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V.63, 1993/94 & V.64, 1994/95 NO.2

Fall 1993

JOE Kim '93

Infectious Diseases

INSIDE:

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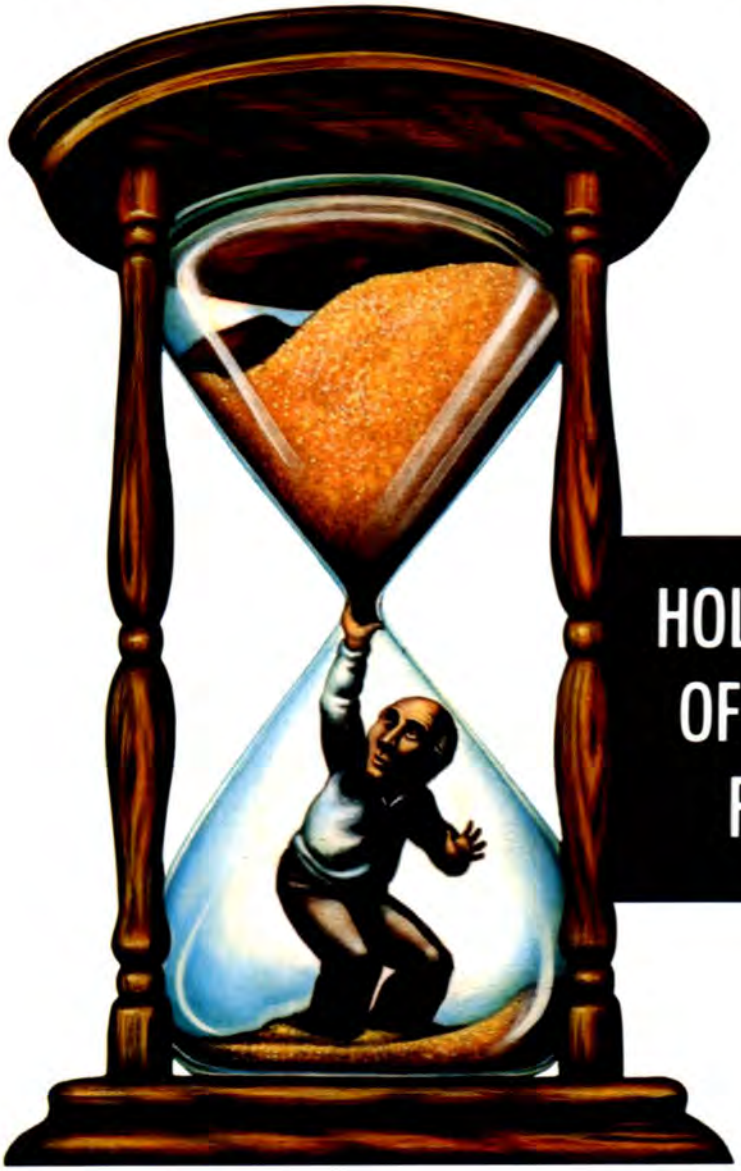

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THE NEXT ISSUE:

PLASTIC & RECONSTRUCTIVE SURGERY

SUBMISSION DEADLINES

ARTICLES
initial copy ..... March 4/94
final revised version April 1/94

ARTWORK ..... April 1/94

COVER ART:

The practice of draping crosses near coastal margins to warn passing ships of the presence of epidemic infections has existed in Europe and South America for many centuries. The cover depicts a mixed media painting of a cross on the seashore at Lima, Peru from a photograph taken during the Peruvian cholera epidemic, part of the seventh cholera pandemic, which claimed 500,000 lives worldwide in 1991-92.

- Joe Kim, Meds '96

GUIDELINES TO AUTHORS

The purpose of the U.W.O. Medical Journal is to provide a single forum for original articles based on clinical or research medicine of topical or historic relevance. Since the readership of the Journal is interdisciplinary, articles published will attempt to reflect the wide range of medical disciplines. The Journal will consider empirical, theoretical, and research reviews. Book reviews will also be considered. The Journal reserves the right to refuse articles that do not comply with the Journal's publication criteria.

MANUSCRIPT SUBMISSION: Each submission must include three (3) copies of the full manuscript PRIOR TO the submission deadline. Late submissions will not be accepted for publication. Authors are expected to submit the final revised version of the manuscript on 3.5" computer diskette along with three (3) copies of the manuscript (the Journal prefers Apple Macintosh® Microsoft® Word or Wordperfect® 5.1). All figures must be camera-ready and artwork must be black and white.

MANUSCRIPT PREPARATION: Manuscripts submitted should be set with one inch margins and typed single-spaced. Original research and review articles should have an abstract that clearly states the relevance of the article to the medical discipline being reported on in no more than 150 words. This dimension should be elaborated upon in the introduction. Original research articles should have experimental methods, results, and discussion sections that follow the introduction. Results and discussion sections may be combined if appropriate. The discussion section should be concise and focus primarily on the findings being presented and their important implications. Authors should rely on articles or information published in recognized journals and sources. References should be listed in numerical order and within the text in the following format:

1. Manev H., Favaron M., Guidotti A., & Costa E. Delayed increase of Ca^{++} influx elicited by glutamate: role in neuronal death. *Molec. Pharmacol.* **36**:106-12 (1989).

(With 3 or more authors, either all authors may be listed or the 1st author followed by et al.)

The Journal reserves the right to edit articles to correct grammatical or stylistic errors.

AUTHORSHIP: All medical students and members of the Faculty of Medicine of U.W.O. are invited to submit manuscripts for publication. Medical students are certainly encouraged to collaborate with medical staff who specialize in the medical sub-discipline being reported on. Manuscripts will also be considered from medical faculty (including interns and residents) from universities and medical institutions other than U.W.O.

MODES OF COMMUNICATION: Authors should submit along with their manuscripts a cover letter including a return address, telephone number, and fax number (where available). The final revised version of the manuscript on 3.5" computer diskette should be sent (with (3) photocopies of the manuscript) to:

The Editors
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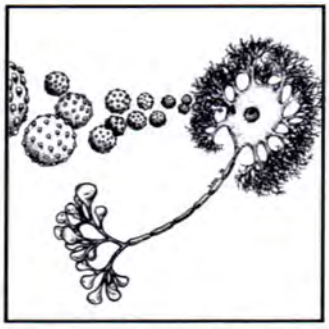
The U.W.O. Medical Journal is an interdisciplinary medical science publication, established in 1930. The Journal is published two times each academic year: Fall, & Spring. Subscription is $17.00 per year. All material published in the Journal reflects solely the views and opinions of the authors of the material printed and not necessarily the editorial staff of the Journal.

FEATURE SECTION —INFECTIOUS DISEASES

Neurologic Sequelae of HIV-1 Infection (P. 27)

!!MEDICAL HUMOUR!!



Pyogenic Hepatic Abscess (P. 35)

HUMAN IMMUNODEFICIENCY VIRUS-1 (HIV-1) TRANSMISSIBILITY AND THE LAW

Legal issues related to human immunodeficiency virus-1 (HIV-1) and acquired immunodeficiency syndrome (AIDS) are evolving more rapidly, perhaps, than any other subject in recent Western law history. Among these issues is the relation of AIDS to the criminal code—specifically disease transmission as an offence. Of particular interest in this regard is what constitutes an illegal act of disease transmission and what retributive measures exist for such acts. Analysis of two cases in which individuals were accused of committing criminal acts related to HIV-1 transmission will reveal that existing laws are insufficient to deal with AIDS-related legal matters.

Case 1

R. v. Ssenyonga *(April 30, 1993), Doc 1560 (Ont. Gen. Div.).*[1]
Offences: *Aggravated sexual assault; consent. Accused [of] infecting complainants with HIV-1.*
Decision: *Acquitted; courts rejecting arguments of consent, fraud, and public policy.*

The accused, knowing he was infected with HIV-1 and without telling this to the three complainants, engaged in sexual intercourse with them, thus exposing them to the risk of HIV-1 infection, which they subsequently contracted. The accused motioned for a directed verdict of acquittal. This motion was granted based on the ground that each of the three complainants freely and voluntarily engaged in sexual intercourse with the accused without the use of a condom. The court upheld that although the complainants may not have consented neither to transmission of HIV-1, nor even to that risk, the evidence was incontestable that they did consent to the application of force inherent in the acts of sexual intercourse; this force was not in itself excessive or dangerous. Furthermore, since the complainants were under absolutely no misapprehension as to the nature of the acts in which they were engaging, there was no evidence of fraud. Ultimately, since section 265(1)(a) of the criminal code was designed to control the non-consensual direct or indirect application of force by one person to another, and not to prevent HIV-1 transmission among the body politic, the Crown's public policy arguments could therefore not prevail.[1]

Case 2

R. v. Thornton *(August 14, 1989), O.R. (3rd) 480, 42 O.A.C. 206, 3 C.R. (4th) 381, [1991] C.C.L. 3659, affirmed (June 4, 1993), Doc. 22312 (S.S.C.).*[2]
Offences: *Causing bodily harm by criminal negligence. Accused [of] endangering lives of public by knowingly donating contaminated blood contributing an unlawful act.*
Decision: *Convicted; 15 months imprisonment.*

The accused was infected with HIV-1 and tested positive on two occasions for AIDS. Despite this, he donated blood to the Red Cross. The accused appealed the decision on the basis that his conduct was not an offence, that it was not proven to have endangered anyone, and that he lacked the guilty mind. The appeal was rejected. The common law upheld that every person was to refrain from potentially malicious conduct. According to the court, the accused personally knew the danger to which the public was subjected consequent to his donation of contaminated blood and thus had the requisite guilty mind. In light of the potential serious harm and damage to the lives and health of the public, the accused was properly convicted.[2]

These cases are characterized by similarities and differences—some are obvious and some are not. In both cases, notwithstanding knowledge of being infected with HIV-1, the accused engaged in baleful activities. Despite the parellelism of these acts, one individual was convicted and one was acquitted. In law, for conviction of a crime to be maintained, the commission of an offence must contain two components, proven beyond a reasonable doubt. These components are *mens rea* (guilty mind) and *actus reus* (guilty act). In addition, *mens rea* and *actus reus* must exist in the background of the offence charged. Taken alone, each case appears to involve acts with both *mens rea* and *actus reus*. But this is not true when the offences are measured against the charges; this is where weaknesses in the law in relation to AIDS become punctuated.

No specific legislation which exists is designed to deal with offences related to HIV-1 infection and AIDS. Thus, such offences must be categorized under existing sections of the criminal code. Ssenyonga was charged with aggravated sexual assault pertaining to sections 265(1)(a) and subsequently 273 of the criminal code. Section 265(1)(a) states that:

> A person commits an assault when without the consent of another person, he applies force intentionally to that other person directly or indirectly.[3]

Section 273 of the criminal code states that:

> Every one commits an aggravated sexual assault who, in committing a sexual assault, wounds, maims, disfigures, or endangers the (1) life of the complainant. (2) Every one who commits an aggravated sexual assault is guilty of an indictable offence and liable to imprisonment for life.[3]

Under the letter of the law, therefore, the accused was found not guilty of assault and thus of aggravated sexual assault. Thornton, however, was charged with criminal negligence causing bodily harm pertaining to section 221 of the criminal code. This section states that:

> Every one who by criminal negligence causes bodily harm to another person is guilty of an indictable offence and liable to imprisonment for a term not exceeding 10 years.[3]

Thus, the accused was properly convicted. Had Ssenyonga been charged under s.221, he too might have been convicted.

A further example of how existing laws are insufficient to deal with AIDS-related offences is based on retributive measures. In regard to case 1, the accused was acquitted and thus received no penalty. In regard to case 2, the accused received 15 months imprisonment; there were no identifiable victims. Had there been any victims, the accused's sentence may have increased but only to the maximum 10 years. Although AIDS is a fatal disease, it is not immediately so. Furtheron, although there is a section of the criminal code designed to deal with criminal negligence causing death (s.220) with a potential liability of life imprisonment, section 227 of the criminal code would likely prevent an AIDS-related offence from being categorized under s. 220. Section 227 of the criminal code refers to death within one year and one day:

> No person commits culpable homicide or the offence of causing the death of a person by criminal negligence...unless the death occurs within one year and one day from the time of the occurrence of the last event by means of which the person caused or contributed to the cause of death.[3]

Thus, qualifiers such as s.227 preclude existing laws from exacting just punishment.

Thus, within the context of the criminal code as it exists today, current laws are inappropriate and improperly utilized for unlawfaul acts of HIV-1 transmission. In the cases described, two points are clear. First, the offences committed are remarkably similar—an individual knowingly infected with HIV-1 transmitted or attempted to transmit the disease, or risk thereof, to innocent, unassuming people. Second, neither section of the criminal code under which the accused individuals' were charged appear sufficiently equipped to provide for due course of law. In case 1, the accused was charged with aggravated sexual assault, possibly because of the potential maximum penalty of life imprisonment, but the charge was inappropriate for the offence. In case 2, the accused was charged with causing bodily harm, not death, by criminal negligence; the charge was bodily harm perhaps because of the potential leniency of the penalty, and because although AIDS is fatal, it isn't immediately so (at least not within one year and one day).

Clearly, the capability to transmit HIV-1 infection represents a danger to health and life. Conspicuous by its absence is a specific set of laws designed to accommodate AIDS-related offences, especially the unlawful commission of HIV-1 transmission. These laws will have to strike a balance between the civil rights of the HIV-1-infected population and the uninfected population—a difficult task since the AIDS population already suffers from discrimination and is unlikely to seek testing or help from public agencies unless reassured that they will be neither further ostracized nor have liberties removed.

I would like to thank Ross and Anne and the entire Journal staff for helping to produce this fine issue, which features infectious diseases. Be sure to read Stitches In Time — it's guaranteed to make you smile. And please take a moment to read A Note to Our Readers on page 10. Enjoy!

Jeffrey Politsky, Meds '94
Editor-In-Chief

1 Canadian Current Law. July 30, number 7 (1993). Case Law Digest 6998.
2 Canadian Current Law. July 30, number 7 (1993). Case Law Digest 7000.
3 Criminal Code of Canada. R.S.C. 1993.

Inequities Of Gender Discrimination

Recently I attended a continuing medical education conference entitled "Gender Inequities in the Classroom." The objective of this conference was to increase awareness of gender discrimination. However, the ensuing discussion used exaggerated examples of gender differences in a futile attempt to explore the issue of gender discrimination. These examples included issues such as the ratio of female to male medical school admission applications and alcohol consumption patterns at all-female parties. I was angered by these ridiculous examples and the overt discrimination created by a discussion of gender differences.

Gender discrimination refers to the ability to distinguish between men and women. This 'rightful' form of discrimination involves acknowledgment of the basic features that distinguish both sexes. Gender discrimination may also be defined as unfair treatment based on a person's gender. The prejudicial basis of this latter form of discrimination makes it 'wrongful'. This 'wrongful' form of discrimination deserves attention and analysis in an effort to reduce its prevalence in society.

Acknowledging basic features that distinguish one gender from another may create greater acceptance and understanding among men and women. Attempts to magnify these differences, however, will serve only to further alienate members of each gender from one another. For example, an all-female party organized to rally support against overt gender discrimination merely perpetuates it by intentionally excluding one sex from such an event.

A large proportion of efforts to reduce the incidence of 'wrongful' discrimination find basis with the apparently trivial differences between men and women. Yet men and women do not adopt the same societal roles and should be treated differently accordingly. Essential to the continued effort to decrease 'wrongful' discrimination is the confirmation that 'wrongful' discrimination stems from prejudice and dislike, not anatomical and societal characteristics. The continual analysis of the basic gender differences between men and women will trivialize the entire effort to eliminate 'wrongful' discrimination and will ultimately pit the sexes against each other ad nauseum.

Anne Silas, Meds '94
Associate Editor

Business Quarterly and *The UWO Medical Journal*: Are We Poor Cousins?

I learned a few weeks ago that The University of Western Ontario Business School publishes an extremely well respected and well known serial, *Business Quarterly* (BQ). The status of BQ in the field of business management may be comparable to that of the New England Journal in the field of Medicine. BQ is edited by a retired business professor on a part time contract and employs a full time staff of two.

The original Business School journal was started in 1932, and was managed entirely by students. The earliest copies of *The UWO Medical Journal* (UWOMJ) also date from about that time. A major difference between the two publications is that the UWOMJ is still managed by students. BQ is an ancillary unit of the University, like Food Services and the Book Store, while the UWOMJ is a subaccount of the Hippocratic Council. BQ's yearly budget is about one million dollars; that of the UWOMJ is around $20,000. BQ has a subscription circulation of about 10,000 at a cost of $39 per year; the UWOMJ has a circulation of approximately 2000 and a subscription fee of $17 per year, however, most of the readers are unfortunately not subscribers. Further, BQ represents a professional business school whose reputation is among the best in North America, established, in part, on the strength of the popularity and esteem of their serial. On the other hand, UWOMJ represents a professional school whose reputation is possibly the best in Ontario.

The difference in the historical development of the two publications has been the degree of faculty involvement. From the beginning, BQ has operated with support from Faculty members in the form of an advisory council, and subsequently, a consulting editor. Eventually the Dean of the School took financial responsibility for the publication and, only five years ago, appointed the present Editor, who accepted the challenge of making BQ self-supporting. The UWO Medical Journal, meanwhile, has carried on with a new Editor every few years and consequently a new vision, a new quality ethic and a new policy, for better or for worse. We need a wider subscription base, a greater sense of pride and greater Faculty involvement, including the Dean's Office. If the experience of our cousins at the School of Business is any indication, this is one opportunity the School of Medicine can't afford to pass up.

Ross Mantel, Meds '95
Associate Editor

A NOTE TO OUR READERS

The UWO Medical Journal is currently in its 63rd year of publication. The Journal has undergone many changes over the past 62 years—some for better, some for worse. During the first 45 years or so, the Journal was strong and consistently good; during the subsequent 15 years, the Journal suffered from a decline in interest, faculty support, and consequently quality. This decline was truly unfortunate.

The University of Western Ontario Faculty of Medicine is highly respected, nationwide and beyond, for a variety of reasons. These reasons include undergraduate and graduate medical education, clinical practice, and scientific research. To those of us who are involved with the Journal, the UWO Medical Journal should be another unique aspect of the University of Western Ontario Faculty of Medicine which stands out and adequately parallels the other efforts of the Faculty. Since September 1991, the Journal has progressed toward this goal.

This is now the third consecutive year that the Journal has experienced improvements and increased interest. One need merely to look at the Journal to appreciate its attractive appearance. The body of the Journal is similarily better as well, with a feature section for each issue, and a more diverse range of topics, including Faculty News, general articles, humour, and education. The Journal has also improved in ways that aren't so obvious—an excellent publishing company, guaranteed income from advertising, and many hours from a hard-working Journal staff. (See Editorial Staff, page 3)

An ancillary component of the Editorial Staff is the Advisory Council. The Council, which is composed of both Faculty members and medical students, was designed and created just over one year ago in order to ensure the maintenance of Journal quality over time. The creation of the Council was a large step forward for the Journal.

Faculty support of the Journal has come not only through the formation of the Advisory Council, but through subscriptions as well. The income generated through advertising accounts for a large percentage of Journal expenses—but not all! So, in an attempt to generate further revenue, the Journal staff and Advisory Council decided to initiate a subscription drive targeting Faculty members. There have been many positive responders, a few negative responders, and a large number of non-responders.

Some readers have shown resentment toward the subscription drive either for having been asked to pay a fee for something that was never requested, or for merely being bothered. The Journal sincerely regrets any ill-will generated because of the subscription drive.

The Journal is asking Faculty members to show their committment to the Journal in the form of a $17 subscription because we believe that the current Journal is something the Faculty of Medicine can not only be proud of, but can benefit from as well. And we hope we can count on your support in this manner. To demonstrate our committment to the Faculty, the Journal will continue to send copies to all Faculty members. The Journal believes that, after you have read this issue, you will agree that the Journal is a very worthwhile cause to support and that you will want to be part of our growth.

Thank you for your understanding and your support. With best regards,

Jeffrey Politsky, Editor-In-Chief
Anne Silas, Assoc. Editor
Ross Mantle, Assoc. Editor

P.S. The Journal's "Friends & Patrons" list is on page 11. 'Friends' are those who have subscribed to the Journal; 'Patrons' have subcribed and made (tax deductible) charitable donations (of $20 or more) to the Journal.

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DEAN'S CORNER:
NEW FACILITIES FOR THE L.M.C.C. PART II EXAM

By Jim Silcox, M.D., Meds '67
Assistant Dean, Student & Faculty Affairs.

If you have had a chance to drop in on the new Learning Resource Centre lately you may have noticed a little office off the main lobby that is a beehive of activity. It is our new standardized patient office. Thanks to startup funding from the Medical Council of Canada, we have been able to hire Linda Ladner as the co-ordinator for this new teaching resource. She is currently involved in our first big standardized patient project which will be the Part II exam of the Medical Council.

As most trainees know, in order to get a Licensure of the Medical Council of Canada (L.M.C.C.), candidates must pass Part I of the Medical Council of Canada Qualifying Exam at the end of Medical School, complete a year of post graduate clinical training, and then successfully complete part II of the exam. The first run of the Part II was last year in Calgary and Toronto (although pilots had been run before that). This year, since more provinces require the new L.M.C.C. credential, more centres will be running the exam. We will be joining six other sites, U.B.C., U. of Calgary, U. of Ottawa, U. of Toronto, Sherbrooke, and Dalhousie, to run the exam simultaneously on the weekend of October 30 and 31.

The exam is in the objective structured clinical evaluation (O.S.C.E.) format. It will be composed of ten, ten-minute patient stations and ten couplet stations. The couplet stations will be composed of a five minute patient "encounter" followed by a five minute question response time called a "post encounter probe" or "PEP" station for short. Each of the patient stations will have a trained, standardized, patient programmed with a story or set of signs and symptoms. The candidates will have a "hint" as to the patient's problems prior to entering the room but will have to carry on from there in the allotted time. An examiner will sit in each room as well and mark the candidate on her or his performance. When the buzzer sounds, the encounter must stop and the trainee moves to the next room in the style of the old "bell ringer" exams that most of us remember from Meds and pre Meds.

Linda's job is to recruit and train the patients according to the contract laid down by the Medical Council. This means "auditioning", then assigning cases appropriately (you can't have healthy 22-year-olds playing asthmatic senior citizens), and then coaching and rehearsing and refining their role playing till it truly becomes standardized. Station number six must look exactly the same to a candidate in London, as it looked to a candidate in Vancouver or Halifax. We have had excellent cooperation from people from all walks of life for this project and many have had experience in amateur theatre so their portrayals should be very lifelike.

As you might imagine, security for such an exam is important. The exam takes four and a half hours (including a half hour intermission) and runs twice over on Saturday and twice on Sunday so a total of four cohorts of forty each can "write" here in London. The Saturday morning exam and afternoon exam are identical but the afternoon cohort will register and be closeted before the morning group are finished so there should be no communication between the groups. The Sunday exam is a different exam but equivalent in terms of difficulty. You might think that the time zone differences might prove to be a security problem, however, by the time the Dalhousie morning group get out of the exam the Vancouver afternoon group will already have gone in. The large number of examiners and standardized patients involved are all sworn to secrecy as well.

If Linda looks a bit frazzled the week of the exam bear with her. The logistics of getting our groups of candidates, physician examiners, and standardized patients parked, registered, fed, watered, deregistered and finally out of the building will rival the efforts of Cecil B. deMille when he filmed his mob scenes for the Ten Commandments. Nevertheless, as of this writing all is going well. We have a specialized site staff of about twenty, plus the resources and amenities of St. Joseph's Health Centre to thank for the smooth progress to date.

Within ten days of the Part II exam, Linda will be at it again, helping Dr. Rieder run another O.S.C.E. for the exit exam of the clerkship. She will have little time to rest on her laurels! In fact, now that she is established, it is our hope that departments will use her services more and more as time goes by. Teaching in a Problem Based Learning format or in Clinical Methods can be significantly enhanced if there is a patient for students to work with. We envision the day when course coordinators will be able to call her and "order" patients with certain programmed signs and symptoms for use in a teaching clinic for a specified time and place. This "off the shelf" approach could have applications in all Health Science faculties, and indeed in other programs like social work and education. In time her office and position can evolve into a faculty wide resource. Visionaries have even suggested that this service could extend into the community where we might help agencies like the Police or Fire Departments train personnel to deal with the public. If we sound excited and enthusiastic it is because we are! Drop in sometime when you are in the Learning Resource Centre to see how things are going. Ω

CLASS REPORTS

Med's 94

THE S.A.P. REPORT

by Anne Silas, Justin Amann, & Jeffrey Politsky

JP: Well guys, clerkship is nearly over. In fact, by the time our trusty fans read this report we'll each be off in our own elective world.

JA (beginning to sing): Look's like we made it,...

AS (cringing): Uggh. Just cuz you're tall doesn't give you the right to sing.

JA: Alright then, ye of one foot below, let us peruse our minds for remnants of clerkship experiences gone by.

AS: Failing that, we'll just make it up! Jeff, you're up—what's your personal best?

JP: Well, there's actually two. But I'll tell the second one as a nice segue into Debbie P's most embarassing moment.

JA: So then, tell us.

JP: 'Twas a dreary, solemn night. The wind howled at the moon (earlier in the day the sun also howled at the moon). Sharp cracks of rain were whipped against the hospital windows with a tremendous thrust.

AS: Good Grief. What a shmooze.

JP (ignoring A.S.—he's good at that now): The chief surgical resident handed me the pager—my very first time. Boy, I thought (my thoughts were shallow)! I'm not just a clerk anymore, now I'm a clerk with a pager! Not soon after, I received my first call:

> 'Mr. H. has a fever of 38.7. He's 6 hours post-op,' the nurse said. 'Hmmm,' I answered (it was all I could think of). 'I just thought I'd let you know,' she stated. 'Of course, thank you,' I replied quickly, and hung up.

—FEVER, FEVER—OMEGOD—FEVER. What do I do? Look up the causes—too many—holy s___—now what? I know, I'll get a doctor, a real one, someone with knowledge—grey hair, stethoscope, and an unstained lab coat. Where doctor? Where doctor? Hmmm, the O.R., that's it, after all, the poor sod's post-op. Look, there's Dr. Wood, he likes me (??).

> 'Dr. Wood, Dr. Wood,' I cried. 'Oh hi Jeff, how are you?' 'Dr. Wood? I need a Dr.' 'Well, what's wrong Jeff?' he said soothingly. 'I just got my first page—a patient has a fever—38.7!!' I exclaimed. 'Oh dear,' he said with a grin, 'what do you think caused it?' he asked.

THINK? THINK! NOW?! Can't think, brain gone, Ug, Ug.

> 'I'm not sure Dr. Wood, but he just had an operation,' I answered. 'Hmmm. Well Jeff, what does the patient look like, is he in pain?'

PATIENT? LOOK LIKE? PAIN? Ohhhh! The Patient! I should examine the patient! You stooopid idiot! You forgot to see the patient!

> 'The patient was vague, sir, but I'll go back and get the straight goods,' I managed to squeak out. 'Good thinking Jeff, and don't forget to rule out the causes of post-op fever. If you're still unsure, consider talking to the surgeon (why bother me, clerk!), he said reassuringly.

Post-op fever! So that's it.

I then proceeded back up to 4 NW after reading some text, examined the patient, and informed the nurse that this patient's temperature would likely dissipate over time and respond to some tylenol. About two hours later, I got another call from the same floor about the same patient:

> 'Mr. H. is in pain, his wound has broken open, what should we do?' the nurse asked.

OPEN?! He's dehisced?! OMEGOD—Doctor, Get a Doctor. I know, Dr. Wood...

JA: What a horrible experience! Is Dr. Wood okay?

JP: Very funny. How 'bout you Anne?

AS: Moi? Well, one of my worst experiences came on a quiet day in the Paeds emerg. I was working with Jeff P. and Dr. Reider—they were both looking for someone to bug, I mean something to do. I was filing my nails when, suddenly, I got a phone call. It was a guy named Dan, a lonely respiratory therapist working at the south street campus. He said he remembered me from my surgery rotation.

> 'Hi! It's Dan! 'Member me?' he asked. 'No!' I replied. 'I'm a respiratory therapist; I'm at south street. Are you busy?' 'Yep!' I answered, not wanting to prolong this. 'Oh! Well, I thought maybe we might get together; I could come over there if you want—we could breathe into the same bag.' he sounded pathetic. 'Gee, Dan, I'm awfully busy right now (yeah, right!!); this isn't a good time for me.' I sounded off. 'Okay, there's always tomorrow—is Jackie there?'

I then proceeded to recount the conversation to Jeff. Jeff then announced to Dr. Reider that Dan, the respiratory man, had just asked me, Anne, out for breakfast, to share two scoops of raisins in a package of Kellogg's Raisin Bran. That's all I heard for the rest of the afternoon—Dan and Anne and two scoops of raisins in a package of Kellogg's Raisin Bran.

JP (smiling & blocking his privates): Sorry, we were bored. But tell me, how did the date end?

AS: Swine! Okay, Justin, you're turn.

JA: Actually, rather than dispel rumours of my upright and steadfast performance during clerkship, I prefer to live vicariously and tell about other peoples' blunders and mishaps.

JP: Fine with us Justin! Why don't you regail us with the yarn about Debbie and Dr. Maxwell's crotch? I think I've told it to you in sufficient detail.

JA: Indeed! This will be a pleasure. As the story goes, it was a Friday before Chistmas, late in the afternoon. Dr. Maxwell, decked in surgical greens, was lecturing to a

group of surgery clerks about dissecting aneurysms. I believe, Jeff, that you were one of those clerks.

JP: Oui! C'est vrai.

JA: As the lecture progressed, Debbie's neck began to feel sore. We know this to be true because her head was reposed downward, at a rather peculiar angle, obviously to gain relief from the pain she was feeling (heaven forbid that it may be another, less virtuous, reason). Little did Deb know (???), though, that her positioning was distracting the grand puba. After 5 minutes, or so, Dr. Maxwell finally spoke up: '(Looking down at his unit) Excuse me, Debbie, but is there something wrong with my crotch, because you can't seem to take your eyes off of it!' Poor Deb, she was beet red—laughter was hard—absolute hysteria for at least 10 minutes. Anyway, just thought we'd record this for Deb's sake. Nobody really knows why she was staring at him that way.

JP: Sounds suspiscious.

AS: Even more suspiscious is the clerk who sold his soul by paying to be off call. 'Nough said.

JA: We can't forget about Ken and Harry. On surgery, Ken's resident accidently set a patient on fire, which Ken promptly put out. Then, clerk Ken got chastized for contaminating the sterile field. And good ol' Harry. He'll be a researcher I tell you.

AS: Whadya mean?

JA: Harry wanted to know if naloxone really is an opiate antagonist. So, he found a patient who was particularly morphine-sensitive for his study. He then gave him just the right dosage of morphine! He followed this with some Narcan (that's thinking on your feet!) and successfully reversed the morphine effect. Now, he's known in medical circles as 'the narc.'

AS: Please, let us not forget the story of the clerk and the wrong orifice. One day on an emerg rotation, a green clerk was sent in to a female patients' room, a.k.a. 'young Dr. _____,' as he was introduced by the resident. 'Dr. _____ is going to do a rectal exam in order to feel your mass; go ahead Dr.' After a couple of minutes, our young clerk/Dr. looked up and said to the resident, 'I'm sorry, I can't seem to palpate the mass.' The patient quickly intervened at this point, 'Perhaps that's because you're not in my rectum!!' The resident then left the room, since he couldn't control his laughter in public.

JP: Poor chap. Oh well, that's all we have to say this time 'round. Look out for the final S.A.P. Report ever, in the next issue. For those of you who are wondering, yes, the JJ Report is no more; the new model (the S.A.P. Report) is apparently 50% more invasive. Ω

Meds '95

by Jamie McNabb

What to say, what to say, what to say? I guess we could welcome one another back from summer vacation, but by the time this has gone to press, that little formality will have taken care of itself ad nauseum. So, let's just forget that one, shall we? I think it would be better if I just forged ahead and relayed all the juicy little tid-bits that have been cooked up over the first couple of months of 3rd year.

Well, nothing has happened. Zip. Zero. Nada. Alright, there were a couple of pubs, Ocktoberfest, maybe a few private get togethers of 6 or 8 people eating spinach dip and exchanging gossip, but there didn't seem to be any one big blow-out where everyone got together and whooped it up as a class. Maybe that's what this space in the *Journal* should address this time around.

The more I think about this, the more I've seen it coming. It is not a phenomenon that has reared its ugly head just for our class alone. We're not, as a group , such bad folks that we should be singled out for such a fate. I'm sure it happens to every class at some point along the line, and I guess now it's our turn.

We're not the Class of '95 anymore. I think it's more appropriate that we be called "the Multiple Sub-Classes of '95." We've all found those around us with whom we feel most comfortable. These are the ones we call when we want to go out, or hang out with when we want company. I guess it's only natural. But inherent in this segregatory process is the fact that not only do we choose who we want to be with, but we also identify those we want to be without.

Remember the first day of Medicine when we were all milling about outside AuditoriumA, tempering our own excitement with the awkward nature of being thrown together with a bunch of near total strangers? I guess this whole process started then; how, I'm not so sure. Maybe it was the way we looked ("Will you look at the nose on that guy?") or how we dressed ("Can you believe it's after Labour Day and she's still wearing white?"), but no matter, we were all doing it. We liked certain things about some, and disliked things about others, allowing only a few

exchanges between the "in" and the "out" piles.

Don't get me wrong. I don't think that we should start looking now for a ninety-six bedroom bungalow with a lovely backyard on a major bus route so we can all live as one big happy family, that's unrealistic. After all, most leases don't come up until April or May. I also don't think we should get together once a month at a pre-arranged time and place for a group hug. But maybe we could remember once in a while that, like it or not, we are all linked by a common bond - we're the ones who will graduate as physicians in 1995, come hell or high water. All of us face similar obstacles, especially in this, our clerkship year, and we all have to get by them. On that basis alone we have more in common than we might at first have thought.

So when you're going about your business this year, and you're just finishing a day where you've felt like a complete fool every time you offered an answer, and you pass by one of your classmates on your way to Kavorkian's office, stop and chat...briefly. Maybe we'll find that the "Out" pile is a little smaller than we once thought. Ω

Meds '96

by Jay Nathanson

Here We Go Again

Welcome back. I hope everyone had a fabulous summer and is refreshed, recharged and ready to learn. It sure is nice not to be known as the "first years" anymore. Speaking of first year, ours ended with a blast. As the rest of U.W.O. was leaving for home, Meds '96 (having a couple more months to go) brought in the summer with a "hot-tub" party at Kirk's. With that out of our system, we bared down for exams. Finally, the interminable Phase I ended, and we bid adieu at the bar-b-que and piñata party hosted by Drs. Anderson and Garcia. The revelry began again with the first week of September, as sleepy-eyed members of Meds '97 (and a few dedicated Meds '96ers) found their way to the UH patio for what was to be the mother of all orientation weeks. Congratulations to Tara and Marcie, who certainly outdid themselves in running such a great orientation that all of us wished that we were in first year again (Well, maybe not. But they were pretty darn close). I don't know, but Fanshawe will never be the same now that we actually all know each other — not that it stopped us from showing Meds '97 how to party.

Anyway, good luck to all in the new year, and a special welcome to Meds '97. Remember, if we could do it, so can you.

P.S. Congratulations to Lisa Klassen (nee Rupke) on her marriage and to Mike Horsey, Joe Kim, and Steve Gallant on their engagements this summer. Ω

Meds '97

by Angelo Mikrogianakis, Heather McMulkin, and Japheth Noah

Accept them and they will come.... Accept them and they will come." The ghostly voice haunted the Admissions Committee continuously. What could it mean? Why could only they hear it? The entire group had become confused and frightened.

The voices became louder and more persistent as the hot days of summer began. On July 9th the voices reached a deafening crescendo. Then, suddenly, they disappeared as quickly and mysteriously as they had begun. There was no explanation, everyone was just happy it had ended.

Beginning on July 11th, the joy and celebration spread through certain homes across the country. Plans were made, suitcases packed, transportation arranged and accommodations reserved. In early September the migration began. Ninety-six people were on their way to London and U.W.O.. They did not know what awaited them there or what the future would bring.

It was not until the morning hours of September 8th that both their and the Admissions Committee's questions were answered. They had all come in search of a dream!... to form the "Class of Dreams", U.W.O. Meds '97.

The theme of this year's orientation was particularly inviting, "Go hard... or go home." The Dean's BBQ was a relaxing way to spend our first evening together. Some of the most common phrases heard were: "You're from New Brunswick too!?", "Which one is Angelo?", "Why did they give us RED hats?", and "I'm so glad that I don't have to cook tonight". An interesting event some of us attended was the Western vs Guelph football game. We had to wear our Meds '97 T-shirts and hats to get in. Our suggestion to next year's orientation committee is not to give out red and white hats to new students when Western is playing Guelph because those are Guelph University football colours! Yes, we were cool.

Apparently our class consists of 38 females, 56 males and two cross dressers! At the Fanshawe Park picnic we had a large turnout but were unable to get enough girls to participate in the traditional "boat race". Luckily, Mike and Angelo/lina quickly volunteered to take the girls' places and willingly donned bras, makeup and creative new hair styles. Meds '97 maintained such a high party atmosphere throughout September that the entire class lost their body defense mechanisms and got the flu! Since we have classmates from Toronto, Ottawa, Montreal, Fredericton, Halifax, London, rural Alberta and Vancouver, the origin of this flu is an epidemiologist's nightmare!

During preceptor day some of us were initiated in various fields of medicine and a few of us got to appreciate our own ignorance in surgery.

In essence, the orientation was memorable, the Faculty was great and most importantly, Meds '96 deserves to be commended for their excellent work. Thanks also to the upper year classes, whose orientation expertise was probably transduced from Meds '94 through '95 to Meds '96 via neuromuscular or gap junctions. Ω

HIPPOCRATIC COUNCIL

WHAT'S BEEN HAPPENING IN ONTARIO, THE REST OF CANADA AND BEYOND...

by Ambrose Au, Meds '95, V.P. External.

This past year has seen much activity within the health care forum resulting from changes in government policies and agendas.

Social Contract

By now, most people are familiar with the Ontario government's social contract talks which were directed at deficit reduction. When the dust settled in August, the OMA and the provincial government signed and ratified an interim agreement that will last until early 1996. Based on this agreement, total OHIP expenditures will be reduced over a three-year term. Expenditures in excess of the limit will be the responsibility of the profession. The government has already taken steps to reduce overall expenditures (tightening eligibility criteria for health insurance). The OMA has also recently advised physicians to reduce their individual billings by 5% for the current fiscal year. This is in an attempt to prevent the need for "clawbacks." In addition, OHIP will be holding back 4.8% of billings which will be returned to those physicians who at the end of their fiscal year, are successful at reducing billings.

In an attempt to improve physician resource management, physician supply will be stabilized over the next three years. During this period, out-of-province physicians without formal Ontario medical training will not be eligible to bill OHIP for services. In addition, International Medical Graduates wishing to be licensed in Ontario will require certification (by the CFPC or RCPSC) as well as at least one year of Ontario postgraduate training. Certification of all new Ontario graduates will continue to be the prerequisite to licensure. The government has promised to develop further plans to promote voluntary retirement and to enhance physician distribution to underserviced areas. Many other initiatives are being developed to improve physician resource management.

In addition, a number of management changes are being initiated to address issues such as health-card fraud, public education, delisting, and third-party services.[1]

Other Ontario Business

The Clinical Clerkship stipend, once a part of the Ministry of Health's Clinical Education Budget, has been formally eliminated. Only those students who are currently completing their clinical clerkship will be entitled to a smaller percentage of the original stipend.

The Council of Ontario Universities released a discussion paper in August. This paper proposed increases of 30% to tuition by 1995-96 in most undergraduate programs. As well, second-entry professional programs, such as medicine and law are to have tuition realigned to double the rate for undergraduate arts and science students. The rationale for the latter include proportionally smaller tuition fee contributions to total costs of programs such as medicine and dentistry, as well as the potential earnings of graduates from such programs.

U.S. Training Visas

Students who are interested in completing their residency training south of the border should know that the doors are closing rapidly. In order to receive a J1-VISA required for training, students require sponsorship letters from the government of Canada. Such a letter will be granted to medical graduates only for the following reasons: if the province in which the candidate intends to seek licensure can show that the training is consistent with the province's existing physician resource plan; if the candidate has obtained pre-arranged employment or return-in-service commitment in Canada; or if the candidate is licensed and undertaking further clinical training in his field of practice. Under Ontario's current physician resource management plan, graduates are unable to seek training in the U.S.

The alternative H-1B-VISA for postgraduate training requires all candidates to have passed all three steps of the USMLE. This visa is currently under review in the U.S. Sources indicate that this visa will in all likelihood not be offered in the near-future.

Postgraduate Training

Following last year's CIMS match surprise in which 96 Canadian graduates were left unmatched (double that of the previous year), postgraduate deans and program directors were left scrambling to avoid repeating this disastrous outcome once-more. At this point, the National Coordinating Committee on Postgraduate Medical Training is maintaining its recommendation that all Canadian medical graduates be guaranteed postgraduate training. Unfortunately, some Provincial Deputy Ministers of Health have indicated that they may not be able to fund sufficient entry level positions to cover the size of the graduating class. Plans to restrict access of International Medical Graduates to postgraduate training have been discussed as have plans to ensure that students funded through the Department of National Defense do

not take up spaces funded by the Ministry of Health. The results of these initiatives is yet to be seen.

On a more positive note, CIMS has agreed to set up a PGY1/PGY2 registry in which residents wishing to transfer to other training programs may enter a central registry which will help them trade programs with other residents. The process will remain confidential until a match is made at which time the program directors will be notified and given the choice of accepting or declining such an exchange.

The provinces are currently investigating the use of training cards as a mechanism of funding postgraduate trainees. Traditionally, the Ministries of Health have allocated funding directly to postgraduate training positions. As a result, students could only apply to positions which received government funding. Under the proposed changes, the funding would be directed towards the postgraduate trainee himself/-herself. Each graduate would then receive a training card which would guarantee the holder full funding for training for the duration of their program. This would reduce the number of funded but vacant positions (e.g. anatomical pathology) and make tracking of expenditures easier for the Ministries of Health. Other issues concerning training cards are currently being evaluated by the provinces.

CFMS Annual Meeting

Thirty-six delegates met on October 1-3 in St. John's, Newfoundland to participate in the 13th Annual General Meeting of the Canadian Federation of Medical Students (CFMS). The CFMS represents over 5500 Canadian Medical Students attending all 13 anglophone medical schools across the country. Reports were presented from all the participating schools as well as from the four regional directors. Discussions centered around postgraduate prelicensure training (acceleration of career decision making, access, portability, and MCCQE Pt II), postgraduate training in the U.S., and rural medicine among other issues. The CFMS continues to participate in many national forums which direct policy decision.

References

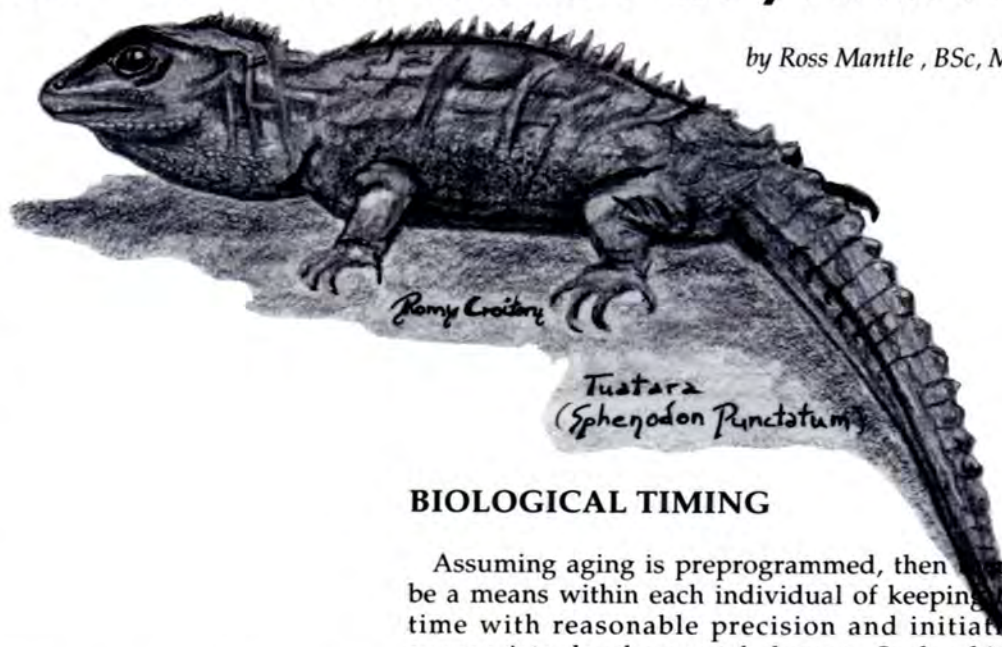
1. *Synopsis of the OMA/Gov't 1993 Interim Economic Agreement. Ontario Med. Rev. 60 (8):15-20 (1993).*

Ω

This year, UWO sent three delegates to the CFMS-AGM: Lesley Horton - Meds '94 (Ontario Director), Ambrose Au - Meds '95 (Sr. Rep), and Elin Ringstrom - Meds '96 (Jr. Rep). We will continue to represent UWO medical students to the Canadian and Ontario Federations by means of regular meetings, information and feedback sessions, and active lobbying. Please do not hesitate to contact any of us with your concerns or interests.

In Search of the Clock: Investigating the Relations of Senescence and Circadian Rhythmicity

by Ross Mantle , BSc, Meds '95.



ABSTRACT

Recent advances on the decay of circadian rhythmicity as part of the mechanism of mammalian senescence are explored. Appropriate historical and scientific background information is provided along with concepts of experimenation and intervention.

INTRODUCTION

Humanity is a tool-making species, conditioned by the constant presence of machinery to accept that the eventual wear and decay of any mechanism is inevitable. In keeping with this, the aging of the body is compared to the wearing out of old machines and assumed to represent a similar process. In fact, the resemblance is only superficial. Aging in mammals is a pre-programmed stage of development brought about as purposefully as puberty and similarly determined by evolutionary forces. Two basic pieces of evidence support these ideas and run counter to aging hypotheses which postulate an inevitable accumulation of damage, genetic errors, or toxins: First, every species has a characteristic lifespan. Within phylum Chordata (the vertebrates) at least, lifespan is more precisely regulated in higher forms such as mammals, than in lower ones, such as fish. Second, the rectangularization of human survival curves with improved social conditions and medical care indicates that, although the average lifespan has increased over the past few centuries, the maximum spans achieved have not. In humans, death occurs no later than one hundred years or so after birth.[1]

ABOUT THE AUTHOR:

Ross Mantle is a third year medical student at the University of Western Ontario. He received a BSc degree from the Laurentian university. This article is a condensed version of a Problem-based learning (PBL) honours project. The Journal encourages students to submit condensed versions of such projects for publication.

BIOLOGICAL TIMING

Assuming aging is preprogrammed, then there must be a means within each individual of keeping track of time with reasonable precision and initiating the appropriate developmental changes. Such a biological "clock" would require, by analogy to mechanical clocks, an oscillator with a fixed frequency (the "pendulum"), a means of adding up the oscillations to mark off larger blocks of time, and a way of communicating or acting on this information (the "hands").

Circadian rhythms are daily cycles entrained to the rotation of the earth by certain cues, called zeitgebers (time givers) such as light, temperature and the tides. For most species, the most potent zeitgeber is light. In the absence of external stimuli, true circadian rhythms continue, but with a period that is usually slightly faster or slower than 24 hours. An oscillating mechanism consisting of a series of enzymatic protein conversions forming a cyclic cascade, has been proposed as a general model. Although little solid experimental evidence exists to support this idea, the pendulum of our internal clocks may have evolved from the synthetic response of the organism's enzymatic machinery to the daily pattern of stresses imposed on it by the environment. The accuracy of the period of a circadian rhythm running in the absence of environmental cues can be better than ±0.01 h/cycle in single celled yeasts.[2]

The means by which a biological clock might mark off the passage of days, months and years is the least understood component of biological timing. In order to explain four day estrous cycles, menstrual cycles and other timed occurences involving intervals which are much longer than one day, the "resonance hypothesis"

postulates a beat phenomenon between two oscillators operating at slightly different frequencies. Beats in the levels of neurohormones may trigger developmental changes including senescence.[3]

THE MAMMALIAN HYPOTHALAMIC-PINEAL AXIS

THE PINEAL

The pineal gland was named for its pine cone shape and resides in the brain. Phylogenetically, the pineal organ is known to have been a third, median eye in the foreheads of the dinosaurs and many primitive present day vertebrates. The closest living relative of the dinosaurs, the tuatara of New Zealand (*Sphenodon punctatum*), is a large lizard which still exhibits a well-developed third eye in the middle of its forehead. The third eye may have a lens and retina, although the eye never approaches the image-forming capability of the lateral eyes.[4] The pineal organ, or epiphysis, is found in the brains of among the most primitive of vertebrates and the most advanced (with the possible exception of one mammal, the nine-banded armadillo).[5] Over the course of evolution the pineal gland has been highly conserved. Pineal eye information keeps organisms in synch with their environments, communicating not only whether it is night or day, but also the season, most likely based on whether the days are lengthening or shortening. Such information is necessary for migration, seasonal changes in plumage or fur colour, food storage and hibernation behaviours, and breeding.

THE SUPRACHIASMATIC NUCLEI (SCN)

This portion of the brain is now considered the master circadian oscillator in birds and mammals. The SCN is an oscillator which can function independently, but which is also entrained to the ambient photoperiod through its connection with the optic chiasm. Once the SCN, entrained to external lighting, reaches the "night" portion of its cycle, nerve impulses are sent to the pineal, which responds with an increased activity in the rate limiting synthetic enzyme for melatonin, N-acetyltransferase. Melatonin is then secreted, feeding back to the SCN in a classic loop arrangement.[6,7]

MELATONIN AND PINEAL SECRETIONS

Melatonin is synthesized almost exclusively in the pineal.[8] In primitive vertebrates, melatonin causes clustering of melanin pigment within melanocytes leading to an overall depigmentation of the skin.

The first inkling of a broader range of function for the pineal came when Otto Heubner observed that tumours which destroyed the pineal in young children resulted in precocious puberty. High levels of melatonin have been found to suppress gonadal development, such that rats kept in continuous light (so that nighttime pineal secretion of melatonin is suppressed) have increased gonadal development, and nighttime melatonin levels drop by 75% over the course of puberty.[9] Melatonin is secreted at night in both nocturnal and diurnal animals.

The pineal is associated with psychiatric disease in humans, particularly affective, schizo-affective and schizophrenic disorders. Evidence of disturbances in circadian rhythms in these patients has led to the speculation that the cause of many of these problems is desynchronization, improper phase relationships or beat phenomena (especially in bipolar affective disorder) in internal timing mechanisms.[5] Perhaps the most dramatic example of the psychiatric effects of pineal function involves the successful treatment of seasonal affective disorder with light.[10]

THE ANTI-AGING EFFECT OF MELATONIN

A group of scientists in Switzerland recently made a discovery which may have very profound implications for the future practice of medicine. In the course of a three year experiment in which mice were given nightly doses of melatonin starting at 1.6 years of age, the melatonin group lived 20% longer on average than controls.[11]

Only two other experimental manipulations are known to significantly increase lifespan in mammals: subsistence level caloric restriction and hypophysectomy.[12] The former effect was originally observed in 1935 by McCay and colleagues and has since become a cornerstone of aging research with a large number of new discoveries being made each year.[13] Food restriction can retard aging to the extent

that lifespan is increased up to 30%. Hypophysectomy has been shown to have similar, though smaller (~11%) life-prolonging effects with or without efforts to replace pituitary hormones. Hypophysectomy may also be combined with food restriction.[14,15] For a review of the effects of food restriction and the manipulation of endocrine glands on aging, see Everitt and Meites, 1989.

THE MELATONIN EXPERIMENT

A three year experiment was conducted in which ten black male mice were given drinking water containing 0.01 mg/ml melatonin. Both the ten mice in the experimental group and ten controls were allowed access to drinking water only at night, from 6 pm to 8:30 am. The mice were kept in cages with burrows in which the mice could sleep during the day. A constant 12:12h light-dark cycle was maintained at a temperature of 23°C. The average lifespan was 2.06±0.22 years (752±81 d) in the controls, and 2.62±0.22 years (931±80 d) in the melatonin group. This represents an increase in lifespan of about 20%, significant to $p<0.01$.

At least two methodological criticisms of this work can be raised. One involves the use of syngeneic mice (strain C57BL/6J). As is well known, highly inbred strains of lab mice may have precisely determined lifespans due to the consistent development of a fatal lesion such as a brain tumour at a certain age. The administration of a drug which is effective against that specific ailment may prolong life without retarding the actual aging process. The Swiss experimenters, however, believe that melatonin acts on aging itself chiefly because of the youthful appearance, activity patterns and body weight of the mice on melatonin. Another possible source of error in interpretation in the melatonin experiment is the constant 12:12 h light-dark cycle. Mice are seasonal breeders with a four day estrous cycle. Since all the subjects were male, estrous cycling would not be expected to play a role. However, the lack of seasonality may have had an effect on the outcome of the experiment.

These results have since been replicated with other syngeneic strains and using females. Starting melatonin at one year rather than 1.6 years actually shortened survival in C3H/He female mice by inducing ovarian cancer, although longevity enhancement was retained when the melatonin was started at a later age.[16] Similar trials involving both males and females in natural (seasonal) lighting would be interesting.

POSSIBLE MECHANISMS FOR THE ANTI-AGING EFFECT OF MELATONIN

Armstrong and Redman theorize that melatonin acts as a nightly synchronization signal which entrains all of the daily rhythms in the body so that they may act in concert. A decrease in the amplitude of the melatonin signal with age might therefore result in progressive desynchronization of the body's rhythms and consequent loss of function in all systems, leading eventually to death.[17] According to their interpretation of the melatonin experiments, exogenous, nightly melatonin strengthened the natural nightly level so that internal synchronization could be maintained for a longer time. This "progressive desynchronization" theory of aging is not new, and was probably first elucidated by Aschoff in the nineteen sixties in the US.[18] Several current papers document the decrease in the nightly melatonin pulse in humans.[19-21] Nightly melatonin peaks decrease in a fashion that is roughly exponential with increasing age.[22]

EFFECTS OF PINEALECTOMY

Pinealectomy has been shown to produce a syndrome similar to that seen in aging, including a rise in cholesterol, triglycerides and circulating phospholipids (Pierpaoli et al, 1991), hypertension, loss of electrolyte balance, diabetes-like symptoms, dissociation of rapid eye movement sleep from slow-wave sleep, elevation in alkaline phosphatase, increased formation of abdominal fibrous tissue (adhesions), increased skin pigmentation, and reduced formation of prostaglandin E1 and thromboxane A. Many of these symptoms can be countered by administration of exogenous melatonin at the appropriate time (early subjective evening).[17]

RANDOMIZED CLINICAL TRIAL OF MELATONIN IN HUMANS

The very low toxicity of melatonin[23] and the fact that it has been used to good effect in clinical trials on sleep, psychiatric disorders and jet lag[10,24] together with the evidence concerning its effect on the longevity of mice suggest that the time may be appropriate for clinical trials on humans. A medium scale randomized clinical trial involving a modest dose of melatonin at night only (some authors suggest 2.5 mg/d)[17] and enlisting subjects in later life, perhaps starting at age 65, would provide invaluable opportunities to study the effect of the substance on sleep patterns, depression, infection, hypertension, blood cholesterol, tumorigenesis and, over an extended period, longevity.

I would like to thank Drs. Flummerfelt and Walker for their practical advice.

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AN INTERVIEW WITH DR. LeRICHE

by Susan Huh, Meds '97

INTRODUCTION

Dr. Nicole LeRiche began her 16-year association with the UWO Faculty of Medicine in 1977 as an intern. After obtaining her FRCPC in Internal Medicine, she engaged in clinical studies in rheumatology at the National Institute of Health (NIH) in Maryland from 1982-84. Since her return to London in 1985, she has served on numerous committees, published several papers, and taught both undergraduates and graduates. She and her husband, Dr. John Howard, have also found the time to raise three children. Dr. LeRiche was appointed as "Deputy Dean" in the Spring of 1993; this title has since been changed to Associate Dean of Academic and External Affairs.

RHEUMATOLOGY

Why did you choose to subspecialize in rheumatology?

"I like internal medicine, and I think rheumatology really spans a lot of internal medicine as an intellectual discipline... There's a need for rheumatologists. There are so many people who could benefit from seeing a rheumatologist there's usually an oversupply of patients.

Knowing that I wanted to be able to control my hours to a greater extent than I would be able to if I were doing general internal medicine was a prime consideration, because at that time I knew that my husband and I would want to have children and I knew that my husband was also doing internal medicine. That was one way we could negotiate that difficulty of having enough time for ourselves, our family and so on. It was a combination of things that helped me make the decision."

BEING AN ASSOCIATE DEAN

How did you become an Associate Dean?

"You really have to ask Dr. McMurtry as to how I came here- Dr. McMurtry is the one who asked me whether I would do what I am doing. I think some of it occurred as a result of the fact that I was invited to be part of the Strategic Planning Exercise which went on last year. Last year, because of the fact that Dr. McMurtry had recently arrived on site, he wanted to a have a good idea about a number of issues within the faculty.

Early in January, when he was making selections for Assistant and Associate Deans, he asked me if I would be interested in the post of "Deputy Dean". My first reaction was one of amazement, but the more I thought about it the more interesting it sounded. Certainly, it was nothing I necessarily would have applied for myself.

What is the role of an associate dean?

"My role as I see it is to do a number of different things. I have responsibility for so-called clinical affairs, which is looking after the Faculty Practice Plan; this plan involves how faculty are paid. In addition, I may stand in for the Dean if he's absent. I'm on a number of task forces which have been struck within the faculty as a result of the Strategic Planning Exercise. I think by being on a number of task forces, I have a fair idea of what's happening in all of them, so there will be a minimum of duplication in other task forces.

I think what Dr. McMurtry had originally intended was that the "Deputy Dean" act as a "backup" — to stand in for him as needed. The official title of Associate Dean of Academic and External Affairs merely reflects the breadth of things that he'd like me to be involved with, and that I'd like to be involved with."

What kind of an impact will your position have on faculty and students?

"The kind of impact that I'll have is more easily seen with faculty. By extrapolation, if faculty feel better about things in general then students will feel better about things in general.

I think what we're trying to do is make changes which will better reflect what people do, how they're rewarded, and how we carry on day-to-day operations within the faculty. As an example, there's a communications task force... trying to look at communications in general across the faculty. I like to think of that as not only the cut-and-dry memo-sending that goes on, but in fact how we talk to one another. Is there a sense of belonging, and cohesion, a sense of *esprit-de-corps* within the faculty itself?... I think that if we can find ways of recognizing people in meaningful ways so that they feel that they're part of the faculty, that feeling will grow...

Bear in mind the difficulty at times in how to get various parts of the faculty talking to one another on several levels: "talking" in the sense of doing research with one another, how to teach most effectively, how to do the best patient care you can, that kind of thing... I see my role perhaps as a facilitator of those processes; I have no illusion that one person can do it, but if there are a number of people whose aim it is to improve a number of those things, it's more likely to happen."

Do you still find time to practice?

"I had a very full clinical practice before I started this position, and still do. [laughter] It's a little bit of a challenge to try to fit everything in. I still feel a great responsibility to continue to see patients, but I have had to cut back a little bit, because of the fact that I'm doing a lot more with the Faculty. It's funny, I was reflecting on that a few weeks ago... I think it gives me a perspective that is really critical, that I'm still doing the

day-to-day stuff that many of my colleagues are also doing... I think it's very important not to become divorced from what our primary goals are, which I see as teaching medical students, doing research, and seeing patients. All those things are very important."

STRENGTHS OF UWO MEDICAL SCHOOL

"I think one of the things that I found really refreshing when I came here, was the fact that people seemed to be very approachable. I think and I hope that students feel that. At times I worry that there are perhaps unnecessary barriers that exist, students presume things about consultants and vice versa. But I think on the whole there' a reasonably cordial atmosphere here.

I think that the quality of teaching is good. I'm concerned, and this is being addressed in the curriculum, about overstuffing people with facts. But I think that certainly the kinds of trainees with whom I work are excellent. They're well-trained, they're knowledgeable, they're kind people, they're the kind of doctors that I would want to go to. I think on the whole, that whether it's the admissions policy or just the institutional ethos in general the people are delightful."

PROBLEM-BASED LEARNING

Why is the school moing toward a more completely problem-based learning curriculum, considering the success rate of Western's graduates?

"I think there is a recognition on the part of not only physicians practicing within the system, but the public as well, that physicians who have very good communication skills, and who are empathic would be preferred. I think this is more easily taught within the context of a small group, and examining a variety of different problems from a number of different angles."

WOMEN IN ACADEMIC MEDICINE

"Young women may be starting to select themselves out of doing science and things like that which are prerequisites for medicine ultimately, because there's sort of a societal view that this isn't really women's work. I think that's happening less and less.

There may not now be the active discrimination which existed before, but unfortunately there may well be barriers...

There are some things within the system which do make it harder for women to either become part of the system, or to succeed in the system. I think that we're trying to make changes that will make that... easier. Certainly Dr. McMurtry is, I think, very aware of that difficulty."

Why hasn't the increase in female enrollment in medical school been accompanied by an equivalent increase in all specialties of medicine?

"A lot of reasons. A lot of it is self-selection... women want flexibility, and certainly my friends doing family practice probably have greater flexibility. If they want to have children, they can take that time off to be home with their child much more easily. The more one subspecializes, the more difficult that becomes because it's more difficult to replace you in a particular situation."

THE STATE OF CANADIAN HEALTH CARE

"I think that many people didn't realize that there has beens and is a finite quantity of resources. Unfortunately what happened is that people were spending as if there weres no tomorrow...

Things seem a lot bleaker when one has been raised in an environment of incredible plenty which then becomes restricted. I think that this is the issue which we are all grappling with. The feelings of frustration are understandable because we have come to enjoy a very good standard of living on the whole...

If we as a profession recognize what our goals are, and where we want to spend money and how we want to spend our time, we can still do what we want to do... we must all be accountable for our spending... `we're all part of the system, and we all have responsibilities to try and make the best uses of the resources that we have'...

I'm concerned by the fact that things have become so provincial, because I see myself as a Canadian, I don't see myself as only an Ontarian... Everything else is becoming more global- why are we becoming more perochial? But it's an understandable reaction because everybody feels threatened."

PERSONAL GOALS

"I like to think of life as a series of adventures and that various things occur and you're lucky enough to meet interesting people... I suppose that a major goal is in trying to be the best physician that I can be, to learn as much as I can, and as well to try to convey that desire to other people... perhaps we have to be more in touch with and allow ourselves time to think about those important things which make up life. In a peculiar way, we as physicians are so intensely involved in other people's lives that we forget the big picture and don't think about how amazing life is."

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FEATURE SECTION

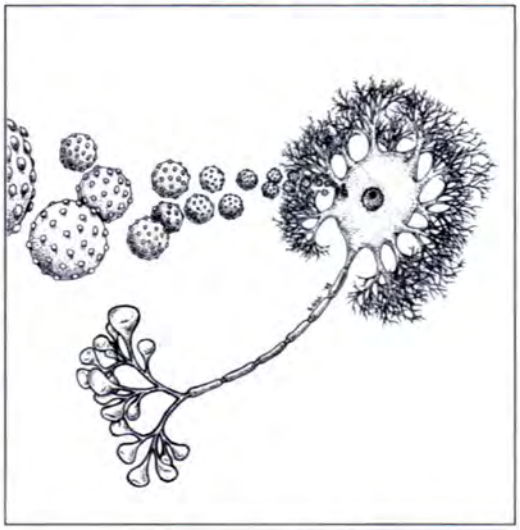
This issue's feature section is Infectious Diseases. Articles in this issue include The Neurologic Sequelae of HIV-1 Infection, Pyogenic Hepatic Abscess, Septic Arthritis, and more.

NEUROLOGIC SEQUELAE OF HUMAN IMMUNODEFICIENCY VIRUS-1 (HIV-1) INFECTION

by Jeffrey M. Politsky, MSc, Meds '94,
David M Pelz, MD, FRCP(C), Meds '75, & Thomas W. Austin, MD, FRCP(C), Meds '65

ABSTRACT

Human Immunodeficiency virus-1 infection is a commonly occurring and an incompletely understood illness which can have severe effects on the central nervous system. Theories of disease transmission relate to immune-mediated transfer, endothelial cell infection, and cell-specific susceptibility. Neuropathologic alterations include diffuse and focal brain changes, and may occur secondary to enhanced cellular immunity, increased secretion of viral proteins, and/or excitotoxic mechanisms of cell damage. Central neurologic findings include the AIDS dementia complex and acute and subacute focal brain diseases. Recognition of the neurologic signs and symptoms of human immunodeficiency-1 virus infection clinically and through the use of neuroimaging techniques is critical for effective therapy. Despite therapeutic intervention, prognosis of human immunodeficiency virus infected patients remains guarded.



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Dr David Pelz is an Associate Professor in the Deparments of Diagnostic Radiology and Nuclear Medicine and Clinical Neurological Sciences at the University of Western Ontario. He is a staff Neuroradiologist at University Hospital who received his MD at The University of Western Ontario in 1975, followed by post-graduate training in Diagnostic Radiology and Neuroradiology. He is currently the Director of Undergraduate teaching in Diagnostic Radiology and Nuclear Medicine.

Dr. T.W. Austin is an Associate Professor of medicine at the University of Western Ontario. He is acting chief of Infectious Diseases at Victoria Hospital in London, Ontario. Dr. Austin graduated from the Doctor of Medicine program at the University of Western Ontario in 1965. He received post-graduate training in Infectious Diseases from a variety of academic institutions in Canada and the U.S. Dr. Austin is currently involved in undergraduate, graduate, and continuing medical education. As well, Dr. Austin is the author of numerous publications, which include journal articles, abstracts, and book chapters.

INTRODUCTION

Systemic human immunodeficiency virus-1 (HIV-1) infection is a common yet incompletely understood illness. This illness, specifically the late phase of acquired immunodeficiency syndrome (AIDS), is complicated by direct central nervous system (CNS) infection and by neurologic disease from the onset of the initial illness. Neurologic sequelae of HIV-1 infection relate to the acquisition of opportunistic infections and the development of CNS neoplasms. Early recognition of the neurologic signs and symptoms has implications for both diagnosis and management of HIV infection and AIDS. Further, diagnosis and management can provide clues to the underlying mechanisms of HIV-1 infection. This paper provides an overview of the neurologic complications of HIV infection, including theories of transmission and neuro-pathology. As well, the clinical neurologic findings of HIV infection are outlined — recognition of these signs and symptoms has diagnositic and therapeutic significance.

TRANSMISSION

The exact mechanism of transmission of HIV-1 and HIV-1-related secondary infections into the CNS is currently unknown. Possible mechanisms of transmission are based on findings that hematogenic and/or neuroglial cells may be preferential targets for HIV-1 and HIV-1-related secondary infections.[1-5] One theory is immune-mediated transfer of viral particles.[1] For example, although microglial cells are the primary target of retroviral infection, these cells lack CD4 receptor sites (the HIV-1 cell surface receptor protein). These cells do, however, have high affinity receptors for immunogloblulin, making antibody-mediated uptake into brain tissue a possible mechanism of infection.[1] Other studies also implicate neuroglial and hematogenous cells as being involved in the transmissability of virus particles.[2,3] This involvement is based on the observation of budding of HIV-1 particles from cell membranes of multinucleated giant cells (macrophages) and monocytes predominantly, although neuroglial cells are also

involved.[2,3] These findings suggest ingestion, digestion, and replication of HIV-1 by brain macrophages.[2,3]

Another theory suggests endothelial cell infection as the primary mechanism.[4] For example, immunohistochemical localization of CD4 and HIV-1 antigens to cerebral and lymphatic venular endothelial cells supposes either natural occurrence or induction of CD4 protein in various endothelial cells, thus allowing HIV-1 to be transmitted from circulating infected leukocytes to targeted tissues.[4] This study also suggests that the high HIV-1 immunoreactivity of macrophages and multinucleated cells in post-mortem tissue may be due to immune-mediated sequestration of HIV-1 antigens from initially infected hematogenous cells.[4]

Neuroglial cells also appear to be sensitive to HIV-1-related secondary infections. For e.g., one 37 year old HIV-1-positive man with a history of pneumocystis-carinii pneumonia died of disseminated cytomegalovirus (CMV) infection and an anaplastic astrocytoma.[5] CMV-bearing astrocytic cells were found throughout the tumour, but not elsewhere. As well, CMV-bearing endothelial cells were noted in several capillaries within the tumour. Microglial nodules and multinucleated giant cells (MGCs) were also found in the tumour and also stained positive for CMV. These authors concluded that astrocytoma cells are permissive to CMV, that these cells are more susceptible to CMV infection and replication than normal tissue, and that the entry of CMV may be due to alterations in the astrocytoma blood brain barrier (BBB) and the hyperplastic endothelial cells.[5] These factors may play a role in the development of opportunistic infection in the presence of other CNS neoplasms.

NEUROPATHOLOGY

Neuropatholgic studies carried out on post-mortem brain tissue from HIV-1-positive induviduals are critical in furthering our understanding of the neurologic sequelae of HIV-1 infection and AIDS. These studies have revealed that specific areas of the brain are preferentially affected in HIV-1 infection. As well, HIV-1 and HIV-1-related secondary infections have a predilection for certain neuronal cell types. The development of HIV-1-related secondary infections represents an important aspect of neurologic disease in AIDS. Clinically, these opportunistic infections may lead to the development of AIDS dementia complex (ADC). Pathologically, these infections signal the terminal stage of AIDS. Although some explanations are forthcoming, the mechanisms underlying these various pathologic changes remain unclear.

Neuropathologic alterations occurring in AIDS are associated with the cerebral hemispheres,[6,10-12] basal ganglia[6-9] brain stem structures and spinal cord,[24] inferior olivary nuclei,[13] corticospinal tracts,[6] and the eye.[14,32-36] Primary histopathologic findings in brain tissue from AIDS patients can be divided into diffuse and focal changes. Diffuse changes include cortical atrophy, white matter pallor, vascular calcification, multinucleated cell encephalopathies, and vacuolar myelopathy.[5,8,9,14-16,18-22] Focal changes include the acquisition of various opportunistic infections, encephalitides, malignant neoplasms, and progressive multifocal leukoencephalopathy (PMLE).[9,12,13,15-17,19-22]

DIFFUSE CHANGES

Cortical atrophy is the most consistent finding in the cerebral hemispheres of AIDS patients with neurologic sequelae.[10,11,23,25] Cortical changes are characterized by significant neuronal loss in the frontal cortex[11] and other foci,[10,23] along with decreases in neuronal density,[11] perkiaryon volume fractions,[11] and widened sulci.[25] A less common finding is cerebral spongioform changes of the white matter, characterized by small rounded vacuoles.[23,25,31] A more diffuse sponginess, *status spongiosis*, characterized by looser and coarser microcystic cavitations has been observed in the gray matter.[23,25,31]

Subcortical structures are commonly involved in AIDS patients with neurologic complications. The most common histologic finding is diffuse white matter pallor with astrocytic reaction.[25] Also common is dystrophic calcification of blood vessels in the basal ganglia.[6-9] The observation of MGCs is an indicator of more severe neurologic disease. Changes in these brains are found mostly in the deep gray structures and white matter and include gliosis, perivascular and parenchymal foamy macrophages, formation of microglial nodules, MGCs, and lymphocytes.[9,15,18,25-28] Multinucleated cell encephalitis is also called HIV encephalitis because of the correlation between the presence of MGCs and opportunistic infections. (see figure 1)

The most common pathologic finding in the spinal cord of HIV-1 infected patients with clinical neurologic symptoms is vacuolar myelopathy.[12,13,25,29,30] Clinically, vacuolar myelopathy is similar to subacute combined degeneration secondary to vitamin B_{12} deficiency; pathologically, the two entities are distinct since in the former, serum B_{12} levels are normal.[30]

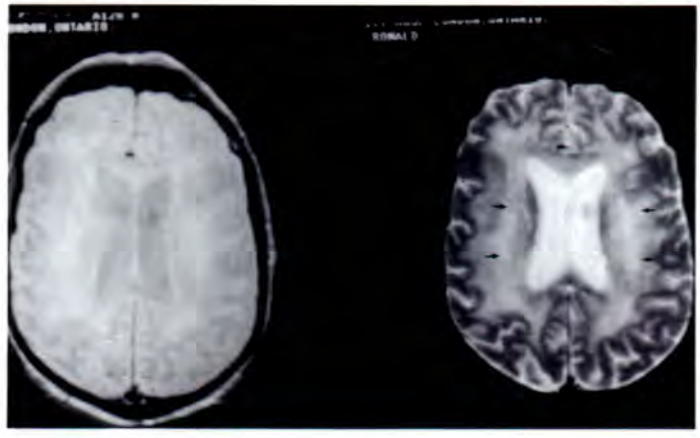

Figure 1
Axial proton density and T2 weighted images in a 40 year old male with AIDS. Diffuse deep white matter high signal in both cerebral hemispheres (arrows) was pathologically proven to represent HIV encephalitis.

Ophthalmic changes include ocular motor nerve palsies, papilledema, CMV optic neuritis, cortical blindness, conjugate gaze palsies, and altitudinal visual field defects.[14] Retinal microvascular abnormalities in HIV-1 infected patients can also occur—in fact, ocular microangiopathic syndrome is common in these patients.[32] The major retinal microvascular alterations are cotton-wool spots;[33] other changes include retinal hemorhages, ectasia of conjunctival vessels, and conjunctival blood-flow sludging.[34-36] These retinal changes can be remarkably similar to those in diabetes mellitus and systemic lupus erythematosis.[32]

FOCAL CHANGES

Major focal pathologic changes in the brains of AIDS patients include opportunistic infections and neoplasms. The most important pathologic processes are cerebral toxoplasmosis, PMLE, and primary CNS lymphoma.[9,15,16,18-20,22,25]

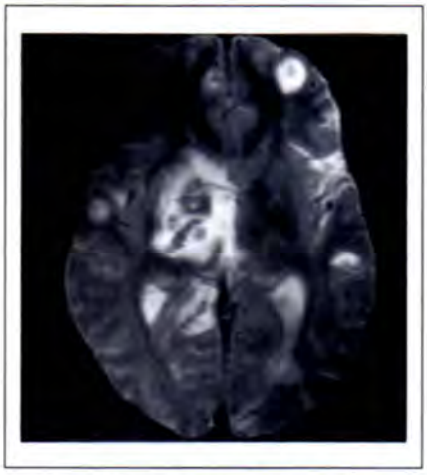

Figure 2
Axial T2 weighted MR image of the brain in a 33 year old female with AIDS. There is a large irregular high signal mass lesion in the deep right temporal lobe and there is a smaller nodular high signal mass in the left frontal lobe. These both represent manifestations of cerebral toxoplasmosis.

Cerebral toxoplasma (see figure 2) lesions are multifocal and have a predilection for the basal ganglia and the cortex.[25] Papovavirus, or PMLE, tends to be localized to the white matter and is associated with an absence of inflammatory infiltrates (see figure 3).[19] Primary CNS lymphoma may also have multiple foci and is usually identified in the white matter.[25] (see Fig 4)

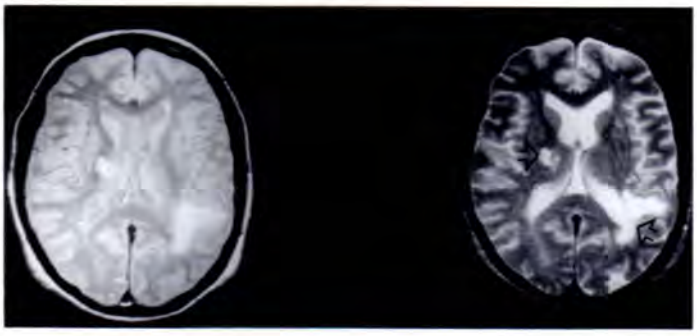

Figure 3
Axial proton density and T2 weighted MR images in a 62 year old female. Irregular high signal changes are seen in the periventricular white matter adjacent to the atrium of the (arrows) left lateral ventricle and also in the posterior limb of the right internal capsule. These were pathologically proven to represent PMLE.

Currently, there is no decisive explanation for the neuropathologic changes in AIDS. One theory suggests a hypersensitivity reaction.[4] The interaction between the CD4 antigen (Ag) and Ag-presenting cells leads to enhanced cellular immune activity. The interaction of immune related Ag's on CNS vascular endothelial cells leads to a breach of the BBB and could lead to the acquisition of opportunistic infections and HIV vasculitis.[4] Another possibility is that AIDS-associated neurologic disease is correlated with higher levels of HIV-1 Ag in tissues, which ultimately leads to increase secretion of viral proteins or viral induction of cytokines. These substances then bind to glial cells and neurons stimulating a positive feedback loop (with further secretion of viral proteins and/or cytokines).[28] Finally, an excitotoxic mechanism of damage has been proposed.[37,38] In this theory, the final common pathway of damage may involve voltage-dependent calcium channels and NMDA receptor-operated channels, in much the same way as damage occurs in stroke, seizures, and trauma.[37,38]

CLINICAL PRESENTATION

The clinical presentation of HIV-1 infection has been subdivided into four distinct phases (see table 1).[39] The development of neurologic signs and symptoms in AIDS is usually associated with phase IV illness, but distinct symptomatology such as ocular and psychiatric findings may occur at earlier stages. Nonetheless, the presentation of neurologic sequelae is an indication of advanced disease.

Clinically, neurologic findings of AIDS fall under various categories. Some of theses categories include ocular, psychogenic, myelopathic, and central findings. The bulk of this discussion concerns the central neurologic findings, which can be subdivided further into diffuse (AIDS dementia complex) and focal brain disease.

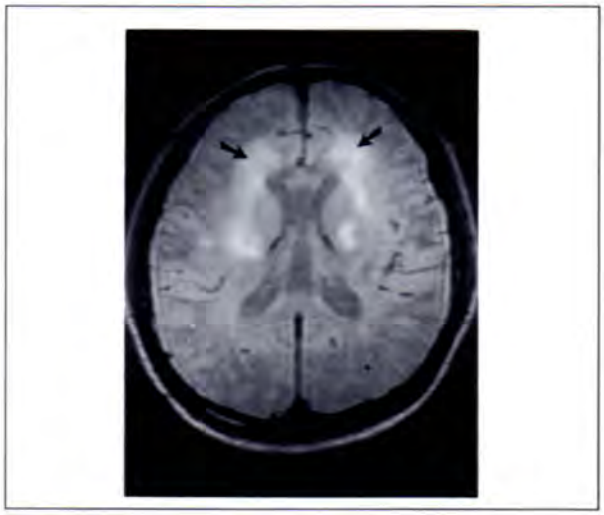

Figure 4
Axial proton density MR image in a 41 year old male with AIDS. Irregular periventricular high signal lesions (arrows) are seen bilaterally which represent primary CNS lymphoma.

TABLE 1
CLINICAL STAGING OF HIV-1 INFECTION[39]

Stage	Clinical Findings
I	Acute HIV Infection
II	Asymptomatic Carriers
III	Persistent Generalized Lymphadenopathy
IV a)	Constitutional Disease
b)	Neurological Disease
	i) HIV-related
	ii) Opportunistic Infections & Neoplasms
c)	Secondary Infectious Disease
d)	Secondary Neoplasms
e)	Other Conditions

OCULAR FINDINGS

Ocular changes and ophthalmoscopically visible changes have been observed in AIDS patients with clinical stage III and IV disease.[24,34,36] The most common occular finding appears to be limitation of central eye movement.[24] Less common, but occuring equally frequently are peripheral eye movement limitations, abnormalities of vision, and abnormal spontaneous eye movements.[24]

PSYCHOGENIC FINDINGS

Psychologic disturbances appear to be related in part to the patient's awareness of being HIV-1-positive. These changes include depression, anxiety, and adjustment reactions.[40,41] The asymptomatic stage of HIV infection is not associated with significant cognitive impairment.[41] Cognitive disturbances, which are associated with clinical neurologic symptoms and which may be revealed by neuropsychologic testing include difficulty with complex sequencing, impaired fine and rapid motor movement, and slowed verbal fluency.[19,25,42]

MYELOPATHIC FINDINGS

Transverse myelopathies are rare, but can occur secondary to spinal lymphoma and infection with herpes zoster.[25] Polyradiculopathy secondary to CMV or combined CMV and herpes simplex virus infections also occur and can be severe.[25] The most common spinal cord finding is progressive vacuolar myelopathy. These patients present with gait disturbance, ataxia, and spasticity. Bladder and bowel dysfunction also occur as myelopathy progresses.[25]

CENTRAL NEUROLOGIC FINDINGS

Diffuse Brain Disease
(AIDS Dementia Complex)

Although a certain percentage of diffuse brain disease relates to metabolic encephalopathies occurring secondary to systemic disease such as pneumonias with hypoxia and generalized sepsis, the commonest CNS complication of HIV infection is a constellation of neurologic signs and symptoms referred to as the AIDS Dementia Complex (ADC).[25]

AIDS dementia complex usually manifest itself after patients acquire AIDS-defining systemic illnesses such as opportunistic infections or neoplasms (see table 2). The complex can occur, however, in the absence of these major systemic illnesses and is thus a separate entity among diagnostic criteria of AIDS.[43,44]

Early symptoms relate to cognitive deficits, such as difficulty concentrating, impaired memory, and inability to perform complex tasks.[19,25,26,42] In earlier stages of illness, formal mental status testing may be quite normal. With increasing severity, however, results become abnormal and include apathy, poor insight, impaired recognition, recall, attention, and calculation.[19,25,26,42]

Gross and fine motor dysfunction become evident with the appearance of gait disturbances, poor balance, and eye and hand incoordination resulting in patients tripping, falling down, dropping items, and finding themselves unable to eat or write.[19,25,26,42,45] Motor dysfunction can sometimes be detected early on by recognition of abnormal or pathologic reflexes such as glabellar, snout, and grasp responses, as well as generalized hyperreflexia. Also, disruption and slowing of rapid sequential and alternating tasks involving fingers, wrists, and feet occur. Other early signs include ocular dysmotility, disruption of smooth pursuit, and slowed saccadic movements.[25]

TABLE 2
DIFFUSE BRAIN DISEASE COMPLICATING HIV INFECTION[25]

Level of Consciousness	Complicating Disease
Depressed	Metabolic Encephalopathies
	Toxoplasmosis ("encephalitic" form)
	Cytomegalovirus Encephalitis
	Herpes Simplex Encephalitis
	Acute HIV-1 Encephalitis
Preserved	AIDS Dementia Complex

End stage presentations of ADC include bowel and bladder incontinence, a complete or nearly complete vegetative state, and marked reduction of arousal.[25]

One author has suggested that the "ADC" is really seronegative neurosyphilis.[46] This notion was formulated on the basis of five AIDS patients who were all diagnosed with ADC. Despite being seronegative for neurosyphilis, the patients all showed a dramatic improvement in function and a marked reduction in impairment following either intravenous (iv) infusion of penicillin G or oral administration of doxycycline (the treatments for neurosyphilis).[46] Although neurosyphilis can't be ruled out despite seronegativity, this reasoning is questionable on a few counts. First, only two of the five patients underwent investigations beyond simple serum and cerebrospinal fluid (CSF) studies. Further, these two patients received computed tomographic (CT) scans but neither magnetic resonance imaging (MRI) or brain biopsies. The latter two procedures are currently the most sensitive diagnostic tools for the neurologic complications of HIV-1 infection. Thus, diagnostic attempts in these patients were incomplete. Second, the positive response to penicillin may have occurred because of another undiagnosed infection also sensitive to this therapy. Third, although the possibiltiy exists that the severe immunosuppression in HIV infection may render serologic tests for syphilis unreliable, substantial evidence is available to suggest that serologic tests for syphilis are indeed sufficiently reactive.[47]

Focal Brain Disease

Apart from the diffuse brain processes discussed, a variety of focal brain disorders develop in AIDS patients. These focal disease processes may be acute or subacute in onset (see table 3), thus making clinical recognition important for appropriate therapeutic intervention. Acute processes are usually due to vascular events or seizures. Some vascular events such as transient ischemic attacks or strokes may lead to permanent brain injury, but most have a benign course.[48]

TABLE 3
Focal Brain Disease Complicating HIV Infection[25]

Onset	Complicating Disease
Acute	Vascular Disorders
Subacute	Cerebral Toxoplasmosis
	Primary CNS Lymphoma
	Progressive Multifocal Leukoencephalopathy
	Tuberculous Brain Abcess (*M. tuberculosis)*
	Cryptococcoma
	Varicella-Zoster Virus Encephalitis
	Herpes Simplex Encephalitis
	Subacute CNS Syndromes

Most focal disorders are subacute in nature and evolve over days to weeks. Cerebral toxoplasmosis, primary CNS lymphoma, and PMLE (papovavirus) are three of the most important focal disorders. These disorders evolve rapidly over days, intermediately (days to weeks), and slowly over weeks, respectively.[50-52] These disorders can produce overlapping, but often distinct neurologic symptoms. For example, cerebral toxoplasmosis usually produces a focal deficit along with a generalized encephalopathy leading to confusion or clouded consciousness.[49,50] PMLE, on the other hand, produces focal deficits without any effect on consciousness until end stages of infection.[52] CNS lymphoma can produce "frontal" or global mental dysfunction when the lymphoma is associated with a significant mass effect or is located deep in the frontal or periventricular region.[51]

DIAGNOSIS

A number of investigative procedures exist which, when used in combination with clinical findings, may lead to correct diagnosis of CNS complications of AIDS. Among these investigations, serum and CSF studies are the most specific,[46,53-57] whereas neuroimaging and brain biopsy studies are the most sensitive.[8,58-63] Venipuncture and lumbar puncture, to obtain serum and CSF, respectively, are inexpensive and useful techniques to identify the presence of viral or bacterial-specific proteins, immune complexes, and altered cell counts.[46,53-57]

For patients with neurologic symptoms who either require further localization of disease or whose CSF and serum results were non-specific, neuroimaging techniques and brain biopsy are often necessary. There appears to be some discrepancy as to which procedure is the most sensitive among CT scan, MRI, and brain biopsy. For e.g., in 149 patients examined with toxoplasma abcesses, CNS lymphoma, and PMLE, MRI was found to be more sensitive than CT scan in detecting lesions, especially PMLE.[58] CT scan was unable to distinguish mass lesions due to toxoplasmosis from those due to lymphoma.[58] Other studies have also found MRI to more consistently reflect the histopathologically documented extent and distribution of CNS disease.[8,59-61] Brain biopsy has also been used to achieve definitive diagnosis. For example, in one study stereotactic brain biopsy was performed after gadolinium-enhanced MRI or contrast-enhanced CT scan.[63] After the biopsy material was examined cytologically, histologically, immunohistochemically, and by polymerase chain reaction, a definitive diagnosis was achieved in 92% of the cases.[63] In another study, definitive diagnosis was reached in 96% of cases.[64] Brain biopsy is considered to be a safe effective means of diagnosis in this patient population.[63-66]

PROGNOSIS AND TREATMENT

The effectiveness of treatment, and thus the prognosis, of AIDS patients with neurologic sequelae clearly depend on early and correct diagnosis and intervention. Even with these measures, the prognosis of HIV-1 infected and AIDS patients is bleak. The extent of neurologic involvement is also a key factor in patient outcome. For example, Mundinger et al. studied the survival of 41 AIDS patients with neurologic involvement based on neuroimaging results.[67] The mean survival of patients with initially normal imaging results was 700 ± 89 days compared with 326 ± 65 days and 202 ± 97 days for patients with cerebral atrophy and focal lesions, respectively. The mean survival for patients with both cerebral atrophy and focal lesions was only 78 ± 44 days.[67] Further, these authors found that, compared with initially normal imaging, the risk of death increased 3.6 times with cerebral atrophy, 6.4 times with focal lesions, and 19.3 times with both.[67]

Medical therapy for neurologic complication of AIDS usually involves antimicrobial agents for opportunistic infections. To be effective, these agents must cross the BBB and the blood-CSF barrier. Currently, there are only a few such agents in use. Zidovudine is an anti-retroviral thymidine analogue which has been shown to be effective in reversing ADC to a lesser stage in most seropositive HIV patients with mild end-stage ADC.[19,25,68]

In light of the possible overlap between ADC and neurosyphilis, a therapeutic trial of iv penicillin or oral doxycycline may be warranted for patients who either don't respond to zidovudine, or who may in fact have neurosyphilis.[46]

Cerebral toxoplasmosis is the most commonly occurring opportunistic infection to cause encephalitis or multifocal brain lesions in AIDS patients.[25,69,70] Although this parasitic infection is associated with high morbidity and mortality, a good response to therapy and an improvement in patient survival has been shown.[25,69,70] A therapeutic trial should be initiated in patients who show neurologic signs and symptoms and have the characteristic lesions as evidenced by neuroimaging or biopsy techniques. The most effective anti-toxoplasma treatment currently available is the combination of pyrimethamine and sulfadiazine, which causes sequential blockade of folic acid metabolism in the parasite.[25,69,70] Therapy lasts for approximately three weeks, and may require the addition of folinic acid.[69-71] Pyrimethamine-clindamycin combinations have shown some efficacy in treating cerebral toxoplasmosis and may be used in patients with a sulfa allergy.[69-71]

Like toxoplasmosis, CNS lymphoma also produces neurologic symptoms secondary to mass lesions. Unlike toxoplasmosis, however, few effective treatments are available for CNS lymphoma—steroids may be able to reduce signs and symptoms secondary to increased intracranial pressure, but little else.[58]

DISCUSSION

Over the last ten years, HIV-1 infection has been shown to be a devastating illness with far-reaching effects on mankind. HIV-1 infection affects a number of organ systems, including the brain. This paper has provided an overview of the neurologic complications of AIDS. These complications are difficult to treat and to control. Progress is continually being made in understanding and managing these sequelae, but much work still remains. As a result of previous research, various theories explaining the causation of AIDS have been postulated. Of these theories, the possibility that neuronal damage in AIDS is mediated through excitatory amino acid activation and increased inracellular calcium appears promising. The combination of NMDA receptor activation, enhanced inositol phospholipid metabolism, and toxic calcium influx leading to neuronal cell death may be involved in the pathogenesis of a variety of neurodegenerative diseases such as dementia of Alzheimer's type, olivopontocerebellar atrophy, cerebrovascular accident, and Huntington's disease;[72-75] recently, this mechanism of cell damage has been extended to include the ADC.[37,38] Developing mechanisms to arrest excitotoxic cell damage are complex since they would involve both extracellular and intracellular processes. Expanding on this notion may lead to new therapeutic strategies for the treatment of the neruologic sequelae of HIV-1 infection and AIDS.

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Ω

PYOGENIC HEPATIC ABSCESS

by Glen Hooker, Meds '94

INTRODUCTION

An hepatic abscess is a localized collection of pus in the liver. Such an abscess may be bacterial (pyogenic), parasitic, or fungal. The present discussion will be limited to the pyogenic type. Further, this paper will focus on the changes in epidemiology and etiology, and the recent advances in diagnosis and treatment.

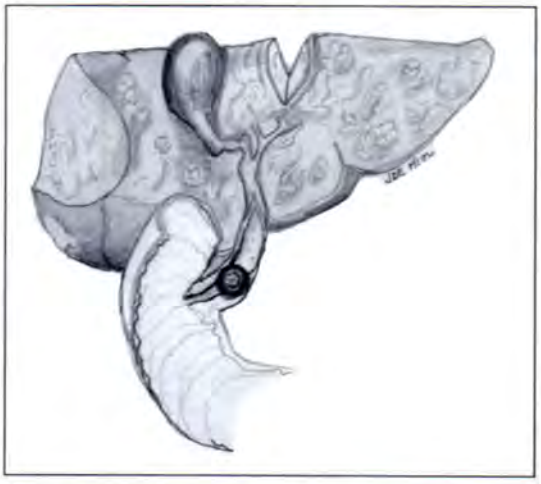

Figure 1: The liver is riddled with multiple abscesses, secondary to a stone in the common bile duct.

EPIDEMIOLGY

In the United States, pyogenic abscesses account for 80% of all liver abscesses; pyogenic abscesses occur in 8-15 people per 100,000 population.[1] The incidence is higher in countries where medical care is not readily available.[2] Despite recent advances in diagnosis and therapy, the incidence of pyogenic liver abscess has remained stable, probably due to increased survival of patients who have intra-abdominal diseases.[2] Males are affected more than females (3:2 ratio).[3] The peaks of occurrence are during the first year of life and between 60 and 80 years of age.[4] There appears to be no racial susceptibility.[5]

PATHOPHYSIOLOGY

In order for a pyogenic liver abscess to develop, at least two pathologic processes must occur. The liver must be both exposed to bacteria and vulnerable in some way to the bacteria.

Bacteria may reach the liver via the portal vein, the hepatic artery, the biliary tree, or by direct spread. Portal venous spread starts as thrombosis of mesenteric veins at the site of an inflammatory process, commonly an intra-abdominal infection such as appendicitis or diverticulitis. Septic emboli, which reach the liver via the portal vein, are subsequently formed creating foci of intense inflammation in the liver. These foci coalesce to form an abscess. Bacteria may reach the liver via the hepatic artery, as in the case of generalized sepsis secondary to conditions such as bacterial endocarditis, renal infection, or pneumonitis. In infants, bacterial seeding through the hepatic artery may occur secondary to umbilical vein catheterization.[6]

The presentation of bacteria to the liver is insufficient to cause pyogenic hepatic abscess; susceptible liver parenchyma is required as well. Examples of vulnerable liver states include obstructive biliary disease, biliary infections, and liver trauma. In obstructive biliary disease (e.g. cholelithiasis, obstructive malignancy of common bile duct or pancreas; see Fig. 1), or biliary infections (empyema of the gallbladder, cholangitis), bacteria multiply in the bile ducts, and ascend into the liver via the bile ducts. In addition, portal and lymphatic invasion by these bacteria produce pus, which enters the liver directly. Trauma is associated with increased risk of developing a liver abscess via bile leakage, decreased perfusion, hepatic necrosis, direct introduction of bacteria, and hematoma formation. About one-quarter of all liver abscesses are cryptogenic in origin, with no underlying source identified, even after visual and manual exploration of the abdomen.[7]

In adults, conditions associated with the formation of pyogenic hepatic abscesses include malignancy being treated with chemotherapy, colon cancer, diabetes mellitus, and cardiopulmonary disease. In children, associated conditions include malignancy, AIDS, polycystic disease, cholecystitis, necrotizing enterocolitis, and non-AIDS immunodeficiency states (e.g. chronic granulomatous disease).[8]

Normally, an efficient clearing mechanism, involving scavenging reticuloendothelial Kupffer cells, prevents colonization of liver parenchyma by bacteria. But when the presence of bacteria in the liver is complicated by the presence of necrotic tissue, hepatic injury, malignant tumours, microemboli, poor perfusion, or biliary or vascular obstruction[2], the bacteria are able to multiply, invade liver parenchyma, and form an abscess.

PATHOLOGY

Grossly, hepatic abscesses are more likely to appear on the right side of the liver than the left by a 3:1 ratio.[9] Perhaps this difference is due to streaming of the superior mesenteric vein fraction of portal flow into the right lobe of the liver.[10] Multiple abscesses occur as often as solitary abscesses.[2] (see table 1) A solitary

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abscess may vary in size from a few millimetres to several centimetres. The liver itself may be enlarged and adherent to surrounding organs due to capsular inflammation[2]. Microscopically, the liver will display an acute inflammatory reaction with necrosis and hepatocyte cords in the portal triad regions.[2]

MICROBIOLOGY

In more than half of patients with liver abscess, the abscesses contain more than one organism when the abscess contents are cultured. Specific organisms recovered vary greatly.

Organisms found generally reflect biliary or enteric flora. The most common aerobic organisms are *E. coli*, *Klebsiella*, and enterococci (e.g. *Streptococcus faecalis*). The most common anaerobes are *Bacteroides*, anaerobic streptococci (e.g. *Peptostreptococcus*), and *Fusobacterium spp.* Isolated colonies of *E. coli* or *Klebsiella* are suspicious for a biliary source, whereas anaerobe-positive cultures are suggestive of a colonic source[2]. Staphylococci, hemolytic streptococci, or other gram-positive organisms are found if the primary infection is bacterial endocarditis or pneumonitis. Recent studies[11] using improved culture techniques have found non-hemolytic streptococci and normal oral flora to play a more prominent role.

There appears to be an increase in the number of cultures positive for anaerobic and microaerophilic organisms. Possibly, this increase is secondary to improved culture techniques. Cultures positive for anaerobes are usually positive for other organisms as well; thus, broad-spectrum therapy is usually required if anaerobes are present.[12]

DIAGNOSIS

Hepatic abscess is associated with a number of symptoms and signs. Symptoms include fever (often erratic, and spiking to 40-41°C), chills, rigors, right upper quadrant pain, malaise, fatigue, weight loss, night sweats, nausea, and vomiting. Physical findings include right upper quadrant tenderness, pleural dullness to percussion, hepatomegaly, and jaundice.[7]

A number of cellular changes occur which may aid diagnosis of pyogenic hepatic abscess. For example, a leukocytosis of greater than $15x10^9/L$ (often with left shift) and anemia of chronic disease are present in most patients. Most patients have an elevated alkaline phosphatase and an elevated gamma-glutamyl transpeptidase (_-GTP) since a liver abscess is a space-occupying lesion.[12] In some patients an increase in aspartate aminotransferase (AST) and alanine aminotransferase (ALT) may be observed. An elevated total bilirubin may be seen in cholestasis secondary to hepatic structural collapse. Blood cultures are positive for bacteria in about half of patients. Percutaneous aspirates from the abscesses are positive for bacteria in about three-quarters of patients.[13] Aspirating a pyogenic liver abscess reveals a malodorous exudate.[7]

The clinical syndrome of a pyogenic abscess often cannot be distinguished from that of an amoebic abscess. Since aspiration of an amoebic abscess can lead to secondary infection, especially in geographic areas with a large immigrant population, eliminating this possible diagnosis is important. Appropriate serologic tests such as the indirect hemagglutination test are useful in the diagnosis of an amoebic abscess.[14]

In addition to clinical findings, and altered biochemical levels, a number of imaging techniques are available which may aid in the diagnosis of pyogenic hepatic abscess. These techniques include ultrasound, computed tomography, invasive techniques, plain radiographs, and radionuclide isotope scanning.

Ultrasound has an 85-95% sensitivity for the detection of hepatic abscesses and is the most useful screening test when an hepatic abscess is suspected. Ultrasound is cost-effective, more accurate than CT in imaging the biliary tree, and allows for diagnostic or therapeutic drainage or biopsy to be performed during the scan. Ultrasound may also be used intraoperatively to locate small or deep abscesses in the liver.[15] Ultrasound, however, may fail to detect an abscess in a liver that is inhomogeneous or high beneath the thoracic cage.

Table 1
Drug Therapy for Pyogenic Hepatic Abscess

Pathogens	Antibiotic Agents
Gram-negative rods (44%) *Escherichia coli* *Klebsiella pneumoniae*	Treat with single agent: Ampicillin-sulbactam (Unasyn) *or* Ticarcillin-potassium clavulanate (Timentin) *or* Imipenum-cilastatin (Primaxin)
Gram-positive cocci (40%) *Streptococcus spp.* *Staphylococcus spp.*	Treat with two agents: Second- or third-generation cephalosporin *plus* metronidazole (Flagyl) or clindamycin (Cleocin) *or* Ampicillin *plus* chloramphenicol (Chloromycetin)
Anaerobic organisms (8%) *Bacteroides spp.* *Clostridium spp.* *Peptostreptococcus spp.*	Treat with three agents: Ampicillin or antipseudomonal penicillin *plus* a second- or third-generation cephalosporin *or* an aminoglycoside *plus* metronidazole *or* clindamycin
Microaerophilic organisms (6%) *Streptococcus milleri* *Streptococcus mitis*	Use same treatment as for anaerobic organisms

Computed tomography (CT) is the diagnostic technique of choice. Its sensitivity is 95%, and its specificity is 92% for single abscesses and 100% for multiple abscesses.[16] When used with contrast, CT will show the relative hypovascularity at the location of the abscess. CT also allows for simultaneous diagnostic or therapeutic intervention.

Endoscopic retrograde cholangiopancreatography (ERCP) and percutaneous transhepatic cholangiography (PTC) are invasive techniques which are useful if biliary obstruction and ascending cholangitis are suspected. These carry the risk of dissemination of infection. Angiography involves fewer complications and may be 100% sensitive for detection of hepatic abscesses.[17]

Chest x-ray is abnormal in about half of patients, but is neither sensitive nor specific for pyogenic hepatic abscess.[18] X-ray may show right hemidiaphragm elevation, pleural effusion, and basilar atelectasis or infiltrate.[14] A plain abdominal film may show gastric displacement due to liver enlargement[18], and occasionally an air-fluid level in the region of the liver, representing an abscess.

Radionuclide isotope scanning uses labelled tracers that are concentrated in hepatocytes or reticuloendothelial cells. These scans are 80-90% sensitive, but are unable to detect small lesions and are unable to discriminate between solid and cystic structures.[17,19]

TREATMENT

The treatment of the abscess includes intravenous antibiotics and drainage. Treatment should be individualized for each patient.

Antibiotics should be given immediately, by the parenteral route, starting with a broad coverage regimen consisting of a penicillin, an aminoglycoside, and clindamycin or metronidazole. Adjustment of this regimen depends on culture results of abscess aspirates (see Table 1).[6] If cultures are sterile but a clinical diagnosis of hepatic abscess remains, broad-spectrum antibiotics should be maintained. Antibiotics should be given for at least three weeks[20]; some physicians recommend therapy for up to 12 weeks. Antibiotics should be given

for 1-2 days before drainage is begun[2]. Oral therapy may be used in the final week or two of treatment if clinical improvement continues. Antibiotic treatment alone, without drainage, has been referred to in the past as a "last resort" in the primary treatment of these abscesses, and several studies proclaim its inadequacy.[2,13,15] Recently, however, that drainage is necessary only if the patient does not respond to antibiotics within 48 hours, or if the patient deteriorates clinically, has been suggested.[21] In the case of microabscesses, where drainage is difficult by any method, antibiotics alone are the mainstay of therapy. Monitoring the efficacy of antibiotic-only treatment, by sizing the abscesses using repeat ultrasound imaging, is imperative.

In addition to antibiotics, drainage of the abscess is also critical to a successful treatment outcome. Drainage may be percutaneous or open. Two decades ago, open drainage was much more common than percutaneous drainage as a primary therapy. Through the 1980's, the two were performed on an equal basis.[7]

Percutaneous drainage became more popular in the late 1970's as an adjunct to open drainage and as a primary treatment. Percutaneous drainage is the current "gold standard" for diagnosis of a pyogenic hepatic abscess,[6] and is 86-92% successful as a treatment. Percutaneous drainage involves first localizing the abscess under ultrasound or CT guidance. A tract to the abscess is then produced using a needle, guide wire, and dilator; a drainage catheter is subsequently inserted into the cavity. Such a catheter would be left in place for 2-3 weeks; early removal is associated with recurrence of abscesses.[22] This type of drainage may be used as definitive therapy, or pre-operatively before open drainage either if the patient is not responding to antibiotics or a search for the primary site continues. The percutaneous method of drainage is ideal for abscesses which are solitary, accessible by needle, deep-seated, or adherent to the abdominal wall.[7] With this method, however, there is an increased likelihood of secondary procedures; as well, the underlying source of the abscess may remain unknown. Further, failure of this method may result if the abscess is multiloculated, if its contents are too viscous to drain via a catheter, or if the catheter is dislodged from the abscess.[23,24]

Open drainage is the classical treatment of liver abscesses. This method is ideal for concurrent drainage of another (e.g. appendiceal) abscess, drainage of multiloculated abscesses, or those that are not easily accessible by needle. Open drainage is usually undertaken on a patient after the percutaneous method had failed[2]. Open drainage is associated with a higher rate of complications and mortality. Thus,

raw comparisons of surgical versus percutaneous treatment are not appropriate without consideration of underlying conditions and location and accessibility of abscesses. Complications include septicemia (most common), effusions, empyema, rupture into right subphrenic space, and pneumonia.[7] Three methods of open drainage exist: the transpleural approach, which is useful for high posterior lesions; the transperitoneal approach, which is the most preferred method since it allows inspection of the entire abdominal cavity for an underlying source, and provides the best mobilization of organs for drainage; and the extraperitoneal approach which may begin posteriorly near the 12th rib or via an anterior retroperitoneal dissection.[2]

Recent suggestions[16] for treatment have included the use of laparoscopic investigation for liver abscesses. Many patients with liver abscesses, however, have dense right upper quadrant adhesions or abscesses, which would preclude successful laparoscopic aspiration. Resection of a portion of liver containing an abscess or abscesses is reserved for areas of infection secondary to hepatic malignancy, or those associated with granulomatous disease of childhood.[2]

PROGNOSIS

Survival has improved due to earlier diagnosis and treatment. Sixty years ago the mortality was 80%, but it is now less than 20%. The primary determinant of prognosis seems to be the underlying condition, with malignancy or immunocompromise having the highest mortality. Prognostic factors include size of abscess, number of abscesses, patient age (more complications in infants and elderly), multiplicity of organisms, timeliness of diagnosis, and presence of immunosuppression or malignant disease.[14,25] If a pyogenic abscess is left untreated, death occurs in 10-30% of patients who have no complications, and in 73% of patients with complications (e.g. rupture, sepsis, hepatic or renal failure).[4,18,26]

SUMMARY

Despite advances in diagnostic technology and new strategies for treatment, the diagnosis and management of hepatic abscess remains challenging. Ultrasound and CT have made possible the detection and early treatment of pyogenic heaptic abscess,[27] thus yielding improved clinical results.[24,28,29] But the incidence of the disease is not decreasing, and the commonly associated factors of malignancy, immunocompromise, and advanced age, are playing a more prominent role in the etiology. The standard of care remains timely diagnosis and prompt institution of treatment. The choice of therapy should be individualized to the patient, considering solitary versus multiple abscess, whether additional problems requiring surgery are present, and the nature of the underlying disease. Morbidity appears to be related to the treatment method, but mortality is related to the underlying disease.

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Ω

THE DIAGNOSIS AND TREATMENT OF SEPTIC ARTHRITIS

by Janet Pope, M.D., MPH, FRCPC

ABSTRACT

The causative agents, demographics and outcome of septic arthritis have changed over the last several years. Staphylococcus aureus remains the most common cause of septic arthritis caused from nongonococcal organisms. Methicillin-resistant joint infections with Staphylococcus aureus have been increasing. Due to better culturing methods more anaerobic cases of septic arthritis are being identified. The most common joint involved in septic arthritis in adults is the knee. However, there are exceptions in certain populations. Intravenous drug use is a risk factor for septic arthritis, often involving fibrocartilaginous joints such as the sternoclavicular and sacroiliac joints. The outcome in these patients is usually excellent. The functional outcome of a septic joint is usually good if the diagnosis is made within two weeks of disease onset. The morbidity with gram negative bacteria is usually higher than with gram positive cocci. Debate about when to intervene surgically in the treatment of septic arthritis continues.

INTRODUCTION

There has been little change in the total number of cases of bacterial arthritis[1] but certain infections are increasing such gram negative bacilli and non-group A streptococci, whereas pneumococci are relatively rare in septic arthritis now. Anaerobes have been cultured more frequently which may reflect better culture techniques. Within certain populations, there may be specific types of bacterial infections, such as Staphylococcus aureus (S. aureus) and pseudomonas in intravenous drug users. So far, there have not been observations of increased septic joints in HIV positive patients, but with AIDS becoming a more chronic disease, it may be tuberculous arthritis or other atypical bacterial joint infections may increase in this immunocompromised population. Bacterial arthritis is the most rapidly destructive form of arthritis. There are two major types of bacterial arthritis: arthritis from Neisseria gonorrhoeae and other bacterial arthritis. The former arthritis is usually more benign and will not be discussed in this review. The pathophysiology, diagnosis and treatment of septic arthritis is discussed.

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PATHOPHYSIOLOGY

Most cases of septic arthritis have resulted from bacterial hematogenous spread. Fewer cases occur from direct spread from joint trauma, arthrocentesis, or local osteomyelitis. Within two days after injection of S. aureus into a rabbit joint, polymorphonuclear infiltration and synovial lining cell hyperplasia occurs.[2-4] Chondrocyte necrosis can occur in two days. Abscesses develop within the joint space. Irreversible joint destruction can occur as early as one week after the onset of infection.

Joints that are damaged are predisposed to infectious arthritis. Rheumatoid arthritis is a risk factor for septic arthritis, as is gout, chondrocalcinosis and osteoarthritis. Intravenous drug abusers are at risk due to recurrent bacteremia. People with sickle cell disease are at risk for certain types of infections including salmonella osteomyelitis or septic arthritis. Others with chronic disease who are immunosuppressed are at an increased risk. These include people with systemic lupus erythematosus, cancer, alcoholism and renal transplantation. The very young and old are at an increased risk of septic arthritis due to impaired host defenses.

The joints commonly involved in adults are the knee and the hip. Children also have these joints involved but have bacterial hip arthritis slightly more often than what occurs in adulthood. See Table 1 for the frequencies of joint involvement. Eighty to ninety percent of septic arthritis is monoarticular. In those with more than one joint involved, the most common organism is still S. aureus and then streptococcus

Table 1
Joints involved in Septic Arthritis

Joint	Percentage of Cases: Adult	Children
Knee	55	40
Hip	11	28
Ankle	8	14
Shoulder	8	4
Wrist	7	3
Elbow	6	11
Others	5	3
More than one joint	12	7

Table 2[6]
Organisms in Septic Arthritis

	Adults (%)	Children (%)
Gram Positive Cocci		
S. aureus	35	27
S. pyogenes, S. pneumoniae, S. viridans Group	10	16
GramNegative Cocci		
N gonnorrhoeae and meningitidis	50	8
H. influenzae	<1	<40
Gram Negative Bacilli		
E coli, Salmonella and Pseudomonas species	5	9
Mycobacteria and Fungi	<1	<1

pneumoniae (S. pneumoniae), group G streptococci and Haemophilus influenzae (H. influenzae).[5]

Aside from Nisseriae gonorrhoeae (N. gonorrhoeae), the most common cause of septic arthritis is S. aureus which occurs in approximately 70% of other bacterial arthritis in adults and 27% of childhood cases.[6] Young children less than five years of age are at risk for H. influenzae which is frequently accompanied by concurrent infection such as otitis media or meningitis. Other gram negative organisms occur rarely in septic joints. However, intravenous drug abusers are at an increased risk of S. aureus in some East coast cities and pseudomonas in the western United States and in Detroit. Table 2 lists the prevalences of certain bacterial pathogens in adults and children with septic arthritis.

DIAGNOSIS

A septic joint usually presents with an acute tense effusion, warmth, erythema, intense pain and markedly limited passive and active range of motion. The mortality rate is doubled in those with polyarticular involvement.[5] Most patients are febrile. The differential diagnosis includes other inflammatory arthropathies. See Table 3 for a list of differential diagnoses. On physical examination, a source of the infection should be looked for as most of the cases are from hematogenous spread. In children, otitis media and meningitis should be ruled out if H. influenza is suspected. Over half the patients with septic arthritis have a peripheral leukocytosis.[7] Both blood and synovial fluid cultures are important for diagnosis. Blood cultures which are positive in 30 to 60%[8,9,10] of cases should be done. Cultures of other areas such as urethra and cervix are important to rule out gonococcal infection. Any symptomatic areas should be cultured such as sputum if the patient has pneumonia, and urine and skin ulcers where indicated. Baseline radiographs should be done. The presence of an effusion is common but erosions are not usually seen early on radiographically. The joint should be aspirated and fully drained.

Synovial fluid is often cloudy. The fluid should be sent for gram stain, culture and sensitivity, acid fast culture where indicated, white blood cell count and differential, red blood cell count, and crystal analysis. The gram stain is positive in 50 to 60% of nongonococcal septic arthritis.[8,11,12] The white count is greater than 50,000/mm^3 in 70%.[13] The presence of red blood cells in a joint with no history of trauma is correlated with an increased risk of septic arthritis. Therefore, any bloody synovial fluid should be sent for culture. The presence of crystals does not rule out septic arthritis. Acute gouty arthritis can also have high white counts, so the diagnosis of septic arthritis should be entertained in a patient with gout who is having an acute flare-up.[13] Polymorphs are abundant with a synovial fluid differential of greater than 80% and usually greater than 95% polymorphs are seen.[13]

The synovial glucose is often less than half of the serum glucose.[14] However this is not definitive as several patients with rheumatoid arthritis have a low glucose. This test is also not sensitive. If the diagnosis of septic arthritis is suspected but not confirmed by the usual tests, then it may be worthwhile to do a gallium scan which if negative, rules out septic arthritis. Usually this is not necessary. Gallium scans are sensitive in detecting septic arthritis but are not specific. Other imaging modalities are usually unnecessary for the diagnosis of septic arthritis.

Table 3
Differential Diagnosis of Bacterial Arthritis

Gout
RA
Lyme Disease
Viral Arthritis
Pseudogout (Chondrocalcinosis)
Reiter's Syndrome
Acute Tramatic or Hemerrhagic Arthritis
Bacterial Endocarditis with Embolization
Rheumatic Fever
Osteomyelitis Near Joint

TREATMENT

Treatment is both local and systemic. A septic joint should be repeatedly aspirated as the effusion reaccumulates. Subsequent fluid gram stains, cultures, white counts and percent polymorphs should be followed and improvement implies successful therapy. The joint is rested with initial passive range of motion a few times a day. There should be no weight bearing for several days. The joint may be splinted, but not in a flexed position or the chance of a flexion contracture occurring is increased. Systemic high dose antibiotics are given often for up to four weeks in nongonococcal bacterial arthritis. Table 4 lists possible antibiotic choices to initiate according to the gram stain and the patient's demographics.

There is debate in the literature about when surgery should be the initial treatment for septic arthritis. Any joint which is difficult to aspirate and to follow clinically, should be treated with surgical drainage. Septic hips are often drained fluoroscopically or by ultrasound guidance in children. If gas forming bacteria are seen on radiograph, this would be an indication for urgent surgical debridement. A post-operative drain is usually inserted. For the surgical treatment of septic arthritis, arthroscopically drained joints are being performed commonly now and open arthrotomies are decreasing. Failure of antibiotics (persistently positive joint cultures) is an indication for surgery. Many of these cases have small synovial abscesses for which a partial synovectomy is performed. In a review of the case series in the literature, Goldenberg et al found that 80% of patients treated medically had complete recovery compared to 47% with surgical treatment.[15] There may have been selection bias where only sick patients with more severe infections were treated surgically. However, because there are no randomized trials comparing surgical to medical treatment, this is the best information to date. Therefore, in most cases of septic arthritis, the initial treatment is medical.

Delay in antibiotic treatment is proportional to poor outcome.[8] If antibiotics are begun within two weeks, 67% of septic joints were found to have complete functional recovery. Whereas, only 27% of joints had complete functional recovery if treatment was initiated more than two weeks after the onset of symptoms. Mortality rate in septic arthritis is increased in the elderly (up to 25%), in those with several joints involved and in those with comorbidity.[11,16] Several of these risk factors for poor outcome are correlated. Functional recovery is decreased in gram negative arthritis compared to gram positive. Intravenous drug abusers who are otherwise well have an excellent recovery in general and may only require therapy for a couple of weeks. These patients are often otherwise young and healthy and have only transient bacteremia with a less severe form of septic arthritis often in small fibrocartilaginous joints such as the sacroiliac joint. A short duration of treatment is usually successful in eradicating the infection; this is fortunate since compliance can be poor.

Sequelae of septic arthritis include flexion contractures, ankylosis, erosive arthritis, sterile post-septic synovitis, decreased range of motion of the involved joint and local muscle wasting. Rarely osteomyelitis occurs secondary to an adjacent septic arthritis.

Table 4
Examples of Empiric Antibiotic Treatment

Gram Stain	Treatment
Gram Positive Cocci	Cloxacillin Vancomycin Cephalosporin
Gram Negative Bacilli	Pipercicillin and Tobramycin Moxalactam Cefotaxime
Gram Negative Coccobacilli	Ampicillin Cefotaxime Penicillin (N Gonorrhoeae)
Total Joint Prosthesis (Irrespective of a Gram Stain)	Vancomycin and Gentamicin
No Organisms on Gram Stain	Cloxacillin and Aminoglycoside Cefazolin and Aminoglycoside Cefotaxime

SPECIAL CONSIDERATIONS

GRAM NEGATIVE SEPTIC ARTHRITIS

There are four groups who are at risk for gram negative septic arthritis. Infants less than two months are susceptible to gram negative bacteremia and can develop septic arthritis. Young children have an increased incidence of H. influenza infections. There has been some ampicillin-resistance of H. influenza over the last decade, so the initial treatment for this infection is often with a third generation cephalosporin. With the vaccination against H. influenza now being widely administered to children in the first year of life, H. influenza septic arthritis could become quite rare. The elderly, especially those with underlying arthritis have an increased risk of acquiring a gram negative joint infection often from urinary tract infections or diverticulitis with septicemia. In some areas, intravenous drug users have pseudomonal infections. The immunocompromised are at increased risk for bacterial joint arthritis including gram negative infections.

RHEUMATOID ARTHRITIS

Patients with rheumatoid arthritis (RA) are at an increased risk of septic arthritis. The signs and symptoms of septic arthritis could be masked in these patients due to their underlying arthritis, use of steroids, and debilitation. In RA, 50% of patients have a peripheral leukocytosis.[7] The most common joint involved is still the knee (50% to 75% in cases series),[17,18] however the elbow is also frequently involved (13 to 38% of cases of septic arthritis in RA). There is an increased tendency for multiple joints to be involved,[19-21] and in one series, 70% had polyarticular septic arthritis.[22] Most septic joints in RA originate from bacteremia. The diagnosis is suspected when inflammation and pain are greater than the patient's other joints. The causative organism is still most often S. aureus, occurring in over 80% of cases.[8,9,12,19,22-24] The synovial fluid white cell count may delay the diagnosis, as 4% of patients with RA without an infection may have a white count of greater than 50,000/mm^3.

JOINT PROSTHESES

Prosthetic joint infections have decreased in the acute post-operative time due to antibiotic prophylaxis, and new techniques in the operating room. The infection rate is now 0.5 to 4%.[25-29] The acute infection is often from staphylococcus epidermidis. Subacute infections can occur in the latter half of the first year post-operatively. These infections are difficult to diagnose and may show loosening on radiograph with pain and joint swelling. Later infections are often from bacteremia (such as post instrumentation) and are usually caused by S. aureus. Treatment involves prolonged use of antibiotics. Sometimes the joint has to be removed. However, the area needs to be sterile before another prosthesis is reinserted. In patients with RA, the risk of prosthetic joint sepsis is three-fold increased compared to osteoarthritis.[25,29,30] It may be the systemic abnormalities of RA that increase the general risk for a prosthetic joint to become infected. Some physicians routinely prophylax patients with prosthetic joint replacements prior to instrumentation and dental work, with a protocol similar to patients receiving prophylaxis for abnormal heart valves. This practice is currently not universal and needs more investigation before becoming routinely advocated.

CONCLUSIONS

Septic arthritis is still relatively common. S. aureus remains the most common causative organism. Monoarticular infections occur in the majority of patients. The usual joints involved are the knee and the hip. The major risk factors for septic arthritis are abnormal joints, immunocompromise and bacteremia. The diagnosis is made by a positive joint culture and gram stain is often positive. Some antibiotic-resistant organisms have increased in prevalence. Specific therapy should be performed using knowledge of the local endemic bacterial prevalences and resistances. The prognosis is good in most cases if antibiotic therapy is initiated promptly.

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OTITIS MEDIA IN CHILDHOOD

by Michael J. Rieder, MD, PhD, FRCPC

INTRODUCTION

Otitis media is a common problem presenting to primary care and emergency physicians. In Canada, the most frequent diagnosis for which antibiotics are prescribed among pre-school children is otitis media. Up to 20% of all visits to primary care physicians in Ontario are for the therapy or follow-up of otitis media. Thus primary care physicians should be comfortable with the management and follow-up of otitis media.

PATHOPHYSIOLOGY

Acute otitis media is an infection involving the middle ear, usually of bacterial origin. Among toddlers, this infection is commonly related to Eustachian tube dysfunction. Eustachian tube dysfunction is more common among toddlers for a number of reasons, including the relatively horizontal location of the Eustachian tube in young children and the relatively large size of periadenoidal lymphatic tissue. Eustachian tube dysfunction is also common after upper respiratory tract infections. In addition, there are some groups, such as children with Down's Syndrome, who are at high risk for Eustachian tube dysfunction.

There are three bacterial species commonly found among children with acute otitis media; *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Branhamella catarrhalis*. Among these organisms, there are appreciable rates of beta-lactose activity among *Haemophilus influenzae* and *Branhamella catarrhalis*. Otitis media caused by *Haemophilus influenzae* is relatively more common among infants and toddlers.

PRESENTATION

There are three principle presentations of bacterial otitis media, acute otitis media, resistant otitis media, and recurrent otitis media. The first, and most common, is acute otitis media, in which a child develops an acute bacterial infection in the middle ear (often after a viral upper respiratory infection). This acute presentation is manifested clinically as pus in the ear, often associated with fever and occasionally accompanied by vomiting.

The natural history of acute otitis media is that, if untreated, the vast majority of these infections will resolve, often after rupture of the tympanic membrane. However, without antibiotic therapy, children tend to have somewhat longer periods of pain and distress than when treated. In addition, the complications of acute otitis media, including meningitis and cholesteatoma formation, appear to be much more common among untreated children.

After antibiotic therapy is instituted, a clinical response is anticipated in 24 to 48 hours. If the child has not improved, or if the child deteriorates, then the child should be considered to have resistant otitis media. In this type of presentation, the child's otitis media is likely caused by an organism resistant to the antibiotic prescribed.

The final presentation of otitis media is that of a child whose otitis media responds to therapy, but, shortly after therapy ends, another episode develops. In this case, the child has recurrent otitis media. Recurrent otitis media may be due to the presence of special risk factors for otitis media, such as Down's Syndrome, allergies, or adenoidal hypertrophy.

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Dr Michael Reider received his MD from the Medical College of Saskatchewan and his PhD in Pharmacology from the University of Toronto. He is currently an Assistant Professor at UWO with cross appointments in the departments of paediatrics, pharmacology and toxicology, and medicine. Dr Reider is also the new undergraduate clerkship co-ordinator.

Table 1
Antibiotic Doses for Otitis Media

Drug	Daily Dose	Frequency of Administration
amoxicillin	25 mg/kg/day	3 times per day
co-trimoxazole	TMP 6 mg/kg/day	2 times per day
erythromycin/sulfamethoxazole (Pediazole)	eryth: 40 mg/kg/day	3 times per day
pivampicillin	50 mg/kg/day	2 times per day
amoxicillin/clavulanate	20 mg/kg/day	3 times per day
cefaclor	25 mg/kg/day	3 times per day
cefixine	8 mg/kg/day	1 time per day

THERAPY

The mainstay of therapy for acute otitis media is the use of oral antibiotics. Traditionally, the use of an aminopenicillin drug such as amoxicillin has been the usual first-line therapy for otitis media (see Tables 1 and 2). In the case of penicillin-allergic patients, co-trimoxazole (Septra or Bactrim) or erythro-mycin/sulfamethoxazole (Pediazole) should be used.

For resistant otitis media, an antibiotic should be chosen which has a different bacteriological spectrum from the antibiotic originally prescribed. There are a number of antibiotics available as secondline therapy, including cefaclor, cefixine, amoxicillin/clavulanate, co-trimoxazole and erythromycin/ sulfamethoxazole.

The same considerations for changing antibiotic therapy apply in the case of the acute therapy of recurrent otitis media. Recurrence and frequency warrant consider-ation for low-dose prophylactic antibiotic therapy or for surgical placement of myringotomy and tympanos-tomy tubes. The only antibiotics which have been evaluated in this role have been amoxicillin and co-trimoxazole. Hopefully, the development of vaccines may resolve some of these therapeutic dilemmas.

Antipyretic and analgesic therapy is important in the symptomatic therapy of otitis media. Acetaminophen is the mainstay of therapy in a dose of 15 mg/kg/dose given every 4 hours as needed. In the unusual case where a child who has had adverse reactions to acetaminophen , naprosyn 20 mg/kg/day divided into two to three doses a day can be used. For single-dose therapy immediately after diagnosis, a single dose of 1 mg/kg of codeine can be used.

Patients with acute otitis media should have clinical improvements in 24 to 48 hours. If the patient has not improved at that time, or if the patient deteriorates, the patient should be seen again. If the patient's symptoms resolve, the patient should be seen in follow-up in two to three weeks. A sterile effusion may persist for up to six weeks after as episode of acute otitis media. Fluid in the middle ear that is not associated with symptoms may not require therapy, but it does need follow-up, especially with respect to the potential for hearing loss. In the case of recurrent otitis media, follow-up will have to address the potential need for insertion of tympanostomy tubes.

Table 2
Cost of 10 Days of Therapy (10 kg child)

Drug	Cost of Drug	Dispensing Fee (Average)
amoxicillin	2.19	10.00
co-trimoxazole (Septra, Bactrim)	1.59	10.00
erythromycin/sulfamethoxazole (Pediazole)	10.99	10.00
pivampicillin	9.57	10.00
amoxicillin/clavulanate	7.75	10.00
cefaclor	11.43	10.00
cefixine	14.58	10.00

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A SAMPLE OF INFECTIOUS DISEASES RESEARCH IN PERU

by Ross Mantle, BSc, Meds '95

The following is a sample of eight concurrent research projects I was exposed to when I travelled to Peru in the summer of 1992 and stayed with Professor Robert Gilman, MD of John's Hopkins University. Dr. Gilman has lived in Lima for eight years engaged in research and publishing papers. In addition to Hopkins, Peruvian universities Universidad Peruana Cayetano Heredia, and Universidad San Marcos arecentres that have been associated with work in infectious diseases. Also involved is Prisma, a well established third world aid and development organization supported in large part by American grants and directed by Dr. Gilman's wife . The wide diversity of tropical infective disease, coupled with the effects of altitude which can be observed in the Andes make Peru an atractive research arena for the infective disease specialist.

Helicobacter pylori (HP)

The relationship between HP, atrophic gastritis, and gastric ulcer has been known for over five years, but is only just now becoming accepted in North American Centres. The further likely relationship between HP and gastric cancer is the subject of research effort by Dr. Gilman. In the third world HP infection rates typically see most of the population infected by age 20, and in some places 50% of the population are infected before one year of age. Rates of gastric cancer are higher and those of peptic ulcer lower than in the first world.

Cholera

Over a year and a half of water and sewage sampling has provided support for the use of sewage monitors to predict cholera outbreaks. Also bioimpedance monitoring has allowed better determination of the state of hydration of cholera patients, allowing for more effective rehydration. [1]

Cysticercosis

Western blot techniques have shown that over 10% of Peruvians and 25% of pigs hae antibodies to T. solium. Current studies are examining the use of sentinel pigs to detect infection in endemic zones. Cysticercosis may be a causative factor in the development of epilepsy.

Cyclospora cayetanesis

A new enteropathogen first described by Dr. Gilman's group which is named after Universidad Cayetano Heredia. Work has begun on basic epidemiology and serology.

Cryptosporidium

Cryptosporidium is also an enteropathogen, but not fatal. Nevertheless, work on nutritional status and diarrhea due to cryptosporidium has revealed changes in growth patterns.

Oximetry

A very useful means of determining repiratory decompensation in children with upper respiratory tract infections living at high altitude. Because the ambient oxygen tension is so low, patients reach the steep portion of the oxygen saturation curve earlier. Oximetry in combination with the World Health Organization (WHO) algorythmare a very powerful diagnostic tool.

Tuberculosis

Patterns of endemicity with respect to age differ in the third world from what might be expected in more developed areas. Dr. Gilman's group is working on a mathematical model of the epidemiology of this condition.

Inca Peanut

Not an infectious disease, but a potentially useful and valuable plant. The Inca peanut, or oilseed Plukentia volubilis was used to make oil by the Inca Indians . Research by Dr. Gilman's groups in collaboration with the University of Arkansas has revealed that the fruit has very high ratios of low saturated fats. Also, the high protein content is a rich source of essential amino acids. Vitamin E content is also high.

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STITCHES IN TIME II - MISADVENTURES IN PSYCHIATRY

by W. David Colby, MSc, MD, FRCP(C)

If you asked me, as a first year medical student, what branch of medicine I planned to undertake, I would have unhesitatingly said "Psychiatry". The idea of flailing at the frontiers of the human psyche was unbelievably enthralling. Delving into the processes, emotions, and even the chemistry of what makes us unique sentient beings (at least in some cases) probably is the most interesting aspect of medical practice. I read the works of Freud, Bettelheim and Brenner and just couldn't wait for my first assignment at 999 Queen Street East, probably the most famous cookie jar in Ontario. I knew that things there would probably be a little bit on the gritty side because, after all, the truly erudite psychoanalytic types carried on their practices at the elegant Clarke Institute of Psychiatry. Nevertheless, I was looking forward to a calm cerebral experience delving into why a patient thought he was Napoleon, or some other equally fascinating delusion.

I was first greeted by the resident who explained the ground rules. "Whenever you are interviewing a patient, make absolutely certain that there is a telephone in the room", he explained.

"How often do you have to call for help?" I asked. He gave me the strangest look.

"You don't call for help", he said with a note of bored sarcasm. "If they give you trouble you pick up the phone and smash them in the face with it." He walked out shaking his head and I meekly followed. We walked into a patient room where there awaited our first subject. He was a small furtive man with greasy hair and eyeglasses that were at least four sizes too large for his face, which created a distinct owl-like expression. He was chain-smoking cigarettes and there was a large filthy ashtray in front of him, full of the detritus of his habit. What a pitiful-looking individual, I thought. A number of diagnoses went through my mind—neurotic? obsessive-compulsive? schizophrenic? forensic case? My thoughts were interrupted by his outburst.

"Hello, I'm Dr. _____, the staff psychiatrist. You must be the new medical student."

Things didn't go so well during this rotation, although I must admit we did see a number of interesting patients. There was a fellow who thought he could identify different neighbourhoods and cities by their characteristic sounds and gave beautiful descriptions of the music in the air composed of city noises. There was a fellow who was trying to enumerate the number of ants in Canada. "I know it sounds strange, but there is a way to do it!" Another one thought he was Jesus Christ and assigned biblical roles to all the significant people in his life. What he worried about was having to relive the crucifixion scene since it was so rough the first time. I felt quite sorry for him. My favourite was this fellow who sat around all day in a black depression doing nothing but moping around the house and watching television. "What kind of shows do you watch?", I asked.

"Happy Days", he replied. He went on to describe how he finally decided to end it once and for all by slitting his throat with a butcher knife. "...and I laid down and waited to die", he said, "...but I didn't die, so I called the ambulance."

"Why did you call the ambulance if you wanted to die?", said the other clinical clerk. "'Cause I didn't want to get an infection, you stupid idiot."

I just couldn't do anything right as far as my staff psychiatrist was concerned. At the end of the year, he kicked me out with one point above a bare PASS level. Needless to say, the very next week my first rotation as a clinical clerk at another hospital was in Psychiatry, and with the same approach and skills, I achieved the highest grade awarded that year on that service. Most of the staff psychiatrists were very interesting and had genuine, deep insight into the human mind. My favourite was an elderly fellow whom I will call "Nutty". During his prime, he had achieved considerable fame for his skills as a diagnostician and therapist and even in his post-retirement capacity- this guy missed nothing. He may have achieved this insight by spending long periods of time as an inpatient on the Psychiatry Service where he worked. Whenever he felt that he was losing it, he would conveniently admit himself **under himself**, write his own orders and treat himself until he felt he should be discharged, all the while leaving his bed periodically to do rounds on his other inpatients on the same service! I left that service with great reluctance because, unlike my experience at Queen Street, I had learned a great deal. Unfortunately, I also learned about the most unpleasant type of psychiatric patient—one whose mere mention sends chills up the spine of any practicing psychiatrist: the borderline personality disorder.

Patients with borderline personality disorder seem to have been placed on this earth for a specific mission: to make the lives of their therapists miserable. They are equipped with every nasty psychological trick in the book: sharply opinionated nature, exaggerated

emotional responses and an ability to incite conflicts wherever they go. Many of these people, of course, end up serving in public office. I will present a brief case history of a typical patient which I saw in my phase of being an Emergency physician.

I looked down on the chart and saw that the chief complaint of this patient was "wants to talk to a doctor". I knew that spelled trouble. It wasn't a good day anyway as I had 75 patients backed up in the waiting room. Nevertheless, I dusted off my best "doctor-patient relationship hat", put it on and went in to see the patient. She was a nurse in her early 60s. "Hello, Mrs. _____, I'm Dr. Colby. What is troubling you today?"

"You're the doctor. You tell me!", she sneered through a Medusa's breath of venom.

"Oh, no!", I thought, "...I can't stand it. Furthermore, I don't have time for this." Nevertheless, the patient went on a long rambling narrative about how she had been prematurely widowed, had been alone for many years but had presented to the Emergency Room because she now had a boyfriend who cared about her. "Say what?", I thought. "Are you having a problem with your relationship?", I asked.

"Of course I am!", she screamed. "The relationship has progressed to the point of where it's getting physical and it makes me nervous. Do something about it!"

Great. An emotional adolescent lands on my doorstep expecting long-term psychotherapy to start in the middle of the busiest afternoon in my life and is hostile besides. I considered handing in my resignation and walking out but I thought I could probably be sued somehow for this. Just when I was about to sign myself in as a patient, what did I hear but the voice of the consulting psychiatrist on call, walking by just outside the confines of the Emergency cubicle. I shoved my hand through the curtains, found a lapel and dragged him in. "Dr. _____, I'd like you to meet Mrs. _____. She has a problem and I would like to refer her to you." This was a classic dump, elegantly executed. The timing couldn't have been better. A few patients later, I noticed out of the corner of my eye Mrs. _____ sashaying out of the hospital with a prescription in her hand. I was then summoned to the other hospital in town since there had been a multiple motor vehicle accident resulting in a large number of critically injured patients suddenly arriving at the Emergency Room and overwhelming the staff there. I jumped into the car and roared across the river to the other hospital and attended a few of these unfortunate accident victims. While I was writing at the chart desk, whom should I see but Mrs. _____ coming in, soaking wet, on a stretcher. The ambulance attendants said that she jumped off the bridge and was fished out of the river by a couple of guys angling from a boat. "I'll handle this", I said to the chart clerk, and I followed Mrs. _____ as they wheeled her into the room. "Mrs. _____, why did you do this?"

"You should have seen the signs!", she hissed. "I'm ready to be taken to my room now." She looked away. I got the picture. This was an act of revenge for not admitting her in the first place.

"But I did see the signs, Mrs. _____", I explained. "That's why I referred you to Dr. _____."

"Shut up and take me to my room", she said.

"I'll see to that when I can", I said icily and left her to chill out for about 20 minutes. When I returned, I informed that I had to do her admission physical. While I was examining her, she suddenly put a satisfied and triumphant look on her face. To my horror, I realized that she had purposely voided her bladder and bowels in order to make my job more unpleasant. Borderline personality disorder.

It was at this point that I gave up any aspirations of being a psychiatrist, forever.

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Jason Bowels M.D., Surgical Resident

By Dr. Michael Rieder

Lifegifts: The Real Story of Organ Transplants

by Sonny Bhalla

Calvin R. Stiller. 230 pp., illustrated. Toronto, Ont., Stoddart Publishing Co. Limited, 1990. $14.95. ISBN 0-7737-2301-3.

Dr. Calvin Stiller's Lifegifts focuses on the sad irony surrounding organ transplants: one person's tragedy is another's good fortune. He juxtaposes informational chapters about the state of organ transplantation with anecdotal chapters that allow the reader a glimpse of the complex emotions and issues at the time of organ donation. This method of writing allows Dr. Stiller to accomplish his goal "to help the general public better understand the process and current potential of transplantation while grasping the correctable tragedy of wasted donor organs."

Dr. Stiller begins his discussion of the state of the art in transplantation technology with a brief history of organ transplantation. He simply and eloquently describes the immune system, the problem of rejection in transplants, and the effects of the introduction of cyclosporine in 1978 on the success rates of various procedures. Using a heart transplant as an example, Dr. Stiller goes on to describe in fair detail the actual technique in an organ transplant operation, and the drama and sense of urgency throughout the procedure. Despite his attention to detail, the discussion is absorbing and the explanations are accessible to the reader with no medical training.

Far more important than the explanations about technique or infrastructure is the author's discussion about the attitudes and misconceptions on the part of the public and the medical community. Public education, Dr. Stiller asserts, is essential to raise the percentage of organs that are actually isolated and used.

A part of what makes this book so accessible to the nonmedical reader is the author's willingness to acknowledge the imperfections of the medical community. Hesitancy on the part of physicians is a significant obstacle that must be overcome before organ transplantation achieves its full potential. Too often, physicians view transplantation as an experimental approach carried out in a few select sites across the country. Nothing could be further from the truth; most organs are transplanted with a full functional recovery rate of 70-75% or better. Doctors must be educated. "Traditionally, doctors have been taught that their responsibility for the patient ends at death."

Dr. Stiller is not afraid to comment on some of the highly charged issues surrounding organ transplants. Finally, Dr. Stiller discusses his vision for the future of organ transplantation, and the obstacles that must be overcome before we can finally cut short the tragic waste of usable organs, and the consequent death of those who desperately need them.

Overall, *Lifegifts* is a short, readable book that concisely outlines the technological and psychosocial issues regarding organ transplantation. The fact that Dr. Stiller is acutely aware of the intense and often conflicting emotions on the part of those considering donation endears him to the reader, and therefore makes his important message that much more effective.

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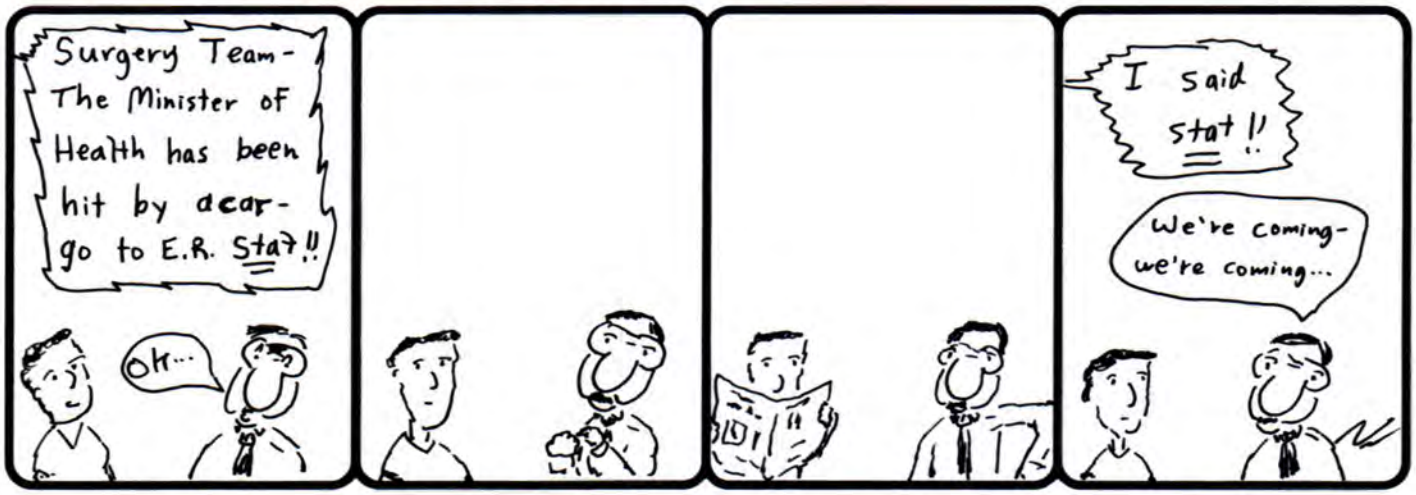
Jason Bowels M.D., Surgical Resident



By Dr. Michael Rieder

THINKING ON YOUR FEET

"Thinking On Your Feet" is an exercise designed to test your clinical decision-making skills based on a case presentation. Below is an exciting patient history with physical examination and laboratory results. Answers may be found on page 53 & 54 or within the case itself. Although this section is called "Thinking On Your Feet," thinking is acceptable in any position. Answer the questions in sequence. Please do not peek at the answers prematurely—this would not be ethical. Compare your responses with those of the case presenter. Award yourself one point for each match.

Scoring:

85 - 100% — Excellent. Patient is recovering nicely;
72 - 84% — Strong Work. Patient is recovering—minor complications;
59 - 71% — Good Eye. Patient likely to survive—some disfigurement;
40 - 58% — Fair. Patient requires critical care & close monitoring;
0 - 39% — Uh-Oh. Red alert—emergency crisis—check A-B-C's.

A CHILD WITH RECURRENT INFECTIONS

A nine year old girl presents with a diffuse papilliform erythematous rash involving her trunk and extremities including her palms and soles. She is on treatment with Septra^{R} for persisting, festering open sores on her extremities, vulva and lower abdomen. Further history reveals she had a severe pneumonia four months before for which she was treated with antibiotics and hospitalized for two weeks. She has had many previous episodes of ear, sinus and chest infections since two years of age but have been worst in the past year. She was born with a congenital heart lesion and had open heart surgery at one year of age. She was fully immunized, had no delay in reaching her milestones and her height and weight are on the 50th percentile.

STOP PLEASE AND ANSWER THESE QUESTIONS:

1. What specific family history do you want to ask?

2. Which physical findings may you expect to detect?

PLEASE CONTINUE...

On examination she is afebrile and in no acute distress. The erythematous rash is noted. She has numerous scars and scabs on her legs and lower abdomen. There is thrush in her oropharynx and she has only some minor cervical lymphadenopathy. Her liver is palpable 3 cm below the right costal margin and her spleen tip is also easily palpable. She has a fixed splitting second heart sound heard over her pulmonic area. The rest of her examination is unremarkable.

STOP PLEASE AND ANSWER THESE QUESTIONS:

3. What is your clinical diagnosis at this point?

4. What is your differential diagnosis?

5. Which laboratory investigations would be indicated?

6. What intervention would you offer this patient?

MEDICAL VOCABULARY

This section is designed to test and expand your knowledge of medical terminology. How many items can you correctly define?

Scoring: [13-15]=Superior knowledge, [10-12]=Above average, [8-9]=Adequate, [5-7]=Fair, [1-4]=Sub-par.

1. **Refsum's Disease.**
a) a ganglioside storage disease producing a distinct maple syrup odour to the urine;
b) the disease complex which occurs secondary to pinworm infection;
c) a rare degenerative disease of aging, commonly involving the speech centres initially;
d) an autosomal recessive, degenerative disorder associated with retinitis pigmentosa, deafness, and polyneuritis.

2. **Indolent.**
a) rude and insulting;
b) inactive, sluggish;
c) treacherous, stealthy;
d) insensible, unconscious.

3. **Peristrumitis.**
a) inflammatory condition of tissues around a goitre;
b) inflammation of a tendon sheath;
c) inflammation of membranes around a sinus, especially a venous sinus of the dura mater;
d) inflammatory condition of the external layer of a vein.

4. **Frottage.**
a) french cottage cheese;
b) the putrid odour produced from the collective decomposition of many corpses;
c) production of sexual excitement by rubbing against someone;
d) reaking havoc.

5. **Oxyecoia.**
a) having a sharp, pointed nose;
b) a genus of amoebas found in the intestinal tract;
c) excess of oxalate deposited in tissues;
d) abnormal sensitivity to noises.

6. **Coprophilia.**
a) attraction of microorganisms to fecal matter;
b) a psychiatric term denoting a morbid attraction and interest in fecal matter;
c) the attraction of spermatozoa to copper—the principle behind copper wire intrauterine devices;
d) (a) & (b).

7. **Proemial.**
a) a late occurrence of a disease process;
b) referring to an early stage of embryologic development;
c) prodromal;
d) malformation of the prosencephalon.

8. **Symphalangism.**
a) the most anterior point of the alveolar process of the lower jaw;
b) web-fingered or web-toed condition;
c) excessive peripheral vascular tone due to sympathetic dysfunction;
d) surgical repair of a divided symphysis.

9. **Trephination.**
a) a long, hollow tube through which sounds are resonated great distances;
b) the process of boring a hole in any flat bone, especially the patella, to allow escape of pus;
c) a reconstructive surgical technique whereby a piece of bone is remodelled;
d) removal of a circular peice of cranium by a trephine.

10. **Hedrocoele.**
a) accumulation of serous fluid in the tunica vaginalis testis;
b) a downward displacement of the caecum;
c) a small bullous rising of the skin which contains serous fluid;
d) a hernia or porlapse through the anus.

11. **Bruxism.**
a) clenching and grinding of teeth, usually during sleep;
b) spasm of masticatory muscles;
c) pain secondary to malocclusion of the teeth;
d) partial paralysis of the upper palate due to inferior alveolar nerve damage.

12. **Egilops.**
a) a Freudian term referring to an unbalanced psyche;
b) an obsolete term for a swelling at the inner canthus of the eye;
c) an inability to resist sexual impulses;
d) (a) & (c).

13. **Progeria.**
a) premature senility syndrome;
b) the syndrome of continuous endometrial sloughing due to an absence of progesterone;
c) the constellation of signs and symptoms due to excess progesterone—weight gain, headache, edema, and depression;
d) the manifestion of infantile behaviours associated with senile dementia.

14. **Kerley Lines.**
a) thickening of interlobular lung septa seen on a chest x-ray;
b) transverse folds of the mucous membrane of the small bowel;
c) growth bands in the dentin of a tooth;
d) lines extending from the upper limit of the obturator foramen to the middle of the neck of the femur, seen on an x-ray of the hip.

15. **Betel Nut.**
a) the nut of the areca palm tree chewed by natives of the East Indies;
b) an extract from the cytoskeleton of the South American Piper Beetle—used as a soporific agent;
c) an Indian delicacy, derived from the giant red-haired beetle, indiginous to the Himalaya mountains;
d) a slang indicating testicular inflammation; a condition restricted to men with a hereditary deficiency of the enzyme which metabolizes betacyanin, a byproduct of beet ingestion.

ANSWERS TO CASE STUDY

1. It appears this child is having an unusual problem with frequent infections and possibly drug intolerance to Septra[R]. If she has an immunodeficiency it may be congenital or acquired. Since congenital immunodeficiencies may be familial, the parents should be asked whether there exists a family history of recurrent infections. The majority of children with AIDS were infected pre or perinatally by their mothers. The maternal history of known HIV infection or recurrent infections is especially pertinent.
2. Congenital immunodeficiencies may be part of syndromes manifesting with dysmorphic features (eg. DiGeorge Syndrome of micrognathia, brachial clefts and congenital heart disease). Children with recurrent or chronic infections may have persistent stimulation of their reticuloendothelial system and thus display hepatosplenomegaly and/or generalized lymphadenopathy. They may also suffer signs of persistent mucosal infections such as thrush (Candidiasis) and herpetic lesions.
3. The history and physical examination are suggestive of recurrent infections due to an underlying immunodeficiency.
4. The immunodeficiencies can be categorized into T cell disorders; B cell disorders; combined T and B cell disorders; neutrophil and complement deficiencies. These may be congenital or acquired. This child seems to have been getting progressively worse since late infancy, although the exact time of onset of an abnormal frequency and severity of infections is difficult to establish. A major clue is the open heart surgery which invariably requires blood transfusions. The Red Cross started screening blood products in the Fall of 1985. Hence, this child was possibly exposed to HIV contaminated blood and HIV infection should be near the top of the differential diagnosis. Furthermore, Septra[R] intolerance is more common in HIV infected patients.
5. A CBC and differential will indicate the numbers of circulating neutrophils and lymphocytes, most of which are T lumphocytes. However, the CD4 cells, a subset of T lumphocytes which are usually decreased in symptomatic HIV infections, may be severely depressed in the presence of a normal circulating lymphocyte count. Hence, the CD4 count should be assessed specifically by flow cytometry. Her HIV antibody status should be determined. Her total and specific immunoglobulin levels should also be measured. A CH_{50} level which determines complement activity is an appropriate screen for most complement deficiencies resulting in immunosuppression. This child was found to be HIV infected, had a low normal lymphocyte count and a CD4 count of 400 which is below the normal level for her age. Her immunoglobulin profile demonstrated polyclonal stimulation with a marked increase in her IgM.

... continued on page 54

6. As one would expect, the aproach to a patient with immunodeficiency is to treat the current opportunistic infection with appropriate anti-infectives while attempting to correct the underlying disorder. The Septra[R] should be discontinued and if the impetiginous lesions relapse they should be cultured. Cloxacillin constitutes the antibiotic of choice since these infections are usually caused by Group A Streptococci and *Staphylococcus aureus*. Oral ketoconazole or fluconazole is usually required to treat mucosal candidiasis in HIV infected patients. Consideration should be given to starting anti-retroviral therapy since the CD4 count is less than 500. Lastly, intravenous immunoglobulin is recommended for chilfren with symptomatic HIV and dysgammaglobulinemia to reduce the frequency and severity of recurrent infections.

ANSWERS TO VOCABULARY

1. **Refsum's Disease.** (d) *Heredopathia Atactica Polyneuritiformis*. A rare degenerative disorder transmitted as an autosomal recessive trait and caused by an absence of phytanic acid alpha-hydroxylase. The disease is characterized by retinitis pigmentosa, polyneuritis, deafness, nystagmus, and cerebellar signs.
2. **Indolent.** (b) Inactive; sluggish; painless or nearly so—said of a morbid process.
3. **Peristrumitis.** (a) Inflammation of the tissues around a goitre.
4. **Frottage.** (c) The rubbing movement in massage; production of sexual excitement by rubbing against someone.
5. **Oxyecoia.** (d) An abnormal sensitivity to noises.
6. **Coprophoelia.** (d) Attraction of microorganisms to fecal matter; In psychiatry, a morbid attraction to, and interest in (with a sexual interest), fecal matter.
7. **Proemial.** (c) Prodromal; an early or premonitory symptom of a disease.
8. **Symphalangism.** (b) Syndactyly; ankylosis of the finger or toe joints.
9. **Trephination.** (d) Removal of a circular peice of cranium by a trephine, a cylindrical or crow saw used for the removal of a disc of bone, especially of the skull, or of other firm tissue as that of the cornea.
10. **Hedrocoele.** (d) Prolapse of the intestine through the anus.
11. **Bruxism.** (a) Clenching of the teeth, associated with forceful lateral or protrusive jaw movements, resulting in rubbing, gritting, or grinding together of the teeth, usually during sleep.
12. **Egilops.** (b) Obsolete term for a swelling, abscess, or fistula at the inner canthus of the eye.
13. **Progeria.** (a) *Hutchinson-Gilford Disease*. Premature senility syndrome; a condition in which normal development in the first year is followed by gross retardation of growth, with a senile appearance characterized by dry, wrinkled skin, total alopecia, and bird-like facies.
14. **Kerley Lines.** (a) Markings on chest roentgram representing thickening of interlobular septa, due to pulmonary edema or cellular infiltration.
15. **Betel Nut.** (a) *Areca Nut*. The nut of the areca palm (*Areca Catechu*) chewed by natives of the East Indies; the nut is so-called because it is chewed with dried *Piper Betle* leaves (an East Indian red pepper plant used as a stimulant and narcotic).

MEDICAL FAX

VITAMIN E UPDATE

Vitamin E (alpha-tocopherol) has been the subject of many recent publications that have attracted much attention from both the medical profession and the lay press. Vitamin E, a primary lipid-soluble antioxidant, is a membrane constituent of the heart myocyte where it plays an acive role in countering oxidative stress. In addition, vitamin E may prevent the oxidation of lipoproteins since the atherogenic potential of lipoproteins increases when oxidized[1].

Vitamin E deficiency may be a risk factor for heart disease. Further, adequate levels of vitamin E may prevent the progression of atherosclerosis[2]. Many current studies are based on the hypothesis that therapeutic vitamin E (or its analogues) may protect the heart from progressive ischemic injury[3,4]. As well, research on peripheral vascular disease indicates that vitamin E may have a positive effect on intermittent claudication[5].

1 *Free Radical Biology and Medicine. 11(1):129-44 (1991).*

2 *Japanese Journal of Clinical Medicine. 51(4):997-1003 (1993).*

3 *Canadian Journal of Cardiology. 9(1):89-93 (1993).*

4 *Free Radical Biology and Medicine. 10(5):315-24 (1991).*

5 *European Juornal of Clinical Pharmacology. 37(6):541-4 (1989).*

PBL PROPOSAL PENNED

Newly appointed Associate Dean Lloyd has released a document proposing that the Faculty of Medicine move to a PBL-based curriculum. McMaster University, Calgary, Toronto, Ottawa, and Dalhousie now all have curricula whose mainstay is PBL. Soon classroom teaching could become a thing of the past. As to whether or not this new trend in teaching is going to make a difference - well, only time will tell.

SIDE EFFECTS CONCEALED FROM THIRD WORLD PATIENTS

According to the current issue of *The New Physician* (vol 42(6):9), a growing number of U.S.-based multinational pharmaceutical companies are selling drugs with incomplete information labels to developing countries. In a study done by the U.S. Office of Technology Assessment (OTA), two-thirds of a random sample of 241 drugs failed to provide information about the side effects of the drugs. For example, one of the drugs being sold overseas was an anti-inflammatory drug that was taken off the U.S. market because it caused a fatal leukopenia. The OTA suggests "the implementation of an international code of conduct for pharmaceutical labelling" to prevent further abuses, since there are no U.S. labelling laws encompassing drugs being produced and marketed by a foreign subsidiary of a U.S. company.

BITTER TASTE IN YOUR MOUTH?

The bitter taste of certain foods and drugs may become a thing of the past. A specific lipoprotein made of phosphatidic acid and ß-lactoglobulin, abbreviated PA-LG, reportedly binds to tongue receptors for bitter substances. A high concentration of PA-LG appears to suppress the bitter taste sensation in humans while leaving other taste sensations unchanged. Phosphatidic acid and ß-lactoglobulin are produced from soya beans and milk respectively. PA-LG may soon be used to fight bitterness in taste buds everywhere.

[Katsuragi et al., Nature. 365:213-214 (1993).]

PARTICLE ACCELERATOR TO FIGHT CANCER

Construction of the world's first medical accelerator is nearing completion in Japan. The 300 million dollar Heavy-Ion Medical Accelerator in Chiba (HIMAC) was designed for use in cancer therapy.

HIMAC is expected to offer cancer treatment programs by March of 1994. Heavy-ion therapy involves bombarding patients with an assortment of ions like neon, carbon and silicon.

Heavy ion therapy is gaining interest for two reasons: First, the mass and charge of heavy ions gives these ions stronger tumour-destroying capabilities than radiation therapy. Second, heavy ion bombardment is more tumour-speciifc than radiation therapy. In addition, aim of the charged ion beam can be finely adjusted using electromagnetic fields, and the ions release most of their destructive energy at the end of their path.

The disadvantages to this form of therapy are high cost and relative ineffectiveness against metastases.

HIMAC offers an alternate form of cancer treatment with potentially less side effects than present treatment regimens. [*Science.* **261**:1270 (1993)]

BENEFITS OF SMOKING IGNORED

Cigaretted smoking may be protective for a number of diseases, but reasearchers, granting agencies, pharmaceutical firms, and ethics comittees are reluctant to promote or permit investigation into the area. "People do not want to be seen to promote smoking in any way, " according to an article inNew Scientist magazine. Nevertheless, some evidence for benefits attributable to smoking exists in Parkinson's, Alzheimer's, ulcerative colitis, rheumatoid arthritis, and even some cancers!

[Mundell, I. New Scientist. 9 October 1993, pp. 14-15.]