of higher education is to bring students to the point of making their own decisions about what is important, they are sometimes not in a position to judge" (Kozma et al., 1978, p. 44).

Objectives are also useful as a basis for independent study,

"for although the ends have not been individualized, the means by which they are reached can be tailored to meet individual requirements." (Davies, 1976, p. 73-4).

Objectives are also useful for curriculum developers because they allow precise definitions of where they intend to go and what they intend to be about. Without this feature, "teachers may have to operate on the basis of intuition and craftsmanship alone, without the benefit of a clearly identified final destination as a map or compass." (Davies, 1976, p. 76).

There are a number of technical advantages of objectives. They are useful in breaking down the subject matter into more manageable pieces and, as such, they can be synthesized into a number of interlocking elements, ensuring that the topic is both consistent and internally coherent (Davies, 1976, p. 74).

The actual development of objectives is one of the most critical decisions which a curriculum planner must make. The decision must define direction to what has to be achieved as well as the goals which are to be to be accomplished. The importance of the decision lies in the fact that it has a vast scope of implications; not only do objectives define a prescription for learning, but they also have implications in terms of content, teaching methods, resources, environment and evaluation procedures required. (Davies, 1976, p. 104).

The question of the appropriate approach to take in the development of objectives has been considered. Tyler (1949) suggests that in organizing a single list of objectives, they



should be stated in a form which makes them helpful in selecting learning experiences and guiding teaching (p. 44). "The most useful form for stating objectives is to express them in terms which identify both the kind of behaviour to be developed in the student and the content area of life in which this behaviour is to operate" (Tyler, 1949, p. 46-7). More recently, Davies (1976) suggests that while there are many ways of writing objectives, no format has yet been shown to be better than any other. "All formats tend to work equally well, and sometimes equally badly...until a clear advantage is demonstrated, common sense suggest that the format chosen should be suitable and appropriate to the situation which it serves" (p. 106). What is perhaps most critical is the specificity of the objectives. "The conscious planner will experiment with varying degrees of specificity until the most effective balance is found between broader expectations and narrower statements of how a student will demonstrate successful learning in a program of study" (Miller, 1987, p. 14-5).

In some instances it may not be educationally advantageous to transform broad, general and somewhat vague aims into precise, unambiguous specific objectives. Myron Atkin (1968) argues that it can unnecessarily restrict the teaching learning possibilities of a situation. Objectives which are too explicit can limit the range of explanation, and teachers can be kept away, or warned off, potentially productive tangents. MacDonald-Ross (1973)

points out that even when objectives have been stated clearly, students will make their own choices about what they learn. Moreover, when behavioral objectives are used, curriculum planners overlook or avoid the important issue of how these objectives are selected (MacDonald-Ross, 1973).

Bearing in mind the advantages, as well as the potential shortcoming of objectives, a list of objectives was developed for each laboratory and tutorial. The objectives were listed for the students and the tutors at the beginning of each laboratory and tutorial. The objectives listed were developed such that they would provide a focus for the students with regard to the concepts of that session for which they were responsible. They provided flexibility in terms of the specific elements of the problem under consideration, thus were not overly directive. Thus, the students were able to seek information in specific areas of interest, without missing the key concepts which were relevant to the problem. Stating the objectives in a general format, also provided flexibility in terms of the resources which the students could use to research the topic.

Other benefits of the objectives were gained; they could be used during the laboratory and tutorial sessions as a framework within which to cover the topic. This would ensure all relevant topics were considered. In addition, the objectives stated could be helpful for evaluation purposes. Knowing the key concepts which were covered by each of the different student groups, test

questions could be developed based on the objectives. This ensured that the test questions dealt with information which each student had received.

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## INTRODUCTION

This manual has been prepared for the use of Teaching Assistants in the Introductory Anatomy and Physiology course HS1B7.

HS1B7 is an introductory Anatomy and Physiology course for B.Sc.Nursing students. The weekly laboratories and tutorials are meant to supplement the lectures which the students receive two times a week. The format of the laboratories and tutorials includes many aspects of problem-based learning. This form of teaching/learning is most likely to be new for both tutors and students.

The purpose of this manual is to help overcome some of the problems which have been encountered in the lab/tutorial sessions, and ensure the smooth and efficient running of these sessions. More specifically, there are three objectives of this manual:

1. Since the tutors for this course come from a wide range of backgrounds, they may not be familiar with all the material which is covered in the laboratories and tutorials. The contents of the laboratories and tutorials are outlined in sufficient detail for the tutors to gain a comprehensive understanding of the topic, thereby filling in gaps of knowledge as they arise.
2. The lab/tutorial sessions have the advantage that the students can discuss the problems in small groups, with the tutor serving as a facilitator to the discussions. However, because of this structure, inconsistencies may arise among the different groups. This has created anxiety for the students as they may be concerned that they might miss some points covered by other groups. The manual will not, however, limit the contents covered in the sessions, but rather will simply ensure that the key concepts are covered in all groups. This will allow the examination of lab/tutorial material, since the examiner can be certain that the relevant material was covered by all the groups.
3. Finally, the manual brings out some topics which may otherwise be overlooked. Of course, other issues may emerge as the session progresses, and the group may decide they would like to investigate these topics further to satisfy their own learning needs.



## THE ROLE OF THE TUTOR

Learning in small groups with a problem-based, self-directed learning format is gaining popularity in several educational institutions. McMaster's School of Nursing adopted this method for its clinical courses, and the transition is being made in the basic science courses as well. The role of the tutors is not one of a teacher, but rather as a group facilitator. As such, the tutor should not use a didactic method of instruction, but rather should guide the students to keep them on track without discouraging useful tangents, and to ensure that the information gained at a session is correct. In addition, the tutor should bring up key points which otherwise would be missed.

## HOW TO USE THE MANUAL

The manual provides supplementary material for each laboratory and tutorial in the course.

For the tutorials much of the information is incorporated in a question and answer format. It is the role of the tutor to try to draw out the answers to the questions posed. If the students have prepared well for the sessions, they should be able to answer many of the questions. Some questions, however, have answers which are not necessarily found in textbooks. These questions require time to think about and additional probing questions before they can be answered. The format used from one group to another will invariably be different. Thus, the tutor may find that rather than pose the questions as they are given in the manual, they should let the students come up with questions which cover the concepts. Again, the tutor's role is to ensure the contents of the tutorials are covered.

Because of the less structured format of the laboratories, with the students working primarily in pairs, the contents covered by the laboratories is presented in a more general manner, as opposed to a question and answer format. The tutor can decide the method which he/she feels most comfortable with to draw this information from the students. The tutor may feel that circulating among the pairs as well as meeting as a whole group at the beginning and end of the session is appropriate.

Finally, it must be emphasized that because the lab/tutorial portion of this course is meant to incorporate some of the features of self-directed learning, tutors and students are encouraged to explore any topic in more detail as they arise.

## SOURCES

The original laboratories and tutorials upon which some of the present laboratories and tutorials are based were prepared by the following faculty members at McMaster University: Dr. Zeba Ansuri, Dr. A.K. Ball, Dr. G.D. Buchanan, Dr. D.H. Carr, Dr. J.E.T. Fox, Dr. H. Groves, Dr. G.J.F. Heigenhauser and George Lewis.

The figures are adaptations from figures in the following textbooks:

1. Van de Graaff, K.M. (1988). Human Anatomy (2nd ed.). Dubuque, Iowa: Wm. C. Brown Publishers.
2. Vander, A.J., Sherman, J.H. & Luciano, D.S. (1985). Human Physiology (4th ed.). New York: McGraw-Hill Book Company.
3. Walter, J.B. (1982). An introduction to the principles of disease (2nd ed.). Philadelphia: W.B. Saunders Company.

## STUDENTS' GUIDE TO TUTORIAL PROBLEMS

You may find yourself wondering how to approach each tutorial problem, and how much detail in terms of the information is required for tutorials. Here are a few points to keep in mind:

1. Follow the objectives listed in the tutorials and laboratories to focus preparation for the sessions.
2. Use the questions posed in the problem as a guide to the concepts that should be emphasized in preparation for the tutorial. These questions are often quite general but will help to provide a focus on the direction of the topic to be dealt with.
3. Anyone can memorize numbers and facts about clinical conditions. That is not the objective of these tutorial sessions. Rather, for a given condition or topic, consider such questions as:
  - a. Why has this condition or situation arisen?;
  - b. What are the underlying mechanisms?;
  - c. What is the physiological or anatomical basis for what is seen?;
  - d. What factors would play a role in the development of this condition?
4. The references which are listed are only **suggested**; other ones could be equally useful and appropriate for your needs.
5. For some tutorial problems, the question of the use of drugs arises. Do not be concerned with specific names of drugs, but rather how and why they work. In order to do this, a good understanding of the underlying condition is essential.
6. Remember that each student will come to each tutorial with a different knowledge base about the problem. This knowledge base will depend on the resources which each student used to deal with the problem, and to some extent, clinical experience. This knowledge should be passed on to the group members. Raise any questions or concerns you have about the topic. Also, don't be concerned if you didn't come up with all the answers. In fact, some interesting issues will arise which are not encountered while researching the problem.
7. Above all, a tutorial is not a beneficial exercise for you unless you ask the question: "Can I **USE** this knowledge?" Applications may not be readily apparent, but if a particular problem is considered from a number of perspectives, you may find ways in which the information will indeed be useful now and in the future.

## Tutorial One

### THE CELL

#### Objectives

1. Review the requirements of the cell.
2. Review the biochemical composition of cells.
3. Review cell organelles and their functions.

---

It is the year 3000 and the chief scientist of the galaxy has assigned you to work on the completion of an artificial planet, 'New Earth' to replace earth as it was known in the year 2000. You are given the task of developing a single cell which will ultimately evolve into a multicellular being such as man. In order to complete this task, you have been advised to review these questions.

What type of environment is necessary for cell survival?

What will this new cell be made of?

What functions will it ultimately be capable of, and what structures must this cell possess to perform these functions?

**Tutor Notes - Tutorial One****THE CELL****Objectives**

1. Review the requirements of the cell.
  2. Review the biochemical composition of cells.
  3. Review cell organelles and their functions.
- 

**Q1. What are the requirements of a single cell?**

1. Nutrients: proteins, carbohydrates, fats

**Q1a. What are the main functions of these molecules?**

Proteins: work as enzymes to catalyze the reactions in the body; may be contractile; provide cell structure

Carbohydrates: provides an immediate source of energy for the body as well as a means for the storage of energy

Fat: insulates and protects the body; a source of stored energy; fat is a component of cell and organelle membranes

2. Ions

**Q1b. What are some of the roles which ions play in cell functions?**

Ions are involved in many cell process including: muscle and nerve functions, the maintenance of proper water concentrations, enzymatic processes, blood clotting, bone development.

This is a good time to introduce the students to the concept of osmosis:

**Q1c. How do ions influence water concentration?**

If two solutions have different concentrations (of ions) and are separated by a membrane which only allows the passage of water, water will move down its concentration gradient until the solutions are iso-osmotic.

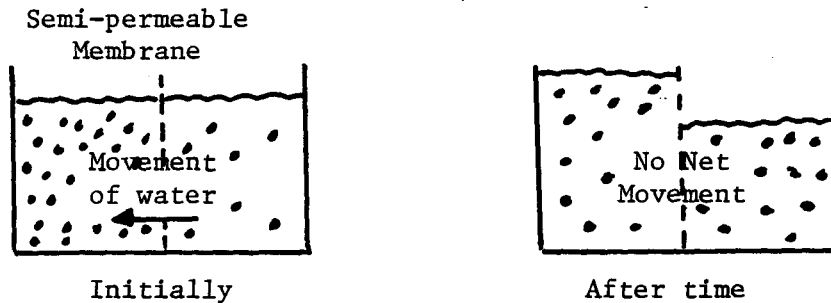


Figure 1A

### 3. Oxygen

Q1d. What is the role of oxygen?

Oxygen is required to release the energy from foodstuffs. This energy is required in order to drive the cell's metabolic activities.

(aside)

Q1e. Why has aerobic metabolism been favoured in evolution over anaerobic metabolism?

The amount of energy, or ATP produced through aerobic metabolism is much greater than that provided in the absence of oxygen. In addition, anaerobic metabolism results in the build-up of lactic acid which increases pH and impairs cellular functions.

### 4. Water

Water is the most abundant substance in the body.

Q1f. What are the functions of water?

Water provides an environment in which reactions can occur, as well as directly taking part in reactions. It also provides a means by which substances can be transported throughout the body.

### 5. Temperature

A temperature which is compatible with an aqueous environment, and one at which metabolic reactions can occur, is essential.

Q2. What will the cell be composed of?

Twenty elements are needed by living organisms; carbon, oxygen, hydrogen and nitrogen comprise 95% of constituents of the organism. These elements will form the molecules of life: carbohydrates, protein, fats, and nucleic acids.

### Q3. What structures do these components make up in the cell?

The way to address this question is to consider some of the functions which are required of the cell, and then discuss what structures are responsible for these functions.

#### 1. Synthesis of new Material

Some structures which are responsible for this ('anabolism') are the endoplasmic reticulum, ribosomes and Golgi apparatus.

#### 2. Production of Energy

The mitochondria are called the 'powerhouse of the cell'. More specifically, the membranes and fluid inside the mitochondria contain enzymes which control some of the chemical reaction by which energy is released from glucose and other molecules.

#### 3. Protection

The cell membrane provides a selectively permeable barrier. It provides a regulatory function by allowing some substances to move into and out of the cell. It can also actively take up or expell various substances which it does or does not require. Thus, the cell membrane provides protection for the cell by regulating its composition.

#### 4. Destruction of Foreign Material

Invaders which do find their way into the cell (for example bacteria) must be destroyed. Lysosomes are vacuoles within the cell which contain enzymes that can destroy such foreign invaders. In addition, old worn out parts of the cell can be destroyed by lysosomal enzymes.

#### 5. Movement

Microfilaments in muscle cells are highly developed and enable cells to shorten or contract. Microtubules, long and slender tubes composed of globular proteins, aid in moving organelles from one place to another. Finally, cilia are hair-like projections from cells which help move extra-cellular particles.

## 6. Reproduction

The nucleus contains the genetic material (chromosomes) that divide to produce two daughter cells which have identical genetic material. In addition, structures within the cytoplasm aid in cell division. Centrioles are structural proteins in the cytoplasm which ensure that the chromosomes are drawn to each pole of the cell as it divides.

## 7. Mechanisms for Absorption and Secretion

Cells must be able to receive the necessary molecules from the external environment as well as be able to get rid of waste products. The primary mechanisms involved in these processes are pinocytosis and phagocytosis. These processes rely on the dynamic nature of the cell membrane and its ability to invaginate, be pinched off, and reform. In addition, some cells in the body are specialized to produce essential molecules which can be used by other parts of the body. An example is cells of endocrine glands. Such cells produce a specific hormone which is secreted from the cell into the bloodstream.

### Q3a. Are all cells of the body capable of performing all these functions?

The 75 trillion cells of the human body have much in common, but those in different tissues vary in a number of ways. These adaptations of different cell types are closely related to that cell's function. Thus, not all cells are equipped to carry on all functions.



## Laboratory One

### THE CELL PART ONE

#### Prerequisite Activities:

Read "Use of the Compound Microscope". Read over the introductory material on epithelial and connective tissue in a histology text. Get the basic concepts of what an epithelium is and what generalized connective tissue is made of.

#### Objectives:

1. To learn to set up, focus and use the light microscope.
2. To examine cells from several sources in order to gain initial understanding of cell structure.
3. To learn how to make simple wet mount preparations.
4. To practice recording microscopic observations.
5. To gain an appreciation of the appearance of animal cells in electron micrographs.
6. To learn to recognize the appearance and intracellular location of cell organelles as shown in electron micrographs.
7. To gain an initial understanding of the major tissue types in the body and how cells are organized into tissues.
8. To study the characteristics of epithelium.

#### PART A - USE OF THE MICROSCOPE AND PREPARATION OF SLIDES

##### Materials:

stained slides (epithelium, muscle and connective tissue)  
microscope and light source  
lens paper

##### Methods:

1. Clarify any portions of the instructions for use of the microscope which you do not understand.
2. Get microscope and light source from lab cabinet and proceed through the instructions for its operation, using a stained histological slide.

3. When you feel you understand how to operate the microscope, have the tutor check your technique.

### Summary Questions

1. What is the basic difference between a microscope and a magnifying glass?
2. What is the function of the sub-stage condenser? The iris diaphragm? Immersion oil?
3. Why focus a slide under the low power objective first, when you know you will need to use oil immersion?
4. What cell structures can be seen in a routinely stained histological slide?

## PART B - PREPARATION AND STUDY OF WET MOUNTS AND SMEARS

### Materials:

Microscope slides and coverslips  
 medicine dropper  
 small beaker  
 dissecting needle  
 filter paper  
 light green stain  
 blood sample  
 stain for blood  
 onion

### Methods:

Work in pairs on this part of the exercise. Two different types of slides will be prepared: a blood film and onion cell slide.

Start preparing the blood film first since it must dry, and be fixed and stained before it can be studied. While it is being processed, make and study the wet mount preparation.

### Blood Smears

1. With a clean slide held horizontally (or lying on the table), place a drop of blood near the right end of the slide.
2. A second slide is held at a 45° angle above the blood slide, touching the slide to the left of the blood drop.
3. Draw the angled slide towards the blood until it just touches it.
4. Push the edge of the angled slide towards the left of the

blood slide, drawing a 'film' of blood behind it.

(Steps 3 and 4 should be done with a fairly quick, smooth motion. The film should appear having a 'thumbprint' shape, and have no streaks).

5. Lay film aside to dry.

6. Stain the slide as follows:

- i. immerse slide in stain for 45 sec.
- ii. dip slide in distilled water and remove quickly
- iii. let slide dry

7. Once the film is dry, cover with a thin film of oil. This embeds the cells in a high refractive index medium. Locate a region of film where individual cells are not piled on top of each other. Sketch the different types of cells which you find.

#### Onion Cell Mount

1. Hold an onion slice with concave side facing you and snap it backwards. A paper-thin sheet of epidermis will be seen at the broken edge.
2. With a teasing (dissecting) needle, tear off a small piece of the epidermis and place it in the centre of a clean slide.
3. Add a small drop of tap water to the piece of epidermis.
4. Cover with a clean coverslip.

#### Technique for Coverslipping a Wet Mount

- a. Prop a cover slip at a 45° angle over the drop of water, supporting it with a teasing needle and steadying it with the thumb and forefinger of the other hand.
  - b. Carefully slide the coverslip toward the water drop until it touches.
  - c. Very carefully let go of the coverslip with fingers and supporting it with only the teasing needle, lower it gently to the surface of the slide.
5. Examine slide under low power and high power. What features of the cell structure can be seen?

As you become frustrated trying to see something, remember that

early microscopists made the basic discoveries about cells and even bacteria this way, until staining methods were developed about 100 years ago.

6. Leaving the slide on the microscope stage, place a small drop of light green stain on the slide just to one side of the coverslip. The edge of the stain should barely touch the edge of the coverslip, but be careful not to get the stain on the top of the coverslip.
7. Touch a piece of filter paper to the opposite edge of the coverslip. The stain will be drawn under the coverslip by capillary action. Watch the tissue through the microscope as this happens and observe the tissue becoming stained.
8. Now, examine the tissue and make a simple sketch of an onion epidermal cell.

#### Summary Questions:

1. What is meant by the term "fixing tissue?"
2. What is the purpose of staining microscopic slide material?
3. You are told that a monocyte is "twice as wide" as a red blood corpuscle. What is its diameter in metric units?
4. What does polymorphonuclear mean?
5. What is the relative number of red cells to leukocytes in a blood film?
6. What is the difference in appearance between plant (onion) cells and animal cells?
7. What parts of a cell can you see in a stained slide using a light microscope?

#### PART C - ELECTRON MICROSCOPE DEMONSTRATION

During this portion of the lab exercise, you will have the opportunity of going to the Electron Microscope Unit, and observe the demonstrations on the operations of a transmission electron microscope (TEM), and a scanning electron microscope (SEM). You will be going to the unit in groups of approximately six, accompanied by a TA where you will spend about five minutes at each microscope. Note the type of images that can be seen with each kind of electron microscope, and try to observe the differences between the two types in terms of a) the principles of their operations, and b) the type of information obtainable. Feel free to ask the operators of the microscopes any questions

you may have concerning the microscopes.

Demonstrations of scanning and transmission electron micrographs will be available in the lab throughout the entire session. Remember that the specimens had to be prepared using special techniques in order that they can be visualized in the electron microscopes. This means that what you are looking at are actually artifacts! From the TEM, observe:

- a. cell membrane, nuclear membrane, smooth and rough endoplasmic reticulum, Golgi apparatus, mitochondria and ribosomes.
- b. compare other subcellular components (ex. lipid, glycogen, contractile filaments) between various cell types.

Note the specific types of information obtainable with the SEM. Can you think of advantages and disadvantages of these microscopes for the study of biological specimens?

#### Summary Questions

1. List at least three major differences between light and electron microscopes.
2. What is meant by the "resolution" of a microscope?
3. What are the basic units of length measurement in microscopy?
4. What makes rough endoplasmic reticulum "rough"?
5. Can you see the cell membrane under the light microscope? Some people said they could.
6. In some cell preparations, you just cannot seem to find the nucleus. Why?

#### PART D - HISTOLOGY OF EPITHELIUM

In this exercise you will try to observe an example of each type of epithelium. (Check the handout sheets for the types such as squamous, cuboidal, columnar etc). A box of histological slides which contains many types of tissue will be provided. Decide which slide will be appropriate; there are a number of different choices. Check the textbook to get hints as to what is likely to be found where.

The objective is to try to determine what features epithelia have in common, and to observe their differences.

Here is a list of slides which will be particularly valuable.

However, remember these slides are not the only ones that allow you to find what you are looking for.

- Slide No. 1 - Squamous epithelium
- 2 - Glycogen
- 3 - Polysachrides
- 4 - DNA in pancreas
- 5 - RNA and DNA
- 6 - Adipose tissue
- 7 - Iron in cells
- 9 - Barr bodies
- 11 - Scalp (non-pigmented)
- 12 - Scalp (pigmented)
- 13 - Meissner's corpuscle
- 62 - Colon (epithelium)
- 72 - Trachea (epithelium)
- 89 - Ovary (epithelium)

## Tutor Notes - Laboratory One

### THE CELL PART ONE

There are three aims of this exercise. One is to give the students practice in the use of the microscope, and it is important to insure that they do so properly. If they are unable to do so, have them review the instructions at the beginning of the laboratory manual.

The second aim of the exercise is to study cell structure. This does not imply that they should learn to classify cells (that will come later). Rather, they should learn that what can be seen by light microscopy is basically cell shape and nuclear shape. It is important that they recognize what cannot be seen as well. Specifically, they must understand that with a light microscope, one cannot see the same things that are revealed by the electron microscope (EM). The popular press and ill-trained teachers often imply that an EM scope just magnifies more than a conventional scope. It is also of value for the student to realize that histochemical stains give important chemical information.

The third, (and unannounced) aim of the exercise is to provide the students with an introduction to some simple techniques. This is just as important as the other aims. Certainly, the students are not expected to be accomplished histology technicians by the end of the period. However, having gone through the procedure once, they will discover that it will be fairly easy to do if they need to make a smear or fresh slide again.

#### PART A - USE OF THE MICROSCOPE

When you check the student's technique, hand them a slide; ie., do not let them begin with a slide already on the stage.

Be certain that they routinely start with low power and then go to higher powers.

You will have three types of slides for the students to use; however, they will not be the same in all groups. One slide will have a columnar epithelium, the second will have skeletal muscle, and the third will have one type of connective tissue. Of course, there will be other tissues on the slides as well, but have the student concentrate only on the one type with each slide. The obvious aim is for them to have a visual image of a typical epithelium, typical muscle fibres, and connective tissue.

### Answers to Summary Questions

1. A microscope (like a telescope) has both an objective lens and an ocular lens. A magnifying glass is simply a convex magnifying lens. Leeuwenhoek's original microscopes were really well-made magnifying glasses.
2. Sub-stage condenser - focusses (or condenses) light onto the specimen.  
  
Iris diaphragm - controls the amount of light entering the condenser (the iris diaphragm serves only to exclude aberrant light rays, not as a dimmer).  
  
Immersion oil - channels light into the lens from the specimen. (Technically, it prevents refraction and loss of light leaving the specimen).
3. Primarily, starting with low power is safer. In addition, by starting under low power, one can get oriented much easier and save time in searching for the area of the tissue to be examined.
4. The structures that can be seen in a routinely stained histological slide are: the shape (or outline) of the cell; the nucleus (and nucleoli), its shape, size and location; large inclusions such as vacuoles; and villi and cilia.

Depending on the stain used evidence of brush borders (microvilli), endoplasmic reticulum, and mitochondria can often be seen. However, this involves understanding the properties of the stains. Most routine stains simply colour the tissue to make it visible and should not be relied on to provide precise identification (ie. cytoplasm is not necessarily pink as it is in the H&E slide).

### PART B - PREPARATION AND STUDY OF WET MOUNTS AND FILMS

Make sure the students make the blood film first and then begin making their wet mount slides while the films are being dried and processed.

Each students must make at least one film and one wet mount, although if there is enough time, encourage them to make more.

Once the blood films have been prepared, have the students sketch the cells they see. Make sure they understand that there are several kinds of white blood cells which have different functions and structural characteristics.



### Answers to Summary Questions

1. Fixing tissue involves the inactivation of the intracellular components. (Most fixatives cause protein denaturation or precipitation).
2. The purpose of staining microscope slide material is to make the specimen visible. (Colours are diagnostic when specific histochemical techniques are applied).
3. The diameter of a white blood cell is about 14  $\mu\text{m}$  (microns or micrometers) or  $14 \times 10^{-6}$  m. (For comparison, a red cell is approximately 7  $\mu\text{m}$ ; it is a useful 'ruler' present in every field!).
4. Polymorphonuclear literally means 'many-shaped nuclei'.
5. The ratio of white to red blood cells is about 1:1000. The exact number is only secondary. They should understand that there are many more red cells.
6. The diagnostic difference is the visible cell wall of plant cells.
7. As previously discussed, the nucleus and the cytoplasm (and sometimes inclusions) can be seen under the light microscope. Make sure the students do not get the notion that they can see organelles such as mitochondria, rough endoplasmic reticulum, ribosomes etc.

### PART C - ELECTRON MICROSCOPIC STUDY OF CELLS

The main purpose of this part is to give the students an opportunity to see some of the structures which are going to be mentioned in the course. In particular, they need to understand that a cell looks very different in an electron micrograph and under the light microscope. They should also appreciate that most organelle membranes are trilaminar, not just the cell membrane. They need to see why the term trilaminar is used.

### Answers to Summary Questions

1. Differences between electron and light microscopes are as follow:
  - (1) the source of energy for image formation is different. The energy source is photons in light microscopy and electrons in electron microscopy.
  - (2) The lenses are different. The lenses in light microscopes are glass, and are magnetic in electron microscopes.

- (3) The resolution is greater with electron microscopes (by over 700 times). The resolution for the light microscope is 0.25  $\mu\text{m}$  and 3.5  $\text{\AA}$  for the electron microscope.
- (4) Observation of living cells and larger specimens is possible with the light microscope and is not possible with the electron microscope.
- (5) There are various other differences such as tissue preparation and cost.

2. The basic units of length measurement in microscopy are:

micrometer ( $\mu\text{m}$ ) or micron ( $\mu$ ); and nanometer (nm).

Make sure the students are aware of conversions among these units:

1 m = 1000 mm  
 1 mm = 1000  $\mu\text{m}$   
 1  $\mu\text{m}$  = 1000 nm

See if they can now convert nanometres to metres ( $1 \text{ nm} = 10^{-9} \text{ m}$ ).

3. The presence of ribosomes on endoplasmic reticulum is what makes it 'rough'.
4. The cell membrane is not visible under the light microscope. People who claim they can see it are making an inference of its presence, not a direct observation.
5. The reason a nucleus is not always observable is simply that some cells do not have nuclei, for example, red blood cells. The required stain to make them visible may not be present. Finally, the section may be cut so that only a part of some cells is present.

The demonstration of the electron microscopes is meant to give the students a chance to see the operation of electron microscopes which they have heard so much about. The important things to stress to the students are the differences in the operation and uses of different types of microscopes; one would choose a particular type depending on the particular needs.

#### **PART D - HISTOLOGY OF THE EPITHELIUM**

Two main purposes are involved:

1. To give the students more time to practice their newly-acquired skill of using a compound microscope.

2. Learn to associate structures seen on slides with textbook figures. This will be useful for the following lab when they will look at a number of slides. They will have seen many of the listed slides in the lectures. It is not important for them to see all the slides, but they should at least try to identify the types of epithelia, and know the difference between squamous and columnar epithelium.

## Tutorial Two

### MRS. WHITE: DECUBITIS ULCER

#### Objectives

1. Discuss the etiology, development and factors contributing to decubitus ulcers.
  2. Consider the functions of the skin.
  3. Gain an introduction to the body's reaction to injury by looking at acute inflammation and the healing process.
- 

Mrs. Emily White, 78, has just been brought into your ward. She has been only able to get from the bed to the chair and to the bathroom with her husband's help since her arthritis became worse, 3 years ago. Her 80 year old husband in the past had helped her move her position frequently but he fell six weeks ago and was hospitalized for a broken hip. Mrs. White has since relied on her neighbors to come in four times a day to help her, however, she was lonely and although the meals looked lovely they didn't taste familiar. Mrs. White felt that she should only ask for a minimum of help, therefore, she remained sitting much of the day in one position. On admission, Mrs. White is noted as being a thin, frail lady, slightly under nourished with a large decubitus ulcer at the base of her spine.

What is a decubitus ulcer? How is it formed? What factors may contribute to their development? Who would be likely to develop them, and where would they most likely occur?

What are the main functions of the skin?

Mrs. White is kept on the ward for several days. What measures must you take in treating the ulcer? What measures should be taken for all patients in order to prevent decubitus ulcers from developing?

Ulceration of the skin will initiate inflammation. Be prepared to discuss the physiological changes that occur with inflammation, and the healing process.

**Tutor Notes - Tutorial Two****MRS. WHITE: DECUBITUS ULCER****Objectives**

1. Discuss the etiology, development and factors contributing to decubitus ulcers.
  2. Consider the functions of the skin.
  3. Gain an introduction to the body's reaction to injury by looking at acute inflammation and the healing process.
- 

**Q1. What is a decubitus ulcer?**

A decubitus ulcer is an area of cell necrosis on skin resulting from the loss of blood flow to the area. Synonyms are 'bed sores' or 'pressure sores'.

Four stages have been described:

Stage I Pinkish-red, mottled skin, the colour of which does not return to normal colour after the pressure has been removed.

Stage II Cracked, blistered, broken skin.

Stage III Broken skin with tissue involvement, exudate and distinct ulcer margin.

Stage IV Extensive ulceration; penetration to the bone and muscle; necrotic tissue and profuse drainage.

**Q2. Why do decubitus ulcers develop and what factors contribute to their development?**

Prolonged pressure to an area may result in the collapse of blood vessels and therefore blood flow to an area will be decreased.

**Q3. Why is blood flow essential to an area?**

Blood is required for the delivery of oxygen and nutrients, as well as for the removal of waste products. Cells cannot survive without proper blood flow.

**Q4. What factors may contribute to the development of decubitus ulcers?**

1. moisture of skin (reduces skin's resistance to trauma)
2. anything which results in decreased movement (for example: drugs (sedatives); age; pain (causing apprehension to move); and depressed a mental state)
3. skin temperature (too cold - decreased blood flow; too hot - increased oxygen demand)
4. scar tissue (not as strong so if there has been a decubitus ulcer, another one is more likely to redevelop in that area)
5. shearing forces/friction - layers of skin moving on each other; most likely sites for this to be a problem is the heels or the sacrum



Figure 2A

**Q5. What patients are more prone to developing decubitus ulcers?**

1. obese (increased weight causing increased pressure)
2. thin (less subcutaneous fat so skin lies in a thin layer over bony prominences)
3. paralyzed (or any immobilized patient)
4. elderly (due to less spontaneous movement and less fat)
5. infections (increased basal metabolic rate resulting in decreased oxygen availability)
6. depressed patients may tend to remain immobile, and may have a depressed immune system

**Q6. What areas are most likely to develop decubitus ulcers and why?**

The back of the head; spines of the scapula; heels; iliac crests; lower sacrum; ribs; ischia; and greater tronchanters are areas which are especially prone because:

1. they are areas with little subcutaneous tissue (thus have less

'cushioning');

2. these are areas which are not adapted to bear weight for long periods of time (such as our feet);
3. in certain positions (such as supine) patients' weight is borne specifically by these sites.

**Q7. What preventative measures would you take to prevent their occurrence?**

1. frequent turning
2. keep skin clean
3. keep weight distribution as even as possible
4. patient education: teach the importance of turning

The end result of a decubitus ulcer is a break in the skin. The skin is the largest organ in the body and it plays an important role in the maintenance of homeostasis.

**Q8. What are the functions of the skin?**

1. protection from injury and disease (outer layer), and ultra-violet light (inner layer)
2. prevent dehydration or water absorption
3. regulation of body temperature

(aside)

**Q8a. How is this achieved?**

Body temperature is regulated by vasoconstriction/dilation at the body surface, and by the secretion and evaporation of sweat.

**Q8b. Why is the regulation of body temperature so important?**

Metabolic processes involve chemical reactions whose rates are affected by temperature. Even slight shifts in body temperature can disrupt the rates of such reactions and produce metabolic disorders.

4. sensory receptors
5. vitamin D production
6. excretion of waste products and regulation of body fluids

much more important for this)

The remainder of the tutorial focuses on the bodies reaction to injury. Local reactions are concerned mostly with changes in the connective tissue. Blood vessels dilate and become more permeable, allowing plasma and white cells to leak into the area. This reaction is acute inflammation.

**Q9. What are the possible agents which can trigger the acute inflammatory response?**

1. physical damage/injury
2. chemical agent
3. infection/Ag-Ab complexes
4. infarction

**Q10. What changes in the systemic circulation are responsible for the increased blood flow to the area?**

1. arteriolar dilation
2. closure of thoroughfare channels between arterioles and venules so blood flows through capillaries

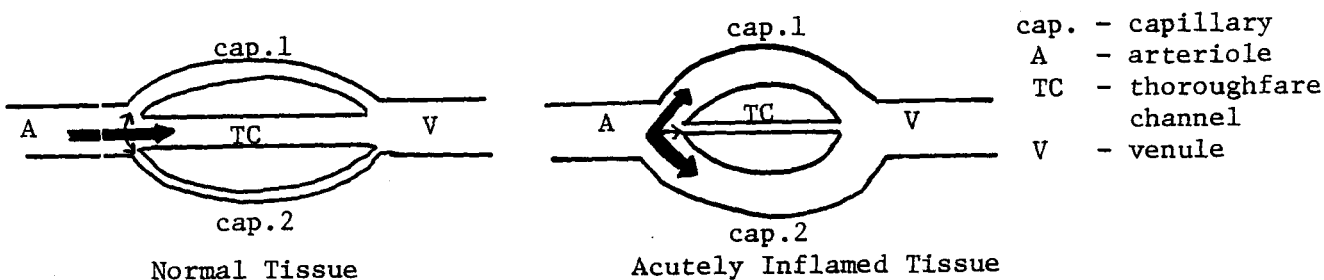


Figure 2B

**Q11. What changes take place within the vessel walls and what effect will this have?**

Spaces between adjacent endothelial cells widen allowing exudate containing plasma, proteins and blood cells to escape from the vascular space into the interstitium (normally only fluid, electrolytes and small molecules are able to leave).

(aside)

**Q11a. How could a scientist study changes in permeability and the movement of protein from the vascular space?**



Proteins could be tagged with a dye or radioisotope, so the accumulation of dye or isotope becomes an index of increased vascular permeability.

**Q12. How will the movement of proteins from the vascular space affect the movement of fluid?**

The plasma osmotic pressure exerted by the proteins will be lost so fluid will leave the vessels to form the 'fluid exudate'. (Fluid shifts and osmosis will be covered in the next tutorial).

The leukocyte infiltration plays an important role in the inflammatory response.

**Q13. What role do neutrophils and monocytes play in the inflammatory response?**

Neutrophils are the first type of leukocytes to emigrate to the site, and they serve two functions: phagocytosis, and the release of chemicals involved in inflammation. Blood monocytes emigrate out of the vessels to become tissue "macrophages": large phagocytic cells.

(Aside) At this point it might be useful to review a bit about cell structure; this situation is a good example of cell specialization.

**Q13a. What structure(s) would you expect to be particularly well developed in monocytes?**

After the cell enters the wound it undergoes changes; it develops extensive endoplasmic reticulum and ribosomes. Now the cell is well equipped to synthesize the enzymes (ie. proteins) required to degrade the ingested debris.

**Q14. How do these cells reach the site of injury?**

White blood cells adhere to the vessel walls and push pseudopodia between adjacent endothelial cells. This is called the 'emigration of white cells'. Chemotaxis plays a role in this process. Initially neutrophils are the predominant leukocytes. Later on these are replaced by monocytes.

**Q15. What are the signs of inflammation? Explain these signs, based on the physiological processes involved in the inflammatory response.**

Inflammation is characterized by redness, swelling, pain and fever. The redness can be explained by the increased blood flow to the area. Swelling, or 'edema' is the result of the fluid accumulating in the extravascular space. The pain which

accompanies inflammation can be explained by both increased distention from the swelling, and the effect of locally produced substances on afferent nerve endings. Finally, fever is the result of endogenous 'pyrogens'. These are chemicals which are released by the neutrophils which are responsible for raising the 'set-point' body temperature.

The healing process is complex and somewhat variable; it depends on the site and extent of injury. A general outline of the process should be considered.

Granulation tissue is formed by the proliferation and immigration of surrounding connective tissue elements. Buds of endothelial cells grow from existing vessels at the wound margin. Because the plasma proteins have leaked, as discussed above, fluid will be bathing the area and it provides an excellent nutrient medium. Differentiation of these vessels occurs; some develop muscular coats and become arterioles and others form thin-walled venules. Fibroblast-like cells multiply and accompany the vascular invasion. They produce collagen and ground substance. Scar tissue forms when the collagen molecules aggregate into fibrils. After about two weeks the process of remodelling takes place; many of the randomly oriented smaller collagen fibres are broken down and reassembled into thick bundles and eventually gather into large fibres that look much like those of undamaged tissue. Similar to monocytes, the endoplasmic reticulum is highly developed in fibroblasts since its primary function is protein synthesis.

Lymphatic vessels and nerve fibres grow into the maturing granulation tissue.

#### **Q16. What factors will influence wound healing?**

##### **1. Local Factors**

- a. blood supply - this is variable from one part of the body to another. For example, the scalp and face have a large blood supply and the legs have poor blood supply.
- b. continued tissue breakdown, such as that caused by infection, or a foreign body. Constant movement may also slow down the healing process if the edges of the wound are continually being disrupted. This results in damage to the delicate granulation tissue.

##### **2. General Factors**

- a. Age - circulation decreases with age; proliferation and synthetic capacity of cells decrease with age.

b. Nutrition - low protein diet may result in defective collagen formation.

## LABORATORY TWO

### THE CELL PART TWO

There are two parts to this lab. First, a series of prepared microscope slides will be provided. Examine these in order to gain a better understanding of various cell types and tissues. You will also get a chance to get your hands wet; a pig's foreleg and dissecting instruments will be provided. A dissection of this joint will be useful as you will actually see the structures in a joint.

#### PART A - HISTOLOGY

##### Prerequisite Activities:

Read the pertinent sections from your histology text book. Bring lecture handouts, sharp pencils, drawing paper, and your histology text book.

##### Objectives:

To learn to identify various cell types and structures in different tissues.

##### Methods:

Study the slides provided, beginning with low power objective, then with high power (40x). 100x lens is to be used only under the supervision of a TA. Whenever possible, make simple, accurate drawings of what is seen, and label the structures. The practice of drawing will force you to observe more critically the shape and colour of different structures. LS and CS on the slide refer to longitudinal and cross-section, respectively.

#### 1. Connective Tissue

Areolar tissue: Slide 62. Collagen fibre bundles are abundant. These are long, red, parallel-strands of fibres. The elongated cells among the collagen fibres are the fibroblasts. Elastin fibres may also be present, but they are more difficult to see.

Reticular tissue: Slide 43 (lymph node). Under 40x lens, look for the light blue fibres (reticular fibres) among the lymphocytes in the lymph nodes. Occasionally, you can see the fibres attached to a large blue cell, which is the reticular cell. They form the frame work of lymphoid organs, bone marrow and liver. Reticular fibres are also found in the lining of the stomach, intestine, trachea and bronchi.

**Adipose tissue:** Slide 6. Fat cells appear as round, empty spaces, but the nuclei of the cells which are displaced toward the periphery of the cells, are still visible. They appear as empty space because the solvents used during tissue processing dissolved away the fat. See also slide 15 (breast). Fat cells are easily identified. Note also the loose connective tissue (mainly collagen) between ducts and groups of cells.

**Mucous connective tissue:** Slide 97 (umbilical cord). It is known as Wharton's jelly in the umbilical cord. The ground substance is jelly-like. Most of the cells seen among them are fibroblasts.

**Hyaline cartilage:** Slide 72 (trachea). The cartilage is the smooth-looking structure filled with holes (lacunae). Chondrocytes are found inside these holes.

**Bone:** Slide 18 (ground bone). There are two types: cancellous (or spongy bone), found inside a bone with a mesh work filled with bone marrow; and compact (or dense) bone, found at the peiphery of the bone. Both are on the slide. Try to identify the Haversian system, lacunae, canaliculi, osteocytes and lamellae.

**Blood film:** Slide 47. Together with cartilage and bone, blood is another example of specialized connective tissue. RBCs should be easy to see. Try to find other blood cell types such as eosinophils, neutrophils, basophils, and lymphocytes.

## 2. Muscle

**Smooth muscle:** This type of muscle is found in blood vessels (slide 40, 41), organs of alimentary canal (slides 53-64), associated with airways (slides 72-74), and many other tissues. Note the shape of the cells, and the position of the nucleus, and compare that with the other types of muscle.

**Skeletal (or striated) muscle:** (slide 33). Note the cross-banding in the muscle cells.

**Cardiac muscle:** Slides 37 (heart muscle) and 38 (intercalated discs). Try to look for LS and CS of the muscle from these two slides, and study the position of the nuclei. Can you find the intercalated discs in slide 37?

## 3. Nervous Tissue

**Cerebellum:** Slide 27. Look for Purkinjie cells. These are large, dark brown cells found between the outer zone, and inner dark,

granular zone. Also, note the dendrites (fine dark lines) radiating from the nerve cells.

**Cerebrum:** Slide 29 (neuroganglia cells). Look for large, dark staining cells with fine projections (multipolar neurons) among the yellow matrix. Some are pyramid-like and others are star-shaped. CAUTION! Large granules surrounding and also inside the tissue, are staining artifacts. Learn to distinguish them from neurons. Astrocytes are also present. Can you find them?

**Spinal cord:** Slide 30. Before putting the slide under the microscope, observe the two regions (white and gray matter) which appear as brown and blue areas, respectively, on the slide. Under the microscope, try to find the motor neurons in the gray matter (large, blue cells with extensions). The dark brown structures you see are RBCs in capillaries and blood vessels.

**Spinal ganglia:** Note the large ganglion cells among the nerve fibres.

### Summary Questions

1. Can you distinguish between collagen and reticular fibres?
2. List two characteristics which can be used to separate the three muscle types.
3. Which of the three muscle types is called voluntary muscle?

### PART B - JOINT DISSECTION

For this part of the lab, work in groups of 4 students.

#### Prerequisite Activities:

Before beginning this exercise, look over the following in the text book in order to have a general idea of the things you will see.

1. The general structure of a typical synovial joint.
2. The histological nature of a tendon and how a tendon joins (blends may be a more appropriate word) with a muscle.
3. A synovial sheath, its general structure and location.
4. A skeletal muscle.
5. A (long) bone. What is the shaft? The marrow cavity? The epiphysis? The diaphysis?

**Objectives:**

1. To examine the structure of a synovial joint and learn how it functions.
2. To see the relationships of tendons to a joint and their anatomic relationships to bones over which they pass.
3. To examine the gross appearance of skeletal muscle and bone.

**Materials:**

dissecting pan  
scalpel  
scissors  
forceps  
fore-leg of pig

**Methods:**

The main objective of this exercise is to study the structure of a synovial joint. However, the material offers an opportunity to see several other structures and make some useful comparative/functional correlations. The specimen is the fore-leg of a pig, and the joint is comparable to a human wrist joint. The material was obtained from a commercial packing plant and each specimen may be cut slightly differently. Therefore, if your specimen shows some feature poorly, or not at all, check the material of other members of your group. One of the specimens will surely have most of the necessary structures.

Step 1. Examine the cut cross-section of the material. Note the relationship of skin, muscle and bone to each other. Next, note the subcutaneous connective tissue beneath the skin. It will probably be fatty. The tela subcutanea serves as a sort of insulating coat. Likewise it provides a pad beneath the skin proper.

Step 2. Look at the muscles. Note that they tend to be in two groups, the flexors and the extensors. You may even see a connective tissue membrane extending from the bone to the skin forming compartments in which the muscle groups lie. If you look at the cross-cut of a muscle you should be able to see white partitions of connective tissue which subdivide the fascicles or bundles of fibres that comprise an individual muscle. The endomysium which surround individual muscle fibres cannot be seen, as these are microscopic. All of the various "mysia" tissue "web" blends into the tendons at either end of the muscle. Thus, when muscle fibres shorten they pull on the bones and cause movement.

- Step 3. Look at the cut section of bone. Note the "ring" of dense (ie. compact) bone which forms the hollow shaft. The cavity inside is the marrow cavity.
- Step 4. Remove the skin from the specimen down to the digits. Look at the muscle tendons as they pass over the wrist joint. Note that some of them lie in small grooves in the bone. At this point they should be surrounded by a connective tissue "tube". These are the tendinous sheaths. They are something like an elongated hollow doughnut and serve to provide a smooth surface for the tendon to slide back and forth across the bone. Carefully slit one of the tendinous sheaths open lengthwise and note the smooth inner surface. Note that the tendon slides back and forth on this well lubricated surface.
- Step 5. Pull at the various tendons and observe the movement of the foot and digits produced. Note that although the muscles (ie. the contractile, red meaty tissue) was located above the wrist joint, they cause movement of the foot and digits below the wrist joint. You might even try to relate some of the muscles to the corresponding ones in your own forearm.
- Step 6. When you are ready to examine the joint proper, flex the joint as much as possible and carefully incise the joint capsule between the ulna and the wrist bones. Open the joint quite widely, but do not sever it completely. Examine the smooth inner surface of the joint. Note the smooth "slick" feel of the surfaces. You should find a small quantity of synovial fluid in the joint cavity. It serves as a lubricant and provides an almost friction-free surface. Examine the surface of the bone in the joint cavity. This surface is covered with cartilage. At some point in the dissection, cut into the cartilage until the bony tissue beneath is reached. How thick is the cartilage cap?
- Step 7. Finally, examine the "sleeve" of tissue which forms the sides of the joint cavity. This tissue was cut in order to open the joint. Note that the inner surface of the "sleeve" is a smooth serous membrane. This membrane is the synovial lining and is the source of the synovial fluid. The outer portion of the "sleeve" is dense regular connective tissue. It comprises the various ligaments, which serve to bind the bones together. (As a general matter, be sure to understand the difference between the terms "ligament" and "tendon". They are histologically quite similar, but anatomically different).



**Summary Questions**

1. Compare a synovial joint and a tendon sheath structurally and functionally.
2. What tissue(s) line(s) a synovial joint?
3. In a few words, describe the structure and function of the fibrous articular capsule.
4. What is the advantage of having a cartilaginous articular surface?
5. What is the difference between the synovial membrane and the articular surface?

## Tutor Notes - Laboratory Two

### THE CELL PART TWO

#### PART A - HISTOLOGY

The main objective of this part of the exercise is to train the students to associate text book figures and description with the actual slides they see. Try to encourage the students to use the text book as much as possible. When the students approach you, although you already know the answers, try to go through the motion of finding the information in the text books. This way they will know how to search for the pertinent information themselves. Try to engage the students in lively discussion about why certain cells or structures are of a particular shape, and what specific functions they may have.

Details on structures, and specific slides are given in the laboratory instructions to the students. They are self explanatory. A few guidelines are given below:

#### 1. Connective Tissue

Try to emphasize the significance of different types of connective tissues in serving different functions in various parts of the body. Many examples are given such as cartilage versus bone.

#### 2. Muscles

Point out that even though there are morphological and functional differences between the muscle types, the mechanisms of contraction (ie. the sliding filament theory) is the same. In cardiac muscle, the intercalated discs may be discernable.

#### 3. Nervous Tissue

Point out the function of Purkinjie cells (functional units in the cerebellum exerting inhibitory influences in relation to the movements of the striated muscles, concerning posture, equilibrium and coordination).

In slide 29, the large, amorphous granules are probably stain deposits from the silver stain used for these slides. Astrocytes are star-shaped cells with radiating dendrites.

#### Answers to Summary Questions

1. In longitudinal section, collagen fibres appear as parallel strands, whereas reticular fibres are always net-like. Long, thick cells (fibroblasts) are located among the collagen fibres, whereas large cells (reticular cells) lie among

reticular fibres and are connected to the fibres.

- 2i. The nuclei. Nuclei are central in smooth and cardiac muscles, but peripheral in skeletal muscle. In addition, smooth muscle fibres have only one nucleus, cardiac muscle fibres have one and sometimes two, while skeletal muscle fibres have many nuclei.
  - ii. Banding Pattern. Smooth muscle fibres lack cross striations under the light microscope. Cardiac muscle fibres bear a slight resemblance to skeletal, but their fibres branch and anastomose so the spaces between them are slit-shaped and the intervening spaces are filled with loose connective tissue.
3. Skeletal muscles are 'voluntary'; their movement is under conscious control.

#### **PART B - JOINT DISSECTION**

The instruction on the exercise sheet should be adequate to follow with a minimum of assistance. The prime point to be gained from the dissection is an opportunity to actually see and feel the interior of the synovial joint.

Points the students should note are:

1. the presence of synovial fluid (it functions to keep the joint well lubricated and helps to nourish the avascular articular cartilage);
2. the 'slick' feel of the articular cartilage;
3. the 'sleeve' of tissue between bones on either side of the joint.

Make sure that the students have a look at the cut cross-section of the antebrachium of the pig and note the relationship of muscle groups to the bone; the relationship of the skin and tela subcutanea to the muscles, etc.; the grooves and tendinous sheaths where tendons slide over the wrist bones. They should also try pulling on different muscles and tendons to produce movement of the digits.

#### **Answers to Summary Questions**

1. Both synovial joints and tendinous sheaths are closed cavities containing a small amount of lubricating fluid. The joints have two cartilaginous articulating surfaces that are connected by a sleeve of synovial membrane; whereas a tendinous sheath is a tube in a tube of synovial membrane.

Both function in a similar manner: two apposed surfaces glide over each other.

2. The answer is contained above: cartilage and synovial membrane line a synovial joint. Make certain that the students understand that the synovial membrane does not cover the articular surface.
3. The articular capsule is best described as a sleeve of connective tissue which encloses the sides of a synovial joint. It bridges from the lateral edge of the articular surface of one side of the joint to the edge of the articular surface on the other side. It functions to (1) help hold the bones in proper alignment and (2) to support the synovial membrane and keep the closed synovial cavity intact.
4. Cartilage makes a smooth bearing surface and is also slightly compressible (ie. it does not shatter under pressure). More important, cartilage can grow and replace worn away material at the surface.
5. As noted elsewhere, the synovial membrane lines the articular ligamentous sleeve only. It is an epithelium which secretes synovial fluid. The membrane originates at the periphery of the articular cartilage and may extend for a considerable distance on the bone and connective tissue before reflecting onto the inner surface of the fibrous capsule. This is particularly true in joints with a considerable range of motion. The articular surface is cartilage which acts as the bearing surface.

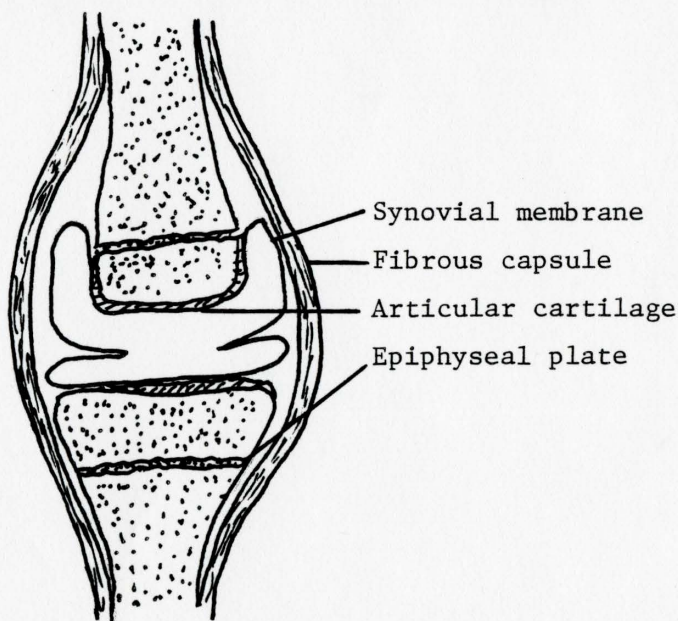


Figure 2A

### Tutorial Three

#### FLUID SHIFTS AND FLUID BALANCE

##### Objectives

1. Provide an introduction to capillary structure and function, and the forces which act at the capillaries.
  2. Discuss the electrolyte and fluid changes that occur in thermal burns of the skin.
  3. Understand what is meant by congestive heart failure.
  4. Describe the fluid shifts in left ventricular failure, and right ventricular failure.
- 

##### Scenario #1

Mrs. Johnson was in the kitchen making dinner when the phone rang. She went to the living room to answer it, leaving her 4-year-old, Peter in the kitchen. It was her neighbour on the phone who had just returned from a trip. Mrs. Johnson was very anxious to hear all about the trip, and therefore she forgot about young Peter and the pot of boiling water she left on the stove. With Mommy on the phone, Peter decided that this was his chance to sneak into the cookie jar. In his climb onto the kitchen counter, he managed to brush his hand against the pot on the stove. It fell to the ground, but not before searing Peter's leg.

When Mrs. Johnson heard his cries, Peter's leg had already been burned quite badly. An area covering roughly eight square centimeters of the outer layers of the skin on his upper leg was burned.

Fluid changes in the body commonly result from changes at the level of the capillary beds. What is the normal structure and function of capillaries, and what forces act there? How will this burn affect Peter's fluid and electrolyte balance?

##### Scenario #2

You are working in the cardiac unit and one of your patients, Fred Hamilton, suffers from chronic congestive heart failure. He has developed a bad cough, and he is coughing up mucous. You also notice swelling in his feet.

What is congestive heart failure? By considering the development of this condition, can you explain the symptoms which Mr. Hamilton has developed? Make sure you distinguish between left ventricular failure, and right ventricular failure. What are the pressures which are involved to account for the fluid shifts?

**Tutor Notes - Tutorial Three****FLUID SHIFTS AND FLUID BALANCE****Objectives**

1. Provide an introduction to capillary structure and function, and the forces which act at the capillaries.
  2. Discuss the electrolyte and fluid changes that occur in thermal burns of the skin.
  3. Understand what is meant by congestive heart failure.
  4. Describe the fluid shifts in left ventricular failure, and right ventricular failure.
- 

The cases of thermal burns and congestive heart failure provide good examples of the principles of fluid shifts which occur in the vascular system. The pressures which determine the flow of fluid into and out of the vasculature are illustrated in these scenarios. In the case of thermal burns, the osmotic pressure is most critical, and the primary force acting in heart failure is the hydrostatic pressure of the blood.

**Scenario 1**

To understand the changes that occur in burns, it is important to go over the normal fluid dynamics that occurs at the capillaries. In order to do this, the structure and function of capillaries as well as Starling forces must be understood. (This knowledge is also necessary for understanding the second scenario).

**Q1. What are capillaries?**

Capillaries are the smallest blood vessels. Their walls are composed of a single layer of endothelial cells. There are many different ways in which these vessels are organized, but all capillary beds form the connection between the smallest arterioles and the smallest venules.

**Q1a. How does the structure of the capillaries relate to their function?**

The endothelial cells are arranged with spaces between, rendering the walls of the capillaries porous. The size of these pores is variable, differing for different tissues. Important substances required by the tissues pass through these pores.

**Q1b. What factors will determine whether or not a substance will leave the vascular space and enter the interstium at a**

### capillary bed?

The permeability of the capillary pores for different substances varies according to their molecular diameters. Water, ions and small molecules (ex. glucose) can pass through the pores. Normally, the plasma proteins and cells in the blood are too large to pass through, though sometimes the proteins can escape. During inflammation, the spaces between endothelial cells increase, allowing the white blood cells and proteins to leave the bloodstream.

Lipid soluble molecules can diffuse directly through the plasma membranes of the endothelial cells, independent of the pores. This is the way carbon dioxide and oxygen enter and leave the capillaries.

**Q1c. What is the most important transport mechanism at the capillaries?**

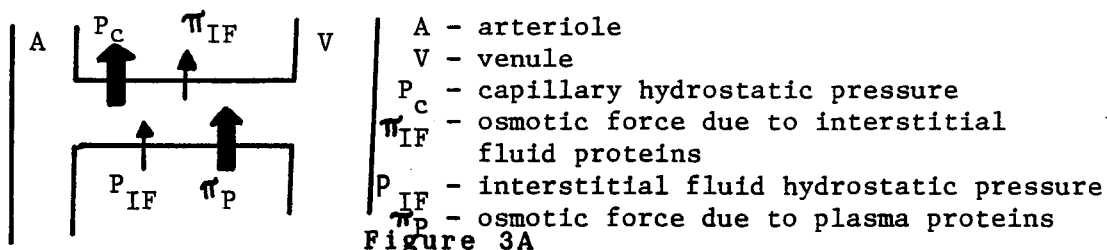
Nearly all substances enter and leave the capillaries by simple diffusion. As the blood passes through the capillary, tremendous numbers of water molecules and dissolved particles diffuse back and forth through the capillary wall, providing continual mixing between the interstitial fluids and the plasma. Despite the rapid rate of diffusion of water, the rates of diffusion into the capillary and out of the capillary are so nearly equal that the volume of plasma in the capillaries remains almost constant.

Because the process involved is diffusion, the net movement will depend on the concentration difference of the molecule in question.

**Q1d. Which tissues of the body would have relatively large pores, and which would have relatively small pores?**

The pores in the capillary beds in the liver are quite large. In fact they are large enough that some small proteins are able to escape from the vascular space. On the other hand, the capillary beds in the brain are almost completely impermeable. This is a protective mechanism and is referred to as 'the blood brain barrier'.

**Q1e. What are the forces which govern the movement of fluid across the capillary membranes?**



The hydrostatic pressure is much greater in the capillary than in the interstitial fluid, so there is a hydrostatic pressure gradient which drives the filtration of protein-free plasma out of the capillary and into the interstitial space. The plasma proteins induce an osmotic flow of water from the interstitial compartment into the capillary.

The forces are different at the arteriolar and venous ends of the capillary. There is net movement out of the capillary at the arteriolar end (filtration), and net movement inward at the venous end (absorption). Over the entire capillary, net movement of fluid is approximately zero. (If net filtration does occur, as in the case of inflammation, the excess fluid can be 'drained' from the region by the lymphatic system).

Having discussed the normal processes occurring at capillaries, you can move on to look at the case of a burn victim, and the effects which burns will have on fluids and fluid shifts in the vascular compartment.

**Q2. What vascular changes will occur at the burn site, and how will this affect the movement of fluid across other capillary beds?**

Intravascular water, electrolytes and proteins are lost through damaged capillaries at the burn site. Proportionally greater amounts of water and electrolytes are lost from the damaged vessels. As a result, the circulating plasma protein becomes more concentrated and the increased osmotic pressure draws fluid from undamaged tissues into all the vascular space throughout the body. The result of this will be generalized tissue dehydration.

The inflammatory process must also be considered. As with any inflamed tissue, the permeability of the capillaries at the burn site will be increased so the plasma proteins will leak out, and carry with it water. This will account for the edema and 'oozing' of serous fluid noted at the burn site.

In addition, intact skin serves as a barrier against the loss of water and heat. When the skin is destroyed by a burn, water and heat are lost. The average water vapour loss from a major burn wound is between 2.5 and 4 liters/day.

### Scenario 2 .

Before beginning to look at this clinical situation, it is necessary to go over the circulatory system. Make sure the students are aware that this is only a brief consideration of circulation. This material will be covered in much more detail when they study cardiovascular anatomy and physiology. However, for this tutorial, it is important to understand the fluid shifts associated with heart failure.



Venous blood returns from the body to the right side of the heart. It drains into the right atrium, then the right ventricle, and from here it enters the pulmonary arteries and then flows to the capillary beds of the lungs, where it is reoxygenated. The blood returns from the lungs to the left side of the heart via the pulmonary veins. It enters the left atrium, then the left ventricle, and it leaves the heart through the aorta. It has now entered the systemic circulation and will perfuse the tissues of the body, before returning to the right side of the heart. (A very simple diagram of this sequence would be helpful).

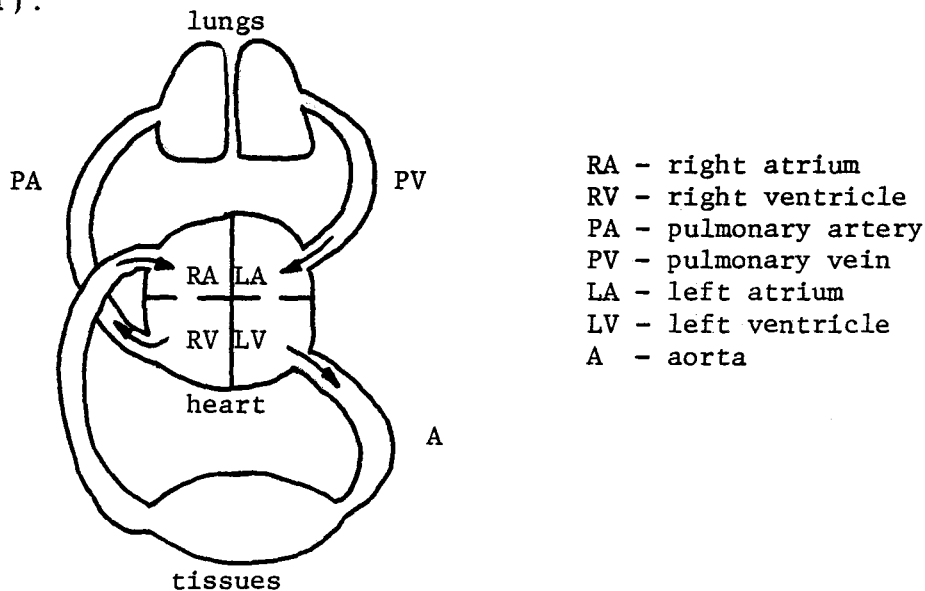


Figure 3B

**Q3. What is heart failure? Distinguish between acute and chronic heart failure.**

Heart failure is not a disease in itself, but rather, the term used for a group of manifestations related to an inadequate pumping action of the ventricles. A widely accepted definition of heart failure is a state in which the heart no longer is able to pump an adequate supply of blood to meet the demands of the body.

Heart failure can be classified as acute versus chronic heart failure. Acute heart failure results from a sudden decrease in the effectiveness of the heart such as in myocardial infarction. Chronic heart failure develops gradually and the patient may initially have only mild symptoms.

**Q4. What happens to intravascular pressure in left ventricular**

### failure?

In left ventricular failure, the left ventricle is unable to pump oxygenated blood coming from the lungs at the volume necessary to meet the demands of the body. When failure first begins, the left ventricle fails to eject its full quota of blood. Compensatory mechanisms exist (such as increased ventricular dilation) but eventually these compensatory mechanisms will not suffice. When this occurs, the amount of blood remaining in the left ventricle at the end of diastole is increased. This increase in residual volume of blood in the left ventricle results in a decrease in the capacity for the ventricle to receive blood from the left atrium. This, in turn, decreases the capacity of the left atrium to receive the full amount of incoming blood from the pulmonary veins and the left atrial pressure increases. This results in an increase in pulmonary venous pressure and capillary pressure.

Q4a. What will the effect be of this increased pulmonary capillary pressure? Before you consider this question, look at a simple diagram of the bronchial tree. Again, this will be covered in detail in second term).

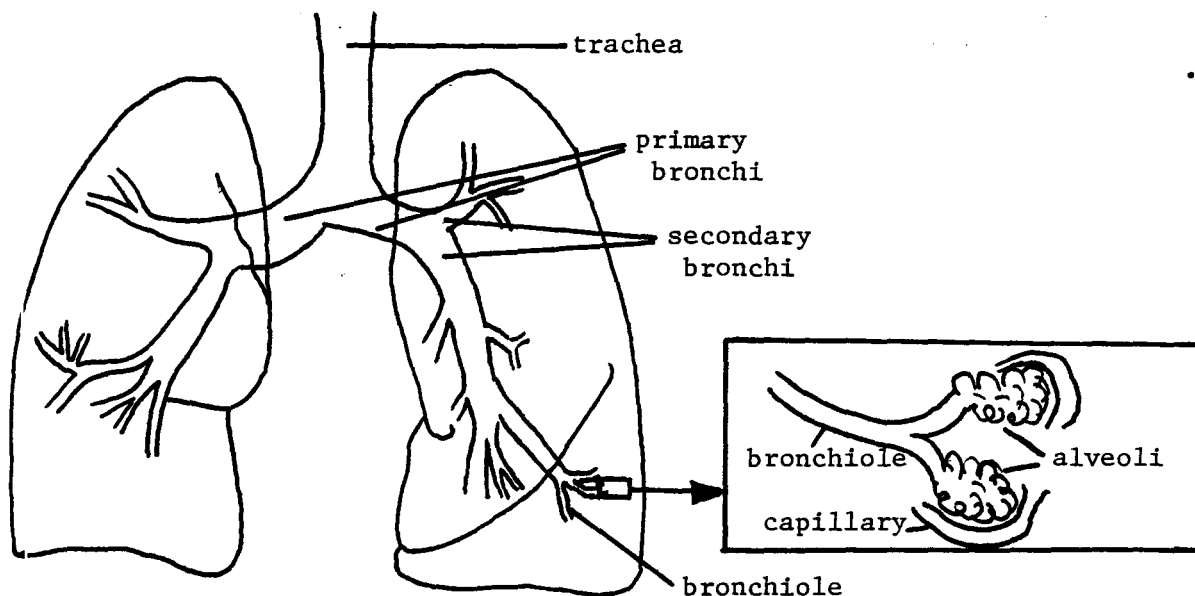


Figure 3C

As the pulmonary capillary pressure exceeds the intravascular osmotic pressure, fluid is forced into the alveoli. Fluid rapidly reaches the bronchioles and the bronchi. It may also reach the pleural space, which is the space between the visceral pleura and the parietal pleura (these membranes line the outer surface of the lung and the thoracic wall, respectively).

Q5. What is the most common cause of right ventricular failure?

**What fluid shifts occur in this condition?**

The most common cause of right ventricular failure is left ventricular failure. Indeed, one rarely sees right ventricular failure without failure of the left ventricle as well. In right ventricular failure, the right ventricle compensates in response to an increase in pulmonary arterial pressure. (You can see that if you continued looking at left ventricular failure, the pressure build-up would reach the pulmonary arteries, then the right ventricle). The right side of the heart would then become less effective and unable to maintain adequate output against the increased resistance within the pulmonary system. The result of this would be blood damming into the systemic circulation leading to peripheral edema.

**Q5a. Explain this resulting edema in terms of hydrostatic and osmotic pressure.**

With the venous congestion in the peripheral vasculature, the capillary hydrostatic pressure increases. (Remember, this is the pressure exerted by the blood against the vessel walls). The capillary hydrostatic pressure would become so great that it would become greater than the osmotic pressure produced by the plasma proteins, which keeps the fluid within the vascular space. This would result in fluid shifting from the vascular space into the interstitium.

**Q5b. In an ambulatory patient, edema first occurs in the feet. Why is this so? What areas are affected next? Would this be different if the patient were bedridden?**

For the blood to return to the heart from the feet, it must act against the force of gravity, thus there is a tendency for blood to pool in the feet. As a result, the hydrostatic pressure is greatest in the feet. As the edema becomes more pronounced, it progresses up the legs into the thighs and the lower trunk. The liver may become engorged, and the pressure within the portal veins of the liver may become so great that fluid leaves the blood vessels and enters the abdominal cavity. The amount of fluid within the abdomen can reach volumes of more than 10 L.

In ambulatory patients, edema will first occur in the feet, and progress from there, as described above. It is most noticeable at the end of the day and may be decreased following a night's sleep. In a patient who is bedridden, pooling in the lower extremities will not occur. Rather, edema may develop in the sacral area, and as it becomes worse, it may progress to the genital region and medial thighs.

## Laboratory Three

### PHYSICAL TRANSPORT OF MATERIALS

#### PART A - FILTRATION

##### Objectives:

To compare filterable materials with non-filterable materials and to demonstrate the importance of pressure induced by the weight of a fluid column.

##### Materials:

funnel	Lugol's solution
filter paper	mixture of charcoal
test tube	copper sulphate
beaker	starch
retort stand & ring	water
medicine dropper	

##### Discussion:

Filtration is concerned with the passage of substances in solution through a membrane. If filter paper, serving as the membrane, is placed in a funnel which is then filled with fluid, the fluid will drip through rapidly when the funnel is full, but as the height of the fluid decreases, the individual drops appear less frequently.

The difference in rate of drop formation depends upon the surface area allowed for filtration and the hydrostatic pressure (i.e., the weight of the fluid column). In this experiment gravity "pulls" the particles of the substance through the pores of the membrane (filter).

Additional force could be exerted by other means. If, for example, the upper part of the filter were contained in a tubular system that was closed and was pressurized with a pump, an increased pressure could be exerted upon the filter. In the circulatory system of the body, both gravity and pumping contribute to the hydrostatic pressure exerted at capillary membranes (the filter). A prime example of filtration in the human body occurs in the kidneys.

In the following experiment, copper sulfate is used as an example of a crystalloid, starch as a colloid, and charcoal as an example of particles in a suspension.

**Methods:**

1. Fold a piece of filter paper as directed, and place it in a funnel. Add a few drops of water to fix the paper in position.
2. Set up a retort stand with a ring support. Place the funnel in the ring over a beaker.
3. Shake the mixture of powdered wood charcoal (black), copper sulfate (blue), starch (white), and pour into the funnel until it almost reaches the top edge of the filter paper.
4. To observe the difference in rate of filtration as the height of the solution in the funnel decreases, count the number of drops passing through the filter in the first 10 seconds. (Make an estimate if an exact count is not possible).
5. When the fluid level is reduced by about one-third, count the number of drops passing through the filter for a period of 10 seconds.
6. Repeat this procedure when the level is reduced by about two-thirds. Record these results.
7. Continue the filtration until the funnel is empty. Observe which substances passed through the filter paper by their color. Check the filter paper to determine whether any colored particles were not filtered.
8. To determine whether starch passed through the filter paper, place approximately 2 cc of the filtrate in a test tube; add a few drops of Lugol's solution. A pale blue to blue-black color indicates starch is present.

**Questions:**

- 1a. What was the number of drops formed in first 10 seconds?
- b. What was the number of drops formed in a ten-second interval when fluid level is reduced by one-third?
- c. What was the number of drops in a ten-second interval when fluid level is reduced by two-thirds?
2. Give a brief explanation of the results obtained in No. 1.
3. What relationship (direct or indirect) was demonstrated between the weight (height) of the fluid column and the rate of filtration?

4. What substances passed through the filter paper?  
What substance did not pass through the filter paper?
5. What is the explanation for the results obtained in Question 4?
6. Where in the human body does filtration occur?

## **PART B - DIFFUSION**

### **Objective:**

To become familiar with the process of diffusion.

### **Discussion:**

Diffusion is the dispersion of substances due to the movement of their ions or molecules. Under appropriate conditions, gas particles may diffuse into another gas, liquid, or solid; a liquid may diffuse into a gas, another liquid, or a solid; and a solid may diffuse into a gas, a liquid, or another solid. Diffusion of solute particles occurs from a region of higher concentration of the particles to a region of lower concentration of the particles. When equilibrium is reached, diffusion occurs equally in all directions. Since the living cells of organisms are not actively involved in the process, diffusion is considered to be a passive transport mechanism.

### **Part 1. Diffusion of a Liquid into a Gas**

#### **Objective:**

To demonstrate the diffusion rate of alcohol into the atmosphere.

#### **Material:**

mercaptoethanol  
petri dish

#### **Methods:**

1. Close all of the doors in the laboratory.
2. One drop of the alcohol will be placed into a petri dish at the front of the room.
3. Obtain the following data, and record them below.
  - a. The exact time the alcohol was poured into the petri dish.
  - b. The seconds required for the first student to detect the

odor.

- c. The seconds required for students in the first row to detect the odor. (Each student will raise his hand as soon as the odor is detected.)
  - d. The seconds required for students in each subsequent row to detect the odor.
4. The experiment will be conducted for a minimum of five minutes.

**Questions:**

1. Did all of the students detect the odor? If not, give a possible explanation for this observation.
2. If the diffusion of the alcohol did not follow a predictable pattern, what factors were present in the environment to cause deviation?
3. Give an example of diffusion of a liquid into a gas in the human body.

**Part 2. Diffusion of a Solid in a Liquid**

**Objective:**

To demonstrate the diffusion of potassium permanganate in water.

**Materials:**

potassium permanganate  
beaker  
tap water

**Methods:**

1. Drop a single crystal of potassium permanganate into a beaker of water.
2. Observe this preparation at the beginning of the experiment and at intervals during the laboratory period. The container should not be touched or disturbed in any way. Record your observations below.

**Questions:**

1. Give a brief explanation as to what happened in this demonstration.
2. Where in the human body does diffusion of a solid through a

liquid medium occur?

### Part 3. Diffusion of a Solid in Agar

#### Objective:

To demonstrate the relationship between molecular weight and speed of diffusion.

#### Materials:

agar in petri dish  
potassium permanganate  
potassium dichromate  
methyl red

#### Discussion:

Agar molecules form a colloid when mixed with water. The molecules of the crystals used in this experiment diffuse through water channels in the agar.

The molecular weight of potassium permanganate is 158; that of methyl red is 269, and that of potassium dichromate is 294.

#### Methods:

1. Place a single crystal of potassium permanganate, a single crystal of potassium dichromate, and a single crystal of methyl red about two inches apart on a film of agar in a petri dish.
2. After one hour, observe the size of the colored ring around each crystal. Record your observations below.
3. At the conclusion of all observations, discard petri dishes in white garbage bins.

#### Questions:

1. The molecules of which substance diffused most rapidly?
2. What was the relationship (direct or indirect) between molecular weight of the substance and rate of diffusion?
3. What part of the cell can the agar be considered to represent?
4. Where in the body does diffusion of this kind occur?



**PART C - DIALYSIS****Objective:**

To demonstrate the types of substances that are dialyzable.

**Materials:**

dialysis tubing	Lugol's solution
distilled water	1% Silver Nitrate
thread	solution of sodium chloride
beaker	glucose
2 test strips	albumin
3 test tubes	starch

**Discussion:**

Since some qualitative tests are to be made in this experiment, it is important that certain precautions be taken to prevent contamination. Because chlorides are present in tap water, only distilled water should be used throughout this exercise to prepare solutions and wash test tubes or other glassware.

**Methods:**

1. Rinse all equipment (beaker, dialysis tubing, and three test tubes) with a small amount of distilled water. Knot one end of dialysis tubing.
2. Place a prepared solution containing starch, sodium chloride, glucose, and albumin in a dialysis tube. Be very careful not to spill any liquid down the outside of the membrane. Do not touch the membrane on the part that is to be placed in the water (i.e. below the planned waterline) because of the salt contained in perspiration. Tie off top of dialysis tube with thread.
3. Place the dialysis tubing in a beaker of distilled water.
4. After one hour perform the following tests on the water in the beaker to see which, if any, of the materials placed in the dialysis tubing have diffused through it.
  - a. Sodium chloride. Place about 2 cc of the beaker water into a clean test tube and add several drops of silver nitrate ( $\text{AgNO}_3$ -). The formation of a white cloudy precipitate indicates the presence of sodium chloride. **NOTE:** Do not put test tube contents down the drain as it contains silver. Discard silver precipitate into glass containers provided at each bench.
  - b. Starch: Place about 2 cc of the beaker water into a test tube. Add a drop of Lugol's solution. A blue-black color

is positive for starch.

c&d. glucose and albumin: Place about 5 cc of the beaker water into a test tube. Use this solution to wet a Hemacombistick or Bililabstick. Read the glucose and protein levels by using the color key on the side of the teststix bottle.

**Questions:**

1. Which substances passed through the membrane?
2. Which substances did not pass through the membrane?
3. From your observations, which type of compound is dialyzable, crystalloids or colloids?
4. In which direction, in terms of concentration of particles, does dialysis occur?
5. Based on the results of this experiment, which components of blood would you expect to remain in the blood vessels and which could move out of the capillaries to form tissue fluid?

**PART D - OSMOSIS**

**Objective:**

To demonstrate the occurrence of osmosis using an osmometer.

**Materials:**

Osmometer demonstration  
test tube  
test strip

**Methods:**

1. Examine the osmometer on the cupboard near the door. It contains a 10% NaCl sucrose solution dyed with methylene blue.
2. Note the level of the fluid in the tube at the beginning of the laboratory period and again near the end of the laboratory.
3. At the end of the lab period, one person from each group should remove a small sample of beaker water and test for sodium and glucose as in exercise C.

**Questions:**

1. Give a complete explanation for the results observed in the experiment.
2. How would an increased strength of the solution in the osmometer affect the final height of the column in the osmometer?

**PART E - HEMOLYSIS AND CRENATION****Objectives:**

To demonstrate hemolysis and crenation.

**Materials:**

3 test tubes	blood
microscope slides	0.9% NaCl
microscope	3.0% NaCl
cover slips	distilled water
graduated cylinder	

**Discussion:**

The term hemolysis is used to indicate lysis of erythrocytes (RBCs) that results in the loss of hemoglobin from the cell. A 0.9% (or 0.15 M) solution of NaCl is isotonic for RBCs. Hemolysis may occur when erythrocytes are placed in a sufficiently hypotonic solution. Hemolysis also occurs when the RBCs are placed in a solvent (e.g., ether) that dissolves the plasma membrane, or in cases where solute particles can penetrate the plasma membrane.

When RBCs undergo lysis, the blood becomes a transparent cherry red color (instead of a dull opaque color), and the hemoglobin becomes uniformly dissolved in the surrounding liquid. Thus, a change from opaque blood to transparent blood may be regarded as an indication of the occurrence of hemolysis.

When cells are placed in hypertonic solutions they may become wrinkled in appearance due to shrinking of the protoplasm. A loss of water from the cell due to osmosis is known as crenation.

**Methods:**

1. Add 3-5 drops of blood to a test tube containing 2 cc of 0.9% (or 0.15 M) NaCl solution. Wash graduated cylinder.
2. Add the same amount of blood to a second test tube containing 2 cc of distilled water. Wash graduated cylinder.

3. Add the same amount of blood to a third test tube containing 2 cc of 3% NaCl solution.
4. Compare the transparency of the three solutions by looking at a printed page through each tube. Record observations below.
5. Using a clean medicine dropper each time, mount one or two drops of the solution from each of the three test tubes on clean glass slides. Cover with a cover glass and observe under the microscope (on high power).
6. Draw three or four cells from each test tube.

#### Questions:

1. What happened to the erythrocytes placed in 0.9% NaCl?
2. Describe the appearance of the erythrocytes placed in distilled water.
3. Describe the appearance of the erythrocytes placed in 3% NaCl.
4. In what kind of solution were the erythrocytes in Questions 1, 2, and 3, (hypotonic, hypertonic, or isotonic)?
5. Explain why you would expect crenation to occur in a 10% glucose solution.

#### PART F - BROWNIAN MOVEMENT

##### Objective:

To observe, indirectly, the movement of molecules as demonstrated by Brownian movement.

##### Materials:

1% Leishman's dye	cover slip
medicine dropper	microscope
microscope slide	

##### Discussion:

Each particle of dye is an aggregate of many molecules. Motion is due to unequal bombardment by the molecules of the water environment. This action was first noticed by the botanist and army surgeon Robert Brown, for whom it is named.

**Methods:**

1. Take a small drop of 1% Leishman suspension and place it on a clean slide by means of a medicine dropper.
2. Cover the suspension with a cover glass.
3. Observe under the high power of the microscope.

**Questions:**

1. Was the pattern of movement of particles directional or random?
2. Which particles moved most rapidly, the larger or the smaller ones?
3. What property of matter is demonstrated by Brownian movement?

**PART G - SOLUBILITY****Objective:**

To demonstrate differing solubilities in polar and non-polar solvents.

**Materials:**

Erlenmeyer flask 100 ml  
Water  
Petroleum ether  
Marker pen  
CuSO<sub>4</sub> crystals

**Methods:**

1. Pour 30 ml of Petroleum Ether in the flask.
2. Pour 30 ml of water in the flask.
3. Shake. Note which is the top and which is the bottom layer.
4. Add a few CuSO<sub>4</sub> crystals. Shake. In which layer does the color appear? Why?
5. Dip the marker pen in each layer. Which layer becomes colored? Why?
6. Shake the mixture. Will the two colors mix? Why?

**Questions:**

1. Why do the two solutions not mix?
2. Why do the two solutions always return to the similar layer?
3. Why is  $\text{CuSO}_4$  marker ink soluble in one layer and not in the other?
4. Relate solubilities in lipid and water phases to the cell structure. How do fat soluble molecules enter the cell? How do water soluble molecules enter the cell?

## **Tutor Notes - Laboratory Three**

### **PHYSICAL TRANSPORT OF MATERIALS**

This is a straightforward exercise with a number of experiments that demonstrate some transport processes. Stress the places within the body where some of these processes occur. Most of the questions deal with observations which are made in the experiments. Answers to some of the other questions are outlined below.

#### **PART A - FILTRATION**

As discussed in the introduction in the students' manual, the force of gravity contributes to filtration. Thus, the rate of filtration, depends on the height of the fluid column; there is a direct relationship between the height (ie. the weight of the solution) and the rate of filtration. Therefore, the rate should decrease as the height decreases.

In this set-up, two important factors determine which substances are filtered: size and solubility. The smaller the substance the more likely it will be filtered, and the more water soluble the substance, the more likely it will be filtered. (The effective size of the molecule depends on the amount of water that associates with the molecule). One final consideration in this set-up is particles will tend to plug up the pores in the filter paper, resulting in decreased filtration rate independent of the hydrostatic pressure.

There are many examples of where filtration occurs in the body. As blood passes through any capillary bed, it is filtered across the endothelial cells lining the vessels, and enters the interstitium. The hydrostatic pressure of the blood in the vessels is the driving force for this movement.

#### **PART B - DIFFUSION**

Diffusion is the dispersion of substances as a result of the movement of their ions or molecules. Net diffusion of any substance in any state always occurs in the direction of high concentration to low concentration until equilibrium is reached, at which point, diffusion occurs equally in all directions. This will be observed in three examples of diffusion.

Before looking at the specific examples of diffusion, consider the factors that affect the diffusion of molecules in any medium. These factors include: the distance involved; the concentration and molecular weight of the molecules; and the temperature. Diffusion occurs more rapidly when the distances are shorter,

when the concentration of the diffusing substance is greater, when the molecular weight is lower, and when the temperature is higher. In addition, other factors unique to various situations may play a role in the rate of diffusion.

### 1. Diffusion of a Liquid into a Gas

When mercaptoethanol is poured into a dish, the odour becomes apparent very quickly to the students who are close to it. Whether or not a particular student detects the odour depends on the receptor sensitivity of the olfactory system within that individual. (Some people do not have the sensation of smell). The further away from the petri dish, the longer it will take them to smell the mercaptoethanol, due to the time required for the liquid to diffuse through the air. Air currents may be present that would disrupt the predicted pattern of diffusion of the alcohol; one would predict that it would diffuse equally in all directions.

An example of diffusion of a liquid into a gas in the human body is the case of the evaporation of sweat. Evaporation of water from the skin and lining membranes of the respiratory tract is one process by which the body loses heat and water. The transformation of water from a liquid state to a gaseous state requires thermal energy. Thus, when water vaporizes from the surface of the body, the heat which is required to drive this process is utilized, resulting in cooling.

### 2. Diffusion of a Solid in a Liquid

In this experiment, the potassium permanganate molecules will dissolve into solution, and diffuse in the predictable way. With time, the molecules are expected to diffuse away from the crystal, to become evenly dispersed throughout the solution.

Examples that illustrate the reverse of this process are any situations in the body in which a precipitate is formed. A **calculus** is a mass of precipitated material that is derived from a secretion and deposited in an excretory duct. The causes of the formation of calculi vary, but often result in an increase in the crystalloid content of the secretion. The presence of a solid mass often acts as a nucleus around which the crystalloids precipitate. Common sites for the formation of calculi are within the urinary or the biliary tract.

### 3. Diffusion of Solid in Agar

As discussed above, the rate of diffusion varies inversely with the size of the molecule. However, the results seen in this experiment will be affected by other factors such as the rate at which the crystals will go into solution. Ionic charges of the molecules may also affect the rate of diffusion through the water



channels of the agar. Nevertheless, the molecules of the crystals should diffuse evenly from the centre of the crystals.

The agar in the experiment represents the cytoplasm of the cell. An example of diffusion of this sort would be the diffusion of intercellular substances through the cytoplasm. Glucose is carried into the cells lining the gut by a carrier mechanism, however, once it is in the cell, it diffuses through the cytoplasm to the other side of the cell (basolateral surface). It can then leave the cell to be taken up by the blood.

### **PART C - DIALYSIS**

The process of dialysis allows the separation of substances based on their physical properties. Depending on the size and solubility of the particles, as well as the dialysis membrane, certain substances are able to pass through the membrane, while others remain in the dialysis tubing.

Compounds dialyze from high concentration to low concentration. From this experiment, one expects the sodium and chloride ions, and glucose to move out of the capillaries to form tissue fluid.

### **PART D - OSMOSIS**

Osmosis is most simply thought of as the diffusion of water. Like any molecule, it will diffuse down its concentration gradient. This movement is termed osmosis. Particles within water are said to have osmotic pressure because the water will tend to diffuse toward them as it moves down its concentration gradient. The movement of water across a semipermeable membrane will be from the pure water (high concentration) to the solution concentrated with NaCl and sucrose.

However, another force acts in this set-up; the force of gravity tends to oppose the movement of water up the column in the osmometer; this force will increase as the height of the column of water increases.

### **PART E - HEMOLYSIS AND CREATION**

This is a special case of osmosis. Fluid moves in or out of red blood cells depending on the concentration of the solution surrounding the cells. One would expect the cells to remain the same in the isotonic solution (0.9% NaCl); to undergo cell lysis when placed in a hypotonic solution (distilled water - the cell contents are concentrated relative to distilled water, thus the water moves down its concentration gradient into the cell); and the cell is expected to undergo crenation (shrink) when placed in

a hypertonic solution (the concentrated salt solution tends to draw fluid out of the cell).

#### **PART F - BROWNIAN MOVEMENT**

Molecules and ions are constantly moving. Their random movement in solutions is termed 'Brownian Movement'. A particle travels along a straight line until it collides with another particle. It then moves in another direction, only to collide again and change direction once more. This movement is random and accounts for the mixing of molecules that occurs when different kinds of substances are put together.

#### **PART G - POLAR AND NON-POLAR SOLVENTS**

This exercise demonstrates to the students the characteristics of polar and non-polar substances, specifically, that they do not mix. Focus on the chemical characteristics of the solvents used to understand this phenomenon.

The two solutions (water and ether) do not mix because the ether is a relatively non-polar solvent. (It is not necessary to go over the atomic structure of polar versus non-polar bonds; just make sure the students realize that it is the characteristics of the elements making up the molecules that determine the polarity of the bonds in that molecule).

The molecules that make up cell structures are important in this regard. The hydrophobic/hydrophilic (ie. polar/non-polar) properties of the cell membrane phospholipids determine the formation of the bilayer membrane structure. This structure makes the passage of other non-polar molecules, such as lipids, relatively easy, and the passage of polar molecules more difficult. (Of course there are factors other than the polarity of the particle which determine the ease which it passes through the cell membrane). Polar molecules overcome the transport problem through the membrane by passing through the membrane by ways of protein channels.

## Tutorial Four

### ROBERT SMITH: CERVICAL RIB

#### Objectives

1. Briefly review the anatomy of the vertebral column.
  2. Discuss the pathology of cervical ribs.
  3. Discuss the normal neurovascular supply and its relation to the complications arising with a cervical rib.
  4. Discuss the mechanisms of pain.
  5. Given the complication which arose during surgery, discuss briefly the anatomy of the lung and the possible mechanisms responsible for Dr. Smith's difficulty in breathing after the surgery.
  6. Discuss the regeneration of nervous tissue.
- 

Dr. Robert Smith, 38 arrives to give you a lecture on the nervous system with his right arm in a sling and tells you he has just had surgery to remove a cervical rib. Are there normally ribs attached to the cervical spine? What do you know about cervical ribs?

When Dr. Smith was in his early twenties, he became aware that he could not carry anything with his right arm. Even to carry his books as a student produced severe pain of the upper arm. If he lifted his arm above his shoulder, his fingers became numb and the whole upper limb pained. He was unable to lie on his right side to sleep.

In his early 30's, he found he could not carry his daughter around. He had also lost his fine motor control. The loss of motor control was most apparent to him when he was operating the electron microscope. Rotating the knobs became difficult and painful to him. At this time the presence of a pair of cervical ribs was discovered on routine chest x-ray. The rib on the right side consisted of bone and cartilage and was compressing the brachial plexus and subclavian artery. What is the anatomical explanation for the neurovascular problems associated with a cervical rib? What symptoms would you expect from a cervical rib? In what ways are cervical ribs treated?

Before his surgery, Dr. Smith complained of pain. What do you know about the mechanism of pain? What would you suspect to be the cause of Dr. Smith's pain?

After the surgery, Dr. Smith found he was unable to breathe easily and the apical tone of the right lung was found to be collapsed. Two mechanisms were suggested: one neural and one pleural. Explain how these conclusions were arrived at.

Two months after the surgery, Dr. Smith can move his arm freely without pain, he can lie on his right side and, with physiotherapy, his muscle tone has recovered. However, his little finger and the adjacent side of the 4th finger still have no feeling. What nerve would you expect to be involved? Would you expect the nerve damage to be permanent?

## Tutor Notes - Tutorial Four

### ROBERT SMITH: CERVICAL RIB

#### Objectives

1. Briefly review the anatomy of the vertebral column.
2. Discuss the pathology of cervical ribs.
3. Discuss the normal neurovascular supply and its relation to the complications arising with a cervical rib.
4. Discuss the mechanisms of pain.
5. Given the complication which arose during surgery, discuss briefly the anatomy of the lung and the possible mechanism responsible for Dr. Smith's difficulty in breathing after the surgery.
6. Discuss the regeneration of nervous tissue.

#### Q1. How many ribs do most people have, and where do they attach?

Each person usually has twelve pairs of ribs - one pair attached posteriorly to each of the twelve thoracic vertebrae. The first seven rib pairs are true ribs; they are directly joined to the sternum by their own cartilage. The remaining five pairs are false ribs. They are so named because their cartilages do not reach the sternum directly. Instead, the cartilages of the upper three false ribs join the cartilages of the ribs next above. The last two ribs are called floating ribs; they have no cartilagenous attachments to the sternum.

#### Q2. What do you know about 'cervical ribs'?

Ribs which articulate to the seventh cervical vertebrae are present in 0.5 - 1% of the population. Cervical ribs may be unilateral or bilateral. They are variable in size. Usually they have a head, neck and tubercle with varying amounts of body.

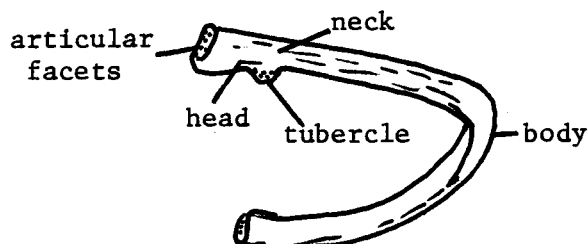


Figure 4A

In addition, cervical ribs often have associated anomalous fibromuscular bands extending from them which may also be responsible for the problems associated with this condition.

**Q3. What are the neurovascular complications associated with cervical ribs, and what is the anatomical explanation for these complications?**

Some people who have cervical ribs may exhibit no symptoms, however others may experience neurological and/or vascular problems because of the extra rib. This is due to the potential for compression of the brachial plexus and/or the subclavian artery and vein; these structures may be arched over the extra rib.

**Q3a. What is the brachial plexus?**

In order to understand what the brachial plexus is, it is necessary to have an understanding of the organization of spinal nerves.

Afferent nerve fibres enter the spinal cord on the dorsal aspect, through the 'dorsal root', and efferent fibres leave via the ventral root. Dorsal and ventral roots from the same level combine to form a spinal nerve. Spinal nerves branch, and the largest branch, the 'ventral ramus', combine with ones from other levels to form a 'plexus'.

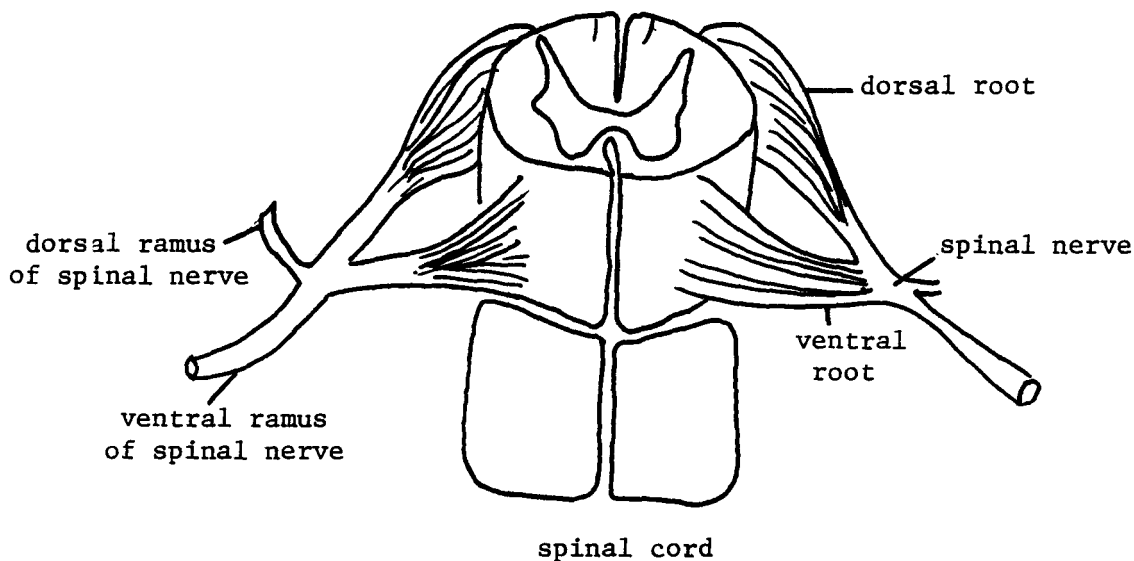


Figure 4B

The brachial plexus is a collection of ventral rami of spinal nerves C5, C6, C7, C8, and T1. It runs obliquely and laterally and passes between the scalene muscles, over the first rib and behind the middle third, of the clavicle to enter the axilla.

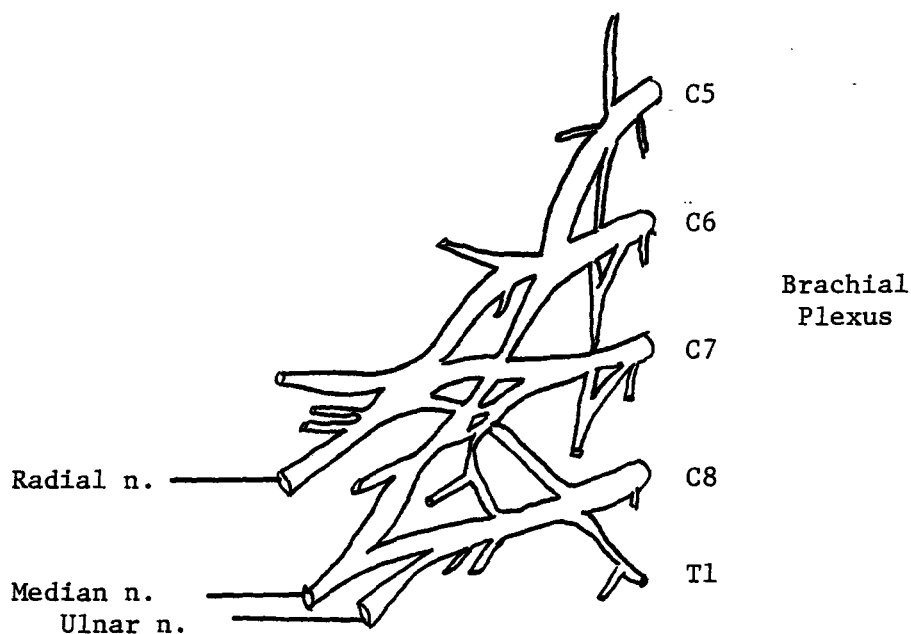


Figure 4C

It innervates the entire upper extremity plus a number of shoulder and neck muscles on one side.

**Q3b. What is the subclavian artery?**

The left subclavian artery is one of the three major arteries originating from the arch of the aorta. Another artery which originates from the arch of the aorta is the brachiocephalic artery. It divides to give rise to the right common carotid artery and the right subclavian artery.

The left and right subclavian arteries carry blood to the arms on their respective sides. Branches of the subclavian arteries also supply blood to parts of the shoulder, neck and head.

**Q3c. Given that the neurological and vascular complications of a cervical rib are compression of the brachial plexus and subclavian artery and vein, what symptoms would be expected?**

Possible effects of the compression of the brachial plexus includes pain and tingling of the hand and forearm, and wasting of the hypothenar muscles of the hand. This muscle is innervated by the ulner nerve which is most likely to be affected by the cervical rib, since its nerve fibres originate from the lowest two spinal nerves of the brachial plexus.

The possible vascular symptoms include: ischemic muscle pain; temperature and colour changes; numbness in the fingers; possible ulceration and gangrene (though this is rare); absence of a

radial pulse; and the possible development of emboli to peripheral vessels of the upper limb.

Compression of the subclavian vein could lead to pooling of blood and edema.

**Q3d. What other conditions may cause the same symptoms as those seen in people who have cervical ribs?**

The same neurovascular changes could possibly be seen in people who have fractured their clavicle or first rib; have drooping shoulders from neurologic disease, injury or poor posture; or have muscle hypertrophy of the scalene muscles. All these conditions have the potential to compress the brachial plexus and/or subclavian vessels.

**Q3e. What treatments are available for cervical ribs?**

Mildly symptomatic patients with paresthesias noted on prolonged arm elevation respond well simply by avoiding the activities or positions that precipitate the symptoms. Elevating the arm may be all that is required to relieve the pressure and the symptoms. Physical therapy with specific exercise designed to improve posture and strengthen the shoulder girdle muscles may be all that's required. However, many patients who have undergone months of physical therapy, transcutaneous nerve stimulation, osteopathy and chiropractic can attest to the general ineffectiveness of these methods.

The only type of relief which will be effective in the patients with severe symptoms is surgical alteration of the mechanical cause of irritation or compression of the neurovascular structures. This involves the complete removal of the cervical rib plus any anomalous fibromuscular tissue.

Mr. Smith said he experienced pain. As an aside, consider some aspects about the mechanisms of pain.

**Q4. What receptors are involved in the conduction of pain, and what stimulate them?**

The receptors which give rise to pain when stimulated are small, usually non-myelinated afferent fibres called 'nociceptors'. Nociceptors have different stimuli; some respond to mechanical, chemical or thermal stimuli. They also have different thresholds to these stimuli.

In some conditions, accumulating chemicals cause the pain threshold to lower, thus inflamed tissue may be more sensitive to pain.



Afferent nociceptors synapse onto two different types of interneurons and from here information is transmitted to higher centres. There are two pathways to the higher centres:

- i. a 'Specific Pathway' which goes to the cerebral cortex and the thalamus to convey information about where and how strong the stimulus was.
- ii. a 'Non-specific Pathway' which goes to the brain stem, reticular formation and another part of the thalamus. Information conveyed by this pathway deals with the aspect of pain which is duller and longer lasting.

**Q4a. What could be causing the pain in Dr. Smith's case?**

One of the stimuli for pain is the lack of oxygen, or 'anoxia', and this may be the case for Mr. Smith since blood flow to his arm may be impaired. In addition, any pain-causing chemicals may accumulate in the area, again because of the impaired blood flow.

Direct stimulation of the pain fibres (nociceptors) due to compression will also contribute to the pain.

**Q5. After Dr. Smith's surgery, he was unable to breathe easily and the apical tone of the lung was found to be collapsed. How do lungs normally remain expanded, and what possible mechanisms could be responsible for the collapse of Dr. Smith's lung?**

The lungs are surrounded by two pleura (serous membranes). The visceral pleural membrane adheres to the outer surface of the lungs and the parietal pleural membrane lines the thoracic wall. The space between the two pleura is the 'pleural cavity'. It contains a thin film of serous fluid which lubricates the adjacent pleural surfaces and reduces friction between them as they move against one another during breathing.

Lungs normally remain expanded due to the fact that atmospheric pressure is greater than the pressure in the pleural cavity.

The 'pleural mechanism' which could account for the collapse of the apical portion of the lung would be injury of the parietal pleural membrane during the surgery. This would result in the loss of the pressure difference between the atmosphere and the pleural cavity, so air would rush from the atmosphere into the pleural cavity allowing the lung to collapse.

The 'neural mechanism' would explain the collapsed lung if the phrenic nerve was injured during the surgery. The right and left phrenic nerves innervate the diaphragm. If it was cut, the

diaphragm would not contract and expand the lung, so the lung would collapse.

Finally, Dr. Smith has found that after two months, his little finger and the adjacent side of the 4th finger still have no feeling.

**Q6. What nerve is involved?**

The ulnar nerve supplies the small muscles of the affected areas. It is a mixed nerve; it carries both motor and sensory fibres. Therefore, both motor and sensory functions will be impaired.

**Q6a. Would you expect the nerve damage to recover?**

Neurons cannot divide. If the cell body is damaged it cannot be repaired. However, axon damage in the periphery can undergo repair.

With myelinated nerves, Schwann cells in the region between the cut portion of the fibre and the next Node of Ranvier enlarge, proliferate and become phagocytotic. Neurofibrils sprout out and invaginate into the cytoplasm of the Schwann cells. The Schwann cells phagocytose the fragmented axons.

Many of the neurofibrils degenerate, but one may reach an appropriate end organ and persist to form a replacement. The final process involves the reformation of the myelin sheath by Schwann cells.

**Laboratory Four**  
**NEUROMUSCULAR PHYSIOLOGY**

**Prerequisite Activities:**

1. Read over and understand the relevant material concerning the structure, biochemistry and mechanisms of contraction of striated, cardiac and smooth muscle.
2. Understand the following terms: threshold, motor unit, neuromuscular junction, tension generation, action potential, cross-bridges, receptor, neurotransmitters, and gap junctions.
3. Read the laboratory exercise and be prepared to answer the questions.

**Objectives:**

To demonstrate properties of muscular contraction of skeletal, cardiac and smooth muscle.

**PART A - GENERAL PROPERTIES OF MUSCULAR CONTRACTION**

Muscle cells are able to convert chemical energy (ATP) into mechanical work. We have described the arrangement of the contractile proteins, actin and myosin within the myofibril and discussed how these proteins interact with each other to result in a shortening of the muscle. This laboratory will demonstrate the functional differences of the three types of muscle. There will be one smooth muscle, one striated muscle and one cardiac muscle experiment for each group.

**Materials:**

A two-pin electrode (stimulator) connected to a variable voltage-variable frequency stimulator

cotton thread

lever

smoked-drum Kymograph

frogs

pH indicator paper

dissecting kit

stand and clamps

incubation baths

physiological solutions

neurotransmitters

**Methods:**

1. Double pith the frog.
2. Dissect out the gastrocnemius muscle and tie a thread tightly around the achilles tendon. Place the frog in a prone position and pin the knee securely to a board. Tie the other end of the thread to the lever.
3. Identify and isolate the sciatic nerve in the thigh. Place the nerve gently across the two pins of the stimulating electrode, taking care not to over-stretch the nerve.
4. Place the smoked drum of the Kymograph against the lever. Note that the speed of the Kymograph can be adjusted from between 1 to 4 inches/min.

The Effect of Increasing the Strength of Stimulation on Force/Degree of Contraction

5. Set the Kymograph speed at 3 inches/min
6. Stimulate the sciatic nerve at a frequency of one stimulus per 2s. Gradually increase the intensity of stimulation from 0 volts until a maximal contraction occurs.

Describe the results using the terms: sub-threshold, threshold, sub-maximal, maximal and, graded response.

**Questions**

- 1a. What is an "all or none" property?
- b. What is a motor unit?
- c. When an axon "fires", does the motor unit exhibit an "all or none" response?
- d. In your view of the answer given to 1(c), and your present observations, how do you think a striated muscle grades the degree/force of contraction? Use the term recruitment of motor units in your answer.

The Effect of Increasing the Frequency of Stimulation on Muscular Contraction

7. Set the stimulus intensity to give a contraction of approximately 50% of maximum. Set the Kymograph speed at 4 inches/min. Begin stimulating the muscle at a frequency of 1 stimulus/2s. Gradually increase the frequency of stimulation.

**Questions**

- 2a. At the lowest frequency of stimulation did the muscle completely relax between contractions? Would you call the contraction of the muscle at this frequency a "twitch" response?
- b. At what frequency did the muscle contractions begin to fuse?
- c. Define "genesis of tetanus" and "tetanus" and state at what frequency tetanus occurred.

**Muscular Fatigue**

8. Maximally stimulate the muscle at greater than tetanic frequency. Describe your results paying particular attention to the duration that the maximal contraction could be sustained.

**Questions**

- 3a. Does muscular fatigue occur in normal muscles?
- b. What do you predict will be the pH of a fatigued muscle and why? Cut the fatigued muscle and touch it inside with a piece of pH indicator paper to confirm your hypothesis.

**Part B - CARDIAC MUSCLE**

1. Double pith the frog.
2. Open the chest and expose the heart. Slit the pericardium and place the bent pin through the apex of the heart. Tie one end of a piece of thread to the pin and the other to the recording lever and position according to previous section. Apply enough stretch to the preparation so the heart beat is recorded on the smoked drum.
3. Remember to keep the heart moist by drops of physiological buffer.

**Questions**

4. What is the sequence of the contraction events? Do the chambers beat in unison or sequentially? How does the frog heart differ from the mammalian heart?
- 5a. Drop a few drops of norepinephrine solution on the heart. How do you explain the changes? How does this relate to the heart rate changes in man?

- b. Drop a few drops of acetylcholine solution on the heart. What does this do? Why?
- c. Can you produce tetanus? Why?

### Part C - SMOOTH MUSCLE

A section of rabbit small intestine will be provided.

1. Tie a ligature on each end and suspend in the incubation chamber so that one end is attached to the lever and the other is fixed in the bath. Fill the bath with physiological saline.
2. Bubble the solution in the bath with compressed air.
3. Keep the bath warm by adding warmed water to the surrounding container.

### Questions

- 5a. Add acetylcholine (10 drops). How does the tissue respond? What is the rate of contraction?
- b. Add norepinephrine before washing out the tissue. What is the response? How does it differ from the heart's response? Why?
- c. Can you produce tetanus? Why?

## Tutor Notes - Laboratory Four

### NEURONMUSCULAR PHYSIOLOGY

The purpose of this laboratory exercise is to reinforce some of the concepts which have been discussed in the lectures on muscle types and nerve-muscle interactions.

While there are a few questions given to the students in their laboratory manual, they are not sufficient for a full understanding of the concepts being demonstrated. Therefore, some information has been provided which covers topics which should be discussed with the group as they go through the exercise. A summary of the topics is provided at the end of these notes.

#### PART A - GENERAL PROPERTIES OF SKELETAL MUSCLE CONTRACTION

The sciatic nerve-gastrocnemius muscle preparation demonstrates some of the basic processes and mechanisms for muscle contraction. Nerve cells that innervate skeletal muscle fibres are called 'motor neurons'. Their cell bodies are located in the spinal cord or the brain stem. The terminal of the motor neuron is branched so that a number of muscle fibres are associated with one motor neuron.

When an action potential is propagated to the axon terminal of a motor neuron, voltage-sensitive calcium channels in the plasma membrane open, allowing calcium ions to diffuse into the axon terminal. This movement of calcium into the nerve terminal triggers the fusion of transmitter vesicles located in the nerve terminal, to release their contents (acetylcholine). Acetylcholine is released into the extracellular cleft separating the nerve and muscle membranes (this region is called the 'neuromuscular junction'). The acetylcholine then diffuses across the cleft and binds to the receptor sites of the muscle fibre membrane (the 'motor-end plate'). The interaction of acetylcholine on the muscle membrane stimulates the opening of ion (sodium and potassium) channels in the end-plate membrane. Slightly more sodium enters the muscle fibre relative to potassium leaving the cell, thus the membrane depolarizes. The amount of depolarization is referred to as the 'end-plate potential' (EPP). (It would be a good idea to go over this process on the board; use a diagram and include the sequence of events).

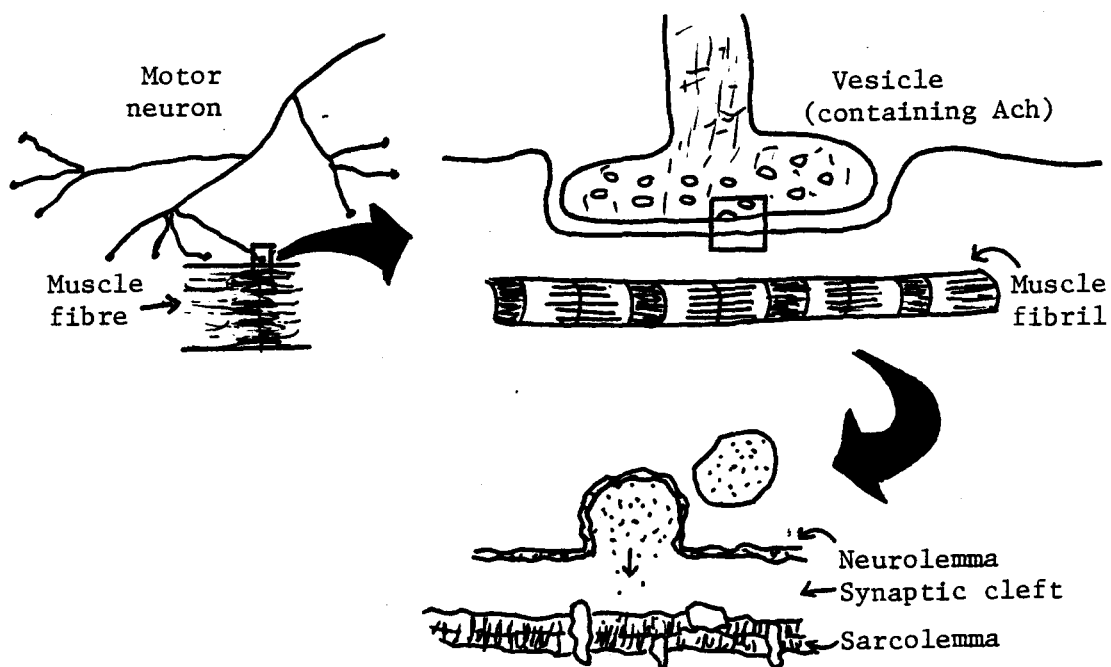


Figure 4A

The events by which this membrane depolarization is converted into cross-bridge interaction, and therefore the actual muscle contraction, is termed 'excitation-contraction coupling'.

The bridge between the electrical events and the mechanical events of the muscle fibre lie in the cellular structure of the muscle fibre. The action potential is propagated throughout the sarcoplasm by a system of intracellular tubules, which are continuous with the extracellular medium surrounding the muscle fibre. As an action potential is propagated through these tubules ('transverse' or 'T-tubules'), the release of calcium from the nearby lateral sacs of the sarcoplasmic reticulum is triggered. These lateral sacs are positioned very close to the myofibrils, so the released calcium can bind to the troponin-molecule. This binding enables the formation of actin-myosin cross-bridges, thereby producing muscle contraction. (This is a simplified account of the process; your group may decide to review the sliding filament theory which has been covered in class, but they may not feel it is necessary).

It is important to note that in skeletal muscle the amount of calcium released by a single action potential from lateral sacs of the sarcoplasmic reticulum is sufficient to produce nearly complete saturation of all troponin sites, so that all of the cross-bridges are 'turned-on'.



A 'twitch' is the mechanical response of a muscle fibre to a single action potential. It is important to understand the time frame in which the electrical and mechanical events occur. Because a single action potential in a skeletal muscle fibre lasts only 1-2 ms, whereas the mechanical response lasts for up to 100 ms, it is possible for a second action potential to be initiated during the period of mechanical activity. If a second action potential does reach the motor-end plate before the fibre has relaxed completely, a contractile response results in which the peak tension is greater than that of the single twitch. This increased mechanical response to subsequent action potentials is referred to as 'summation'.

A maintained contraction in response to repetitive stimulation is known as 'tetanus'. At low frequencies of stimulation, the tension may oscillate as the muscle fibre has time to partially relax between stimuli, and 'unfused tetanus' results. Higher stimulation frequencies results in 'fused tetanus' in which there are no oscillations. The tension produced during tetanus may be five times as great as that produced by a single twitch.

Why is the tension developed during tetanus greater than that generated by a twitch? The answer involves the 'series elastic component' (SEC) of the muscle. This refers to all the connective tissue which the cross-bridge interactions impart their force to, such as the tendons. In a single twitch, the external tension generated in the SEC is still rising at the time when the cross bridge tension is declining from its peak values (this occurs because calcium ions are actively being pumped back into the sarcoplasmic reticulum). Therefore, the peak tension developed by the SEC during a twitch is never as great as the maximum tension that can be generated by the cross-bridges, simply because of the lack of time. This problem is overcome as the duration of contraction increases (as in the case of tetanus).

### Answers to Questions

- 1a. A stimulated muscle contracts, or a nerve fibre propagates a nerve impulse either completely or not at all. This phenomenon is termed the 'all-or-none' property.
- b. A motor unit consists of one motor neuron, plus all the muscle fibres it innervates. The number of muscle fibres within a motor unit varies from as few as 10 (as is the case in some muscles of the eye), to several hundred (for instance, motor units may contain 1700 muscle fibres in the gastrocnemius muscle).
- c. Each muscle fibre in a motor unit is controlled by the same neuron, thus the electrical activity in a motor neuron controls the contractile activity of all the muscle fibres in

that motor unit. It follows, then, that the motor unit will exhibit an 'all-or-none response'.

d. There are two ways the contractions of skeletal muscle can be graded:

i) increase the total number of individual muscle fibres which are contracted by recruiting more motor units, or;

ii) increase the tension produced by each contracting muscle fibre by increasing the action potential frequency, thus producing summation of contractions and tetanus.

3a. Muscle fatigue does occur in normal muscles. Several factors have been implicated in fatigue of the contractile mechanisms including the accumulation of lactic acid, and the depletion of ATP stores in the muscle cells.

b. One would expect the pH of the muscle to be lower in fatigue because of the production of lactic acid.

## PART B - CARDIAC MUSCLE

Cardiac muscle fibres have some characteristics which are the same as in skeletal, but many important differences exist. Like skeletal muscle, the individual myocardial cells are striated, but they are much shorter and have branching processes at their ends. Adjacent cells are joined end-to-end at 'intercalated discs'. There are two types of membrane junctions at these discs: desmosomes, which hold the cells together and where the myofibrils are attached; and gap junctions, which allow action potentials to spread from one cardiac muscle cell to the next.

In addition to the ordinary type of cardiac muscle fibres, there are areas in the heart which contain specialized cells. These are termed 'conducting cells' and are essential for normal excitation of the heart. These cells are able to spontaneously depolarize. This occurs through a progressive reduction in the membrane permeability to potassium. They are in contact with ordinary cardiac fibres via gap junctions, thus the action potentials for this conducting system can spread to other myocardial cells.

The heart is innervated by both divisions of the autonomic nervous system. Because it lacks somatic innervation, cardiac muscle is involuntary. The postganglionic sympathetic fibres terminate upon the cells of the specialized conducting system, as well as the ordinary myocardial cells of the atria and ventricles. These neurons release norepinephrine. The parasympathetic fibres release acetylcholine. They innervate the conducting system and the atrial myocardial cells, but not the

ventricular myocardium.

Like the other muscle types, contraction of cardiac muscle is triggered by depolarization. It is crucial that the two atria of the heart contract at the same time and the two ventricles contract at the same time in order to ensure efficient pumping of the blood. This coordination is made possible by the gap junctions which allow the spread of action potentials from one cell to the next, and by the specialized conducting system which facilitates the rapid and coordinated spread of excitation.

A brief description of the spread of depolarization throughout the myocardium follows. Of the group of cells which are capable of autonomous spontaneous rhythmical self-excitation, those of the sinoatrial (SA) node have the highest intrinsic rate (100/min). Therefore, they set the pace for the excitation and the contraction of all the myocardial cells. From the SA node, the wave of excitation spreads via gap junctions to the cardiac cells of the atria. The spread of excitation is also carried by some specialized conducting fibres from the SA node to the atrioventricular (AV) node, which is located at the base of the right atrium. Excitation is carried from this node through the conducting fibres called 'the Bundle of His'. The Bundle of His divides into left and right branches which in turn branch into 'Purkinjie' fibres that spread throughout the left and right ventricles.

#### Answers to Questions

- 5a. Norepinephrine increases the heart rate by increasing the slope of the pacemaker potential, thus causing the pacemaker cells to reach threshold more rapidly. Norepinephrine does this by increasing the flow of calcium ions into the SA-nodal cells (and calcium ion movements have similar effects to those of sodium on the membrane potential).
- b. Acetylcholine decreases the heart rate by increasing the permeability of the membrane to potassium, so it takes longer for the cell to reach threshold. The resting heart is under the control of the parasympathetic system, so at rest the heart rate is lower than its intrinsic rate of about 100 beats/min.

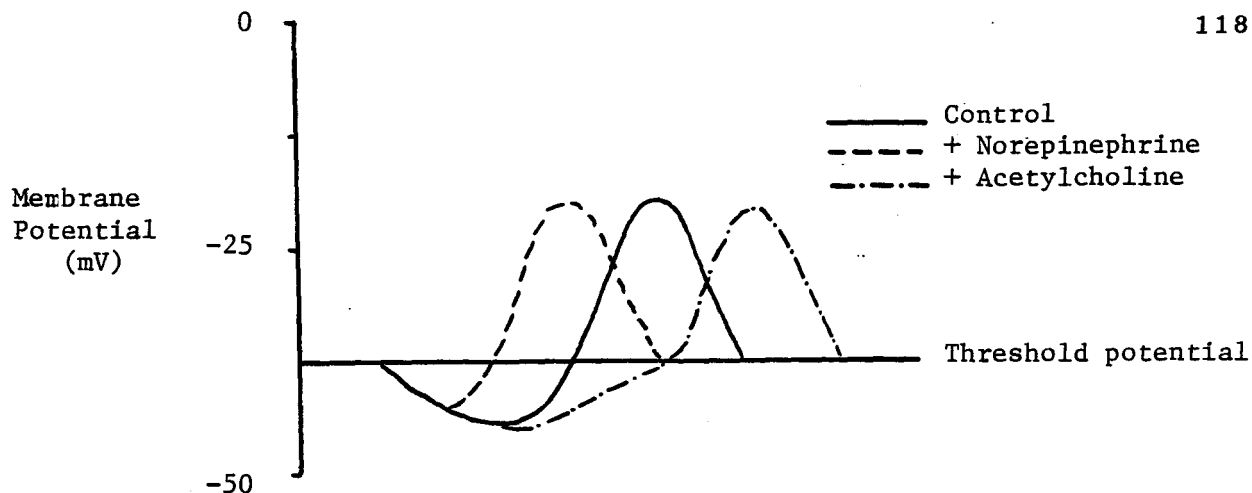


Figure 4B

- c. A tetanic state cannot be produced in cardiac muscle because the repolarization period is relatively long (200 ms). During the repolarization period, another action potential cannot be initiated.

#### PART C - SMOOTH MUSCLE

Smooth muscle uses cross-bridge interactions between actin and myosin filaments to generate force, and calcium ions are involved in the control of cross-bridge activity. Despite such similarities, the differences between smooth muscle cells and the other muscle fibre types are abundant. The structural organization of the contractile filaments, the process of excitation-contraction coupling, and the time course of contraction are quite different in the other two muscle types.

The cross-striation pattern which is seen in skeletal and cardiac muscle fibres is lacking in smooth muscle fibres. Like cardiac muscle cells, the nerve supply comes from the autonomic nervous system, thus, smooth muscle is not normally under direct voluntary control. During embryological development, the smooth muscle cells do not fuse together. Therefore, differentiated smooth muscle cells are individual spindle-shaped fibres, containing a single nucleus.

The excitation-contraction coupling of smooth muscle cells involves calcium, but not in the same way as in skeletal muscle cells. Calcium from either intracellular stores in the sarcoplasmic reticulum, or from the extracellular fluid, enter the cytosol and triggers contraction. Relaxation is brought about by the removal of calcium from the cytosol through the action of calcium pumps either in the membrane of the sarcoplasmic reticulum, or in the plasma membrane.

The speed of contraction of smooth muscle fibres is relatively slow because the mechanisms for rapidly activating and relaxing the contractile apparatus of the skeletal muscle fibres are absent in smooth muscle fibres. In addition, unlike skeletal muscle, a single action potential releases sufficient calcium to turn on only a portion of the cross-bridges in smooth muscle cells. Because of this, the tension can be graded by varying the magnitude of the changes in the cytosolic calcium concentration.

The cytosolic calcium concentration may remain at a sufficient level such that a low level of cross-bridge interactions are maintained. This low level of tension constitutes 'muscle tone' in these fibres.

There are several inputs which affect the contractile activity of smooth muscle cells. First, some smooth muscle cells have the ability to generate spontaneous action potentials. The plasma membranes of these cells depolarizes and repolarizes on a rhythmical basis. When threshold is reached during the depolarization phase, an action potential is generated. Such spontaneous changes in the membrane potential occur with cycle times ranging from seconds to several minutes. These cyclical changes are termed 'slow wave potentials' and are thought to arise from the cycling of the sodium/potassium pump at the membrane.

In addition to being innervated by nerve fibres from the autonomic nervous system, some smooth muscle cells are sensitive to a variety of hormones. Neurotransmitters and hormones can have either excitatory or inhibitory effects (ie. can depolarize or hyperpolarize the smooth muscle cell membrane).

The calcium concentration can also be varied by many local factors, including paracrine substances which bind to receptor sites on the smooth muscle membrane; oxygen concentration; the ion composition of the extracellular fluid; and osmolarity.

### Answers to Questions

- 5a. Acetylcholine has a stimulatory effect on the smooth muscle of the gut.
- b. Norepinephrine has an inhibitory effect on the smooth muscle of the gut.

## SUMMARY

A lot of information has been covered. A summary of what has been covered may help you organize the laboratory, and give you a better focus of the topics to be discussed in this exercise.

### A. Skeletal Muscle Contraction

- a) Motor neuron/skeletal muscle interaction at the neuromuscular junction
- b) Transduction of electrical events into mechanical events
- c) Tension development: twitch; summation; tetanus

### B. Cardiac Muscle

- a) structure
- b) conduction cells, and spread of excitation
- c) role of the autonomic nervous system

### C. Smooth Muscle

- a) structure
- b) excitation-contraction coupling; the role of calcium
- c) concept of tone
- d) inputs which affect the contractile activity of smooth muscle cells

## Tutorial Five

### JANE NURSE: IMMOBILITY

#### Objectives

1. Learn the muscles used for bearing weight, and the changes in the muscles which are used in walking with crutches and with a walking cast.
  2. Understand what is meant by atrophy.
  3. Discuss the difficulties facing a student with a broken ankle, and the physical and mental obstacles that such a student would encounter.
  4. Discuss the assets which a Nursing student would have in this situation.
- 

#### August 15

Jane Nurse is so excited. She has been accepted into Nursing at McMaster. She and her mother have shopped for a new wardrobe, and she has bought all her books and supplies. This is an exciting yet frightening time - so many new things to come: university classes, residence life, campus life.

#### August 25

Disaster struck! Jane went racing down the stairs to the beach at her cottage. She caught her foot in a tree root and fell. Jane's right ankle has swollen badly and she cannot put her weight on it. A cast is applied and Jane is instructed not to bear any weight on this foot for three weeks. She is given a pair of crutches and instructed on their use. She is told to return in a week for evaluation.

When she returns, she is told that in two weeks she will be ready for a walking cast, and six weeks after that the cast can be removed.

#### September 7

Classes begin at McMaster.

What muscles are normally used to bear weight? What muscles are used in walking with crutches? With a walking cast?

What state will Jane's foot be in when the cast is removed?

Finally, consider some of the problems which Jane will have when

she starts school. What are some of Jane's assets in dealing with her injury?

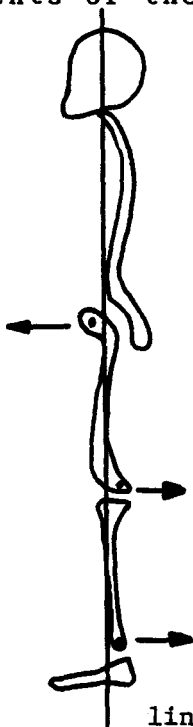


**Tutor Notes - Tutorial Five****JANE NURSE: IMMOBILITY****Objectives**

1. Learn the muscles used for bearing weight, and the changes in the muscles which are used in walking with crutches and walking with a walking cast.
  2. Understand what is meant by atrophy.
  3. Discuss the difficulties which a student with a broken ankle would be faced with, and the physical and mental obstacles that such a student would encounter.
  4. Discuss the assets which a Nursing student would have in this situation.
- 

**Q1. What muscles normally bear weight?**

It is important to realize that the force which the muscles are acting against in the maintenance of an erect position, is the force of gravity. Thus, one must consider the line of gravity through the body, as this is what determines what the natural tendencies for the movements of the joints are.



Arrows indicate the natural tendencies for the joints to move

Figure 5A

Starting from the top, the muscles of the neck are required to maintain the head. Specifically, the dorsal muscles of the neck, or the neck extensors serve this purpose. The **splenius** and **semispinalis capitis** muscles are located at the back of the neck. They arise from the vertebrae and insert on the skull, thus maintain the head in an extended position. The **trapezius** muscle aids in extending the neck, as well as preventing the shoulders from drooping.

Muscles of the **erector spinae** muscle group extend from the sacrum to the skull. These muscles are responsible for keeping the back extended, thus maintaining it in an erect position.

The pelvis must be stabilized by the anterior muscles which flex the hip. The muscles which perform this function are the **iliacus** and the **psoas major**. The **quadriceps femoris** can also flex the hip, and it may help the other two muscles to keep the pelvis stabilized.

Because the line of gravity falls in front of the knee, there is a tendency for it to extend. The **tensor fascia lata** is a small muscle located on the lateral thigh. It pulls on a strip of connective tissue (the fascia lata, which is continuous with the iliotibial tract), and when it contracts, it locks the knee in position. The **gastrocnemius** muscle arises from the femur, and inserts on the calcaneus bone via the Achilles tendon, thus it acts over two joints: the knee and ankle. It also causes flexion of the knee, to oppose the tendency for the knee to extend.

The line of gravity falls in front of the ankle joint, thus the plantar flexors are required to stabilize the joint when standing erect. The plantar flexors are the **gastrocnemius**, **soleus**, **plantaris**, **peroneus longus**, and **tibialis posterior**.

In addition to the weight bearing muscles, the bones of the feet (the talus, calcaneus and metatarsals) are well adapted to bear weight.

## Q2. What muscles are used when walking on crutches?

With Jane's foot in a cast, and she is walking with the use of crutches, the weight has shifted to the upper extremities.

Start at the tips of her fingers and work your way along her upper extremities to determine the muscles which she will be using in this case.

Her fingers will be in a flexed position, as she holds onto her crutches. The intrinsic flexors of the hand are the **flexor pollicis brevis** (it flexes the thumb), and the **lumbricales** (there are four of them, and they flex the digits at the metacarpophalangeal joints. The extrinsic muscles of the digits are

located in the anterior surface of the forearm, and are the **flexor digitorum superficialis**, **flexor digitorum profundus**, and **flexor pollicis longus**.

The wrist is in a slightly extended or neutral position, and to prevent further extension of the wrist, the muscles required to maintain this position are the **flexor carpi radialis**, **flexor carpi ulnaris**, and the **palmaris longus**.

As Jane applies the weight of her body on the crutches, her forearm extends. This force is provided by her **triceps brachii**.

Finally, the **latissimus dorsi** and the **pectoralis** muscles adduct the arms to help support Jane on the crutches.

The foot which is in a cast must be 'carried' and this requires the use of the hip flexors (the **iliacus** and **psoas major** muscles), and the knee flexors. Knee flexion is provided by the hamstrings, of which there are three: the **biceps femoris**, **semitendinosus**, and **semimembranosus**.

**Q3. Finally, what muscles will Jane use when she has a walking cast?**

In order to lift her casted leg and swing it around, Jane will rely on the hip abductors and rotators. These actions are necessary because the casted leg will be longer, and she does not have the use of her knee joint to swing her leg through.

The **gluteus maximus** and **gluteus minimus** rotate the thigh laterally and the **gluteus medius** rotates the thigh medially. The **gluteus medius** and **gluteus minimus** are also abductors of the hip as is the **tenor fascia lata**. The **sartorius** also assists in the action by externally rotating the hip.

The **quadratus lumborum** provides lateral flexion of the vertebral column, which is necessary to 'lift' the leg up. In addition, the **internal and external oblique** muscles laterally rotate the abdominal wall to assist in swinging the lifted leg around.

**Q4. What is meant by muscle atrophy? Distinguish three types of atrophy.**

Atrophy refers to a decrease in the size of the cells and a corresponding decrease in the size of the affected organ. Atrophy of any cells in any organ may occur. Atrophy can be classified as: disease atrophy, aging atrophy and disuse atrophy.

Disease atrophy of muscle tissue may be caused by a disease which directly affects the muscles themselves, or a disease which affects the nervous system. Not only will such a disorder prevent the use of the muscle, but nerve fibres provide a trophic

influence on muscle tissue. Aging atrophy refers simply to the normal aging process of tissues and organs of the body. Disuse atrophy, which is applicable to Jane, is a local atrophy resulting in a decrease in the size of muscle fibres and muscle strength, owing to a loss of sarcoplasm within the muscle fibres.

Atrophy is a reversible process. When exercise is resumed after disuse atrophy, the fibres in healthy muscle tissue will undergo 'hypertrophy'; they will increase in size and strength. This increase can be attributed to an increase in the number of myofibrils accompanied by a strengthening of the associated connective tissue. It is a rare occurrence to find hyperplasia of muscle fibres (increased cell number), and increases in muscle mass are considered to occur solely from an increase in the size of the individual fibres.

**Q5. Consider some of the specific problems which Jane will face.**

The students should be able to come up with many obstacles which Jane will encounter. She will be unable to participate in many athletic events which are a major part of orientation. When classes begin, she will have difficulties in getting from one class to the next and may miss some course material. Carrying books or a tray of food may pose a problem. She will have to find a seat in the aisle in order to extend her casted foot out. Stairs, weather (carrying an umbrella) and transportation are some obstacles in the environment which Nurse Jane may have problems with. The stress of school, of living alone for the first time, and added physical work she will have in walking on crutches, will leave her fatigued. She may develop muscle soreness as a result of the extensive use of some muscles (in her upper extremities) which have not been used to any great extent in the past.

Jane may also face some mental problems; her inability to participate in recreational events may leave her frustrated or depressed.

**Q6. What are some assets which Jane has in dealing with her injury?**

Because Jane is in McMaster's Nursing Program, her classmates will undoubtedly be sympathetic to her condition and will help her out in any way they can. Jane is youthful, and has a great deal of energy, which will make coping easier. Her disposition may be an asset or a liability; she may be a patient, outgoing and determined person and these characteristics would be assets. On the other hand, if Jane was shy and had difficulty asking for assistance, she would have a harder time coping.

Q7. Finally, are there any benefits which may arise from this injury?

While the injury may seem to be nothing but a problem for Jane now, she may be able to use this disability in her future career. Presumably she will be able to empathize with patients she may see who are in the same predicament, and her first-hand experience may help in her nursing care of such patients.

## Laboratory Five

### LIVING ANATOMY

#### Prerequisite Activities:

Read over this material beforehand and look up any terms and names of muscles with which you are not familiar.

#### Objectives:

1. to gain an understanding of the mechanical and muscular factors involved in the erect posture.
2. To examine coordinated muscle action and the roles of prime movers (agonists), antagonistic muscles, synergistic muscles, and stabilizing muscles.

#### Materials and Methods:

The important feature of this exercise is that it provides an opportunity to study living anatomy, which is after all what health professional are concerned with in their work. Each of you will be expected to perform the activities described in the exercise and to observe these as your lab partners also perform them. It would be ideal if the members of the class could wear gym clothes. While we will not insist that this be done, you are urged to do so if possible. In any event, make certain that you wear appropriate clothing so that you can participate in the exercise(s) described below.

#### PART A - FUNCTIONAL ANATOMY OF THE TRUNK - STANDING ERECT

When one is standing properly erect, a vertical line passing through the centre of gravity of the body would extend from the middle of the skull (approximately where it joins the cervical vertebrae) in front of the thoracic and lumbar regions of the vertebral column, pass through the sacral promontory, and from there downward behind the hip joint, but in front of the knee and ankle joints. In order to understand how this position is maintained, we need to consider two areas: the trunk and the lower extremity.

The problem in maintaining the vertebral column erect is the same as trying to keep a stack of spools or barrels erect. (The fact that the vertebral centra are not in a vertical column but curved is not really relevant in this respect). The muscles responsible for this are the true dorsal muscles which lie on either side of the spinous processes of the vertebrae, in the "gutters" formed by the spinous processes and the ribs or transverse processes of the lower vertebrae. The more superficial fascicles of these

muscles are called the erector spinae and are primarily the ones which maintain the column erect. (The deeper fascicles also help, but, as well, are concerned with rotatory movements of the vertebrae).

Looking from the back, it is obvious that the left and right erector spinae act like "ship's rigging" to stabilize the column laterally.

**EXPERIMENT** - You can verify this function by sitting on a stool and placing your fingers on the erector spinae in the middle of your lumbar region (just above the waist) as your lab partner lifts upward with hands placed under your arms. You will feel the erector spinae slacken as the weight is removed from the vertebral column. Conversely, have your lab partner push against one shoulder (laterally) and note the increase in tension on the side being pushed as the muscles resist the force.

Now that you have an idea of how the muscles feel when contracted or slack, sit or stand erect and note that both left and right erector spinae are under some degree of contraction. Bend laterally and note that if you bend left, the right group of muscles is under more contraction than the left, and vice versa.

What you have been examining is the stabilizing effect. That is, two groups of muscles with opposite actions. Both are under tonic contraction in order to maintain the skeletal structure in a stable position.

Now what about front-back movement? Note on a skeleton that the erector spinae muscles lie behind (dorsal) the centre of the vertebrae. Thus, when they contract they tend to pull the vertebrae backward. However, which muscles act as antagonists and pull the vertebrae forward? Actually, none! Remember the centre of gravity is in front of the vertebral column and the dorsal muscles hold the vertebrae erect by opposing the antagonistic action of gravity. Actually, there are muscles which can bend the vertebral column forward (ie. flex), but they only act when one flexes against resistance.

This is easily demonstrated by lying supine and sitting up (against the force of gravity). Note that the abdominal muscles contract immediately, pull the thorax toward the pelvis and flex the spine. Question: If you were lying down and wanted to sit up (unassisted) without using the abdominal muscles (or at least use them minimally), how could you do it?

When standing, keeping the vertebral column erect is only part of the problem. The rest involves the lower extremities. There are three joints which must be stabilized in the lower extremity; the ankle, the knee and the hip.

The ankle joint is capable of some lateral movement called eversion (sole of the foot outward) and inversion (sole of the foot inward), but its chief movement is like a hinge joint which allows us to point our toes up (dorsiflexion) and down (plantarflexion). When standing erect, we would expect that the flexors (the gastrocnemius and soleus) and the extensors (chiefly the tibialis anterior) would be in tonic contraction to counterbalance each other and keep the joint stable. In fact, you will note that only the flexors are contracting. The reason is that the line of gravity falls in front of the ankle and only flexors need counter this force to stabilize the ankle. At this point you might logically ask whether or not the line of gravity passes through the ankle joint, and then less work would have to be done to stand erect. You can test this as follows:

**EXPERIMENT:** Standing without shoes, have someone palpate your calf muscles (gastrocnemius, with soleus beneath) and note the degree of tension. Now, stand with your heel resting on a slight elevation (about one inch). This thrusts the ankle joint forward slightly toward the line of gravity and the degree of contraction of the calf muscles should decrease. Now, if you repeat this experiment with high heels (about 3" heel height), you will discover that the tibialis anterior muscle begins to contract as well. (The tibialis anterior lies just lateral to the "shin bone" and its tendon is the large one which crosses the front of the ankle. The reason is that if the ankle joint is in the line of gravity, the flexor and extensor muscles must act in concert as "rigging" to stabilize the joint).

What about stabilizing the knee joint? Actually this is no problem. First, the line of gravity falls in front of the knee. Thus, the tendency would be for the knee to bend forward. However, the structure of the joint prevents hyperextension. Second, the gastrocnemius muscle actually takes its origin from the femur above the knee and since it is contracting to stabilize the ankle it would tend to slightly flex the knee anyway. Third, and more important, a small muscle called the tensor fascia lata (which is located on the lateral thigh about the position of the pocket seam in trouser) pulls on a strip of strong connective tissue which passes down the side of the thigh to the knee joint. When the knee is fully extended, contraction of the tensor fascia lata effectively locks the knee joint in position. (This occasionally proves to be embarrassing in military formations, where it is possible to stand at attention and actually fall over like a tree trunk while fully conscious).

With the hip joint, the line of gravity passes behind the joint and it is necessary for the flexors to be active against the pull of gravity to effect stability. The pure flexors of the hip are the iliacus and psoas muscles. They arise from the ventral (front) aspect of lumbar vertebrae and the ilium of the pelvis.



For this reason if one stands relatively still for a long time, one feels some discomfort in the lower back. The reason is that these muscles have been pulling forward against the lower vertebral column to stabilize the hip joint. The large knee extensor muscle on the front of the thigh, the quadriceps femoris, can also flex the hip and if one moves about, it shares the work of the hip stabilization with the iliacus and psoas. Hence, walking is less fatiguing than standing still.

You can verify the action of the quadriceps by standing with your fingertips touching the front of your thigh and rocking backward slightly. You will feel the muscle tighten as it counters the tendency of gravity to pull the hip into extension. Repeat the maneuver while your lab partner pushes against your back (to counter the force of gravity) and note that the quadriceps do not actively contract.

## **PART B - FUNCTIONAL ANATOMY OF THE UPPER EXTREMITY**

**Note:** Skeletal material as well as models of the hand will be available in the '2J' laboratories. It will be helpful if you will bring your Anatomy textbook with you.

Beginning at the sternoclavicular articulation, palpate the clavicle, the acromion process of the scapula, and the spine of the scapula. Also, locate the inferior and superior angles of the scapula.

Using an illustration as a guide, try to trace the outline of the trapezius muscle. Its upper border forms the lateral contour of the neck. The lower border is rather difficult to locate.

A thin sheet of muscle stretches from the margin of the mandible downward to the area of the first two ribs. This is the platysma muscle, which tenses the skin in the neck. Its development varies widely in individuals. See if you can demonstrate its presence.

Try to abduct the shoulder against resistance to demonstrate the outline of the deltoid. Note that the deltoid hangs down from its bony origin much like epaulettes on a uniform. You might note further that if you hold someone's arms closely against their side, it is fairly easy to prevent them from abducting the limb. If you allow them to get their elbows away from their side it is much more difficult. The reason is that the deltoid, although it is the chief abductor of the shoulder joint, cannot initiate abduction due to the angle of its fibres. The supraspinatus, which lies deep to the deltoid, actually moves the joint into a slightly abducted position, after which the deltoid fibres can begin moving the limb effectively.

With the shoulder partly abducted (about  $45^{\circ}$ ), try to adduct against resistance. You will note that the anterior and posterior parts of the deltoid contract, but not the lateral (middle) fibres. You can also see the structures which form the anterior and posterior border of the axilla (arm pit). These muscles, the pectoralis major anteriorly and the latissimus dorsi posteriorly, are actually the chief adductors of the shoulder joint. Since they originate in the vertebral column, they also are important movers of the shoulder girdle.

Try to extend the elbow joint against resistance to demonstrate the action of the triceps brachii. Now, with the forearm horizontal and the elbow against the side, try to pull your arm back (this is, by the way, extension of the shoulder joint). Does the triceps contract during this action? Why?

Sit with your forearm resting on the laboratory bench surface. Try to flex your elbow against resistance while (1) your hand is pronated, (2) your hand is half pronated (or half supinated) and (3) while your hand is supinate. In which position do you have the most power? The least?

You should have found that you had the most strength when your hand was supinated. The reason has to do with the tendon of insertion of the biceps brachii muscle, which attaches to the radial tuberosity. When the hand is in other than a supinated position, the tendon is wrapped around the radius. Thus, contracting the biceps not only flexes the elbow, it also tends to bring the hand into supination. To prevent this, other muscles must resist the supination and hence counter some of the force of the biceps, making it less efficient in performing flexion.

Two other muscles participate in elbow flexion. The brachialis muscle is under the biceps and cannot usually be demonstrated. It is not a large muscle, but its ability to perform flexion is not affected by the position of the hand and forearm. The brachioradialis muscle also flexes the elbow. This muscle extends from the lateral distal side of the humerus to the distal end (styloid process) of the radius. This muscle is actually a post-axial muscle (and hence, radial nerve innervated) despite the fact that it performs flexion. You will note that unless the hand is in a half pronated position this muscle will tend to bring the hand into that position. Thus, its action is resisted by other (antagonistic) muscles in some instances.

A number of muscles lie in the forearm and some of them cannot be easily palpated. However, you should undertake to locate and demonstrate the function of the major ones.

The flexor carpi radialis, flexor carpi ulnaris, extensor carpi ulnaris and extensor carpi radialis longus and brevis muscle

constitute the so-called "corner" muscles. While keeping the fingers relaxed, try flexing the wrist against resistance and locate by palpation the flexor carpi muscles. In the same way, locate the extensor carpi muscles. (You might wish to outline in grease pencil or coloured chalk the position of these muscles). If you place your thumb and fifth digit together and flex your wrist, you should see a tendon become prominent in the middle of the wrist. This is the palmaris longus tendon. The muscle inserts into a "web" of connective tissue (the palmar aponeurosis), not on the bone. Some of you will not have a palmaris longus muscle as it is absent in about 20%.

If you wiggle your fingers without moving the wrist you will be able to see and feel the common flexors and the common extensor of the digits. Again, you might wish to mark the position of these muscles with a grease pencil.

You should note that the extrinsic muscles which serve the digits obviously cross the wrist, and, of course, assist in flexion and extension at that joint.

There are several extrinsic muscles which serve the thumb, second digit (index finger) and fifth digit (little finger). These are difficult to palpate separately but you can demonstrate their actions and can certainly locate some of the tendons as they cross the wrist.

What is the anatomical "snuff-box" and what structures form it? (It is produced at the wrist when the tendons of the extensor pollicis longus on the inside and the extensor pollicis brevis on the outside are tensed so as to pull up two ridges of skin).

It is difficult to palpate the intrinsic muscles of the hand. However, you can demonstrate their actions and distinguish these from the actions performed by the extrinsic hand muscles. For example, with the fingers straight, flex the metacarp-phalangeal joint (the knuckle) and hold the hand in that position. You will soon note that your hand begins to "feel tired". Now, clench your fist tightly and note that after a minute or so, you feel the muscular strain in your forearm, and not your hand.

Finally, you should, with the aid of your anatomy text, locate and palpate as many of the bony landmarks of the forearm, wrist and hand as possible. An understanding of their normal relationships can prove most useful in trying to assess whether an individual has sustained a fracture.

## **PART C - FUNCTIONAL ANATOMY OF THE LOWER EXTREMITY**

Owing to the exquisite coordination of muscles in a normal

individual, we seldom realize that walking, reduced to its simplest terms consists of falling forward and catching one's self by using one leg as a brace to stop our fall. We are reminded of this, however, when we "trip" since even a slight impediment in swinging the leg forward can send one sprawling forward.

Observe someone walk slowly. Note when starting from a standing position the weight of the body shifts to one leg, which frees the other to move. As the body begins to lean (fall) forward, the hip joint of the "free" extremity is flexed to lift the foot clear of the ground. The knee will flex passively. (The muscles controlling the knee do, in fact, undergo some contraction to ensure smooth coordinated movement.) At the ankle, the extensors of the ankle (the tibialis anterior, chiefly) contract actively to hold the toes clear of the ground. If they did not, the foot would drop down and it would be necessary to flex the hip and knee even more to avoid dragging the toes. Such an exaggerated stepping is seen in individuals with a damaged peroneal nerve which causes "foot drop".

As the limb swings forward, the knee goes into extension by inertia and the hamstring muscles with the help of the gluteus maximus, brake the swing of the limb.

As the advanced foot strikes the floor, note that the heel makes first contact. At this time, the ankle joint (which is above and in front of the heel), tends to continue its movement forward. Unless the extensors of the ankle are contracted, the foot will rotate as in plantar flexion and "slap" the floor. If you have tried to walk when your foot has "gone to sleep" you will have experienced this sensation.

As the heel of the advanced foot strikes the floor, the knee is in extension but the limb is not vertical. When the weight of the body shifts onto the advanced limb, there is a brief period, in which the knee must be held in active extension by the quadriceps femoris. Otherwise it is likely to flex ("buckle") with the result that the individual will fall backward. (Remember, in standing the knee can be "locked" in extension almost without muscular action, and in the stride forward, it was able to swing into full extension passively).

What happens to the hip joint as the weight is taken up by the advance limb? Remember in order to step forward, the hip was flexed to lift the foot from the ground. Now, it must be pulled into extension. This is accomplished by both the gluteus maximus and the hamstring muscles.

You can verify the action of the gluteus maximus by walking slowly while palpating the gluteal muscle. Note that it actively contracts as you move forward onto the advanced foot.

As soon as the limb is vertical it is in essentially the same situation as when you were standing still, except that now all the weight of the body is on the one limb. (The opposite limb is now going through the motions we have previously considered). This state lasts only an instant, however, as the body continues to move forward. At this point one of two things could occur. If the leg muscles maintained the ankle fixed, the heel would lift from the ground and the weight being borne by the limb would be transferred to the distal metatarsal heads. Soon the foot would be pulled forward and the process of hip flexion, knee flexion and ankle dorsiflexion would be repeated to get the limb in front of the body to act as a brace during the next step. This is not the normal way of walking, but anyone who has worn stiff boots, an ankle castor walked with muscles tensed to "splint" a sore ankle has experienced this mode of walking. It is also the mode of walking for someone wearing high heels, if they are not accustomed to them. However, the geometry of the foot is different owing to the shoe maintaining the ankle in a plantar flexed position even at rest.

The normal action of the trailing foot in walking is as follows. As the trunk moves ahead of the foot, the ankle extends (dorsiflexes) somewhat, maintaining heel contact. To do this the calf muscles must relax somewhat. (Remember they were contracting to keep the ankle stable). Then, when the body has moved far enough that the foot is about to be dragged forward, the calf muscles contract vigorously. This plantar flexes the foot immediately and the foot acts like a lever and pushes forward (a movement called "push off"). Then the actions previously described occur to swing the limb to the front where it catches the body.

In some individuals the push off is divided into two phases. The heel will be pulled off the ground before the sudden plantar flexion which propels the body forward. This gives one a "bouncy" gait. Such a gait is more costly in terms of energy expended as the muscles must actively support the weight of the body against a considerable torque. However, it serves to "cock" the foot so that at push off reaction time is lessened and force is increased. As a result, this gait is more commonly seen among athletes.

**EXPERIMENT:** Walk normally and have your lab partner analyze your gait. Walk with ankle stiff and note the rolling gait and tendency to drag the foot forward along the floor. If you can execute the two phase push off, walk 10 steps in that manner, then 10 steps normally and note the difference in exertion by the calf muscles. Finally, without shoes, walk normally and note the action of the toes. What do they do? Do they contribute significantly to walking? What would be the effect on walking with the loss of the toes?

One last aspect of locomotion needs to be examined: the pelvis. When standing erect the pelvis is supported in a horizontal position by the lower extremities (ie. the sides are at equal height). When one foot is lifted, however, the pelvis tends to drop laterally toward the unsupported side. To prevent this (or at least check it) the abductors of the hip (gluteus medius and minimus) contract on the supported side to counter this movement. At the same time the erector spinae on the unsupported side shorten and pull up of the pelvis. (The erector spinae on the supported side also contract to fix the vertebral column against the pull of the opposite erector spinae). Collectively, these actions can prevent the pelvis from sagging toward the unsupported side. However, if nothing else happened, we would still fall sideways. Remember the centre of gravity is medial to the limb which is supporting the body. To move the centre of gravity over the foot which is in contact with the ground, the body tends to sway laterally toward the supported side. As well, the trunk rotates toward the side of the limb on the ground.

You can demonstrate these motions by standing still and lifting one foot from the ground, then slowly step forward. In normal walking, the balance which you require to stand on one foot is never quite attained, since the next step begins before balance is effected. Demonstrate this by walking normally and stopping quickly in mid stride (ie. one foot raised).

### SUMMARY QUESTIONS

1. Paralysis of the gastrocnemius and soleus muscles should induce what problem of locomotion?
2. Paralysis of the extensors of the ankle (tibialis anterior, extensor digitorum longus, extensor hallucis longus) would lead to what sort of problem in walking?
3. In running, as in walking, power is applied during the powerful plantar flexion caused by gastrocnemius and soleus contraction at "lift-off". However, some of the world's best distance runners have remarkably thin legs. Can you explain this apparent paradox?

## Tutor Notes - Laboratory Five

### LIVING ANATOMY

The main objective of this exercise is to induce the students to relate anatomical facts to the living body. In addition, they should develop an understanding of the functioning of opposing muscles, as well as relating structure to function.

Surface anatomy is an important part of the study of gross anatomy. To know what lies beneath the skin helps in the overall understanding of gross anatomical structures. The best way to study surface anatomy is by studying living subjects. The use of textbooks and models can reinforce the information which is covered as one proceeds through the exercise.

It is the role of the tutor to ensure that the students complete the exercises and to guide them to appropriate resources to clarify any problems the students encounter. Not all the possible landmarks and muscles which can be examined by palpation are covered; encourage students to discuss and examine muscles and functions other than those listed if the opportunity is available.

## Tutorial Six

### OSTEOSARCOMA

#### Objectives

1. Discuss the effects on the gait which would be encountered by a patient with a leg amputation.
2. This tutorial should provide an overview of some aspects of cancer, with specific reference to osteosarcoma.
3. In this discussion of cancer, osteosarcoma will be dealt with in more detail. Diagnosis, treatment and physical problems associated with osteosarcoma will be considered.

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Two young men who have been in the public eye in the past ten years or so for their coping with osteosarcoma of a leg are Edward Kennedy Jr., son of Teddy Kennedy, and Terry Fox. Both these men had a high amputation of the leg affected, and each learned to compensate for the loss of that limb. This tutorial focuses on the implications of a malignancy in a limb. Also, you should be able to discuss some aspects of cancer.

Use your knowledge about the muscles of the lower limb to determine what, if any, changes will be required in terms of the muscles used for walking in patients with transfemoral amputations. Can you think of other ways, besides gait changes, in which an amputee would be affected?

What is cancer? What are tumours? How is cancer treated? What do you know about chemotherapy?

Osteosarcoma is a rare form of cancer. Be prepared to discuss this disease. Consider the following: the definition and incidence of osteosarcoma; the sites it commonly affects; diagnosis; signs and symptoms; available treatments; and prognosis.

In addition to the regular tutorial session, for the second hour you will have the opportunity to listen to a young adult who has had osteosarcoma, discuss the disease and the effects of a prosthesis. If you have any questions about any aspect of walking with a prosthesis, or cancer, this individual will be an excellent resource. Students from past years have enjoyed this session tremendously, as well as learning a great deal about the topics.



## Tutor Notes - Tutorial Six

### OSTEOSARCOMA

#### Objectives

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Consider some of the affects which a prosthesis will have on a patient who have received a transfemoral amputation.

**Q1. What will the affect of the prosthesis be on the muscles used for walking?**

The effect of the prosthesis on the gait of an individual will depend in part on the level of the amputation, and the prosthetic device. Without a functional knee, the hip ab/adductors will be called into play in order to clear the prosthesis off the ground. In addition the abdominal muscles will be needed to lift the prosthesis. Such problems are overcome by either a below-the-knee level of amputation, or a prosthetic device which has a knee.

(These points will be covered in more detail in the second part of this tutorial session when you will have the opportunity to speak with a young adult who has had a leg amputated).

**Q2. What other possible physical problems would such an individual face?**

With the change in the muscles which are used, amputees commonly develop 'scoliosis', a curvature of the spine. Pressure points on the stump may lead to the development of pressure sores and necrosis. Psychological problems may result as the patient may have difficulty in accepting his handicap, and may develop a poor self-image. Finally, the individual will experience "phantom pains" when the nerve fibres in the stump are stimulated and send afferent impulses to the CNS.

**Q3. In the broadest terms, how would you define cancer?**

While cancer is a general term referring to many diseases, all cancers have the common characteristic of involving uncontrolled

proliferation of un-differentiated cells.

**Q4. Often you associate cancer with 'malignant tumours'. What are benign and malignant tumours?**

First, tumours can be defined as masses of new cells, the growth of which is not under the control of the organism, and which serves no useful function for the host.

Benign tumours are those which grow evenly from their centre, and remain at the site of their origin. Examples of benign tumours are some moles and warts. Once they have been removed surgically, benign tumours seldom recur.

Malignant tumours are composed of atypical cells with aberrant chromosomes. The cells divide rapidly, and they grow irregularly and invade surrounding tissue. Malignant tumours have the ability to 'metastasize', which means that they are able to spread to distant sites. Malignant cells are disseminated through the body via lymphatic and blood vessels, or may spread to other areas by direct invasion. Millions of cells may be shed by malignant tumours each day.

**Q5. What are some common treatments for cancer?**

- i. surgery
- ii. radiation
- iii. chemotherapy

With reference to the third treatment listed, it should be emphasized that no drugs yet available are truly selective for malignant cells.

**Q5a. What is the usual mechanism by which these 'antineoplastic' drugs work?**

Antineoplastic drugs work by inhibiting cell proliferation. The drugs are selective only to the extent that they are more toxic to cells in the body which divide at a relatively rapid rate.

**Q5b. Given this mechanism of action for these drugs, what problems would you expect with their use?**

All antineoplastic agents exert substantial toxicity on some normal cells of the body. Tissues which are composed of cells which have short generation times are most susceptible to be affected. Thus, gastrointestinal, epithelial and hematopoietic tissues are most likely to suffer.

**Q5c. What would be the major factor in determining whether a patient would be treated using chemotherapy versus surgery?**

Surgery is the usual treatment for cancers which do not appear to have metastasized at the time of diagnosis. However, if the cancer has spread, surgery may be life-saving, such as in the case of space occupying lesions causing pressure; otherwise surgery is of little value in the cases of cancer in which metastasis are already present.

On the other hand, chemotherapy is the most important method of therapy when metastasis is present. Since these are the patients with the poorest prognosis, chemotherapy is often associated with success rates lower than for surgery.

Turn now to a discussion about **osteosarcoma**. Consider the following in your discussion:

1. definition
2. incidence
3. sites most commonly affected
4. diagnosis
5. signs and symptoms
6. treatments available
7. prognosis

1. Osteosarcoma can be defined as a malignant neoplasm derived from osteoblast cells in which there is osteoid production (this is the organic part of the intercellular bone matrix).
2. The ages of presentation are usually between 10 and 25 years. It is more common in males; the ratio of male to female patients is about 2:1.
3. Osteosarcoma may arise within any bone of the skeleton, but more than 90% arise within the long bones. About 75% are around the knee at the epiphyseal plate area, just below the periosteum.
4. The majority of patients with osteosarcoma can be diagnosed with a reasonable degree of confidence from the appearance of the lesion on x-ray film. Biopsies of the tissue expected to be malignant are used to confirm the diagnosis.
5. There is an increase in the size and the number of blood vessels present around the tumour. There is also an increase in the local temperature. As the tumour increases in size, the skin over it stretches and becomes taut, thin and has a glossy appearance. The earliest symptom is pain, usually over the site of the tumour. Pain may be intermittent, but is always located in the same area. Finally, the tumour growth may impinge on other structures including muscles, nerves and blood vessels.

6. Removal of the primary lesion by 'adequate surgery' is the acceptable management of the primary tumour.

Q6. What needs to be considered in determining the level of amputation? What surgical procedure would you recommend for tumours arising below the knee? In the proximal femur? In the distal femur?

Two important considerations in determining the level of amputation are first, the possibility of 'skip metastasis' which are metastasis occurring within a single bone or across a joint. They are relatively common in osteosarcoma. Second, the functional limitations associated with the surgical procedures must also be considered in determining the level of amputation.

The minimal functional difference between below the knee and above the knee amputation is a good reason why the amputation level for tumours below the knee should be transfemoral (and lesions below the elbow should be transhumeral). This minimizes the risk of skip metastasis.

Hip 'disarticulation' (amputations at a joint) is the preferred treatment for tumours at the proximal femur.

The appropriate level of amputation for tumours arising in the distal femur, the most common site for osteosarcoma, is controversial. One must consider the significant functional limitations of hip disarticulations as compared to transfemoral amputations. However, stump recurrence following transfemoral amputation which have been reported to be as high as 30% must also be considered. The surgeon must decide whether the risk of local recurrence is worth the functional benefits of an above the knee stump.

Q7. What variables would influence the prognosis of the patient?

The stage of the disease (which reflects the presence of metastasis and the surgical accessibility of the primary lesion) at the time of diagnosis, and the subsequent treatment determines the prognosis of the patient.

## Laboratory Six

### LOCOMOTION ANATOMY

This 'Musculoskeletal Lab' is your introduction to practical Anatomy in the Anatomy lab using prepared human materials. You should bring your textbooks to this lab and be well prepared.

#### Objectives:

1. A review of the musculoskeletal system.
2. Actual visualization of major muscles and their relationship to the joints they cross.
3. Realized that each muscle 'compartment' (ex. flexor or extensor compartment) usually has one main nerve supply.

This lab will consist of demonstration of the skeleton, selected muscles, joints and their movements under the headings of:

#### 1. Neck and Thorax

##### NECK:

- neck moving muscles especially sternocleidomastoid and trapezius
- accessory nerve (eleventh cranial nerve)

##### THORAX:

- intercostal muscles
- the diaphragm and phrenic nerve
- accessory muscles of respiration

#### 2. Abdomen and Back

##### ABDOMEN:

- muscles of anterior abdominal wall

##### BACK:

- extrinsic back muscles
- intrinsic back muscles (superficial, intermediate and deep)

#### 3. Upper and Lower Limbs

##### UPPER LIMB: chief flexors, extensors and rotators

- important injection sites
- main nerves of flexor and extensor compartments

##### LOWER LIMB: Chief flexors, extensors, adductors of hip and knee

- chief flexors, extensors and rotators of ankle joint
- main nerves in each compartment
- important injection sites
- fractures, dislocations, arthritis of hip joint in the elderly

## Tutor Notes - Laboratory Six

### LOCOMOTION ANATOMY

Major muscle groups should be identified, as well as their major nerve supply. Exact points of origin, insertion and minute functions should not be emphasized. This information is available in any textbook.

#### 1. Neck and Thorax

##### NECK:

Causes and results of paralysis or fibrosis of the sternocleidomastoid and trapezius should be discussed.

THORAX: A brief mention of intercostal nerves and phrenic nerve should be made. Referred pain to the shoulder travels along the phrenic nerve following diaphragmatic irritation.

#### 2. Abdomen and Back

##### ABDOMEN:

The three layers of muscles, directions of their fibres and similarities to intercostals should be pointed out. Laxity of these muscles may give rise to some kinds of hernias.

##### BACK:

Avoid details of intricate muscle actions. Spasm of intrinsic muscles of the back may give rise to backache, as well as vertebral joint problem. (Discuss disc herniation, scoliosis, kyphosis, lordosis).

#### 3. Upper and Lower Limbs

##### UPPER LIMB:

Intramuscular injections in the deltoid area, especially in children should be avoided. Complications of such injections include fibrosis of the deltoid, and paralysis of the axillary nerve. Injections into the triceps should be avoided since this may damage the radial, branchial or ulnar nerve and the profunda brachii artery. Demonstrate the brachial plexus.

##### LOWER LIMB:

In children under 2 years of age, subcutaneous fat may be mistaken for gluteus maximus. In adults, injections may be given in the upper outer quadrant of gluteus maximus to avoid injuring the sacral nerve. Injections into anterior or lateral thigh are often given in infants. This is because quadriceps femoris is the largest muscle in the body and at birth this area has a relatively large mass. Compare shoulder and hip joint. Geriatric problems in the hip joint should be mentioned briefly.

## Tutorial Seven

### CONGENITAL HEART DEFECTS

#### Objectives

1. Understand the differences between adult and fetal circulation.
2. Develop a thorough understanding of the fetal circulation and the special adaptations necessary for life in utero.
3. Understand the structural anomalies involved, and the effects of some congenital heart defects.

-----

Mrs. Devlin is in labour and, within the next few minutes, baby boy Devlin will be delivered. For the past nine months, the baby has depended upon his mother circulatory system for the delivery of oxygen and nutrients, and the removal of carbon dioxide. Now, however, the baby will be independent; clearly changes will have to occur in his circulatory system.

The circulatory system of the fetus is different from that of adults. How is the blood in an adult oxygenated? How, and why is this different in the fetus?

Make sure you have a good understanding of the blood flow in the fetus, and why these specializations are critical. Trace the flow of blood through the fetus. Above all, keep in mind WHY blood travels the route it does.

Some structures have a specific function in the fetal circulation. What do these structures become in adults: umbilical artery; umbilical vein; ductus venosus; ductus arteriosus; and foramen ovale?

As soon as baby Devlin is delivered changes occur in his circulatory system. What are the two main changes in the vascular resistance which occur at birth?

While Mrs. Devlin was on the maternity ward, she talked to Mrs. Congenita, who had just given birth to baby Connie. Mrs. Congenita explained to Mrs. Devlin that baby Connie had a ghastly 'blue' appearance when she was born. Her doctor informed her that baby Connie had a congenital heart defect called 'Tetralogy of Fallot'.

Four relatively common birth defects are: atrial septal defect (for example, patent foramen ovale; patent ductus arteriosus; coarctation of the aorta; and Tetralogy of Fallot). Describe these defects. What are the consequences of these defects to blood flow?

What are some of the possible causes of congenital heart defects?



**Tutor Notes - Tutorial Seven****CONGENITAL HEART DEFECTS**Objectives

1. Understand the differences between adult and fetal circulation.
  2. Develop a thorough understanding of the fetal circulation and the special adaptations necessary for life in utero.
  3. Understand the structural anomalies involved, and the effects of some congenital heart defects.
- 

Before discussing fetal circulation, a brief review of the adult circulation is in order.

**Q1. How is the blood in an adult oxygenated?**

In an adult, the blood is oxygenated as it flows from the right side of the heart then through the lungs where oxygen is taken up by the blood and carbon dioxide is released. The oxygenated blood returns to the left side of the heart via the pulmonary veins. From here it is ejected by the left ventricle then into the systemic circulation, before returning to the right side of the heart.

**Q2. How does this differ in the fetus?**

Obviously this route by which the blood is oxygenated cannot operate in the fetus as its lungs are not exposed to the atmosphere. Thus, in the fetus, the lungs are not functional with respect to the transfer of gases; rather, gas exchange occurs in the placenta.

**Q2a. Before looking at the specifics of the fetal circulation, there are two main specializations which exist in the flow of blood in the fetus to ensure the proper oxygenation of all tissues. What are these two special arrangements?**

To ensure adequate oxygenation of the fetal organs, the fetal circulation is arranged in a way such that several sites of intercommunication or shunts are present. In addition, preferential flow or streaming of the blood occurs to limit the disadvantage of the intermixing of oxygenated and deoxygenated blood.

**Q2b. Where is the fetal blood most highly saturated with oxygen, and where does it go from there?**

The umbilical venous blood is the most highly saturated blood in the fetal circulation. Therefore the distribution of this blood is very important to ensure that all the fetal tissues receive appropriate oxygenation.

Once the blood has entered the intra-abdominal portion of the umbilical vein, a portion of this umbilical venous blood supplies the liver. However, much of this highly oxygenated blood bypasses the hepatic circulation through the **ductus venosus** which directly connects the umbilical vein to the inferior vena cava.

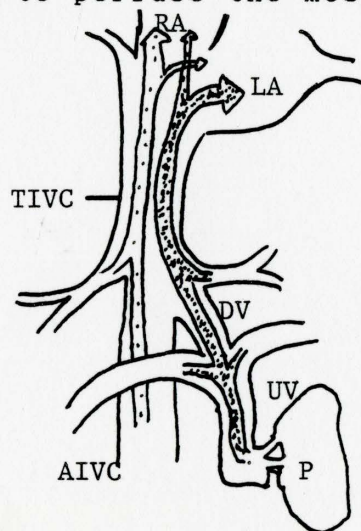
**Q2c. What other vessels, besides the ductus venosus drain into the inferior vena cava?**

Blood returning from the systemic circulation via the abdominal inferior vena cava, as well as blood returning from the liver, will join the blood which has been shunted through the ductus venosus. It is important to realize that these vessels will carry blood which is not well oxygenated, compared to that of the ductus venosus.

**Q2d. Does the blood from these different vessels mix? Why is this important?**

The two streams, one from the abdominal inferior vena cava plus the right hepatic vein and one from the ductus venosus, demonstrate definite streaming within the thoracic inferior venal cava, to minimize mixing of the blood. The well oxygenated blood derived from the ductus venosus occupies the dorsal and leftward portion of the inferior vena cava, while the other 'stream' occupies the anterior, rightward portion of the inferior vena cava.

This arrangement tends to prevent the mixing of well and poorly oxygenated blood. As will be seen, the well-oxygenated blood can go on to perfuse the most important organs of the fetus.



- RA - right atrium
- LA - left atrium
- TIVC - thoracic inferior vena cava
- AIVC - abdominal inferior vena cava
- DV - ductus venosus
- UV - umbilical vein
- P - placenta

Figure 7A

**Q2e. The blood now enters the right atrium. Where does it go from here?**

Once again the process of streaming occurs. This is a result of thin membranous structures called *crista* found in the right atrium, and the position of the *foramen ovale*, a hole between the left and right atria.

The *crista dividens* is positioned such that it overrides the orifice of the inferior vena cava and as a result, it splits the inferior vena caval blood stream into an anterior and rightward stream (remember this carries the less well oxygenated blood) which then is directed to the tricuspid valve and then into the right ventricle. The other stream is dorsal and leftward (carrying blood from the *ductus venosus*), and it is preferentially streamed through the *foramen ovale* into the left atrium.

**Q2f. Blood from the superior vena cava and the coronary sinus (blood which has perfused the cardiac muscle itself) also enters the right atrium. Which pathway would this blood take?**

This blood follows a pathway similar to that followed by the rightward stream of the inferior vena cava. The *crista interveniens* directs the superior vena caval blood towards the tricuspid valve which it passes through to reach the right ventricle. It makes sense that this is the pathway which is taken because like the rightward stream of the inferior vena cava, these vessels carry relatively poorly oxygenated blood.

**Q2g. In the adult, blood is ejected from the right ventricle into the pulmonary arteries. Is this the same pathway as that in the fetus? Where does the blood which is ejected from the left ventricle go?**

Only a small portion of blood leaving the right ventricle goes on to perfuse the lungs. A greater portion passes through another shunt, the *ductus arteriosus* which feeds into the descending aorta, then back to the placenta for reoxygenation.

Blood which is ejected by the left ventricle enters the ascending aorta, and from here, this relatively well-oxygenated blood goes on to perfuse the brain, the head, the upper limbs and the upper thorax.

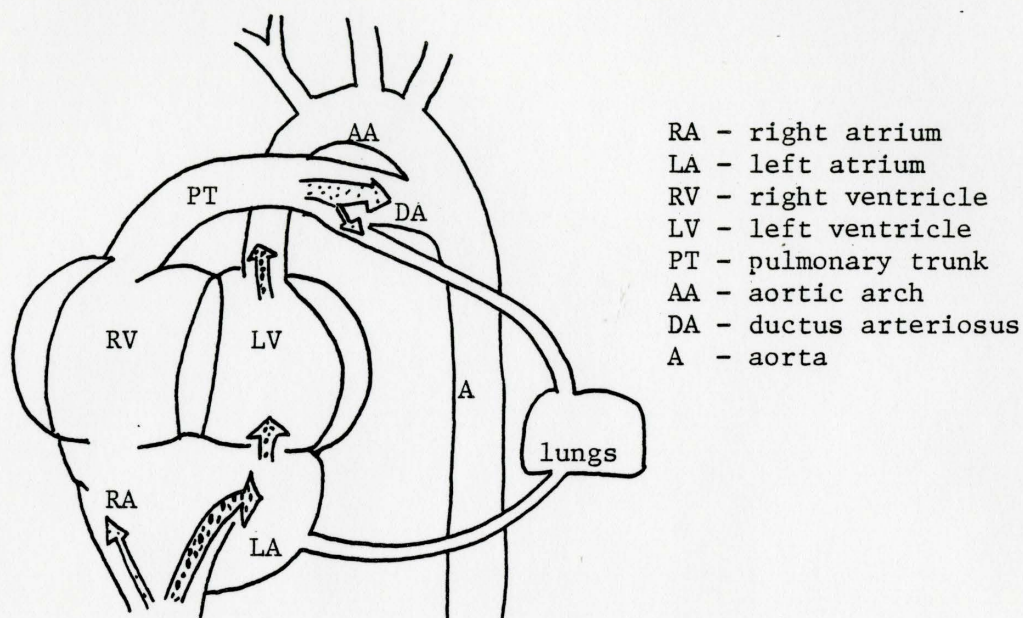


Figure 7B

**Q3. Many of structures which have been mentioned are unique to the fetus. What structures do they become in adults?**

Umbilical artery - Medial umbilical ligament

Umbilical vein - ligamentum teres hepatis or round ligament of the liver

ductus venosus - ligamentum venosum (a fibrous cord in the liver)

ductus arteriosus - ligamentum arteriosum (complete closure at about 6 weeks)

foramen ovale - fossa ovalis (a depression in the interatrial septum)

**Q4. Clearly some changes must occur in the fetal circulation at the time of birth. These changes result in part from the changes in vascular resistance. First, what changes in vascular resistance occur in the fetal circulation, and second, what effects do these changes have on the structures which are unique to the fetal circulation?**

Two main changes occur at birth with respect to vascular resistance. The loss of the great amount of blood flow through the placenta results in a sharp increase in systemic pressure. This results in an increased pressure within the aorta, as well as the pressure in the left chambers of the heart. With the expansion of the lungs that occurs with the first breath of the neonate, the resistance of the pulmonary vessels decreases

markedly (in the fetal lungs, the blood vessels are compressed). Thus, pulmonary arterial pressure falls, as does the pressures within the right chambers of the heart.

In the newborn, the combination of high left atrial pressure and low right atrial pressure cause a tendency for a shunting of blood from the left side of the heart to the right through the foramen ovale (of course this is the opposite way the blood flowed in the fetus). The greater pressure on the left side causes the small valve that lay over the foramen ovale on the left side of the atrial septum to close over the opening, thereby preventing further flow.

The combination of increased systemic resistance with the elevated aortic pressure, coupled with the decreased pulmonary resistance causes a shunting of blood from the aorta to the pulmonary artery shortly after birth. This change in oxygen tension of the blood is thought to be the stimulus for the contraction of the smooth muscles of the ductus arteriosus which occurs at birth, resulting in 'functional closure'. The ductus arteriosus becomes anatomically closed during the second month of life as the lumen becomes completely occluded by the growth of fibrous tissue.

Turn now to some of the anomalous heart conditions which are present in the neonate. Discuss the following congenital heart defects, with consideration of: the structural anomaly, the effects, and the treatments:

1. atrial septal defect (patent foramen ovale)
2. patent ductus arteriosus
3. coarctation of the aorta
4. tetralogy of Fallot

#### **Atrial Septal Defect (Patent Foramen Ovale)**

Atrial septal defects cover a number of defects in the septum between the atria; patent foramen ovale is a common atrial septal defect. It is the most common congenital cardiac anomaly found in adults, and is more prevalent in females. Surgical correction is best done in childhood. In early life, most patients are asymptomatic, but in early adulthood, there is often the onset of pulmonary hypertension.

It is usually associated with a left to right shunt (ie. blood will pass from the left ventricle back into the right ventricle thereby increasing the pressure within the pulmonary arterial system).

In all left to right shunts, blood is shunted directly from the

left heart back to the right heart without going through the systemic circulation. Compensatory mechanisms exist to maintain cardiac output and as a result, extra work is required by the heart itself. The magnitude of the amount shunted depends on the size of the defect, the pulmonary vascular resistance, and the relative compliance of the left and right ventricles. The extra work load placed on the right side of the heart explains the pulmonary hypertension, as well as the right ventricular hypertrophy and atrial arrhythmias, which may develop.

### **Patent Ductus Arteriosus (PDA)**

Failure of the ductus arteriosus to close following birth is another common congenital abnormality which occurs predominantly in females (2:1). The structural anomaly is an opening between the left pulmonary artery and the aortic arch. Practically all PDA cases are detected and surgically corrected in early childhood. Most patients with PDA are asymptomatic, and the abnormality is usually compatible with survival to adulthood. Symptoms which may appear are exertional dyspnea and fatigue with increased pulmonary resistance.

The patent ductus is accompanied by a variable degree of left to right shunting. The left to right shunt may cause pulmonary congestion and pulmonary artery hypertension. A significant volume of blood is shunted back across the ductus into the lungs instead of through the aorta. This puts strain of the left ventricle and left ventricular hypertrophy, and congestive heart failure may result.

### **Coarctation of the Aorta**

In this condition there is a severe narrowing of the aorta near the site of the fetal ductus arteriosus which produces high resistance to the flow of blood in the aorta. This results in elevated pressures in the aorta proximal to the stenosis, and left ventricle, and a possible back pressure into the lungs.

The life expectancy in uncorrected coarctation of the aorta is shortened. The average life span is reduced to about 35 years, with almost 90% mortality by the age of 50. The disease is often diagnosed in late childhood in asymptomatic patients who are found to be hypertensive or it may be detected from an abnormal routine chest x-ray film. The surgical treatment is resection and anastomosis, which is usually performed when the patient is 7-10 years.

If uncorrected, significant symptoms such as congestive heart failure are likely to occur in early adulthood. The most common causes of death in patients with coarctation of the aorta are congestive heart failure, aortic rupture or dissection of the

aorta.

### **Tetralogy of Fallot**

There are four anomalies associated with this defect: pulmonary stenosis, ventricular septal defect, right ventricular hypertrophy, and a shift of the aorta (such that the aorta originates from the right ventricle rather than the left, or it overrides the interventricular septum).

These anomalies are best understood if one considers the 'initial cause' of the defect which occurs in the embryologic development of the heart. During the fourth week, the aorticopulmonary septum divides the truncus arteriosus between the aorta and the pulmonary trunk. If this division is unequal, the diameter of the pulmonary artery will be decreased, while the diameter of the aorta will be increased.

The pulmonary stenosis decreases blood flow to the lungs and results in hypertrophy of the right ventricle. If the obstruction is severe enough, the pressure within the right ventricle will be greater than that on the left side, so that blood will flow through the foramen in the developing interventricular septum, thus by-passing the pulmonary circulation. As a result of this right to left shunt, the systemic blood will be poorly oxygenated and cyanosis may be present. Because of their cyanotic appearance, these babies are sometimes called "blue babies".

Almost 50% of children without surgical correction will die before the age of 5 years, and only 5% will be alive at 25 years. Patients with repaired tetralogy of Fallot do well, with 75% of them being alive and active on a long-term follow up.

Relief of the symptoms may be obtained by the "Blalock-Taussig" operation. In this surgical procedure, the end of a systemic artery (usually the left or right subclavian artery) is joined to the side of the left or right pulmonary artery. As a result, some of the mixed arterial-venous blood in the aorta flows through the shunt into the lungs for oxygenation.

The nature of the disease in the uncorrected condition shows a gradual increase in the severity of the pulmonary stenosis with worsening of the symptoms. The most common causes of death are, hypoxia, cerebrovascular accidents, and congestive heart failure.

**Q5. Finally, what are some possible causes of congenital anomalies?**

One of the most common causes of congenital heart defects is a viral infection such as rubella during the first trimester of pregnancy. Congenital heart defects are also thought to have a

genetic component because the same defect has been seen with an increased incidence in siblings and in succeeding generations.



**Laboratory Seven**  
**HEART & LUNG ANATOMY**

**Prerequisite Activities:**

Read sections on heart and respiratory system in appropriate text. Be familiar with upper and lower respiratory passages, heart, pericardium and great vessels. **Bring anatomy text to the lab.**

Students will work in groups of about 4.

The dissection material consists of a pig's heart with lungs and trachea attached.

**PART A - DISSECTION OF THE HEART**

**Objectives:**

1. To examine the gross structure of the heart (including valves, chambers and coronary vessels).
2. To examine the large vessels that enter and leave the heart.
3. To study the relationship of the heart to other mediastinal structures.
4. To examine the relationship of the pericardium to the heart, mediastinum, and diaphragm.

**Materials:**

pig heart and lung  
dissecting instruments  
dissecting pan  
applicator sticks

**Methods:**

Step 1. Examine the external appearance of the heart and determine its relative position in the body. Look at the anterior surface of the heart and visualize its relationship to the chest wall, diaphragm and lungs. Follow the aorta, note its relationship with the esophagus, identify the vagus nerves, and locate the paraaortic lymph nodes.

Step 2. Identify the pericardium (or its cut edges if it has been removed). The left and right phrenic nerves can be seen

on the lateral aspect of the pericardial sac. From what spinal segments does this nerve arise?

- Step 3. Cut the pulmonary arteries and veins to separate the heart from the lungs. Identify the external wall of the right ventricle, left ventricle, right atrium, left atrium and the right and left auricles. What is the difference between an atrium and an auricle?
- Step 4. Locate the anterior and posterior interventricular sulci (sulcus = singular), the atrioventricular (or coronary sulcus). What structures lie in the sulci?
- Step 5. Trace the coronary arteries to their origin. They are called "end arteries" or terminal arteries. This means they have few anastomoses. What is an anastomosis, and what are the implications for the myocardium?
- Step 6. Note the relationship of the aorta and the pulmonary trunk as they emerge from the heart.

#### Right Atrium

- Step 7. Examine the relationships of the atria. Locate the superior and inferior vena cava and note their relationships. Into which atrium do they drain? Use an applicator stick to probe these structures.
- Step 8. Cut a large flap in the front of the right atrium. Examine the interior and note a portion of the wall is smooth (derived from the sinus venosus), while the pectinate muscles form the ridges on the "sculptured" wall (derived from the primitive atrium). Locate the coronary sinus. What is it? Examine the auricle. What is its function?
- Step 9. Examine the interatrial septum and locate the fossa ovalis. This is the obliterated foramen ovale. Probe to see if there is a patent foramen ovale. Would this cause a functional defect in post-natal life. Why? In what direction would blood flow through this foramen if it remained patent?

#### Right Ventricle

- Step 10. Extend the incision past the tricuspid valve. Note the thickness of the wall. Examine the structures in the chamber, specifically the trabeculae carneae, papillary muscles and chordae tendineae. The chordae tendineae attach the papillary muscles to the cusps of the atrioventricular valves. What is the function of the

papillary muscles?

Step 11. Extend the incision through the pulmonary valve and up the pulmonary trunk.

### Left Atrium

Step 12. Make an incision in the left atrium and examine the chamber of the left atrium. What veins empty into this chamber? (Although the veins may have been removed, the orifices may be present).

### Left Ventricle

Step 13. Extend the incision past the bicuspid valve and down to the apex of the left ventricle. Compare the wall thickness and the structures in the chamber with those of the right ventricle. Examine the bicuspid valve. Find the circumflex branch of the left coronary artery and great cardiac vein lying in the coronary sulcus (cut in cross section).

Step 14. Extend the cut from the apex up past the aortic valve. Examine the valve and locate the orifices of the left and right coronary arteries.

### Valves

Step 15. Remove the atria and trim the aorta and pulmonary trunk so the valves can be seen from above. Compare the right and left atrioventricular valves. How are they similar? How do they differ? Compare the aortic and pulmonary valves. Note the differences between the two types of valves (atrioventricular vs. aorta/pulmonary). How do they function? Note the origins of the right and left coronary arteries with respect to the aortic valve cusps. Finally, note the relationships of the orifices of the four valves.

### Conducting fibres

Step 16. Finally, cut away the wall of the left ventricle to expose the interventricular septum from the left side. Try to locate the conducting fibers (part of the bundles of His) that lie beneath the endocardium. They appear as whitish branching fibers.

**PART B - DISSECTION OF THE LUNG****Objectives:**

1. To examine the structure of the larynx, air passages and lungs.

**Methods:**

- Step 1. Arrange the specimen in its normal anatomical position. Note that the mediastinum lies between the two pleural cavities. The contents of the mediastinum include: 1) the heart within its pericardium, 2) vessels proceeding to and from the heart, 3) the trachea 4) structures in transit between the neck and the abdomen, as well as a number of other structures such as the thymus and lymph nodes.
- Step 2. Trace cranially along the esophagus and trachea noting their relationship. (Which is anterior?). Look for lymph nodes, evidence of the thymus gland, and for the thyroid gland.

Larynx

- Step 3. Examine the larynx. Identify the following: hyoid bone; thyroid cartilage; cricoid cartilage; epiglottis; glottis and vocal cords. Examine the relationship between the epiglottis, tongue and glottis. Note how these structures interact during swallowing. Do you think there is a great danger in accidentally passing a gastric tube into the trachea? Why or why not? A branch of which nerve innervates the intrinsic muscles of the larynx?

Trachea

- Step 4. Next, examine the trachea. Note that it contains cartilaginous "rings" in its wall. Why? Are they really rings? Follow the trachea to the bifurcation of the primary bronchi. Each bronchus enters the hilum of the lung. What other structures enter (or leave) the hilum?

Bronchi and Lungs

- Step 5. Before proceeding, insert a glass tube (with rubber tubing attached) into the trachea and tie securely. Next, inflate the lungs and allow them to deflate several times. Why do the lungs deflate when air is not forced into them?

Step 6. Note the smooth serous membrane covering the surface of the lung. What is its name and function?

Step 7. Now, examine the surface features of a lung. (You might wish to cut the lung free of the trachea). There are substantial differences in the anatomy of the pig and human lungs (specifically, the shape of the lungs and the arrangement of the lobes). Note that the lung is partially subdivided into lobes by fissures. Examine the surface of the lung for evidence of indentations of the ribs; in life the lungs lie against the rib cage, and clear indentations of the ribs are seen in human lungs in situ. These indentations are not likely to be seen in the pig specimens because they are fresh and the indentations will have disappeared.

The pleural cavity is only a "potential" space. Why? Note the mediastinal surface of the lung is molded by the heart and aorta.

Step 8. Next, insert the glass tubing through the primary bronchus and into a secondary (lobar) bronchus, or continue to a tertiary or segmental bronchus. One secondary bronchus serves each lobe of the lung. Force air through the tubing and note the response of the lung. Does the entire lung inflate? If not, which portion inflated? What does this exercise illustrate about the bronchial tree?

## Tutor Notes - Laboratory Seven

### HEART & LUNG ANATOMY

The aims of the exercise are: (1) to learn the anatomy of the heart, its location in the body and its relationships to adjacent structures; and (2) to learn the anatomy and relations of the larynx, trachea, bronchi and lungs.

#### PART A - DISSECTION OF THE HEART

Questions are distributed throughout the steps. Answers and the steps in which they appear are given below. Students should be encouraged to take time to examine the demonstration material.

Step 2. The phrenic nerve emerges from the third, fourth and fifth spinal segments. ("3, 4 and 5 keep the diaphragm alive").

Step 3. The atria are relatively thin-walled chambers that receive blood returning to the heart (from the systemic circulation or the lungs). An auricle (and appendage of the atrium) acts a reservoir. It is important when stroke volume (hence venous return) increases above normal limits.

Step 4. The coronary vessels that supply blood to the wall of the heart lie within the sulci.

Step 5. The basic pattern of the arteries is 'tree-like'. An anastomosis is a connection between two arteries (or two veins). If one vessel is occluded, the other can (in theory) supply the terminal distribution of both vessels and prevent ischemia (lack of blood) of the tissue.

The lack of anastomoses among branches of the coronary arteries means that, following occlusion of a branch the tissue supplied by that vessel usually dies from lack of blood supply. This is an 'infarct'. There are anastomoses at the arteriolar level, but these types are too small to provide adequate blood flow following a sudden occlusion. However, they may enlarge sufficiently to provide adequate blood flow if blockage develops gradually (this may occur in atherosclerosis).

Step 6. The aorta and pulmonary trunk twist around each other (counter-clockwise if viewed from above).

Step 7. The venae cavae empty into the right atrium. Their openings face each other along the posterior atrial wall. Developmentally, the smooth portion of the wall was

derived from the sinus venosus. (Another term used for the smooth portion of the adult right atria is 'sinus venarum'). The trabeculated portion was derived from the primitive atrium. The coronary sinus, which drains the coronary veins, empties into the right atrium between the orifice of the inferior vena cava and the tricuspid orifice.

Step 8. The auricles provide reserve volume capacity for the atria.

Step 9. A patent foramen ovale occurs frequently (ca. 20%) but seldom causes any dysfunction. The explanation lies in the fact (often overlooked or misunderstood) that developmentally there are two interatrial septa. During fetal life blood passes under the right septum ('septum secundum'), through the foramen ovale in the left septum ('septum primum'), and into the left atrium. After parturition the decrease in the pulmonary vascular resistance results in a decrease in the pressure in the right atrium and ventricle. The pressure in the left atrium is then higher than in the right. Thus, the left septum is forced against the right septum and the foramen is closed functionally. Only when the foramen is exceptionally large, or the right septum is small, do they fail to overlap and shunting occurs. In this case oxygenated blood passes from left to right. This is classified as one of the acyanotic heart diseases and does not result in a 'blue baby'.

Step 10. The chordae tendineae attach the papillary muscles to the cusps of the atrioventricular valves. They prevent the valves from opening back into the atria when the ventricles contract. They do not pull the valves open (this is a common misconception).

Step 12. The pulmonary veins (usually four in number, frequently more in pigs) empty into the left atrium.

Step 13. The wall of the left ventricle is thicker than the wall of the right. The chambers of one ventricle may appear larger. However, their capacity is the same, since with each contraction an equal volume of blood is expelled from each side of the heart. (Otherwise there would be an accumulation of blood in either the pulmonary or the systemic circulation).

Step 15. The atrioventricular valves have large trap-door-like cusps. They differ in that the left has only two cusps (bicuspid or mitral valve), while the right has three (tricuspid valve). The aortic and pulmonary valves are alike in structure (they were derived from a single

four-cusped valve). These cusps are called semi-lunar cusps. They hang from the walls of the vessels like pockets. When the ventricles relax, blood begins to return toward the heart. The cusps fill and close the lumen of the vessel.

## **PART B - DISSECTION OF LARYNX, BRONCHI AND LUNGS**

- Step 3. The hyoid bone may have been removed from the specimen. It is easily seen on the plastic model.
- Step 4. Approximately twenty 'U-shaped' rings of hyaline cartilage prevent the trachea from collapsing. (If they were full 'O' rings they would impinge on the esophagus lying immediately behind the trachea, and interfere with swallowing).
- Step 5. Lung tissue is rich in elastic fibres, therefore they tend to deflate. Elastic tissue contributes about one third to the recoil tendency of a lung. The surface tension of the fluid lining the alveoli (even in the presence of surfactant) contributes two thirds. If adequate amounts of surfactant are not present, the effort required to inflate the lungs can become enormous. The recoil tendency of lung tissue contributes to the negative pressure between the layers of visceral and parietal pleura (pleural cavity). If air is introduced into the pleural cavity the lungs will collapse.
- Step 6. The pleura (visceral layer cover the lungs and parietal layer lines the cavity) is a serous membrane that produces a thin watery fluid to lubricate the pleura and permit the adjacent surfaces to slide against each other.
- Step 8. The students should note carefully the nature of the broncho-pulmonary segments and understand that these structures are anatomically and functionally distinct even though their boundaries are not easily visible.



## Tutorial Eight

### CATHERINE THOMPSON: DEEP VEIN THROMBOSIS

#### Objectives

1. Discuss the normal process of hemostasis.
2. Discuss the pathological conditions that predispose a patient to deep vein thrombosis. Include causes, signs and symptoms, and treatments.

-----

Mrs. Catherine Thompson, a 69 year old grandmother was admitted to hospital for replacement of a severely degenerated hip joint. The surgery went well and the patient's recovery was uneventful until two days post-op, when the patient complained of discomfort in her right leg. The leg was slightly swollen and tender. The pain increased and the leg developed a slight 'bluish' discolouration and felt cold. The superficial leg veins became distended.

In order to discuss what has happened to Mrs. Thompson, it is necessary to understand the mechanism of venous thrombus formation. Make sure you are prepared to discuss the main processes leading to the development of a venous thrombus.

What has happened to Mrs. Thompson? What are the signs and symptoms of this condition? What complications may arise?

Finally, consider what the mechanisms are by which drugs could act to prevent this condition and to prevent progression of the thrombus. Consider how Nursing care can also be important in preventing the development of DVT.

**Tutor Notes - Tutorial Eight****CATHERINE THOMPSON: DEEP VEIN THROMBOSIS****Objectives**

1. Discuss the normal process of hemostasis.
  2. Discuss the pathological conditions that predispose a patient to deep vein thrombosis. Include causes, signs and symptoms, and treatments.
- 

Before considering the pathology of Deep Vein Thrombosis (DVT), it is important to consider the normal physiological response to a damaged vessel, namely thrombus formation.

**Q1. What is the initial response when a small blood vessel is severed?**

When an arteriole, capillary or venule is severed, the immediate inherent response is vasoconstriction. This is only a transient response (lasting only about one minute) but the effect is that it slows the flow of blood to the affected area.

**Q2. The next step in the process of hemostasis is the formation of a 'platelet plug'. Do platelets normally adhere to blood vessels? What role do platelets play when a vessel is disrupted?**

Platelets do not adhere to intact endothelial cells which line the vessel walls. However, when a blood vessel is disrupted, the endothelium is damaged and as a result the underlying connective tissue, containing collagen fibres, is exposed. Platelets adhere to collagen, and when they do, the platelets release a number of substances including thromboxane  $A_2$  and serotonin. These substances stimulate additional (adjacent) platelets to adhere to the attached platelets, aggregate, and form a platelet plug at the site of the disrupted vessel.

A platelet plug can completely seal breaks in blood vessel walls, but it is only one part of the hemostatic process: blood coagulation.

**Q3. What is meant by a 'cascade'? Explain the cascade which occurs in the hemostatic process.**

A cascade simply refers to a series of steps or events, with one step triggering the next. A cascade mechanism often has an amplifying effect, as the activation of one step leads to an even greater activation of the following step.

Coagulation involves a cascade of plasma coagulation proteins with the end result being the formation of fibrin from its inactive precursor, fibrinogen. This final step is catalyzed by the enzyme thrombin.

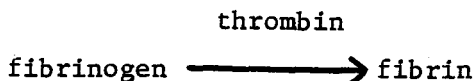


Figure 8A

Coagulation can be activated by two pathways: intrinsic and extrinsic. The initial event in the intrinsic pathway is the activation of Factor XII or "Hageman Factor". This is simply a protein which circulates in the blood but is normally inactive. It becomes activated when it comes in contact with the damaged vessels wall (specifically the underlying collagen molecules). This event starts the cascade of the activation of a series of plasma proteins which normally exist in the circulation in inactive forms. The last two steps are the conversion of prothrombin to thrombin, and the conversion catalyzed by thrombin of fibrinogen to fibrin.

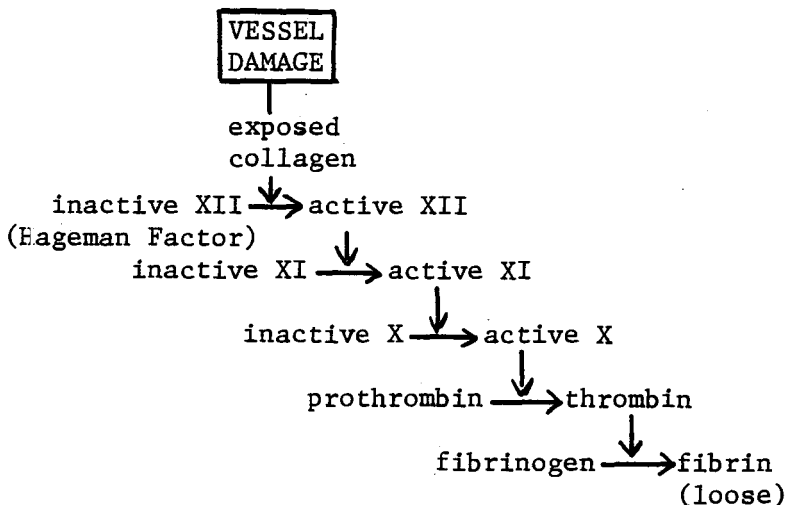


Figure 8B

#### Q4. What does fibrin do?

The action of thrombin on the fibrinogen molecules is the removal of several polypeptides, allowing the remaining molecules to bind to each other to form the polymer 'fibrin'. Initially, fibrin is a loose mesh of interlacing strands which are stabilized and strengthened by the formation of covalent cross linkages. In the development of this thrombus, many erythrocytes and other cells may become trapped in the fibrin meshwork.

**Q5. What is needed to form the covalent cross linkages, and what produces this?**

The plasma protein "Factor XIII" is the enzyme which catalyzes the formation of the cross linkages. It is interesting to note that thrombin is what activates this plasma protein. This makes sense; as it catalyzes the reaction in which fibrin is formed, it also catalyzes the reaction whereby the enzyme responsible for the cross-linking of fibrin is produced.

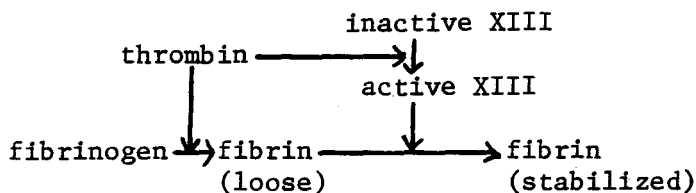


Figure 8C

**Q6. The process which has just been discussed is called the "Intrinsic Clotting Pathway". There is also an "Extrinsic Clotting Pathway". What initiates this pathway?**

Damaged tissue releases "tissue factor" (the term "tissue thromboplastin" is also used) which activates the extrinsic pathway. The two pathways emerge in a common pathway beginning at the step of the activation of Factor X that then catalyzes the reaction of prothrombin to thrombin.

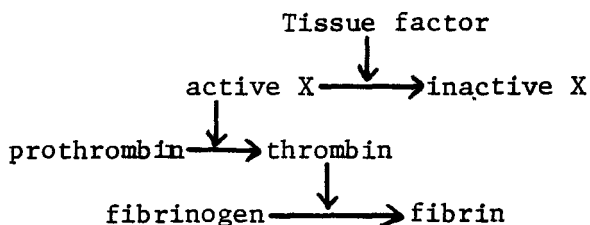


Figure 8D

Clearly, haemostasis is an important physiologic process. However, thrombosis can also be pathological in nature.

**Q7. What is happening to Mrs. Thompson? Describe the development and signs and symptoms of this condition.**

Mrs. Thompson demonstrates the signs and symptoms of DVT. It is a commonly seen complication of venous diseases. It develops

acutely over a period of a few hours, or up to 1-2 days.

If a thrombus is not large enough to affect circulation, the patient may be asymptomatic. The patient may also show no symptoms if adequate collateral circulation has developed around the obstruction. However, once a thrombus becomes large enough to significantly decrease venous drainage or completely close off a vessel, signs and symptoms develop. DVT most commonly occurs in the leg, and in this case, the circumference of the ankle, calf and lower thigh can increase markedly. The area is also characterized by pain and tenderness.

**Q8. What are some possible causes of thrombi formation?**

Three major causes which may contribute to, and explain the development of DVT have been suggested:

1. Since under normal circumstances the initiation of blood clotting is primarily dependent on the state of the blood vessel lining, even minor transient alterations in this surface could initiate clot formation. Trauma to the vessel walls could be caused by cannulas, needles, irritant drugs or bacterial sepsis.
2. Thrombi development may come about as a result of stasis or pooling of the blood. This may be the result of congestive heart failure, trauma, or any condition which renders a patient bed-ridden.
3. It is possible that people who develop thrombi have a hyperactive clotting mechanism. This could be a result of a deficiency in the amount of normally occurring circulating anticoagulants.

**Q9. What is the primary concern of patients with DVT?**

The major concern of DVT is the potential occurrence of a pulmonary embolism. A thrombus may be dislodged from the veins, pass through the right side of the heart, and become lodged in the pulmonary arterial circulation.

**Q10. Patients may want to rub or massage their calf because of the discomfort they feel. Why should they not do this?**

This may cause the thrombus to break away from its site of attachment on the vessel wall, and cause an embolus to form.

**Q11. If a embolism does not form, what problems may arise?**

If a DVT doesn't dislodge and embolize, the clot usually undergoes lysis, and recannulization of the vein occurs. The valves within the veins are usually destroyed in this process.

This in turn may lead to chronic venous insufficiency, characterized by chronic leg pain, edema and stasis ulcerations.

**Q12. Considering the pathogenesis of DVT, what possible mechanisms could drugs have to treat this disease and to prevent it from developing further?**

The major classes of drugs used in the condition of venous thrombosis are: (1) drugs which inhibit coagulation (these are called "anticoagulants"), (2) drugs which interfere with platelet adhesion and aggregation, and (3) drugs which digest fibrin ('fibrinolytic' agents).

1. Two main anticoagulants are available: Heparin and Vitamin K antagonists.

Heparin acts by accelerating the rate of inactivation of a number of activated clotting factors, including thrombin. Vitamin K antagonists act by interfering with the hepatic synthesis of prothrombin, and factor VII, IX and X.

(aside)

**Q12a. Given the mechanism of Vitamin K antagonists, why is it be given initially in conjunction with another drug?**

Because of its mechanism (the inhibition of the production of some of the clotting factors in the blood), the therapeutic effect of Vitamin K antagonists is delayed until the circulating clotting factors have been cleared from the circulation. It is this delay of 36-48 hours which necessitates the use of a more quickly acting drug (such as heparin).

2. Antiplatelet drugs: While many compounds inhibit platelet function, only a few act as anti-thrombotic agents in vivo. There is evidence that aspirin reduces the incidence of thrombosis in some patients.

3. Fibrinolytic Agents: These drugs lyse venous thrombi which have been formed recently. However, they may also produce serious bleeding, particularly in the post-operative period.

**Q13. The site of thrombus formation (arterial or venous) must be considered when selecting treatment. Why?**

Thrombi consist of both platelets and fibrin, but the relative contribution depends upon the site of the thrombus formation. On the arterial side of the vascular system, where pressure is high and flow is rapid, the thrombus has a large platelet component. This is called a "white" or "arterial" thrombus.

On the venous side, the relative contribution of fibrin is greater and the platelet mass is small. Numerous red cells are trapped in the fibrin meshwork during the formation of the thrombus, hence they are called "red" or "venous" thrombus.

The drugs that affect the cascade leading to fibrin formation are not the same as the drugs that inhibit platelet aggregation; thus, the selection of drug therapy must be based, in part, on the site of the thrombus formation.

## Laboratory Eight

### BLOOD

#### Prerequisite Activities:

1. Read sections on blood in an appropriate text.
2. Be familiar with:
  - a. The formed elements (erythrocytes, leukocytes and platelets) - their functions, morphological appearance and normal values;
  - b. the events that lead to blood coagulation;
  - c. the ABO blood groups and;
  - d. the methods outlined in the lab (note that some of the methods are at the end of the laboratory).

#### Objectives:

In this laboratory, several tests will be performed on a blood sample from a 'patient', and their blood film will be examined.

#### Tests to be done:

1. Clotting time
2. Hematocrit (Hct)
3. White blood count (WBC)
4. White cell differential
5. ABO blood group

#### Materials:

hematocrit tubes  
sealant  
WBC counting diluent  
microscope slides  
Neubauer counting chamber  
tile  
antisera  
applicator stick

#### PART A - CLOTTING TIME

1. Warm citrated plasma and 0.4 Molar  $\text{CaCl}_2$  to  $37^\circ\text{C}$
2. Add 5 drops of plasma to glass tube.
3. Add 5 drops of  $\text{CaCl}_2$  solution to plasma in test tube
4. Start stop watch and mix
5. Tilt tube at 1-2 second intervals. When gelatinous clot forms stop watch and record time.



**PART B - HEMATOCRIT** (Hct - volume of red cells expressed as a fraction of volume of blood)

1. Fill and seal capillary tube.
2. Centrifuge (do all of group members' together).
3. Observe the colour of plasma, the 'buffy' coat' of white cells, and platelets on top of column of packed red cells.
4. Measure hematocrit:

$$\text{Hct} = \frac{\text{height of red cells}}{\text{height of blood cells}}$$

Normal: female - 0.33-0.43  
male - 0.39-0.49

**PART C - WHITE BLOOD COUNT (WBC - # of white cells/litre)**

1. Dilute 0.1 ml of blood in 2 ml of WBC counting diluent and mix (a one in twenty dilution). Mixture must sit for 2 min. to allow red cells to lyse - can be left longer.
2. Place coverglass on clean Neubauer counting chamber.
3. Mix suspension and add small drop to side of chamber so that mixture just fills space between coverglass and platform (do not continue to add more mixture or mop up excess).
4. Allow several minutes for white cells to settle.
5. Locate ruled area under low power objective (lowering condenser slightly and use of fine focus makes it easier to see large cells). Count and record all white cells in each of the large corner squares (1 mm<sup>2</sup> divided into 16 smaller squares). If the cells are evenly distributed, the 4 counts should be similar. (See figure in 'Methods' section - page 4 of this lab).

Calculation:

WBC = total cells counted in 0.4 mm<sup>3</sup> x 20 (dilution)

$$\begin{aligned} & \frac{1}{\text{---} \times 1 \times 0.1 \times 4 \text{ (volume counted)}} \\ & \times 10^6 \text{ (number of mm}^3 \text{ in 1 litre)} \end{aligned}$$

Normal: 3.5 - 10.0 x 10<sup>6</sup>/L

**PART D - WHITE CELL DIFFERENTIAL**

1. Cover dry, stained film with a thin film of immersion oil.

2. Using low power objective, focus on film and locate area of slide to be used for examination (choose area where individual red cells can be seen - avoid thicker end of film where cells overlap, or opposite end where red cells form 'cobblestone' paths).
3. Add a drop of oil to the slide, and carefully turn to oil immersion objective. (Check that microscope is properly illuminated - adjust condenser to focus light on back of film and close diaphragm to cut out excess light). Use fine focus continuously to focus on the fine structure of cells.
4. Observe: Red Cells - general appearance - shape, any variation in size, staining - usually uniform with slightly paler centres

White Cells - several types, nucleated, compare size with red cells.

Platelets - Exposure to injured tissue or thrombin, (an activated coagulation factor) stimulates platelets to aggregate (or clump). (Individual platelets will be seen, however, since the films have been prepared from venous blood into a tube containing an anticoagulant.

5. Count and identify each of the white cells in the field. Move to adjacent field and repeat. Continue until 100 cells are counted (if time is available, repeat for a second slide and compare and average the results).

Calculation: If 45% of the white cells are neutrophils, the value is expressed as neutrophils, 0.45.

Normal:

neutrophils	-	0.40	-	0.75
bands	-	0.00	-	0.06
eosinophils	-	0.01	-	0.06
basophils	-	<0.01		
lymphocytes	-	0.20	-	0.40
monocytes	-	0.02	-	0.10

## PART E - ABO BLOOD GROUP

1. Place 2 drops of blood on a clean tile.
2. Add a drop of anti-A to 1st drop of blood and anti-B to the second.
3. Mix each with a clean applicator stick.
4. Rock and rotate tile slowly.

5. (Antigen on surface of red cell results in agglutination when exposed to specific antibody; for example, Group A cells agglutinate to anti-A). Record results..

	anti-A	anti-B
Agglutination	-----	-----

### Methods:

#### Capillary tubes

Types -unmarked - no anticoagulant  
 -marked - heparin anticoagulant

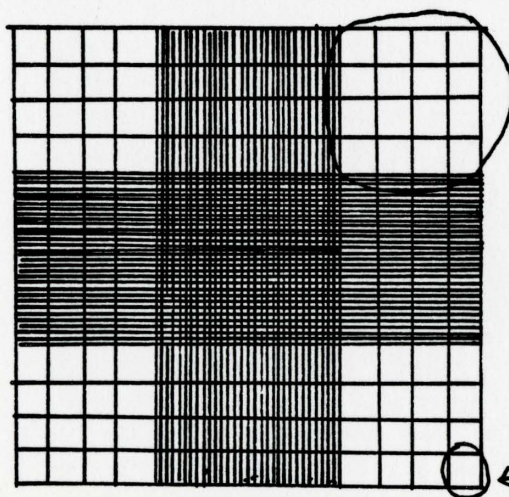
Filling-hold tube at an angle to facilitate filling (avoid bubbles)

-to seal tube, hold tube horizontally and plug dry end th sealant.

#### Preparation of Blood Film

1. Use clean (grease and lint free) slide.
2. Place a drop of blood on the slide.
3. Draw 2nd slide at an angle toward drop of blood and, as blood begins to flow along edge of 2nd slide (this happens very quickly), reverse direction and blood will be drawn out to form a thin film. Use a fairly quick, smooth motion. A properly made blood film will have a 'thumb print' shape and no streaks or globs.
4. Air dry and print name with pencil on thick end of slide.
5. Stain according to directions in lab and allow to air dry.

#### Using a Neubauer Counting Chamber



This is how the counting chamber will appear under low magnification.

Count the cells in these squares and repeat for all 4 corners. Each of these 4 squares measures 1mm x 1mm and is x 0.1mm deep, to give a volume of 0.1ml.

(This is what is seen under high magification).

Patient's Name \_\_\_\_\_

Student's Name \_\_\_\_\_

### BLOOD LAB RESULTS

(\*\*"HAND IN LAB RESULTS AND ANSWER TO THE QUESTIONS FOR MARKING TO YOUR TUTOR BEFORE YOU LEAVE THE LAB TODAY)

Hematocrit\_\_\_\_\_

White Blood Count\_\_\_\_\_ x 10<sup>9</sup>/L

White Cell Differential

neutrophil\_\_\_\_\_

band \_\_\_\_\_

eosinophil\_\_\_\_\_

basophil\_\_\_\_\_

lymphocyte\_\_\_\_\_

monocyte\_\_\_\_\_

Capillary clotting time \_\_\_\_\_ minutes

ABO Group\_\_\_\_\_

### Questions

1. What would likely happen to the hematocrit and haemoglobin of a normal healthy individual who moved from Hamilton to Mexico City? Explain the reason for your answer.
  
2. In a patient with an acute bacterial infection (ex. acute appendicitis) what would likely happen to the:
  - a. white cell count
  - b. differential
  
3. When referring to neutrophils, what is meant by the term 'a shift to the left'?

4. What factor(s) can initiate coagulation?
  
5. How would treatment of a patient with heparin affect their clotting time?
  
6. Why does a blood clot 'retract'?
  
7. Exposure to antigens foreign to an individual can stimulate the production of antibodies. Antibodies to foreign antigens of the ABO blood group system are normally present in adults. These antibodies could be produced as a result of antigenic stimulation following exposure to 'AB-like' substance widely distributed in nature.

In which ABO blood groups are the following 'naturally occurring' antibodies usually found?

Anti-A -----  
Anti-B -----

8. What is the function of platelets? What can occur in severe thrombocytopenia?
  
  
  
  
  
  
  
  
  
  
9. What would the red cells look like if the patient had iron deficiency anemia; sickle cell anemia? Why?

## Tutor Notes - Laboratory Eight

### BLOOD LAB

There is no formal lecture devoted to the topic of "blood"; this laboratory is meant to stimulate students to gather this information on their own.

Students will receive blood samples and slides from 'patients' which have been prepared by the laboratory instructor. The students will be required to analyze the blood to determine: clotting time; hematocrit; white cell count and differential; and the blood type (ABO). The 'correct' values for the hematocrit and blood type will not be available to the students, but the lab instructor will have a record of the answers. The students are aware that they will be required to hand in their results, as well as answers to the questions on the last page of their lab, which will be graded.

#### PART A - CLOTTING TIME

Make sure the students are aware of what is actually happening to the blood as it clots. It may be useful to review the process by which blood clots. (Depending on whether or not you have already had the tutorial, the students may be very familiar with this process, or it may be quite new to them).

Briefly, the coagulation cascade is triggered by exposure of blood to collagen fibres in the connective tissue that lies beneath the endothelial cells lining a vessel (or exposure to glass in vitro). The contact stimulates the activation of 'Factor XII', and the 'intrinsic' pathway of coagulation. 'Tissue factor' generated by the damaged cells activates the 'extrinsic' pathway. The final step in either pathway is the formation of fibrin strands from the plasma protein fibrinogen, catalyzed by the enzyme thrombin. (Again, this will be covered in more detail in the tutorial).

#### PART B - HEMATOCRIT

Blood is composed of a cellular portion which is called 'formed elements' and a fluid portion, the plasma. When a blood sample is centrifuged, the heavier formed elements separate from the plasma.

The blood will have been prepared such that some samples will have low hematocrits, some will have high hematocrits, and some will be 'normal'. Discuss possible reasons for the different observations found among the different samples.

## PART C - WHITE BLOOD CELL COUNT

It will be a useful exercise to see if the students can derive the formula which they have been given to calculate the white blood cell count.

Some of the samples will be prepared such that they have a high white cell count and some will have a low white cell count. Have the students discuss why they may have obtained this result.

## PART D - WHITE CELL DIFFERENTIAL

Once they have tried to complete the differential, the students should compare their results with the 'normal' values (given in their handout). They should go over the structure and function(s) of the five types of white blood cells. (A summary of this is provided for you here).

**Leukocytes (White Blood Cells)** - In each cubic millimetre of blood there are between 5 and 9 thousand leukocytes which can be classified into five separate types according to their respective staining characteristics, as well as their functions in the body. (Make sure that the students are aware that the leukocytes are actively mobile and that they can leave the bloodstream. Indeed, many of their functions are carried on outside the bloodstream).

There are two main categories of leukocytes: granular and agranular:

Granular - neutrophils  
          eosinophils  
          basophils

(These names come from the stain affinities of the cells; for example, a basophil stains with a basic stain and therefore is called 'base-loving').

Agranular - lymphocytes  
          monocytes

A brief description of the structure and functions of the white blood cell types follows:

1. **Neutrophils (or 'Polymorphs')** - (40-75% of total leukocyte count)

a. Structure

-have segmented nuclei with 2-5 lobes with fine interconnecting strands

- the chromatin within the nuclei is condensed and deeply stained
- characterized by having a large number of fine, neutrophilic granules that impart a mauve colour to the cytoplasm
- in addition, they have somewhat fewer, slightly larger, reddish-purple staining granules
- 'Band' Neutrophils are slightly immature, and are recognized by the fact that their nuclei are 'band-like', commonly having the form of a horseshoe.

b. Function

- involved in acute inflammatory response; they adhere to endothelial cells of venules, extend pseudopodia between the cells and migrate into the surrounding tissue
- once outside the bloodstream, they move toward the foreign object (eg. bacteria) which they rapidly phagocytose and destroy
- a significant increase in the proportion of neutrophils in the peripheral blood may indicate a response to an acute bacterial infection
- in this case, it is common to see a greater proportion of immature 'band' neutrophils as the demand for neutrophils is increased

2. **Eosinophils** (1-6% of total leukocyte count)

a. Structure

- nuclei have two lobes, which are often obscured by granules
- they are packed with large, specific granules which stain a distinctive red-orange colour

b. Function

- leave the bloodstream and enter the loose connective tissue associated with wet epithelial membranes (eg. respiratory and digestive tracts)
- they aggregate and phagocytose antigen-antibody complexes at sites where local allergic responses are in progress
- also produce enzymes that inactivate the mediators of inflammation released by mast cells
- therefore, an increase in blood eosinophils can occur in an allergic response

3. **Basophils** (less than 1% of total leukocyte count)

a. Structure

- nuclei commonly have 2 lobes; but can have more
- nuclei are often hidden by their large, blue-staining specific granules in blood films



-these are secretory granules containing heparin and histamine

b. Function

-main function is the involvement in the allergic response;  
antigen-IgE antibody interaction occurs at the cell membrane;  
this interaction triggers the release of histamine

4. Lymphocytes (20-40% of total leukocyte count)

a. Structure

-two size categories:

small lymphocytes (7-8  $\mu\text{m}$ )

medium-sized (or 'large') lymphocytes (12  $\mu\text{m}$ )

--small lymphocytes have a spherical or slightly indented nucleus with abundant dark-staining condensed chromatin

--only a thin rim of slightly basophilic cytoplasm is visible

--there are two different families of small lymphocytes:

B-lymphocytes differentiate in red bone marrow

T-lymphocytes differentiate in the thymus

--(B- and T-lymphocytes are morphologically indistinguishable in a routine blood film)

--medium-sized lymphocytes have slightly larger nuclei

--again, it is rounded, dark-staining, and may have a slight indentation on one side

--in comparison with small lymphocytes, medium-sized lymphocytes have a greater amount of cytoplasm, more free ribosomes and mitochondria, and their rough endoplasmic reticulum and golgi regions are more apparent when viewed by EM

b) Function

--lymphocytes are involved in the immune response

--the small lymphocytes circulate between the lymphatic and blood vessels; this circulation allows them to come into contact with foreign antigens present in the body to which they will respond by initiating an immune response

--very briefly, the initiation of the immune response brings about the production of circulating immunoglobulins ('humoral antibody response')

--a second type of immune response creates antigen-specific cytotoxic lymphocytes ('killer cells') with the capacity to destroy antigenetically different cells ('cell-mediated immune response')

5. Monocytes (2-10% of total leukocyte count)

a. Structure

-largest type of leukocyte

-nuclei in monocytes range from being deeply indented or

roughly kidney-shaped to having the shape of a wide horseshoe (may be confused with medium-sized lymphocytes)

- chromatin is less condensed than that of lymphocytes and therefore stains lighter
- monocytes also possess an abundance of cytoplasm that stains a pale blue-gray
- cytoplasm usually lacks granules, but it can exhibit a few very fine purple staining granules

b. Function

- monocytes are immediate precursors of macrophages. Thus, in acute inflammatory reactions, they leave the venules, enter the tissues to become macrophages

**PART E - ABO BLOOD GROUPS**

In this experiment, the blood sample is mixed with solutions containing antibody A or antibody B. A reaction (agglutination) indicates the erythrocytes in the blood sample have the corresponding antigen.

Erythrocytes contain a large number of antigens from a number of blood group systems; two surface antigens of the ABO blood group are identified as A and B. The erythrocytes of group A blood possess only the A antigen, and the plasma of group A blood usually contains an antibody for the B-antigen (anti-B). Group B blood presents the opposite situation: the erythrocytes have the B antigen and the plasma usually contains the A antibody (anti-A). Group AB blood has erythrocytes with both surface antigens but neither plasma antibody. Group O blood has erythrocytes without these surface antigens, but the plasma contains both antibodies. If group O blood containing high levels of anti-A or anti-B is given to a patient with A or B antigens on their cells, the donor antibodies could damage the recipient's cells. Thus the use of the terms "universal donor" or "universal recipient" should not be encouraged).

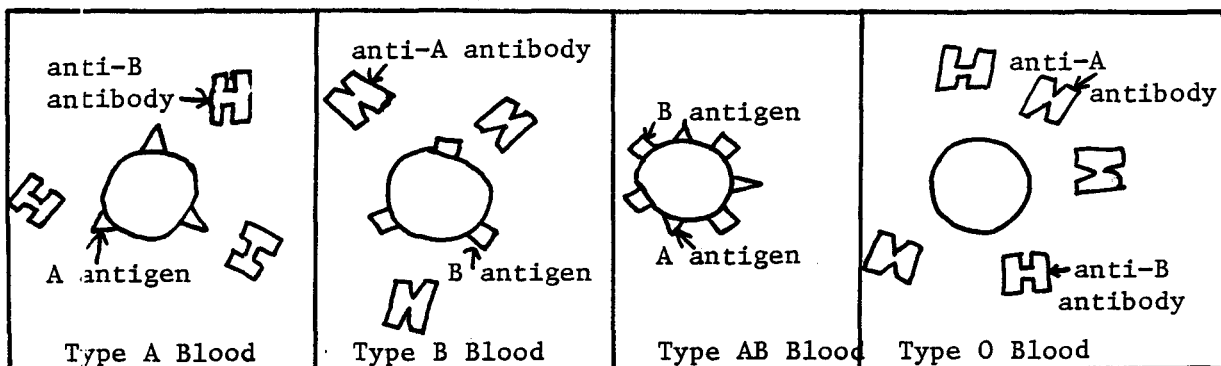


Figure 8A

Transfusions conducted with blood that has not been properly matched with respect to the ABO system can lead to a severe immunological reaction that leads to hemolysis of the donor erythrocytes.

A patient's plasma may also contain antibodies to antigens from other blood groups: antibodies that may have developed in response to exposure to foreign antigens in blood received in a previous transfusion, or to fetal blood that gained access to the mother's circulation. If these patients are given blood containing the antigen they can also have a severe haemolytic transfusion reaction. In cross matching blood, these antibodies are detected and compatible blood that does not contain the corresponding antigen is selected.

## Tutorial Nine

### DRUG X

#### Objectives

1. Understand how coronary blood flow is regulated: how is the oxygen demand and the supply kept equal?
  2. What are the determinants of cardiac oxygen consumption?
  3. Describe what angina pectoris is and the underlying mechanisms for its occurrence.
  4. If you were to design a drug to alleviate angina, what are the mechanisms by which this drug could work?
- 

A 50 year old male patient, Andrew Anderson who suffers from angina pectoris comes into a drug company inquiring about drugs which could relieve his symptoms. You are a research scientist responsible for the development of new drugs. You set out to discover 'Drug X' which will alleviate Mr. Anderson's symptoms. However, before you feel able to undertake this project you decide you must review basic cardiovascular physiology which you learned many years ago in 1B7.

How is coronary blood flow regulated? What way(s) can the heart receive more oxygen? How is this different from other tissues, such as the gut, the kidney or skeletal muscle? How does the content of oxygen affect the coronary vessels?

You remember that the autonomic nervous system played an important role in cardiovascular physiology. What affect does stimulation of the autonomic nervous system have on coronary blood flow?

You begin to think about what factors would be important in your drug development. First you investigate the causes of angina pectoris. What causes angina and what is the reason for the associated pain?

You decide you should focus on the oxygen supply and demand of the myocardium. What determines oxygen demand, and what factors alter these determinants?

Finally, what mechanisms of action would 'Drug X' have in order to alleviate angina?

What possible side effects would you expect from the drugs which you have proposed to use?

## Tutorial Nine

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---

#### Q1. How is 'autoregulation' achieved in coronary blood flow?

Blood flow through the coronary system is regulated almost exclusively by local blood flow regulation within the heart itself. This 'autoregulation' occurs in accordance with the metabolic rate of the heart. Whenever the heart rate and force of contraction of the heart increases, the rate of coronary blood flow increases accordingly, and if the activity of the heart decreases, coronary blood flow also decreases. In this way the oxygen demands placed on the heart are met.

- Q2. There are two ways in which an organ can receive more oxygen: by either increased perfusion of the organ or by increasing the extraction of oxygen from the blood. Which of these mechanisms play a role in the case of oxygen delivery to the heart?

As blood passes through the coronary vessels, most of the oxygen is removed, leaving venous blood deoxygenated. Thus increased extraction of oxygen is not possible in the heart as it is in other tissues, since virtually all of it has been extracted in the normal resting state. Thus, when the oxygen demand is increased, blood flow to the heart must increase. It does this secondarily to vasodilation of the coronary vessels.

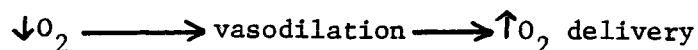


Figure 9A

- Q3. How does the  $PO_2$  of the blood affect the coronary vessels? Specifically, how does the lack of oxygen cause dilation of the coronary vessels?

The means by which lack of oxygen (hence increased oxygen demand) affects the oxygen supply has not been determined but the two principle possibilities that have been suggested are:

1. Oxygen supply has a direct effect on the coronary vessels:  
 $\downarrow O_2$  tension  $\longrightarrow$   $\downarrow O_2$  availability to the coronary vessels themselves, and this causes the vessels to form less ATP, and therefore to dilate automatically;
2. Oxygen has an indirect effect: lack of  $O_2$  causes vasodilator substances such as adenosine compounds to be released by the tissues. (Adenosine acts as a vasodilator in decreasing the release of calcium from the sarcoplasmic reticulum, thereby decreasing the cross-bridge interactions of the vascular smooth muscles).

**Q4. What effect does stimulation of autonomic nervous system have on coronary blood flow?**

It is important to point out that the heart can 'autoregulate' its oxygen supply independently of nervous control, but stimulation of the autonomic nervous system does affect coronary blood flow both directly and indirectly.

The direct effects result from the action of the transmitter substance on the coronary vessels. The coronary vessels are innervated extensively by nerve fibers from the sympathetic nervous system. The release of norepinephrine from these nerve endings generally constricts the vessels.

The indirect effects result from secondary changes in coronary blood flow caused by increased or decreased activity of the heart:

sympathetic stimulation  $\longrightarrow$   $\uparrow$  heart rate and contractility, hence increased  $O_2$  demand  $\longrightarrow$  local blood flow regulatory mechanisms for increasing coronary blood flow  $\longrightarrow$  coronary blood flow increases approximately in proportion to the metabolic needs of the heart muscle.

(The distribution of parasympathetic nerve fibres to the ventricular coronary system is very small, and has an almost negligible effect).

**Q5. Of these two ways in which stimulation of the autonomic nervous systems affects the coronary blood flow, which is more important physiologically?**

The indirect effects described above are more important because they tend to override any direct effects of the neurotransmitter substances on the coronary vessels.

As was discussed above, the oxygen demands of the heart are met by the process of autoregulation. The demands of the heart, or the work which is required of the heart, are a function of the cardiac output.

**Q6. What determines oxygen demand? What factors alter these determinants, namely the rate of contraction, and the force of contraction?**

The heart rate is a function of the inherent autonomous discharge of the sinoatrial (SA) node or 'pacemaker'. This rate is 100 bts./min. However, this changes, since the SA node is under the constant control of nerves and hormones.

The SA node receives nerve impulses from parasympathetic and sympathetic nerve fibres.

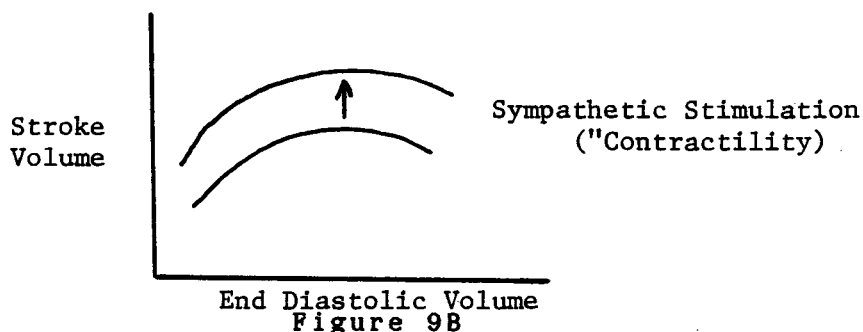
Stimulation of PNS  $\rightarrow$   $\downarrow$ HR (acetylcholine does this by increasing the permeability of the membrane to potassium)

Stimulation of SNS  $\rightarrow$   $\uparrow$ HR (norepinephrine does this by increasing the flow of calcium ions into the SA-nodal cells).

The ventricles never completely empty themselves of blood during contraction. Thus, a more forceful contraction can result in a greater stroke volume. (Recall, stroke volume is the volume of blood ejected by the ventricle with each beat of the heart).

There are two major factors affecting the force of contraction:

1. End-diastolic volume (EDV, the volume of blood in the ventricle just prior to contraction). Recall Starling's Law of the Heart which states that there is a direct relationship between the diastolic volume of the heart, ie. the length of its muscle fibres, and the force of contraction of the following systole. Thus, the more-distended ventricle responds with a more forceful contraction;
2. Sympathetic nervous system. Norepinephrine increases the ventricular strength of contraction at any given initial EDV. This is what is called 'increased contractility'.





Before moving on, it is important that the students discuss the cellular mechanisms by which the neurotransmitters work in this case.

There are two mechanisms by which norepinephrine (and epinephrine) increase contractility. First, they may directly increase the movement of calcium through 'receptor-operated channels' into the cytosol during excitation. This can occur because membrane proteins which constitute ion channels through the membrane are adjacent to the plasma-membrane receptors, and the binding of the neurotransmitter to its receptor may alter the membrane-receptor structure, and in doing so, may permit the receptor to interact with the adjacent ion-channel protein.

The other mechanism involves the second messenger cAMP. The binding of the catecholamines to their receptors may cause the receptors to activate the enzyme **adenylate cyclase** which is located on the inner surface of the membrane. This enzyme catalyzes the formation of cAMP from its precursor, ATP. Cyclic AMP can then diffuse throughout the cytoplasm to trigger other intercellular events. In this case, the intracellular cAMP acts by influencing the transport of calcium through the plasma membrane.

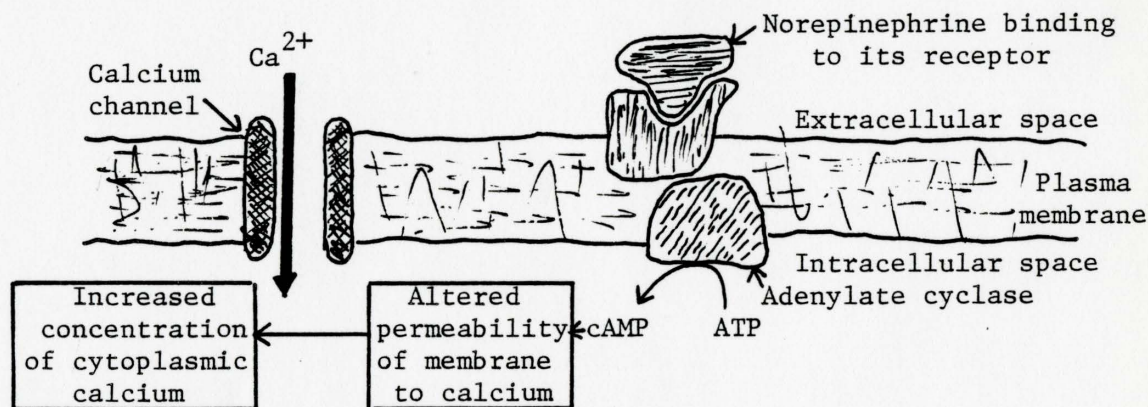


Fig 9C

**Q7. What is angina pectoris? What are the characteristics of the pain, and what is the reason for the pain associated with angina pectoris?**

Angina pectoris can be defined as episodic substernal pain. The pain has been described as a sensation of tightness, compression, pressure, a tearing, ripping or wrenching sensation that begins

in the chest and radiates outward in all directions. The heart itself has no pain receptors. Thus, the pain associated with angina is called 'referred pain' because it is felt in the left arm, the jaw or the neck. The pain lasts for a few minutes. In some people it may be a barely perceptible ache, while in others it may occur rapidly as a severe crushing sensation. The frequency of anginal attacks varies considerably; they may occur as often as several times each day, or may be single, isolated attacks. An attack is typically brought on by exertion, and is usually alleviated by rest.

The pain is a manifestation of cardiac anoxia. It is almost invariably associated with extensive coronary atherosclerosis and the consequent occlusion of coronary blood flow. When the heart doesn't receive enough oxygen, metabolites are formed in anaerobic metabolism, including lactic acid and there is an accumulation of potassium as it leaves the muscle. It is these metabolites which are thought to stimulate the pain receptors around the heart.

**Q8. Myocardial anoxia occurs whenever oxygen supply oxygen demand. Therefore, relief of these episodes is brought about by reducing the myocardial oxygen demand, or increasing the oxygen supply. Given this, what are the mechanisms by which drugs could act which could be used to treat angina?**

**Q8a. First, consider ways in which the oxygen supply could be increased.**

Vasodilators could be used because if the coronary vessels dilate, there will be an increased supply of oxygen to the heart. Adenosine is released by hypoxic myocardial cells and it promotes vasodilation. Therefore, a drug could work by blocking the factors which terminate adenosine's activity (such as its uptake by erythrocytes and other cells). In this way the vasodilatory effect of adenosine on coronary vessels is enhanced.

Recall the direct vasoconstrictory effect of norepinephrine on arterioles. Another vasodilator mechanism would be the inhibition of norepinephrine on the coronary vessels. This could be achieved in a number of ways. Drugs could act by depleting the norepinephrine stores from the nerve ending. The improperly stored neurotransmitter would then be free to diffuse from the protective binding sites within the nerve terminals, and could then be inactivated by enzymes.

Drugs could prevent the release of norepinephrine in response to a nervous impulse.

They could also prevent the interaction of norepinephrine with its receptor on the vascular smooth muscle. Again, this would result in vasodilation.

Recall the mechanisms by which smooth muscle contracts. Calcium is required for the initiation of muscle contraction in response to excitation. Therefore, drugs which inhibit the influx of calcium into the vascular smooth muscle cells could be used to promote vasodilation.

Finally, consider the mechanism by which norepinephrine increases contractility. It increases the movement of calcium into the cytosol via the second messenger cAMP. Therefore, drugs could inhibit the formation of cAMP or increase its rate of breakdown. This would decrease the contractility of the heart, and thereby the myocardial oxygen demand.

(Aside: In theory, oxygen delivery to the heart can be improved by drugs which vasodilate the coronary vessels. However, sclerotic vessels tend to have less capability to dilate than healthy vessels, so that blood may be shunted away from the areas where it is most needed).

Vasodilators which are not necessarily specific to coronary vessels are also effective because they decrease the total peripheral resistance, hence the preload and afterload are also decreased, thereby decreasing the demand placed on the heart.

**Q8b. In what ways could you decrease the oxygen demands of the heart?**

Recall the determinants of myocardial oxygen consumption: heart rate, preload, afterload and contractility. Drugs should be directed toward decreasing any of these factors.

Again, inhibition of the sympathetic nervous system would be effective since norepinephrine increases these factors. Thus, the same mechanisms which were used to promote vasodilation by blocking the effect of norepinephrine would be effective in decreasing the oxygen demands of the heart.

Laboratory Nine SchedulePART A (2J24)      PART B (1R1 - Anatomy Lab)

<u>2:30 - 4:00</u>	<u>Groups 1, 2 and 3</u>	<u>Groups 4, 5 and 6</u>
<u>4:00 - 5:30</u>	<u>Groups 4, 5 and 6</u>	<u>Groups 1, 2 and 3</u>

For PART A (Exercise Physiology), the first hour should be spent doing the laboratory exercise. Following this there will be a half hour discussion about the lab.

There are three stations for PART B (Clinical Anatomy). Spend half an hour at each station, as follows:

	<u>Station 1</u>	<u>Station 2</u>	<u>Station 3</u>
<u>2:30 - 3:00</u>	<u>Group 4</u>	<u>Group 5</u>	<u>Group 6</u>
<u>3:00 - 3:30</u>	<u>Group 5</u>	<u>Group 6</u>	<u>Group 4</u>
<u>3:30 - 4:00</u>	<u>Group 6</u>	<u>Group 4</u>	<u>Group 5</u>
<u>4:00 - 4:30</u>	<u>Group 1</u>	<u>Group 2</u>	<u>Group 3</u>
<u>4:30 - 5:00</u>	<u>Group 2</u>	<u>Group 3</u>	<u>Group 1</u>
<u>5:00 - 5:30</u>	<u>Group 3</u>	<u>Group 1</u>	<u>Group 2</u>

## Laboratory Nine

### PART A - EXERCISE PHYSIOLOGY

#### Prerequisite Activities:

Wear loose clothing, suitable for riding a bicycle, to the laboratory.

#### Objectives:

1. To demonstrate the relationship between oxygen uptake, ventilation, blood pressure, heart rate, carbon dioxide production and lactate production to increasing exercise intensities.
2. To examine the changes which take place during a progressive exercise test.
3. To examine the relationship of aerobic and glycolytic metabolism to exercise intensity.
4. To examine the uses of exercise tests. The energy expenditure of exercise will be considered.

#### Materials:

blood pressure cuffs  
stop watches  
exercise bicycles

#### Methods:

1. One student will exercise on the bicycle at each load setting indicated on the chart, for **one minute**. The remaining students will measure pulse, respiratory rate and blood pressure during the final 15 seconds of that load.
2. The work load will be increased by increments as shown on the chart, and again the measurements should be taken in the last 15 seconds of the workload.
3. Continue until the subject is no longer able to sustain the workload.
4. Repeat the procedure for all group members.
5. Using the data recorded, calculate the oxygen consumption per minute per kilogram body weight at the maximum load you were able to achieve.

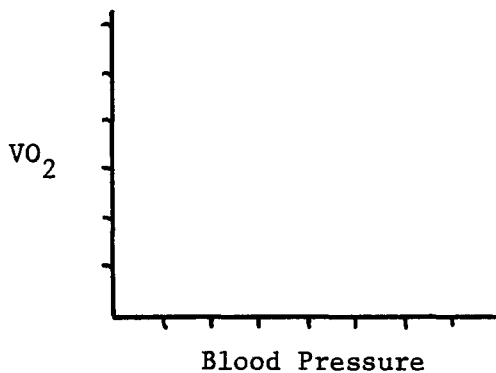
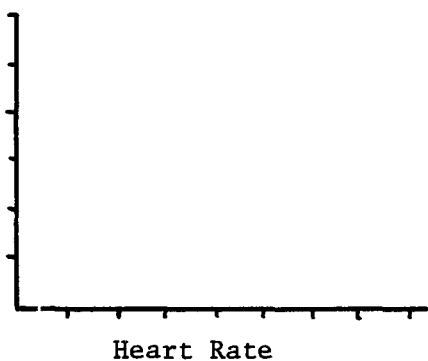
Determine your exercise capacity standing from the following table and chart:

Setting (kg/m/min <sup>-1</sup> )	VO <sub>2</sub> 300 + (setting x 2)	Blood Pressure	Heart Rate	Rate of Respiration
150	600			
300	900			
450	1200			
600	1500			
750	1800			
900	2100			
1050	2400			
1200	2700			
1350	3000			
1500	3300			
1650	3600			
1800	3900			

25 ml/kg-min	poor
25-35	below average
35-45	average
45-55	above average
55-65	good
65 and over	superior

On the graphs below, plot:

heart rate versus VO<sub>2</sub> and blood pressure versus VO<sub>2</sub>



Once you have completed the exercise, the answers to the following questions should be discussed.

1. What were the changes in heart rate, blood pressure and ventilation? How does cardiac output change in a progressive exercise test?
2. What factors will affect the  $VO_{2max}$  of an individual?
3. What are some of the clinical uses of a  $VO_{2max}$  test?
4. If the amount of oxygen consumed in an exercise is known, one can calculate the caloric equivalent, given that 1 litre of oxygen is roughly equivalent to 5.0 kcal. Given this information, can you calculate how many kcal. you have 'burned off' if you exercise for 30 minutes at 50% of your maximal oxygen uptake?

## **PART B - CLINICAL ANATOMY**

It is essential for Nursing students to understand cardiac surface anatomy as a basis for performing cardiopulmonary resuscitation (CPR). Gross cardiac anatomy is included in this lab. As future nurses, you should have an excellent working knowledge of the "vascular system" especially sites for infusion lines and potential sites where deep vein thrombosis may occur. Cardiovascular response to exercise will also be discussed.

### Station 1: Surface Anatomy of the Heart

The heart normally lies on the anterior aspect of the thorax, two thirds to the left of the midline of the chest, extending from the 2nd and 6th ribs. The area overlying it is called the "precondrium". The heart is constantly mobile, therefore, the surface markings of its valves and borders are approximate. The base of the heart is formed entirely by the atrial and lies posteriorly. The apex of the heart lies in the fifth intercostal space just medial to the mid clavicular line. "Apex beat" is the lowest and outermost palpable cardiac impulse in a living subject. This can readily be felt on yourself by the flat of your hand. During CPR, the heart is squeezed between the sternum and the back (which should be supported by a firm surface). Incorrect CPR in which pressure is applied over the ribs instead of the sternum results in fractured ribs, pneumothorax, and other complications.

### Station 2: Gross Cardiac Anatomy

Look at a wet specimen of the heart. Peel away the superficial layers of the pericardium. What are the different layers of pericardium? Discuss the basic arrangement of coronary arteries. The atria are under relatively low pressures, therefore their walls are thin compared to those of the ventricles. Identify the cardiac orifices and the valves guarding them. Examine the origin of great vessels and coronary arteries. How does exercise affect an ischemic heart?

### Station 3: Vascular System

Discuss the pathway of systemic circulation. Carotid, femoral and radial pulses are commonly palpated in clinical practice. Peripheral veins are used for infusion of fluids, drugs etc. In the upper limb, the cephalic vein, in the lower limb the long saphenous vein and femoral vein are often used. The external jugular vein in the neck is used under special circumstances. Scalp veins may be used in infants. Deep veins in lower limbs are prone to deep venous thrombosis. Air embolisms are potential complications in case of neck infusions.



## Tutor Notes - Laboratory Nine

### PART A - EXERCISE PHYSIOLOGY

The study of exercise physiology provides an excellent field within which to review some concepts in cardiovascular and respiratory physiology and metabolism.

This laboratory exercise is by no means a comprehensive study of an aspect of exercise physiology, but rather it serves to introduce the students to a few topics in the field. Specifically, the idea of maximum aerobic capacity will be studied as the students perform a maximal exercise test on a cycle ergometer.

There are a number of physiologic changes which accompany progressive exercise. Before you begin the laboratory, discuss some of the changes you expect to see, and the mechanism(s) involved.

**Heart Rate:** In many types of work, there is a linear increase in heart rate as the work load increases. The increase in heart rate is a result of changes in the autonomic stimulation of the heart. Withdrawal of vagal impulses to the heart, and increased sympathetic stimulation, as well as circulating catecholamines, contribute to the rise in heart rate.

**Blood pressure:** As a result of vasodilation in the vascular beds of the working muscles, the peripheral resistance to blood flow is reduced, but the constriction of other capillary beds, as well as the elevation in cardiac output, causes the blood pressure to rise. It may exceed 175/110 during exercise. The rise in blood pressure will depend in part on the size of the muscle group involved in the exercise. For example, blood pressure would be higher in arm exercise than leg exercise because there is relatively more vasoconstriction (inactive muscle) and less vasodilation (working muscles) in arm exercise. In general, the larger the activated muscles, the more pronounced is the dilation of the resistance vessels.

**Cardiac output:** Cardiac output (Q) increases almost linearly with the degree of exercise, and outputs as high as 6-7 times resting values have been obtained in trained athletes. For most people, values reach a maximum of about 4-5 times of resting levels. The cardiac output of an individual walking up a moderate grade will double from resting levels. At rest, in the supine position, Q is about 4-6 l/min with oxygen extraction of 40-50 ml/min. The uptake of oxygen increases during the first minutes of exercise until a 'steady state' has been reached. At this point, oxygen uptake corresponds with the demands of the tissue (and there is no accumulation of lactic acid). At steady state, the heart rate (HR), Q, and pulmonary ventilation have attained fairly constant

levels. During more severe exercise, anaerobic processes must supply part of the energy. In this case, lactic acid is produced.

Several factors must be considered when one looks at changes in  $Q$ . Recall the equation:  $Q = HR \times SV$ . The increased HR (discussed above) results in increased  $Q$ . The increased systemic pressure results in increased venous return, increased end diastolic volume, and therefore increased stroke volume. (Sympathetic stimulation causes increased contractility of the ventricle, thus directly increasing stroke volume).

Increased metabolism in the muscle results in local vasodilation, which decreases the resistance to venous return and thereby increased cardiac output. Total blood flows as great as 12 - 15 times normal have been recorded immediately following intense muscular activity. Possible vasodilator substances include: potassium, histamine, acetylcholine, adenosine, and lack of oxygen.

**Ventilation:** Alveolar ventilation may increase 10 - 20 times during exercise (ie. from 5 l/min to 50 - 100 l/min). The control mechanisms by which ventilation increases is not known. One might speculate that changes in the blood gas levels stimulate the peripheral chemoreceptors and/or respiratory control centres, however, the  $PO_2$  and  $CO_2$  levels stay quite constant during exercise. (These blood gases could, in fact, be the effectors if the sensitivity of the chemoreceptors was decreased, or perhaps the fluctuations, rather than the absolute levels of the gases could be detected). The ventilatory response might also be a result of the respiratory stimulants, circulating epinephrine, or increased temperature. Receptors in joints and muscles might be stimulated by physical movement, and afferent pathways from these receptors may play a significant role in stimulating respiration during exercise.

Maximal oxygen consumption ( $VO_{2max}$ ) is the highest oxygen uptake an individual can attain during physical work, breathing at sea level. It is generally agreed among exercise physiologists that the evaluation of  $VO_{2max}$  is essential in the evaluation of an individual's capacity to perform aerobic work. This index is related to cardiovascular-respiratory capacity, and has become widely accepted as a criterion for the assessment of 'physical fitness'. At the level of 'maximal oxygen uptake' there is no further increase in oxygen uptake despite increases in the work load. Aerobic metabolism is no longer sufficient for the production of energy of the individual, and the anaerobic systems come into play. As a result, lactate is produced; blood lactate levels reach values of greater than 80 mg/100 ml blood.

It is this 'maximal aerobic capacity' which you will be measuring

in the laboratory exercise.

Before you begin the exercise, discuss what factors might affect  $VO_{2max}$ .

**Muscle Mass:** The demand of the oxygen-transporting system vary with the size of the active muscles.

**Type of Exercise:** Since isometric work (in which the length of the working muscle stays constant) hinders local blood flow, and dynamic exercise facilitates the circulation, it follows that a greater oxygen uptake can be obtained during dynamic exercise.

**Sex:** Before puberty, there is no significant difference in the maximal aerobic power between girls and boys. Thereafter, it is about 20% higher in males (5% higher when corrected for weight and body composition differences). The reason for this difference is likely the higher haemoglobin levels in males.

**Age:**  $VO_{2max}$  decreases by roughly 9% per decade after the age of 20. This decline accompanies other decreases including: lower maximal heart rate; lower maximal breathing capacity; lower vital capacity; and less muscle strength.

**Training:**  $VO_{2max}$  can improve by as much as 30% in children, and 10% in adults.

Exercise testing has become a useful tool for the assessment of respiratory, cardiovascular and metabolic responses to increasing exercise in both health and disease. Exercise prescriptions can be given based on the performance of an individual on a  $VO_{2max}$  test.

The caloric expenditure of various activities can be calculated if the amount of oxygen consumed is known. One litre of oxygen is equivalent to approximately 5 kcal. Therefore, if a 50 kg individual had with  $VO_{2max}$  of 50 ml/kg-min was exercising at 50% of her  $VO_{2max}$  for 30 minutes, her caloric expenditure would be:

$$50\% \times .050 \text{ l/kg-min} \times 50 \text{ kg} \times 30 \text{ min} \times 5 \text{ kcal/l} = 187.5 \text{ kcal}$$

## **PART B - CLINICAL ANATOMY**

This portion of the laboratory takes place in 1R1. The purpose of this lab is to give the students a good 'feel' of clinical cardiovascular anatomy which will form a major part of their daily work as future nurses, such as monitoring intravenous lines and cardiopulmonary resuscitation.

### Station 1. Surface Anatomy of the Heart

CPR should be demonstrated on the model "Rescusit Anne" available in the Anatomy Department. The chest wall, precordium and xiphisternal junction should be demonstrated on a skeleton. A cadaver, preferably with a detachable anterior chest wall would help in demonstrating the relationship of the heart with other thoracic structures. The potential danger of pleural rupture during improper CPR should be pointed out.

### Station 2. Gross Cardiac Anatomy

This module should be as much "hands on" as possible. Several wet specimens of hearts should be kept at hand. Students should be encouraged to hold them and examine them under the instructors' supervision. Models of the heart should also be available.

### Station 3. Vascular System

Briefly discuss the cardiac cycle. Potential complications such as accidental air embolism and deep vein thrombosis, should be emphasized. Main differences between venous and arterial circulation should be emphasized, for example, pressure differences, oxygen tension etc.

**Tutorial Ten**  
**RENAL PATHOLOGY**

Objectives

1. Discuss cystitis; include its cause and its treatment.
  2. Discuss the renal responses to haemorrhage and the physiological mechanisms involved in these responses.
- 

Scenario One

Sandra Smith comes into Emergency. She tells you that she and her husband are just passing through town, returning home from their honeymoon. She would have waited until she arrived home but the symptoms of frequency and pain on voiding are so severe that she needs some assistance.

A mid-stream specimen of urine is obtained and the lab report shows 20-25 red cells and 25-30 white cells per high power field (normal values are zero and 2-3 for red and white cells respectively). A diagnosis of cystitis is made and she is given a prescription for gantrisin and told to force fluids.

What is cystitis? What are possible causes of it, and what are the symptoms? How is it treated? In what ways can the pathogen gain entry to the bladder? Why are females more susceptible to cystitis than males?

Scenario Two

Mr. Jones is brought into Emergency from a bad car accident. He has haemorrhaged severely from a cut leg. He is immediately placed on intravenous fluids.

What role does the kidney play following haemorrhage? Make sure you understand, and are able to discuss the renal mechanisms involved in the maintenance of homeostasis.

## Tutor Notes - Tutorial Ten

### RENAL PATHOLOGY

#### Objectives

1. Discuss cystitis; its cause, and its treatment.
  2. Discuss the renal responses to haemorrhage and the physiological mechanisms involved in these responses.
- 

#### Scenario One

- Q1. What is cystitis? What are the causes? What are its symptoms? Are there any complications associated with cystitis?**

When organisms multiply within the urinary tract, the infected walls become inflamed. If the infection is within the bladder it is called 'cystitis', and if in the urethra, it is called 'urethritis'.

The free flow of urine normally results in the elimination of micro-organisms from the lower urinary tract before they are able to multiply. Any factor which limits the free flow of urine or results in the inability to empty the urinary bladder completely predisposes to urinary infection.

As in any infection, there is an increase in body temperature and the urine may contain inflammatory exudate cells. Another symptom of cystitis is a burning sensation during micturition. Due to hyperalgesia of the nerve endings in the urethra, they can be stimulated by the mere flow of urine. There is also a feeling of urgency to micturate due to the increased sensitivity of the stretch receptors involved in the micturition reflex. This leads to frequent evacuations of the bladder with only small volumes of urine being passed on each occasion.

Chronic polynephritis may develop if the infection ascends into the kidney.

- Q2. What are the routes by which the pathogen can gain access to the bladder?**

The most common route of entry is from the external environment. This is referred to as 'ascending' infection. Organisms can also gain entrance to the bladder through urethral instrumentation. A particularly high risk of infection is associated with long term catheterization.

The infection may be 'hematogenous' or blood-borne. In this

case, the bacteria bypass the reticuloendothelial cells of the liver and spleen, and the lung, pass into the systemic circulation and are filtered at the glomerulus. If urine outflow is obstructed, the organisms may multiply and initiate an inflammatory response.

**Q3. Why are females more susceptible to cystitis?**

Females are more susceptible to infection of the urinary tract because the external urethral orifice is much closer to the rectum, and the urethra is much shorter in females than in males. The absence of antibacterial properties of prostatic fluid, hormonal changes affecting adherence of bacteria to the mucosa, and urethral trauma during sexual intercourse are other reasons that predispose females to cystitis.

**Q4. What treatment is recommended for cystitis?**

Predisposing causes, if found, must be dealt with. Otherwise, the treatment involves the identification of the organisms and administration of the appropriate antibiotic agents. Increased fluid intake is encouraged to promote 'flushing' of the bladder.

In order to determine the micro-organism involved, a sample of mid-stream urine is collected and sent to the laboratory to be cultured so that the types and numbers of bacteria can be identified and their susceptibility to various antibiotics determined. The mid-stream sample will be less likely to be contaminated by surface skin organisms than a sample collected at the beginning of micturition.

**Scenario Two**

The kidney is a very important organ for the maintenance of homeostasis. It does this through the three basic processes of filtration, reabsorption, and secretion. Before you consider the role of the kidney in haemorrhage, briefly discuss each of these basic renal processes.

**Filtration**

Filtration occurs at the glomerulus of the nephron. As the blood flows through the kidney, fluid passes from the capillaries into Bowman's space. The kidneys are perfused by an amount of blood that equals up to 25% of cardiac output, thus over 1 litre of blood is filtered each minute.

The process of filtration involves bulk flow. The composition of the fluid entering Bowman's space is identical to that of the

plasma, with the exception of proteins and blood cells which remain within the vascular space.

### Reabsorption

The process of reabsorption is not bulk flow, as with filtration, but is mediated by transport processes and/or diffusion. As the fluid passes along the tubule, certain substances are conserved as they are reabsorbed from segments of the renal tubules into the peritubular capillaries. In this way, these substances are retained in the body and not lost through the urine. The reabsorption of different substances is under different regulatory mechanisms.

### Secretion

Some substances not filtered from the plasma may be secreted within the renal tubules from the peritubular capillaries, and can then be excreted from the body. (Substances which are filtered may be secreted as well).

### Q5. What is the role of the kidney in haemorrhage?

When there is a loss of isosmotic fluid, as in the case of haemorrhage, the kidney tries to maintain fluid volume and prevent the secretion of sodium and other ions. Of the three basic processes above, filtration and reabsorption are altered in haemorrhage.

Before considering the homeostatic mechanisms involved, it would be useful to consider the components of the process individually.

### Q6. What is the role of renin?

Renin is a proteolytic enzyme produced by specialized cells in the juxtaglomerular apparatus (JGA) of the nephron. It is important because it begins a cascade of reactions which ultimately results in the formation of angiotensin II. Renin catalyzes the breakdown of angiotensinogen into angiotensin I. (Angiotensinogen is a circulating protein produced by the liver). Angiotensin I is then converted to angiotensin II; this reaction is catalyzed by 'converting enzyme': an enzyme which is located primarily within the lung.



Figure 10A



**Q6a. What factors regulate the levels of renin?**

Angiotensin II inhibits renin release through a negative feedback mechanism.

The arterioles of the juxtaglomerular apparatus are innervated by nerve fibres of the sympathetic nervous system. Stimulation of these nerves stimulates the release of renin.

The renin-secreting cells are sensitive to pressure. When renal arterial pressure is lowered, these cells detect this fall in pressure and secrete more renin.

Finally, the macula densa theory proposes that the rate of sodium passing through the macula densa area of the distal tubule acts in some way as a signal for the release of renin. (Recall the structure of the juxtaglomerular apparatus; it is the site where the junction between the ascending limb of the loop of Henle and the distal tubule makes contact with the afferent arteriole).

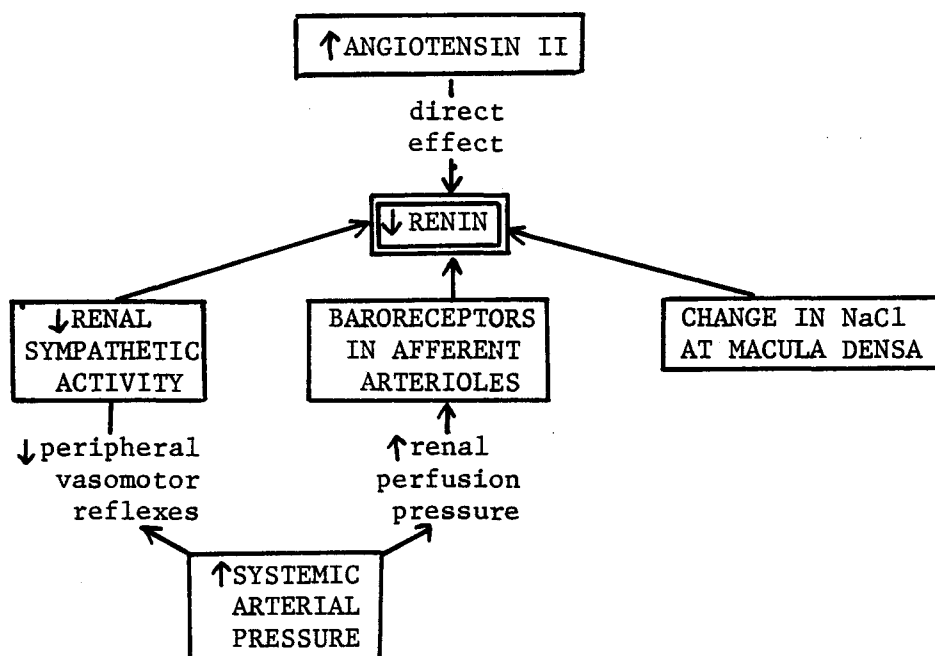


Figure 10B

**Q7. What are the principle actions of angiotensin II? How will these effects help in homeostasis in the case of haemorrhage?**

Angiotensin II has a number of effects including:

1. arteriolar vasoconstriction causing increased systolic,

diastolic and mean arterial pressure;

2. decreasing heart rate;
3. decreasing cardiac output (yet stroke volume is maintained);
4. increasing right atrial pressure;
5. decreasing renal blood flow and hence decreasing glomerular filtration, and;
6. stimulating the release of aldosterone.

Its action of vasoconstriction of the arterioles in the kidney will help maintain blood volume, as this will decrease the amount of fluid which is filtered at the glomerulus, resulting in decreased urine formation. Its action of stimulating aldosterone release is also beneficial for the conservation of water.

**Q7a. What is the role of aldosterone in haemorrhage?**

Aldosterone is one of several steroid hormones secreted by the adrenal cortex. Its primary role is to increase the rate of sodium reabsorption in the nephron, primarily in the distal tubules and collecting ducts. In the presence of aldosterone, almost all the sodium that reaches these segments is reabsorbed.

Thus with haemorrhage, the angiotensin II will indirectly stimulate sodium reabsorption by stimulating the release of aldosterone. The retention of sodium will help maintain the intravascular pressure.

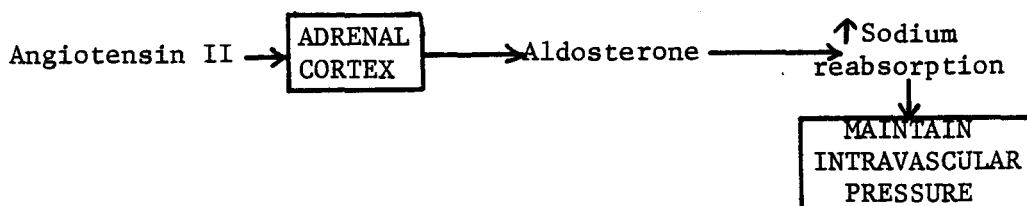


Figure 10C

While renin secretion is the most important regulator of aldosterone secretion, it is also regulated to a lesser extent by sodium and potassium concentrations in the plasma. There are receptors within the cells of the zona glomerulosa in the adrenal cortex, which are sensitive to the concentration of sodium in the plasma. Increased sodium concentration causes a reduced rate of aldosterone and vice versa.

**Q8. What is the role of antidiuretic hormone (ADH) in the maintenance of fluid in the case of haemorrhage?**

The ability for water to be reabsorbed in the late distal tubules and collecting ducts depends on the availability of antidiuretic hormone (ADH). Antidiuretic hormone is a peptide that is synthesized in the hypothalamus and released from the posterior

pituitary. Changes in the extracellular osmolarity controls the secretion of ADH. There are osmoreceptors in the hypothalamus and information is transmitted from there to the hypothalamic cells that produce ADH. An increase in osmolarity stimulates ADH secretion, while a decrease in osmolarity inhibits ADH secretion. Another stimulus for the release of ADH is blood pressure. There are baroreceptors in the left atrium of the heart, which when stimulated in response to changes in blood pressure, send afferent impulses to the hypothalamus to stimulate or inhibit the release of ADH.

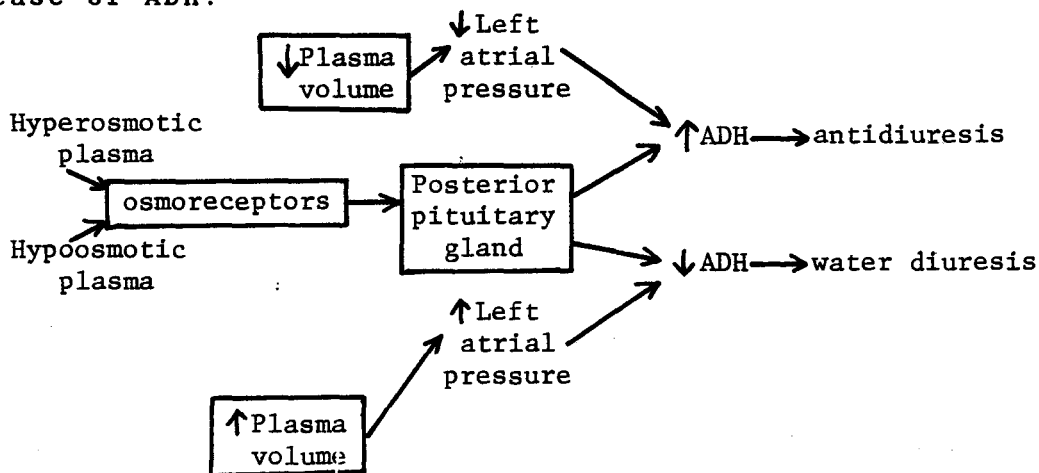


Figure 10D

The way in which ADH works is by binding to specific receptors in the tubular membrane. It is a peptide hormone, and this interaction stimulates the activation of adenylate cyclase which catalyzes the formation of cAMP. Once formed, cAMP induces changes in the luminal cell membrane that increases its permeability to water. Thus water will be reabsorbed, providing there is a concentration gradient. This gradient of increasing osmolarity along the medullary pyramids is established through the 'counter current system'.

**Q9. How does ADH fit into the scheme of the maintenance of homeostasis during haemorrhage?**

The decreased atrial pressure resulting from the loss of fluid and the effects of angiotensin II on the vascular system, stimulates the release of ADH from the hypothalamus which causes the reabsorption of water as it passes through the kidney, as discussed above.

As a final exercise, try to draw up a flow diagram which incorporates all the homeostatic mechanisms involved in the case of haemorrhage.

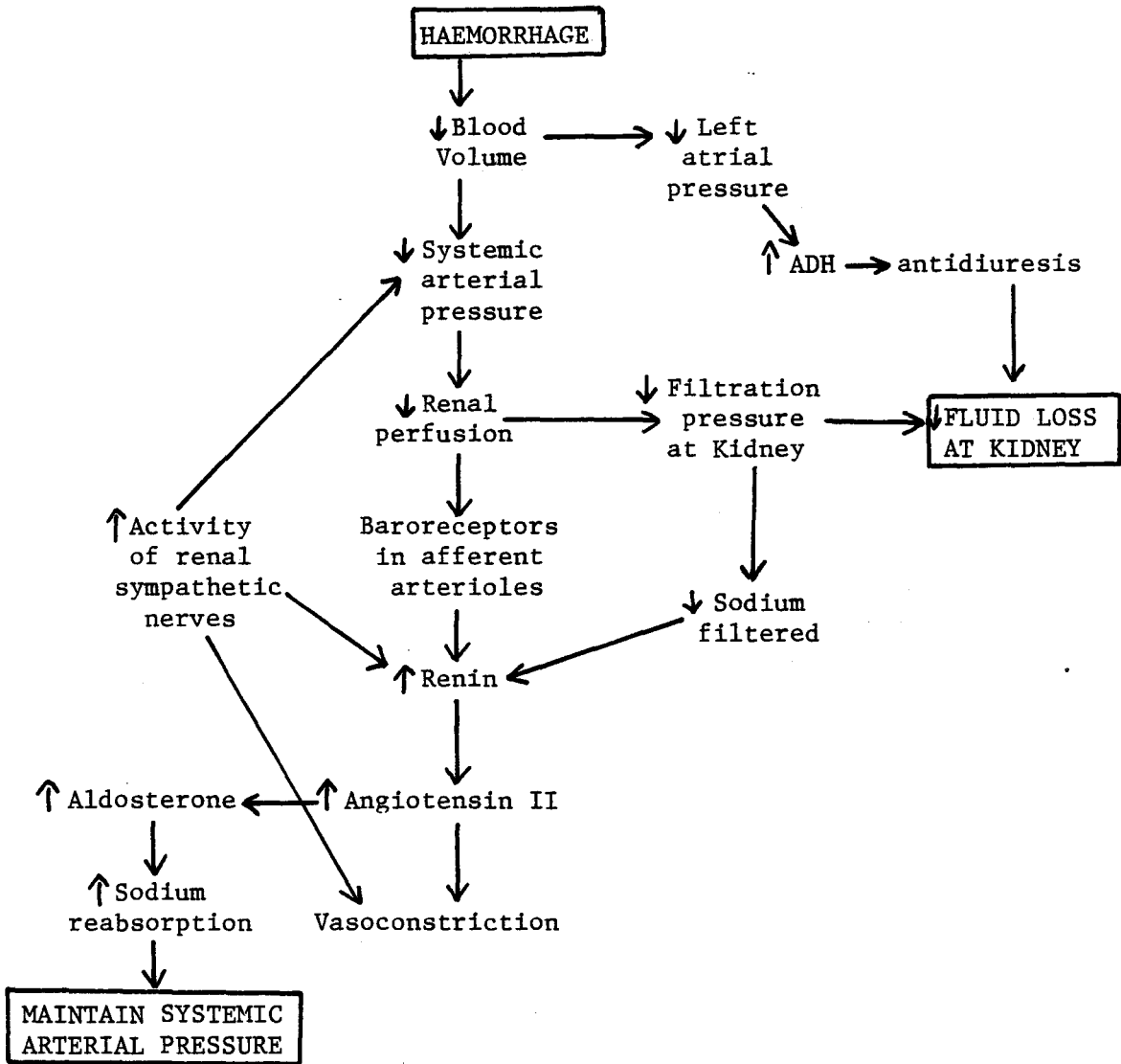


Figure 10E

## Laboratory Ten

### KIDNEY ANATOMY

#### Prerequisite Activity:

Review the anatomy of the kidney and bring your anatomy textbook.

#### Objectives:

1. To examine the gross structure of the kidney.
2. To study the major internal structures of the kidney microscopically including the nephron.
3. To examine the relationships of the kidneys to the rest of the urinary tract and the structures which surround it.

#### PART A - GROSS ANATOMY

Part A of the exercise will be in the Anatomy Lab. Bring your textbook.

<u>Group 1</u>	<u>Group 2</u>	<u>Group 3</u>	
2:30 Sta. 1	Sta. 2	Sta. 3	Groups 4,5 and 6 - Kidney Dissection (2:30-3:45)
3:00 Sta. 2	Sta. 3	Sta. 1	
3:30 Sta. 3	Sta. 1	Sta. 2	
<u>Group 4</u>	<u>Group 5</u>	<u>Group 6</u>	
4:00 Sta. 1	Sta. 2	Sta. 3	Groups 1,2 and 3 - Kidney Dissection (4:00-5:30)
4:30 Sta. 2	Sta. 3	Sta. 1	
5:00 Sta. 3	Sta. 1	Sta. 2	

#### Station 1: Bladder, Ureter and Urethra (2 parts)

- a. The Ureters, Bladder and Urethra and their location in the pelvis. The locations of and the relations of the kidney, ureters, bladder and urethra will be shown in male and female prosections of the pelvis.
- b. Specimens illustrating renal development will be presented and discussed.

#### Station 2: Gross Anatomical Relationships (2 parts)

- a. Posterior relationships of the kidney ie. the relationship of the psoas muscles, quadratus lumborum, diaphragm, transverse

abdominus muscle, lower ribs, and vertebral level. Also, notice the adipose capsule, the renal fascia and the pararenal fat which surround the kidney itself.

- b. Illustrates the relationship of the kidneys to anterior right structures, including right and left colic flexures, liver, duodenum, pancreas and spleen. Note the suprarenal (adrenal) glands which lie just cranial to the kidney.

### Station 3: Renal Blood Vessels

- a. This module is concerned with the blood supply to the kidneys, both internal and external. One portion of the module shows the inferior suprarenal (adrenal) artery. Also, note the location of the other major arteries to the abdominal region: the celiac root, the superior and inferior mesenteric arteries and the gonadal (ovarian or testicular) arteries.
- b. The other part of the module illustrates the vessels within the kidney: the anterior and posterior divisions of the renal artery, the segmented, interlobar, arcuate and interlobular arteries, and the afferent and efferent arterioles associated with the glomerulus.

## PART B - DISSECTION OF THE KIDNEY

### Materials:

fresh kidney  
 dissecting pan  
 dissecting knife  
 magnifying glass  
 applicator sticks  
**Anatomy Text**

### Methods:

Step 1: Before dissecting the kidney, examine it grossly. Note the perirenal fat that may be found on the outside of the kidney. Strip this fat away and examine (feel) the surface of the fibrous capsule on the surface of the kidney. You are actually feeling the kidney capsule. (If the capsule and fat have been removed, remnants of these structures can be found around the hilus).

Next, locate the hilum of the kidney and the structures (artery, vein and ureter) which emerge from it.

Now, gently nick the capsule and peel it away from the kidney. Note that it is closely adherent to the tissue. What kind of tissue is the capsule?

Step 2: Insert applicator sticks into the renal artery and vein (or their branches), and the ureter. Leave these in position so you can follow their course after the kidney is cut open.

Step 3: Using the large dissecting knife, cut the kidney into two 'slabs' beginning at the lateral border (convex side) and cutting toward the hilum. Do not separate the two halves completely. Now lay the kidney open in the dissecting pan.

Step 4: The following areas and structures can be seen with the naked eye: renal cortex, renal medulla, renal pelvis, renal papillae, pyramids, major and minor calyces and renal columns.

Note the relationship of the ureter and the larger arteries and veins to the above structures.

Make a sketch of one half of the kidney and identify the structures mentioned above.

Step 5: With the aid of a magnifying glass, look more closely at the cut surface of the kidney. Note the striations in the medulla (ie. in the pyramids). These are the collecting tubules and straight loops of Henle. Examine the surface of the renal papilla closely and look for the tiny opening of the collecting ducts into the calyces.

Examine the renal cortex. The glomeruli and proximal and distal convoluted tubules give this region a 'granular' appearance. Glomeruli may be seen as small red spots.

Finally, look at the smaller blood vessels in the kidney. Try to locate the arcuate arteries, the interlobar and the interlobular arteries. Understand the relationship of these different vessels to each other and to the nephrons.

### Summary Questions

1. What is the difference between the following: renal hilum, renal pelvis and major calyx?
2. What exactly is the structure called the 'renal pyramid'?
3. Trace the pathway of urine formation as fluid moves from the glomerulus to the urethra.
4. Distinguish between interlobular arteries and interlobar arteries.

5. What landmarks could be used to describe the location of the kidneys?
6. Explain the function of a glomerulus based on its structure.



## Tutor Notes - Laboratory Ten

### KIDNEY ANATOMY

#### PART A - GROSS ANATOMY

The various modules which comprise Part A of the exercise will be conducted in the Anatomy Laboratory (1R6) and will be supervised by the Anatomy Laboratory Assistants. However, you should accompany your group to 1R6 to make sure they work through the modules on time and return to the 2J area without getting lost.

#### Renal Embryology and Anomalies

The students should be reminded particularly that gross malformations of the kidney (horseshoe kidney, fused mass on one side, etc.) do not ipso facto mean that there are any physiological abnormalities. In addition, it is very important that they understand that duplication of the ureters does not provide a 'spare' ureter. That is, a pair of ureters on the same side drain different regions of the renal parenchyma.

#### Bladder, Ureters and Urethra

The following points should be stressed:

1. the location of the kidneys with respect to palpable landmarks
2. the course of the ureter, especially over the pelvic brim and its relation to the vas deferens in the male
3. the position of the bladder when empty versus when full
4. the course of the urethra through U-G diaphragm

#### Gross Anatomical Relationships

The nature of the renal fascia and its extensions should be emphasized. As well, the position of the adrenal glands and the other viscera which lie anterior to the kidney should be noted.

#### Renal Blood Vessels

The segmental nature of the renal arteries, and the fact that they supply discrete sections of the kidney should be emphasized. In this connection, point out that 'supernumerary' renal arteries are not spares, they are simply segmentals arising directly from the aorta. The lack of anastomoses among renal arteries makes them vulnerable to embolization of small thrombi that block blood flow to kidney and produce infarcts.

The apparent differences between left and right renal veins should be noted (in terms of length, and tributarie(s)), and the developmental explanation for it supplied.

The general pattern of the vessels within the kidney should be stressed; however, the details of specific names is of secondary importance. It is important, however, to stress the relative lack of anastomotic connections between the segments of the kidney. Finally the nature of the vasa recta (and their importance to countercurrent mechanism) should be demonstrated.

## PART B - KIDNEY DISSECTION

The kidney dissection is straight-forward. The problem likely to be encountered is variation in the amount of excess material (perirenal fat etc.) which remains on the kidney and the length of the attached ureters and renal vessels.

### Answers to Summary Questions

1. The renal hilum is the medially located indentation (concave region) where the ureter and blood vessels enter or leave the kidney.

The renal pelvis is the expanded portion of the ureter which lies just inside the hilar region.

The major calyces are the two (or three) large projections extending from the pelvis of the kidney. They appear to be part of the pelvic area, but only the common central portion is properly pelvis.

2. The renal pyramid (so-called) is the triangular appearing pattern seen when viewing a cut section of kidney. The appearance is due to the convergence of collecting ducts, etc. toward a minor calyx. (Emphasize that the pyramid is an appearance).

3. The pathway followed by the filtrate during urine formation from the glomerulus to the urethra is as follows: glomerulus, proximal convoluted tubule, loop of Henle (three parts), distal convoluted tubule, collecting duct, minor calyx, major calyx, renal pelvis, ureter, bladder, urethra.

4. The interlobar arteries are found between the pyramids running parallel to the edges, and passing toward the cortex where they form the arcuate arteries. Each pyramid and surrounding cortical tissue represents a primitive lobe - hence the name.

The interlobular arteries are given off at right angles to the arcuates and pass into the cortex.

5. The upper pole of the kidney is about the level of the 11th rib about 1.5 - 2 inches lateral to the posterior midline. The lower pole is about the level of the 3rd lumbar vertebra. The hilus lies at the level between the 1st and second lumbar vertebrae.
  
6. The glomerulus is a highly ornate capillary 'tuft' which provides a large surface area. Since plasma filtrate passes through the 'filtration membrane' formed by the endothelial cells lining the capillaries, the epithelial cells that form the visceral layer of Bowman's capsule, and the intervening basement membrane, it is obvious that the glomerulus is a filter for the blood.

## Tutorial Eleven

### JOSEPH WHITE: DUODENAL ULCER

#### Objectives

1. Describe the normal secretions of the stomach, and the protective mechanisms of the stomach.
  2. Describe what a duodenal ulcer is, its etiology, signs, symptoms, and treatments.
  3. Discuss the possible drug treatments which may be used for ulcers, and their mechanisms of action.
- 

Joseph White, 55, is the president of a company which is suffering in the present economic climate. His stomach 'troubles', which he has had for many years, have been much worse lately. The gas and discomfort have been reduced by eating frequently, but because of the increase in severity of pain, he visited his family doctor last Tuesday.

His doctor told him he had a recurring duodenal ulcer, and he was started on Cimetidine, 300 mg, 4 times a day. What is a recurring duodenal ulcer? What tissues are involved and how long would it take to heal?

Mr. White found that the drug therapy seemed to be working well. On Friday night he felt much better and decided to have a few drinks to relax. He felt great, but woke up Saturday morning with a terrific headache so he took 2 extra-strength Anacin tablets. On Saturday evening he arrived at Emergency, complaining of severe abdominal pain. He is very pale and is sweating profusely. His pulse is 130 and his blood pressure is 90/60. He tells you that he passed a black, tarry stool about one hour ago. The sharp pain just began on the way to Emergency.

Make sure you understand the pathogenesis of peptic ulcers. What individuals may be susceptible to peptic ulcers? What factors are present to protect the stomach and the duodenum from their environment? What factors are thought to play a role in the development of peptic ulcers?

Mr. White's major complaint was the pain he was experiencing. What was producing this pain?

Do the 'tarry stools' tell you anything about the extent of Mr. White's lesion and the location of the lesion? Finally, there are three main types of drugs which are available for treating peptic ulcers. Can you explain how they work? Can you think of any non-drug treatments?

**Tutor Notes - Tutorial Eleven****JOSEPH WHITE: DUODENAL ULCER****Objectives**

1. Describe the normal secretions of the stomach, and the protective mechanisms of the stomach.
  2. Describe what a duodenal ulcer is, its etiology, signs, symptoms, and treatments.
  3. Discuss the possible drug treatment which may be used for ulcers, and their mechanisms of action.
- 

**Q1. What is a duodenal ulcer? Distinguish between acute and recurrent forms. What healing process is involved?**

A duodenal ulcer involves the erosion of the lining of the epithelial layer of the duodenum. There may be single or multiple lesions. It is one of several types of peptic ulcers, which is a general term for lesions in the stomach or the duodenum. Peptic ulcers are found in about 10% of the population at autopsy, and are 10 times more frequent in the walls of the duodenum than the stomach.

It may be an acute or chronic condition ranging from a mild form where the erosion is limited to the uppermost mucosal layer to more severe cases whereby the crater formed penetrates through the mucosal lining or all the way to the smooth muscle layer resulting in perforation of the gastric or intestinal wall. Such a lesion may be fatal. In such a case, the ulceration extends down into deeper layers perforating large blood vessels, resulting in extensive internal bleeding. Acute ulcers occur as a complication of surgery, trauma, toxicity or diseases. Recurrent ulcers are far more common.

The healing process involves the formation of granular connective tissue at the base of the crater and the spreading of the tissue outward to the circumference. The process takes about 4 to 8 weeks for completion. In more than half the patients who have peptic ulcers, recurrence occurs within 2 years.

**Q2. The pathogenesis of peptic ulcers appears to involve the disruption of the normal balance between digestive secretions and protective secretions. Hydrochloric acid is the major ulcer promoting factor; the digestive enzyme pepsin may also contribute. Briefly discuss the secretion of these substances.**

The parietal cells of the gut secrete HCl. The formation of HCl

depends on the reaction of  $\text{CO}_2$  and  $\text{H}_2\text{O}$  catalyzed by carbonic anhydrase to produce  $\text{H}^+$  and  $\text{HCO}_3^-$ . Chloride ion is actively pumped into the cell and combines with the  $\text{H}^+$  to produce  $\text{HCl}$ .

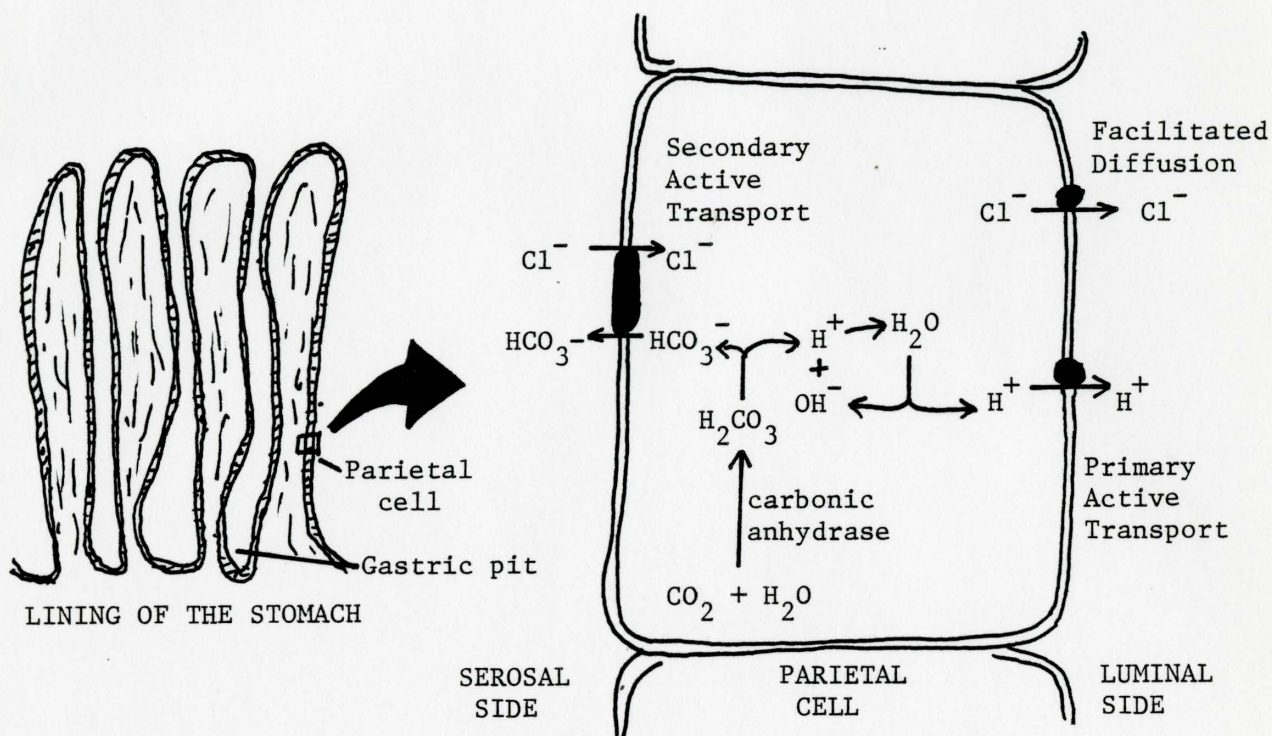


Figure 11A

The secretion of  $\text{HCl}$  and pepsin are mediated by neural and hormonal mechanisms. The vagus nerve regulates secretion; vagal stimulation initiates the secretion of large amounts of acid and pepsin by the parietal cells and chief cells respectively. Vagal stimulation also causes the release of the hormone **gastrin** from the antral portion of the stomach. In addition, gastrin is released in response to distension of the stomach and a number of secretagogues including peptides, caffeine and alcohol.

Histamine also stimulates gastric secretions in a manner similar to that of gastrin.

**Q2a. Individuals who are susceptible to peptic ulcers may have weaker protective barriers against the high acidity in the stomach. These protective factors are called 'gastric mucosal barriers'. What are they?**

The mucous which is secreted by the mucous cells is alkaline which helps to protect the stomach wall by neutralizing the acid. The cells lining the lumen have a low permeability to hydrogen ions, preventing their entry into the underlying mucosa. In addition, the lateral surfaces of the epithelial cells are joined

by tight junctions, that prevent the hydrogen ions from gaining access to the intercellular spaces. Finally, the epithelial cells are continuously being replaced every few days by mitosis.

**Q2b. What additional protection does the duodenum have against acid?**

The alkalinity of the small intestine neutralizes the acid. The pancreatic secretions which contain large quantities of sodium bicarbonate are especially important in neutralizing the HCl of the gastric fluid.

Excess acid entering the duodenum reflexively inhibits antral peristalsis in the stomach, thereby decreasing the rate of gastric emptying. This allows more time for the neutralizing actions of the pancreatic fluid. Since the reflex inhibition subsides as the contents are neutralized, more stomach contents can be emptied into the duodenum.

The presence of acid in the small intestine stimulates the release of the hormone secretin from the intestinal mucosa. This hormone then travels to the pancreas via the blood where it stimulates the rapid release of pancreatic fluid that contain a particularly high concentration of sodium bicarbonate.

**Q3. What factors are thought to play a role in the development of peptic ulcers?**

While the etiology of peptic ulcers is not clearly understood, there are a number of factors which have been implicated in their development. These include: emotional factors (stress, anxiety, anger and hostility); drugs which are potentially ulcerogenic (including aspirin, alcohol, nicotine and caffeine); genetic factors (as suggested by a higher incidence in patients having a family history of peptic ulcers); and gender.

**Q3a. Can you think of any reason(s) which could explain the difference in the incidence of peptic ulcers between the sexes?**

Some possible explanations might be: hormonal, dietary factors, or differences in the level of stress, or any other ulcerogenic agent.

**Q4. Why would Mr. White experience pain?**

The pain associated with peptic ulcers results from irritation of exposed nerve fibres in the region of the ulcer, and contractile spasms of the smooth muscle irritated by the acid.

**Q5. What information can you gain from the presence of 'tarry' stools?**

The tarry stools indicate that a large artery has eroded and partially digested blood is being passed. This indicates that the lesion is not occurring at the lower end of the intestinal tract since the blood has been partially digested.

Q6. The drug treatment for peptic ulcers involves the reduction of acid secretion and/or its neutralization. Outline the pathway of acid secretion, starting from the CNS and point out places where drugs have the potential to act.

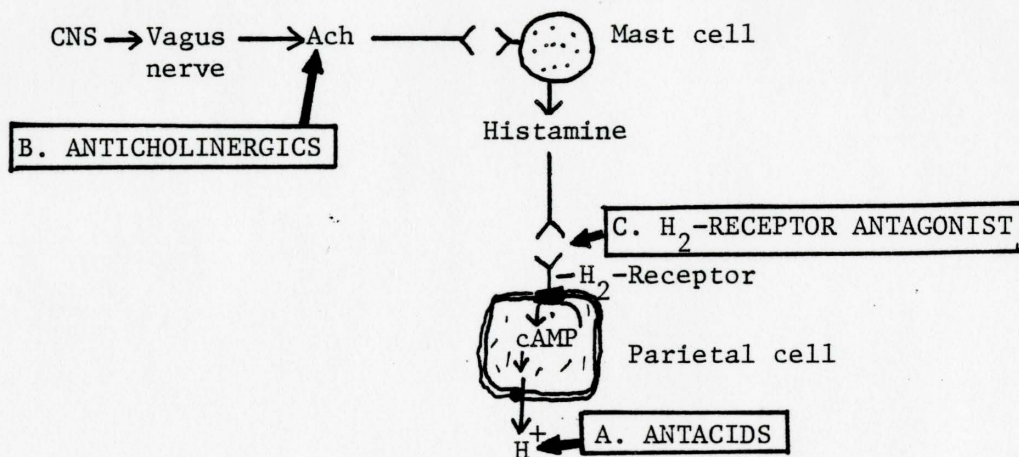
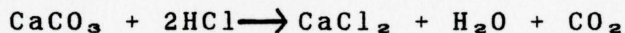


Figure 11B

### A. Antacids

The beneficial effects of antacids are attributed to their ability to neutralize the gastric acid and to reduce the proteolytic activity of pepsin (elevation of the pH of the gastric contents from a normal value of 1.3 to 5 results in complete inactivation of the enzyme).

Antacids which are currently in use are all weak bases which are capable of combining with HCl to form salts and water. 'Tums' is calcium carbonate, and it reacts with HCl as follows:



The selection of an antacid is based on three primary considerations: the acid neutralizing capacity; the risk of adverse effects; and factors influencing patient compliance. Antacids are not widely used because of the associated risks.

### B. Anticholinergics

These drugs prevent the action of acetylcholine at its receptors. With the receptors blocked, acid secretion is reduced as is



smooth muscle motility, thus delaying gastric emptying time. However, the high dose of anticholinergic agents required to reduce acid secretion is almost always accompanied by several adverse effects.

Since these drugs slow gastric emptying time, they work synergistically with antacids; by decreasing emptying they prolong the time available for antacids to work. However, this beneficial effect may be offset by continued presence of food in the stomach that provides a stimulus for prolonged acid secretion.

### C. $H_2$ -Histamine Blocking Agents

Since the secretion of HCl is regulated in part by the action of histamine on its  $H_2$  receptors, blocking these receptors provides a means of inhibiting acid secretion.  $H_2$ -receptor blockers inhibit both basal and induced secretions of gastric acid.

#### Q7. What ways can peptic ulcers be treated without using drugs?

Stress management is recommended for patients suffering from recurrent peptic ulcers. Restricting the intake of alcohol, caffeine and nicotine is sometimes suggested. Frequent small meals are beneficial so that food is kept in the stomach most of the time. The food can neutralize much of the acid and dilute the gastric juice, so that its digestive action on the mucosa is minimal.

## Laboratory Eleven

### ANATOMY OF THE DIGESTIVE SYSTEM

This laboratory takes place in the Anatomy Lab - 1R1 area

The digestive system is examined in a modular form. Each module deals with the three embryological parts of the gastrointestinal tract (GIT) - the foregut, midgut and hindgut. A general reading of embryology and histology of the GIT is required prior to attending this lab. Remember, you will get more out of the session if you come prepared.

#### STATION 1 - 1R6

**Foregut:** This is the area starting from the mouth to the duodenum (as far as the bile duct entrance). Besides the small intestine and the stomach, observe the liver, gall bladder and the spleen. Note the blood supply of the GIT below the diaphragm is derived from the coeliac artery. What are the parts of the stomach? How does its nerve supply affect it? Surface anatomy of important viscera should be practiced on the cadaver. Also observe the attachment of the greater and lesser omentum.

#### STATION 2 - 1R17

**Midgut:** This is the area from the end of the foregut to the junction of the splenic flexure of the transverse colon. What is the significance of mesentery? What is the source of blood supply? Observe surface anatomy of the kidneys. What is referred pain? Why is pain in the umbilical area important?

#### STATION 3 - 1R18

**Hindgut:** This is the area starting from the end of the midgut to the anus. How can you differentiate between the loops of greater and smaller intestine?

#### SCHEDULE

	<u>1R6</u>	<u>1R17</u>	<u>1R18</u>
2:30 - 3:15	1&2	3&4	5&6
3:20 - 4:05	3&4	5&6	1&2
4:10 - 4:55	5&6	1&2	3&4

**Tutor Notes - Laboratory Eleven****ANATOMY OF THE DIGESTIVE SYSTEM**

This laboratory takes place in the Anatomy Lab - 1R1.

The students will spend 45 minutes at each of three stations. (See the schedule on the student's lab outline). It is recommended that discussion be carried out around a cadaver demonstrating as one goes along. Demonstration of peritoneal folds and spaces may require a diagram or chart, as these are relatively difficult to demonstrate on the cadaver. Individual viscera eg. stomach, liver and gall bladder may be demonstrated as separate specimens. Surface anatomy should be emphasized in each module.

**STATION 1**

Detailed discussion of embryology and small branches of blood vessels should be avoided. The concept of subphrenic spaces and lesser sac should be introduced.

**STATION 2**

Pancreas and its relationship to the spleen should be pointed out. Important surface anatomy including that of the kidneys should be emphasized. The function of mesentery and omentum should be discussed.

**STATION 3**

Main gross anatomical differences between small and large intestine should be pointed out. Referred pain and haemorrhoids should also be discussed.

## Tutorial Twelve

### DIARRHEA AND CONSTIPATION

#### Objectives

1. Discuss the causes of constipation.
  2. Describe the normal process of defecation.
  3. Understand the ways in which drugs could be used to overcome constipation. What problems may arise from the misuse of such drugs?
  4. Discuss the causes of acute and chronic diarrhea, the mechanisms whereby diarrhea may be produced, and the ways in which drugs may act to alleviate diarrhea.
  5. Discuss the problem of lactose intolerance and why it is characterized by diarrhea.
- 

#### Scenario One

You are visiting your grandparents and you tell them that you are now studying the digestive tract. Your grandmother proceeds to discuss with you her problem with constipation.

What are some of the causes of constipation? What is the normal mechanisms of defecation?

Your grandmother goes on to tell you that recently she has been taking laxatives in order to have a 'regular' bowel movement. How do laxatives work to alleviate constipation? What problems could develop with repeated use of laxatives?

#### Scenario Two

Roberta Kwitze, age 21, has been sponsored as a student in nursing by the United Church of Canada. Her home is Nigeria. When she arrives she delights in all the new foods available to her, particularly milk. Her local region in Africa does not have cattle for milk production. In fact, she cannot remember seeing any member of her family drink milk after they were weaned from the breast. After about two weeks in Canada, Roberta develops diarrhea and cramp pains.

What is diarrhea (distinguish between acute and chronic diarrhea), what are some of the possible causes, and what are the physiological mechanisms involved in diarrhea? What mechanisms could be used to the control of diarrhea with drug therapy?

At first Roberta is hesitant to discuss her problem with anyone, but when it becomes so severe that she has difficulty coping, she goes to the student health services. After tests for parasites and stool cultures have been examined, changes in dietary patterns are discussed. Milk is removed from her diet and she improves rapidly. What do you think was the cause of Roberta's diarrhea?

**Tutor Notes - Tutorial Twelve****DIARRHEA AND CONSTIPATION**Objectives

1. Discuss the causes of constipation.
  2. Describe the normal process of defecation.
  3. Understand the ways in which drugs could be used to overcome constipation. What problems may arise from the misuse of such drugs?
  4. Discuss the causes of acute and chronic diarrhea, the mechanisms whereby diarrhea may be produced, and the ways in which drugs may act to alleviate diarrhea.
  5. Discuss the problem of lactose intolerance and why it is characterized by diarrhea.
- 

**Q1. What is constipation and what are its causes?**

Constipation may be defined as a decrease in the frequency of bowel movements accompanied by a prolonged and difficult passage of stool, followed by a sensation of incomplete evacuation. It has many diverse causes, including the following:

1. psychological factors - failure to respond to the defecation stimulus or to acquire the habit of regular defecation. Emotional stresses may also be a cause.
2. nutritional factors - a diet which contains insufficient bulk or contains foods that hardens the stool, severe dieting, starvation or dehydration.
3. disease - hypothyroidism, tumours obstructing the intestinal tract, haemorrhoids, or damage to the nerve plexus of the colon that co-ordinated motility.
4. drugs - aluminum containing antacids, anticholinergic agents, opiates, or laxatives when misused.
5. miscellaneous factors - pregnancy, after childbirth, decreased physical activity, or age.

**Q2. What is the normal mechanism of defecation?**

Defecation involves a reflex; when feces enter the rectum, the distention of the rectal walls stimulates the generation of afferent impulses that are sent through the myenteric plexus.

This initiates peristaltic waves in the descending and sigmoid colon forcing feces toward the anus and simultaneously relaxing the internal sphincter. If the external sphincter is relaxed, defecation will occur.

The defecation reflex is weak, but it may be fortified by another reflex which involves the sacral segments of the spinal cord. Signals are transmitted into the spinal cord from afferent fibres in the rectum, triggering a reflex back to the descending colon, sigmoid colon, rectum and anus by way of parasympathetic nerve fibres. These signals greatly intensify the peristaltic waves and thereby are able to convert the relatively weak defecation reflex into a powerful process.

Defecation is controlled voluntarily by contraction of the external sphincter, a skeletal muscle which is kept tonically contracted when a person wishes to prevent defecation. When this is done, the defecation reflex dies out after a few minutes.

### Q3. How do drugs which alleviate constipation work?

Laxatives (cathartics) are used to induce defecation and are commonly classified on the basis of their mechanism of action.

#### 1. Stimulants or Contact Laxatives

Drugs in this category act by stimulating peristalsis. They can do this in a number of ways: by stimulating the stretch receptors or sensory nerves of the intestinal mucosa, by directly stimulating intestinal smooth muscle, or by increasing the pressure within the lumen of the intestine and thereby stimulating peristalsis.

(aside)

Q3a. How could the pressure within the lumen of the intestine be increased?

Inhibition of electrolyte and water reabsorption from the intestinal lumen, or enhancement of water secretion into the lumen would increase intraluminal pressure.

#### 2. Saline or Osmotic Laxatives

This class of laxatives consists of non-absorbable, or poorly absorbable sugars or cations (such as  $Mg^{++}$ ,  $K^+$ , or  $Na^+$ ) and anions. A hypertonic solution of the salts, because of their osmotic effect, causes the retention of water in the intestinal lumen. Increased intraluminal pressure stimulates stretch receptors which in turn stimulate peristalsis.

(In addition to its osmotic action, magnesium is thought to activate the release of the stomach hormone CCK, a hormone

that stimulates intestinal motility and inhibits fluid absorption from the intestine).

### 3. Bulk-forming Laxatives

The ingestion of non-digestible polysachrides and cellulose derivatives, results in the retention of large volumes of water in the intestinal tract. Again, this results in increased intraluminal pressure which stimulates peristalsis and hence facilitates the movement of stool.

This is the way in which dietary fibre acts as a laxative.

### 4. Lubricant or Emollient Laxatives

These laxatives retard the absorption of water from the intestinal lumen and in doing so, they soften the fecal matter. This is the way in which mineral oil works. They may also act by coating the mucosal lining, and fecal material, thus facilitating the smooth passage of the stool down the bowel.

(aside)

Q3b. How might this affect the absorption of some nutrient requirements?

The chronic administration of mineral oil may interfere with the absorption of food and fat-soluble vitamins which may contribute to nutritional deficiency.

Q4. What are some of the risks associated with the misuse of laxatives?

The excessive use of laxatives by some people is often the result of misunderstandings about the normal physiology and pathophysiology of the digestive system. The regular use of laxatives can cause problems such as depletion of water, electrolytes and vitamins. The overuse of laxatives often develops into a habit that is difficult to break. A cycle is initiated if one takes a laxative which results in a complete evacuation of the bowel and fails to appreciate that a delay of a few days is required for the accumulation of sufficient contents in the colon for another bowel movement to occur. Therefore the individual takes another laxative.

With the regular use of laxative, the normal defecation mechanisms may become blunted, and the individual may rely entirely on these drugs for defecation.



**Q5. What is diarrhea? What are some of the possible causes of acute diarrhea and chronic diarrhea?**

Diarrhea is the frequent passage of feces that has increased water content. It is a symptom resulting from a variety of causes.

Acute diarrhea may arise from many factors including:

1. microbial causes - usually bacteria in adults, and viruses in infants. This is the most common cause of diarrhea. It may not be the microbe itself which causes the diarrhea, but rather the toxins it produces.

Infections or toxins often cause diarrhea by altering various ion-transport processes in the epithelial membrane, or by direct penetration of the mucosa;

2. nutritional causes - foods that are excessively spicy or fatty, or have a high content of roughage;
3. drug induced causes - antibiotic-induced diarrhea is quite common and it may result from the mildly irritating properties of these drugs; a side effect of drugs affecting the autonomic nervous system is diarrhea (ex. cholinergic agents); and intestinal infections caused by drug alteration of the normal intestinal flora.

Factors which may contribute to chronic diarrhea include:

1. cancer of the rectum or colon;
2. a number of diseases of the gastrointestinal tract;
3. emotional stress.

**Q6. What are the mechanisms involved in the production of diarrhea?**

1. Osmotic diarrhea occurs when unabsorbed solutes are present in the lumen. They promote water retention.
2. In some diseases including celiac disease and chronic inflammation of the colon, permeability of the bowel to water is decreased.
3. With ulceration or inflammation of the gastrointestinal mucosa, the outpouring of inflammatory exudate often causes diarrhea.
4. Intestinal secretory diarrhea occurs when the net absorption of electrolytes and water from the intestines is reversed so

that fluid is secreted into the intestines. This is the mechanism by which cholera toxin produces diarrhea. It stimulates adenylate cyclase, which increases cAMP levels within the cell. This induces an outpouring of salts and water to such an extent that the colon is unable to reabsorb the load.

5. Hypermotility, a side effect of some drugs, promotes diarrhea.

**Q7. What mechanisms could be used for drug therapy in the control of diarrhea?**

1. Reduced motility of the gastrointestinal tract - the goal is to inhibit peristalsis and/or increase the tone of the circular smooth muscle of the intestines and thereby decrease the frequency of defecation. This is the mechanism by which opium and its derivatives (such as codeine and morphine) produce their anti-diarrheal effects.

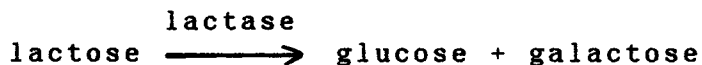
2. Absorbants - act by absorbing fluid as well as the toxins, bacteria and other noxious materials that are responsible for causing diarrhea. However their non-selectivity is a problem; they may also absorb nutrients, digestive enzymes, orally administered drugs and vitamins. Most over-the-counter drugs work by this mechanism.

**Q8. Consider the case of Roberta. Why do you think the cause of her diarrhea is?**

With the removal of milk from her diet, Roberta improved rapidly. This would indicate she was intolerant to lactose.

**Q8a. What is lactose? What is lactose intolerance? Why does lactose intolerance cause diarrhea?**

Lactose is a disaccharide which is found in milk. It cannot be absorbed directly, but must first be digested into its monosaccharide components: glucose and galactose. The enzyme responsible for this breakdown is lactase which is found within the brush border of the small intestine.



Lactase is normally present at birth, but it may decline in some individuals as they mature. This is a fairly common occurrence in many ethnic groups so that by the age of about five they no longer produce this enzyme. In the absence of lactase, lactose remains in the lumen of the small intestine, and its osmotic pressure tends to hold water within the lumen.

The unabsorbed lactose-containing fluid is passed on to the large

intestine where bacteria are able to metabolize the lactose, but in doing so produce large amounts of gas and organic products which inhibit active transport processes. This increases the osmolarity within the lumen, which in turn results in the movement of fluid into the lumen of the large intestine. The end result is the production of diarrhea and gas with associated cramps.

The symptoms of lactose intolerance can easily be overcome by avoiding milk and milk products in the diet.

## Laboratory Twelve

### GASTROINTESTINAL PHYSIOLOGY

#### Prerequisite Activities:

Read this before coming to laboratory.

#### Objectives:

1. To show that glucose uptake across the intestinal wall is an active process (ie. it can occur against a concentration gradient and is carrier mediated).
2. To show that the glucose carrier is stereo-specific, the mucosal solution will contain phloridzin, a molecule which attaches to the mucosal side of the carrier but which is not transported across the membrane. (This competition for the carrier site could also be demonstrated by adding competitive sugars or amino acids).
3. To further investigate the characteristics of the carrier molecules for glucose, and demonstrate its  $\text{Na}^+$  dependence, the external concentration will be lowered by replacing the  $\text{Na}^+$  in the mucosal solution with choline, keeping the solution iso-osmolar. (Why iso-osmolar)?
4. To show that the unloading of the glucose within the cell is dependent upon the maintenance of low intracellular  $\text{Na}^+$  concentrations, ouabain (a digitalis-like compound) will be added to the serosal surface. This compound inhibits the  $\text{Na}^+$  pump, which is presumed to lie on the basolateral surface of the cell. The addition of ouabain produces a build-up of sodium within the cell.

#### PART A - DEMONSTRATION OF INTESTINAL MOTILITY

A segment of intestine similar to the one you will use, except that it is not everted, will be suspended in a glucose solution and attached to a recording device to show active contraction changes in tension. During the laboratory period, various drugs will be added to the tissue bath to demonstrate their effect on intestinal motility.

Observe the intestine in the glucose solution and record your observations.

1. Does it exhibit tone?
2. Are there spontaneous contractions?

3. When the acetylcholine analogue, carbachol, is added to the bath, does the tension change?
4. What happens to the contractions?
5. What happens to the contractions when noradrenaline is added?
6. Are there any changes in tension?
7. Are there spontaneous contractions?
8. What is the neurotransmitter in the GI tract which is excitatory? Inhibitory?
9. What happens to motility in the GI tract when you run a race?

### Part B - INTESINAL MOTILITY

Note: Each group will be divided into 3 smaller groups of 3-4 students.

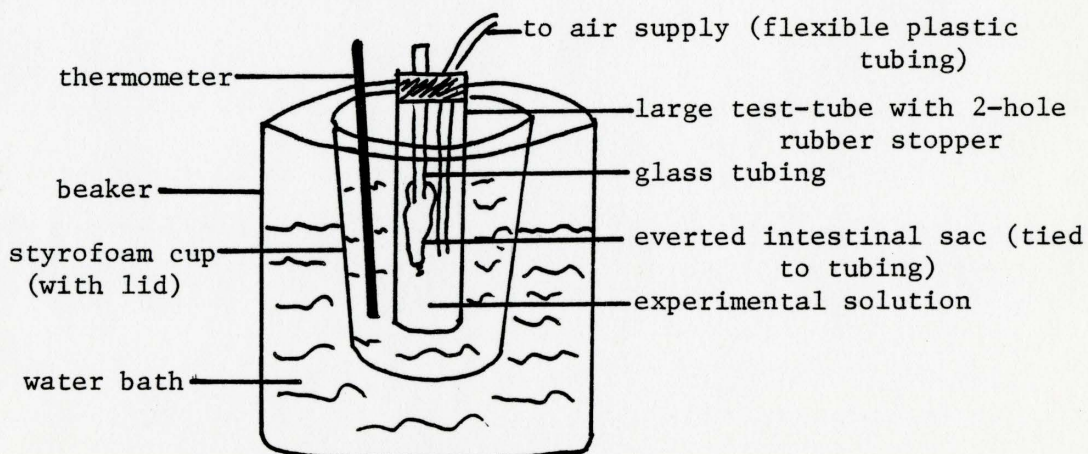
#### Materials:

<u>work bench</u>	<u>drawer/cupboard</u>	<u>central location</u>
styrofoam cup and lid	test tubes	inverted gut segment
scissors	medicine dropper	solutions*
Pasteur pipettes	1000ml beaker	
thread	rubber tubing	

#### \*Krebs Ringer Bicarbonate Solutions:

- A - without glucose
- B - with glucose
- C - with glucose + phloridzin
- D - with glucose + ouabain
- E - with glucose but Na<sup>+</sup> substituted by choline

#### Diagram of Experimental Apparatus:



**Methods:**

The objective of the experiment is to characterize the mechanism of intestinal transport of glucose.

1. The incubation tube consists of a cut-down 15 ml. test tube, a two-hole rubber stopper with a piece of glass tubing inserted into one hole, and a length of flexible plastic tubing with a hard plastic fitting on one end. Place the flexible tubing through the second hole of the stopper (fitting above, of course) so that it is immersed in the liquid to be added to the incubation tube.
2. A water bath in which to place the incubation tube will be needed. This can be made with a styrofoam cup and a large beaker. First make a hole in the centre of the cup lid so that the incubation tube can be inserted and held snugly.
3. Fill the cup almost to the brim with water, place the cup in the beaker and add water to the beaker until the water level is about 1/4 to 1/2 inches below the level inside the cup.
4. Attach a length of rubber tubing from the air outlet on the work bench to the fitting on the flexible plastic tubing and adjust the air flow so that a small, steady stream of bubbles emerges from the tubing inside the incubation tube. Once the air flow is adjusted, do not change it.
5. Bring a small beaker to the lab. prep. room to obtain a specimen of everted gut. This should be handled carefully and kept in a small amount of warm buffered saline (37°C).
6. Insert the glass tube of the incubation tube into one end of the everted intestinal strip. Tie firmly on glass tube. Flush gently with Sol.A using a long thin pasteur pipette to remove bubbles. Then tie off the other end of the intestinal strip to make a sac. **Be sure to keep the tissue wet at all times.**
7. One member of each pair group should fill the styrofoam cup with warm tap water, while another places sufficient Sol. A to immerse the sac in the incubation tube and insert the preparation.
8. As soon as the incubation tube and cup are adjusted properly, fill the beaker with tap water which is slightly warm to touch. Check the temperature of the water in the cup. Throughout the experiment, maintain the temperature in the cup by removing some water from the beaker and replacing it with warm water.

**EXPERIMENT #1: Done by each group of students.**

- a) When the preparation is ready, add Sol. A to the inside of the intestinal sac by using a long thin Pasteur pipette to introduce the solution through the glass tubing to which the sac is attached.
- b) After the preparation has incubated 15 min., obtain a sample of the fluid from inside the sac and a sample of the fluid in the test tube and test for the presence of glucose, using Dextrostix. (Instructions for their use is on the container). Estimate the volume of fluid in the sac. Record volume as: 0 for empty, + for small volume, ++ for medium, and +++ for full. Record glucose reading in mg/dl.

**EXPERIMENT #2: Done by each group of students.**

- a) one member of the group should now flush the intestinal sac with fresh Sol. A. This can be done by repeatedly adding and withdrawing the fluid with a Pasteur pipette.
- b) After flushing the intestinal sac, one member of the pair will fill the sac with Sol. B and the other fill the incubation tube with Sol. B.
- c) Incubate the preparation for 15 min., measure the glucose in the intestinal sac, and estimate the volume of fluid in the sac (hint: this should be your +++)

**EXPERIMENT #3: Done by Group #1 only.**

- a) Flush the sac with Sol. B and change the incubation solution to Sol. C.
- b) Incubate the preparation for 15 min. and measure the glucose in the intestinal sac and estimate the volume.

**EXPERIMENT #4: Done by Group #2 only.**

- a) Flush the sac with Sol. B, change the incubation solution to the Na<sup>+</sup> poor Krebs Sol. E.
- b) Incubate for 15 min. and measure the glucose content of the sac.

**EXPERIMENT #5: Done by Group #3 only.**

- a) Flush the sac with Sol. B and fill it with Sol. D. Leave for 15 min.
- b) Replace the incubation solution in the tube with fresh Sol. B. Do not change the sac solution.

- c) Incubate for 15 min. and measure the glucose content of the sac.

### SUMMARY QUESTIONS

1. Is the carrier for glucose stereo-specific? If so, which is the preferred shape, and what other sugars compete for this carrier?
2. What is the role of  $\text{Na}^+$  in glucose transport?
3. What is the role of  $\text{K}^+$  in glucose transport?
4. It was difficult to show  $\text{Na}^+$  dependence of glucose transport in man in vivo. Can you suggest why?
5. How does fluid move in the intestine?



## Tutor Notes - Laboratory Twelve

### GASTROINTESTINAL PHYSIOLOGY

#### PART A - INTESTINAL MOTILITY

This part of the laboratory consists of a demonstration which will be set up in each laboratory. Make sure that your group observes the material and understands that the demonstration is recording something different from the experiment they will perform.

#### Answers to Questions in Part A

1. Yes, the intestinal strip does (hopefully) exhibit tone.
2. Yes, there are (or should be) spontaneous contractions.
3. Carbachol (same mechanism of action as acetylcholine), added to the water bath, should increase both frequency and amplitude of contractions.
4. Noradreneline should decrease the amplitude and frequency of contractions.
5. From the above, students should be able to deduce that acetylcholine is the excitatory neurotransmitter in the gut and that the adrenergic transmitters are inhibitory.
6. When running a race, gut motility should decrease, due to the stimulation of the sympathetic nervous system.

#### PART B - INTESTINAL ABSORPTION

While the experiment itself is fairly straight forward, there is likely to be some difficulty with mechanical details. (Bear in mind, however, that this is part of the purpose of the exercise; ie. to do something which requires a bit of manual and technical skill). A few technical difficulties that may arise as you proceed through the laboratory are outlined below.

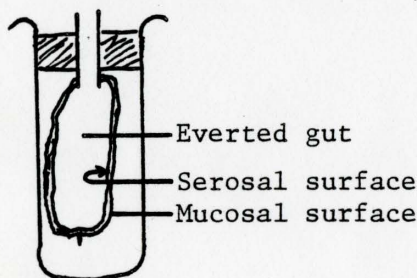
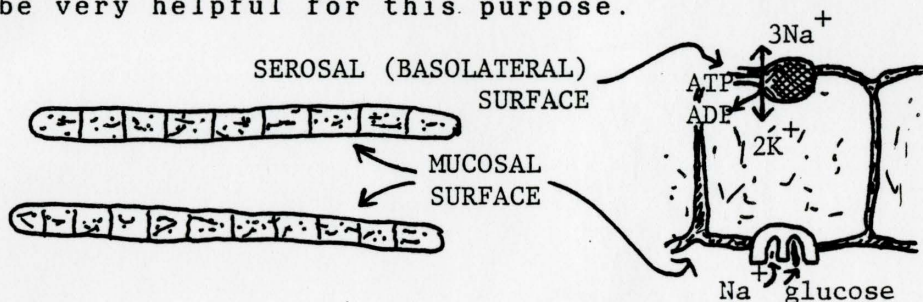
Setting up the water bath and remembering to monitor the temperature of the bath will be a problem. It would be easier to use commercial laboratory water baths. However, learning to work with the available material is a valuable exercise.

Step 4 can cause trouble for the unwary. If the incubation tube and air hose is assembled and then the air is turned on, there is a tendency to "blast" incubation fluid and apparatus all over the work area.

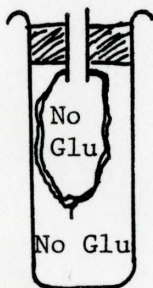
Flushing the sac out completely between runs is not easy to do. However, if they inject and withdraw several changes of fluid, they will get close enough to the right concentration simply by dilution.

The instructions for using and reading the dextrostix are on the container and should not be a problem. Some students try to read too much precision into a colourimetric test.

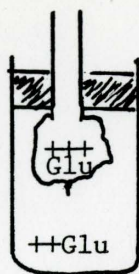
At the end of the laboratory period, you should assemble your group and discuss the results. Before going over the results, it is very important that the students understand exactly what they did, and the theory behind what was expected to happen. A diagram of the set up of the gut, and the different experiments would be very helpful for this purpose.



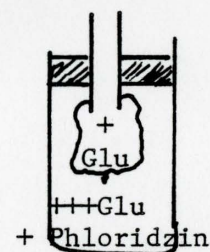
It is most important that the students realize which carriers are on the inside and outside in this set-up, since the gut has been everted.



In Experiment #1, neither compartments contain glucose. Thus, no glucose should be recorded.



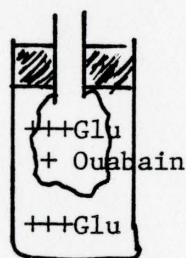
In Experiment #2, both compartments contain glucose. However, after a period of incubation, one would expect the concentration of glucose to be relatively greater in the sac, since it has been transported into this compartment (all the requirements for transport are present).



In Experiment #3, phloridzin has been added to the incubation solution. Since phloridzin is a glucose analogue, it competes for the glucose carrier, thereby preventing the transport of glucose. Thus, the incubation solution should contain a relatively great amount of glucose, while the concentration should stay (or decrease, as it is being metabolized) within the sac.



In Experiment #4, since  $\text{Na}^+$  is required for the transport of glucose (both  $\text{Na}^+$  and glucose must be bound to the carrier for it to function) the glucose concentration will remain relatively high in the incubation solution, and will remain constant (or decrease) in the sac.



In Experiment #5, the sac has been filled with a solution containing ouabain. Since ouabain inhibits the  $\text{Na}^+$  pump located on the serosal side, the concentration gradient for  $\text{Na}^+$  cannot be established, and it remains high in the cell. Since the  $\text{Na}^+$  concentration gradient is necessary for the functioning of the  $\text{Na}^+$  glucose carrier transport, glucose concentration should remain high in both compartments.

It is entirely possible for students to obtain results contrary to expectation. Thus, when they are asked to interpret the results in the Data Correlation section, they will refute the hypothesis or have a novel interpretation. It is important that we not tell them they are wrong! The experiment may be flawed, but data are data. If they did not obtain the anticipated results, be sure they understand what the experiment should show, and let them speculate on what could have produced the results they obtained. Both transport and metabolism of glucose must be considered.

#### Answers to Questions in Part B

1. The carrier for glucose is stereo-specific. The dextrorotary form is the preferred form. A few other sugars compete for the carrier; prominent among which is galactose.
2. Sodium ions serve to bond the glucose to the carrier at the outer surface of the cell membrane.
3. Potassium ions act to 'un-bind' the glucose from the carrier on the inner surface of the cell membrane.
4. The obvious difficulty in showing that glucose transport is sodium dependent in vivo is to obtain a sodium-free local environment.
5. Fluid moves into the intestinal wall by osmosis (it is to be hoped that some of the class will remember that osmosis is really diffusion of water from a region of higher water concentration to a region of lower water concentration).

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